Sunday 2 September 2007

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

MODULATION OF ION CHANNELS FROM PHYSIOLOGY TO PATHOLOGY

99 Potassium inward rectifier expression is regulated by TGFbeta and BMP and increases during differentiation of cardiomyocyte progenitor cells

P. Van Vliet[1], T.P. De Boer[2], J.P.G. Sluijter[1], M.A.G. Van Der Heyden[2], P.A. Doevendans[1], M.-J. Goumans[2]. *[1]UMCU/ICIN, Cardiology, Utrecht, Netherlands; [2]UMCU, Medical Physiology, Utrecht, Netherlands*

Background: Cell transplantation therapy is currently considered as an alternative therapy for heart regeneration. However, spontaneous contractions of stem- and progenitor cell-derived cardiomyocytes may lead to arrhythmias after cell replacement therapy. One of the key components in the regulation of the electrophysiological characteristics of the adult ventricular cardiomyocyte is the potassium inward rectifier (Kir) channel. Kir channels are required during phase 3 repolarization and stabilization of the resting membrane potential of cardiomyocytes. Here we study Kir2.1 and 2.2 expression during cardiomyocyte progenitor cell (CMPC) differentiation into cardiomyocytes and regulation of this expression by TGFβ and BMP.
Methods & Results: CMPCs were isolated from human fetal hearts, differentiated into spontaneous beating cardiomyocytes upon 5-azacytidine stimulation, and showed a fetal ventricular-like electrophysiological phenotype. RT-PCR demonstrated no or low levels of both Kir2.1 and 2.2 expression in differentiated CMPCs. Upon stimulation with TGFβ however, CMPC differentiation improved and Kir2.1/2.2 expression markedly increased. Increased IK1 current after differentiation of CMPCs and hyperpolarization of undifferentiated CMPCs after BMP stimulation suggest functional Kir channel conductance in response to TGFβ and BMP signaling. To determine whether TGFβ and BMP directly regulate Kir 2.1 expression, we performed a Kir2.1 reporter assay in vitro. COS7 cells were transiently transfected with a Kir2.1 promoter luciferase construct and cultured with or without TGFβ or BMP. Kir2.1 promoter activity was enhanced upon ligand stimulation. To test whether increased activity of the Kir 2.1 promoter also resulted in increased expression of Kir 2.1 in CMPCs, we stimulated undifferentiated CMPCs at different timepoints with TGFβ and BMP. Both ligands induced increased expression of Kir 2.1 within several hours. These results suggest a direct effect on Kir 2.1 expression in response to TGFβ and BMP.
Conclusion: Expression of Kir 2.1 and 2.2 is enhanced during CMPC differentiation, when stimulated with TGFβ. Increased IK1 currents, in combination with a more negative membrane potential after stimulation with BMP, could indicate regulation of potassium inward rectifiers by TGFβ and BMP. Concordantly, Kir 2.1 promoter activity is induced by TGFβ and BMP in COS7 cells and its expression is enhanced in CMPCs. This suggests that TGFβ and BMP stimulate Kir 2.1 expression, resulting in hyperpolarization of CMPCs.

100 Anisotropic electrical conduction across mesenchymal stem cell-derived cardiomyocytes improves functional integration in a cardiac syncytium in vitro; the importance of cell alignment

D.A. Pijnappels, M.J. Schalij, A.A. Ramkisoensing, J. Van Tuyn, A.A.F. De Vries, E.E. Van Der Wall, A. Van Der Laarse, D.L. Ypey, D.E. Atsma. *Leiden University Medical Center, Cardiology Department, Leiden, Netherlands*

Background: Cell shape and orientation contributes to anisotropic electrical conduction across the heart. However, little is known about the importance of anisotropic integration of stem cell-derived cardiomyocytes into cardiac tissue. Therefore, we investigated the effect of cell orientation on electrical conduction across stem cell-derived cardiomyocytes developing in a cardiac syncytium.
Methods: Neonatal rat cardiomyocytes (CMCs) were co-cultured with neonatal rat mesenchymal stem cells (MSCs) for 10 days. Cardiomyogenic differentiation of MSCs was assessed by immunohistochemistry, whole-cell patch clamp, and electrical mapping experiments. The effect of cell orientation on electrical conduction was assessed in a model consisting of two CMC fields, cultured onto fibronectin-gelatin pre-coated microelectrode mapping arrays. These fields were electrically separated by a laser-dissected, a-cellular channel (225±5 μm wide). Uncovered coatings in these channels were micro-abraded in a direction either (I) parallel or (II) perpendicular to the channel, or left (III) unabraded. Then, either $50x10^3$ eGFP-labeled MSCs, cardiac fibroblasts (CFBs), CMCs, or a mixture (2:8) of CFBs and CMCs were applied onto these coatings.
Results: MSCs differentiated (±20%) into functional CMCs during 10 days of co-culture with neonatal rat CMCs, as was shown by typical cardiac cross-striation of sarcomeric proteins, intrinsic action potentials, and increased conduction velocity (CV). Application of labeled MSCs, CMCs, or neonatal rat cardiac fibroblasts (CFBs) onto these micro-abraded coatings resulted in uniform anisotropic cell alignment, in contrast to isotropic alignment if applied on unabraded coatings. During 10 days of co-culture, CV across applied MSCs increased significantly ($p<0.01$). However, CV was significantly different between the three configurations ($p<0.05$), being highest in perpendicular (~11.1 cm/s, n=12), intermediate in isotropic (~7.3 cm/s, n=11), and lowest in parallel configuration (~4.8 cm/s, n=11). CMCs ($n>30$), CFBs ($n>30$), and a mixture of both ($n>10$) showed also an alignment-dependent CV, but significantly different from each other ($p<0.05$). CV across the two CMC fields was ±20 cm/s during follow-up.
Conclusions: Neonatal rat MSCs can differentiate into functional CMCs, and show anisotropic electrical conduction according to their cell alignment. This has profound effects on both time course of functional integration and conduction velocity. The present study introduces anisotropic cell alignment of de novo CMCs as a novel determinant of functional integration in host cardiac tissue.

101 Human ventricular scar fibroblasts as target for gene therapy to repair conduction block in vitro; multiple ion channel expression by the myocardin gene leads to acquired excitability

D.A. Pijnappels, J. Van Tuyn, A.A.F. De Vries, S. Knaan-Shanzer, A. Van Der Laarse, D.L. Ypey, M.J. Schalij, D.E. Atsma. *Leiden University Medical Center, Cardiology Department, Leiden, Netherlands*

Introduction: Scar formation after myocardial infarction is associated with slow conduction and conduction block, thereby increasing risk of lethal arrhythmias. Cardiac fibroblasts play a crucial role in the genesis and maintenance of myocardial scarring.
Hypothesis: Disrupted electrical conduction in myocardial scar may be repaired by genetic modification of the scar fibroblasts using Myocardin, a cardiogenic transcription factor, which induces the expression of a wide array of cardiac genes including those of ion channels.
Methods: Neonatal rat cardiomyocytes (CMCs) were cultured in micro electrode arrays (60 electrodes, Multi Channel Systems, Germany), resulting in synchronously beating monolayers. After 2 days, a central conduction block was created by laser-dissection of a 320±30 μm wide channel, dividing the monolayer in two asynchronously beating fields. Then, $50x10^3$ GFP-labeled human ventricular scar fibroblasts (hVSFs) transfected with the Myocardin gene (Myo-hVSF) or $50x10^3$ GFP-labeled hVSFs transfected with the LacZ gene (LacZ-hVSF, negative control) were applied in the channel. In an additional group labeled CMCs (positive control) were applied. Electrical conduction across Myo-hVSFs was assessed for up to 8 days upon external stimulation of the culture, and compared to LacZ-hVSFs and CMCs. PCR and immunohistochemical analysis was performed at day 1 and day 8.
Results: At day 1, the conduction block was repaired by both Myo-hVSFs (n=10) and CMCs (n=11), associated with resynchronized beating of the two CMC fields. However, LacZ-hVSFs (n=9) were not able to repair the conduction block. Conduction velocity (CV) across Myo-hVSFs increased progressively from 2.6±0.4 cm/s at day 1 to 17±0.8 cm/s at day 8 ($p<0.01$) of co-culture. In contrast, a cellular conduction block was present throughout the follow-up after application of LacZ-hVSFs. CV across CMCs was 18.5±0.4 cm/s at all time points. Electrogram characteristics from recordings of Myo-hVSFs changed significantly during follow-up ($p<0.01$), indicating a change to excitation-driven propagation. Myo-hVSFs expressed genes encoding for fast Na^+ ion channels (SCN5A), L-type Ca2+ ion channels (CACNA1C), inwardly rectifying K^+ ion channels (KCNJ3), which are involved in electrical excitability. The expression levels of these genes increased significantly over time ($p<0.05$).
Conclusions: Human ventricular scar fibroblasts (hVSF) expressing Myocardin are able to repair a conduction block over considerable distances, most likely via acquired excitability. hVSFs may be a promising target for gene therapy in treating scar-related arrhythmias.

102 Modulation of the AV-nodal conduction by Connexin40 and Connexin30.2

J.W. Schrickel, M. Kreuzberg, A. Ghanem, K. Tiemann, G. Nickenig, K. Willecke, T. Lewalter. *University of Bonn, Department of Medicine-Cardiology, Bonn, Germany*

Purpose: Connexin30.2 (Cx30.2) and Connexin40 (Cx40) are key gap-junctional proteins in the murine AV-node. Cx30.2 has been shown to contribute to physiological conduction slowing of this specialized tissue. In this context, functional interactions of Cx30.2 and fast conducting Cx40 remained unclear.
Methods: 18 wildtype- (WT), 10 Cx30.2-deficient (Cx30.2-/-), 6 Cx40-deficient (Cx40-/-) and 10 Cx30.2/Cx40 double-deficient (Cx30.2/Cx40-/-) mice were in vivo electrophysiologically investigated using a transvenous right cardiac catheterization.
Results: QRS was prolonged in Cx40-/- (21.3±2.7 ms) and Cx30.2/Cx40-/-(19.9±2.4 ms) compared WT (12.9±1.9 ms) and Cx30.2-/- (14.2±2.0 ms; $p<0.0001$). PQ was significantly decreased in Cx30.2 (35.7±3.4 ms) as compared to all other investigated groups (WT: 46.6±4.0 ms;Cx40-/-: 50.8±6.2 ms; Cx30.2/Cx40-/-: 51.6±5.1 ms; $p<0.0001$); this was independent from a tendency towards P-wave prolongation in Cx40-/- und Cx30.2/Cx40-/- mice. This accelerated AV-conduction was attributable to a significant faster supra-Hisian conductivity with shortened AH-intervals in Cx30.2-/- (28.2±4.3 ms vs. 35.9±4.4 ms; 35.8±1.9 ms; 37.3±5.5 ms, successively; $p<0.0001$). Functionally, a significantly lower Wenckebach-periodicity was present in Cx30.2-/- (basal stimulation cycle-length S1S1: 79.7±7.2 ms), but not in Cx30.2/Cx40-/- (81.5±6.7 ms; $p<0.001$). The HV-Interval was prolonged in Cx40-/- compared to WT and Cx30.2-/- as an indicator for impaired infra-Hisian conductivity in this mouse strain.
Conclusions: No acceleration of AV-nodal conduction is present in Cx30.2/Cx40-/- compared to Cx30.2-/-. This implicates a compensating role of additional deletion of Cx40 on increased AV-conductivity associated with Cx30.2-deficiency. The

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

presence of fast conducting Cx40 in the AV-node is thus essential for faster impulse propagation in Cx30.2-/-. This study strongly implicates functional interactions of Cx40 and slow conducting Cx30.2 in the murine AV-node. The conductive properties of the AV-node under physiological conditions and in pathological states (such as hereditary AV-blocks) might therefore be mediated by a differential expression or activation of such interacting connexins.

103 Conditional and cardiac specific overexpression of the neuronal nitric oxide synthase

N. Burkard[1], A.G. Rokita[2], S.G. Kaufmann[2], M. Hallhuber[2], C. Gebhardt[2], K. Hu[2], L.S. Maier[3], K. Schuh[3], O. Ritter[4]. [1]*University of Wuerzburg, Department of Internal Medicine I, Wuerzburg, Germany;* [2]*Georg-August-Univerity, Department of Cardiology, Goettingen, Germany;* [3]*Georg-August-University, Department of Cardiology, Goettingen, Germany;* [4]*University of Wuerzburg, Cardiology Dept., Wurzburg, Germany*

Introduction: The role of the neuronal nitric oxide synthase (nNOS, NOS1) enzyme in the control of cardiac function still remains unclear. Results from nNOS -/- mice or from pharmacological inhibition of nNOS are contradictory. We hypothesize that the close proximity of nNOS and certain effector molecules like L-type Ca^{2+}-channels (LTCC) has an impact on myocardial contractility.
Methods and results: To test this hypothesis we established a new transgenic mouse model with a conditional, myocardial nNOS overexpression. For generation of this transgenic animal model the Tet-Off-system (BD biosciences) was used.
Analysis of transgenic nNOS overexpression showed a 6-fold increase in nNOS protein expression compared to non-induced littermates (638±23%, n=12, $p<0.05$). Western blot analysis of different tissues verified the myocardial specificity of our inducible nNOS overexpression. Co-immunoprecipitation experiments and immunostainings indicated interaction of nNOS with SR Ca^{2+}ATPase (SERCA2a) and additionally with L-type Ca^{2+}-channels in nNOS overexpressing animals. In vivo examinations of the nNOS overexpressing mice showed a decrease of $+dp/dt_{max}$ compared to non-induced mice (reduction for 52± 17%, n=12, $p<0.05$) and an attenuated response to dobutamine infusion. Intracellular Ca^{2+}-transients and fractional shortening in cardiomyocytes were clearly impaired in nNOS overexpressing mice vs. non-induced littermates ($3.0\pm0.4F/F_0$ vs. $2.2\pm0.2F/F_0$, n=13, $p<0.005$ and 7.7±1.3% vs. 3.8±0.5%, n=13, $p<0.05$). Ca^{2+}-traces after 10mM caffeine application as a measure of SR Ca^{2+}-content demonstrated a significantly reduced SR Ca^{2+}-content in nNOS overexpressing animals compared to non-induced cardiomyocytes. Protein expression of LTCC, SERCA2a, NCX and phospholamban was not changed. Phosphorylation of phospholamban at the Ser16 site was decreased in nNOS overexpressing myocytes (0.85±0.02 vs. 0.32 ±0.005, n=9, $p<0.05$).
Discussion: In conclusion, we demonstrated that conditional transgenic overexpression of nNOS results in an inhibition of myocardial contractility. We suggest that nNOS suppresses the function of L-type Ca^{2+}-channels. Additionally, prolongation of relaxation time in isolated cardiomyocytes from nNOS overexpressing mice indicate that nNOS must have a direct effect on the SERCA2a function (possibly via reduced phosphorylation of phospholamban) and therefore suppresses Ca^{2+}-reuptake into the SR.

104 Partial inhibiton of NCX reduces inward currents but increases Ca^{2+} loading of cardiac myocytes

S. Ozdemir[1], V. Bito[2], K.R. Sipido[2]. [1]*Akdeniz University Faculty of Medicine, Department of Biophysics, Akdeniz, Turkey;* [2]*KULeuven, Laboratory of Experimental Cardiology, Leuven, Belgium*

Recent studies have proposed SEA-0400, a novel and selective blocker of the electrogenic Na/Ca exchanger (NCX) as an antiarrhythmic agent. SEA-400 could block inward currents during the Ca^{2+} transients and if, as suggested, SEA-400 would reduce preferentially outward NCX current it would also reduce Ca^{2+} loading of the cell. However, these putative effects on Ca^{2+} homeostasis have not been studied. We investigated the effects of SEA-400 in left ventricular myocytes from adult pigs (8-10 cells in each protocol). Membrane currents were recorded under whole-cell voltage clamp; Ca^{2+} transients were recorded simultaneous using fluo-3 as Ca^{2+} indicator, intracellular $[Na^+]$ was 10 mmol/L. Experiments were performed at 37±1°C. At 1 μmol/L, SEA-0400 significantly decreased both the forward and reverse mode of the NCX current, when measured during a voltage ramp at similar driving force of 60 mV (by 67±7% and by 50±5, respectively, n=8 cells, mean±SEM); the extent of reverse mode block was larger than of forward mode ($P<0.05$). The amplitude of the Ca^{2+} transients evoked by depolarizing steps from -70 to +10 mV increased significantly (to 1016±230 vs. 466±86 nmol/L at baseline, $P<0.05$); the relaxation was significantly slowed (half-time of relaxation 460±73 vs. 259±19 ms at baseline, $P<0.05$). On repolarization we measured the inward NCX current density and expressed the values as function of $[Ca^{2+}]$i at that time (pA.pF-1.μmol/L-1): inward NCX current density was reduced almost 3-fold in the presence of SEA-400 (-0.62±0.06 vs. 1.79±0.18 at baseline, $P<0.001$). The sarcoplasmic reticulum (SR) Ca^{2+} content was evaluated during fast caffeine application (10 mmol/L for 10 s) and the resulting inward NCX current, integrated and normalized to cell capacitance, used as measure for the SR Ca^{2+} content. SEA-400 significantly increased SR Ca^{2+} content to 3.06±0.58 vs. 1.28±0.08 pC/pF at baseline ($P<0.05$). The peak of the caffeine-induced Ca^{2+} transient was significantly augmented (3107±438 vs. 1013±245 nmol/L at baseline, $P<0.05$) and Ca^{2+} decline was slowed down as expected (tau 1744±361 vs. 767±141 ms, $P<0.05$). On the other hand, despite elevated $[Ca^{2+}]$i, the peak NCX current density decreased (-0.98±0.06 vs. -1.75±0.08 pA/pF, $P<0.05$). In conclusion, SEA-400 effectively reduces the potentially arrhythmogenic inward Na/Ca exchange current during SR Ca^{2+} release. Such a beneficial effect may however be compromised by a higher Ca^{2+} loading of the myocytes and slowed relaxation.

ABLATION OF VENTRICULAR ARRYTHMIAS

105 Electrophysiological predictors of long-term success in patients with electrical storm treated by catheter ablation

C. Carbucicchio[1], M. Santamaria[2], G. Maccabelli[2], M. Moltrasio[2], N. Trevisi[2], F. Giraldi[2], P. Della Bella[2]. [1]*Centro Cardiologico, Univ. of Milan, Arrhythmia and EP Dpt., Milan, Italy;* [2]*Catholic Univ. of the Sacred Heart, Cardiovascular Dpt., Milan, Italy*

Background: Electrical storm (ES), defined as ≥3 ventricular tachycardia (VT) episodes/24 hours causing implantable cardioverter defibrillator (ICD) therapies, is a life-threatening emergency and long-term outcome in survivors is conditioned by ES recurrences. Catheter ablation (CA) has been proposed for the treatment of ES; in this study acute electrophysiological predictors of long - term success have been investigated.
Methods: Ninety-five consecutive patients (pts) (85 M; age 64± 13 yrs) (coronary artery disease, 72; idiopathic dilated cardiomyopathy, 10; arrhythmogenic right ventricular dysplasia, 13), undergoing CA for drug refractory ES were prospectively evaluated. Multiple spontaneous VT morphologies (2-5) occurred in 36 pts. Acute efficacy of CA was defined by standard programmed electrical stimulation: prevention of inducibility of any (clinical and non-clinical) VT was defined as Class A result; suppression of any clinical VT with persistent inducibility of ≥1 non-clinical forms as Class B result; the inability to prevent even the induction of ≥1 clinical forms of VT as Class C result. Long-term analysis focused on sudden cardiac death (SCD), ES recurrence, VT recurrence (not consistent with ES).
Results: Class A result was achieved in 68 pts (72%), Class B in 17 (18%); Class C in 10 (11%). A short-term rhythm stabilization was obtained in all pts during the post-procedural period. At a 22±13 month follow up, all Class A and Class B pts (85 pts, 89%) remained free from ES; 8/10 Class C pts had ES recurrence, which caused SCD (4) or emergency cardiac surgery (4). VT recurrence rate was significantly reduced in Class A vs. Class B (16% vs. 65%, $p<0.0001$) pts and in Class A vs. Class C (16% vs. 100%, $p<0.0001$) pts.
Conclusions: Programmed electrical stimulation predicts long-term outcome in pts treated by CA for ES. Prevention of inducibility of the presenting VT(s) protects from ES recurrence, but not from VT recurrence. The suppression of all inducible forms of VT is indeed required aiming at overall VT prevention. Ablation of clinical VT(s) represents the reasonable procedural endpoint to reduce SCD rate in ES pts.

106 Regional scar encircling catheter ablation (ReScE-ablation) to treat post-infarct ventricular tachycardia

T. Deneke[1], B. Lemke[2], B. Calcum[1], T. Lawo[1], P.H. Grewe[1], A. Muegge[1]. [1]*University Heart Center Bochum, BG Klinik Bergmannsheil, Med. Klinik Ii, Bochum, Germany;* [2]*Bochum, Germany*

Post-infarct ventricular tachycardia (VT) is often electrically and hemodynamically instable impeding excessive mapping strategies during VT. Electroanatomic voltage mapping during normal sinusrhythm can characterize local myocardial function and help to identify VT-exit-regions.
Methods and Results: 65 patients late after myocardial infarction presenting with VT and indication for invasive therapy were included. Left ventricular substrate mapping and ablation of VT was performed only during sinusrhythm.12-lead ECGs of all inducible VTs were recorded. In a first step the left ventricular substrate was mapped differentiating normal, abnormal and scar tissue based on local endocardial bipolar voltage. In a second step the exit site of the target VT was regionalized by pace-mapping. Linear Regional Scar Encircling (ReScE-)ablation along the scar border restricted to damaged myocardium was directed to ablate all inducible VTs. Per inducible VT 0.8±0.3 ReScE-ablation lines were performed. The clinical VT was rendered non-inducible in 95% (62/65) of patients (129/157 inducible VTs successfully ablated; 82%). In 40/62 (65%) patients no VTs were inducible after ablation (complete success), in 35% (22/62) VTs were still inducible (incomplete success). During a mean follow-up of 12±11months (0.2 to 60) freedom from any VT was documented in 83% of all patients.
Conclusions: ReScE-ablation directed towards exit sites of post-infarct VTs is effective in 95% of clinical VTs without the necessity of mapping during ongoing VT. 82% of all inducible VTs could successfully be ablated and complete suppression of any inducible VTs was achieved in 65%. Long-term follow-up documented freedom from any VT in 83%.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

107 Contribution of a new CARTO pacemapping map to localize the isthmus of post-myocardial infarction ventricular tachycardia

L. Groben, I. Magnin, M. Andronache, C. De Chillou, M. Abbas, N. Zhang, E. Aliot. *Brabois University Hospital, Cardiology Department, Vandoeuvre-Les-Nancy, France*

Background/Purpose: Radiofrequency ablation of the anatomic substrate of unstable post-myocardial infarction (MI) ventricular tachycardia (VT) remains challenging. Many mapping strategies rely on the existence of inducible and stable VT. The purpose of this study was to assess the role of left ventricular pacemapping (PMa) used in combination with an electroanatomic mapping system to localize the isthmus of reentrant ischemic VT during sinus rhythm.
Methods: Among 120 radiofrequency ablation procedures performed from 1998 to 2006 for ischemic VT in the Cardiology department, 10 patients meeting the following inclusion criteria were selected: patients for which 1) clinical VT on 12 lead ECG was documented; 2) a complete left ventricular electroanatomic map in sinus rhythm with high density PMa was recorded; 3) a complete and precise left ventricular activation map during VT was available; 4) the mechanism of VT was an endocardial reentry circuit for which the isthmus characteristics could be clearly defined through the means of the activation map. For each site of PMa, the percentage of correlation with the clinical VT expressed through a template matching software was obtained. These percentages were localized on a new electroanatomic map called "percentage of correlation map". 10 "percentage of correlation maps" were directly compared to the corresponding 10 activation maps during VT. Each critical part of the isthmus (7 distinct zones) identified on the VT map was superimposed on the corresponding "percentage of correlation map". The mean percentage of correlation for every isthmic zone for every map could thus be calculated.
Results: Statistical analysis of 405 PMa points belonging to one of the 7 predefined regions of the isthmus shows that PMa (for threshold values $>$ 75%) has good sensitivity ($>$80%) and specificity (76-83%) for identifying the exit zone of the isthmus. On the other hand, sensitivity, specificity and positive predictive value for localizing the central part or the entry zone of the isthmus are mediocre (47%, 61%, 13% and 65%, 61%, 31% respectively). Visual comparison of "percentage of correlation" and VT maps suggests that the isthmus of post-MI VT can be identified by a zone of excellent percentage of correlation located in the direct vicinity of a zone of poor percentage of correlation.
Conclusions: Our study suggests that ventricular PMa can accurately identify the exit zone of post-MI VT isthmuses and visual isthmus identification using our "percentage of correlation" map seems possible.

108 Fixed electrogram-to-QRS complex interval following entrainment from the right ventricle: a new criterion for postinfarction ventricular tachycardia ablation

M. Gonzalez Vasserot, J.L. Merino, R. Peinado, H. Roa, E. Macia, O. Quintero, J.A. Sobrino, J.L. Lopez-Sendon. *Hospital Universitario "La Paz", Madrid, Spain*

Introduction: Entrainment by pacing from the target site for radiofrequency application is a validated technique for mapping and ablation of postinfarction ventricular tachycardia (VT). However, the measurement of the postpacing interval following VT entrainment is often complex due to the pacing artifact and subjective in the presence of fragmented electrograms. Middiastolic electrograms showing a constant activation time with the QRS complex despite VT cycle length oscillations are makers of the tachycardia slow conduction isthmus. The aim of this study was to evaluate the criterion of a fixed middiastolic electrogram-to-QRS complex interval (Eg-QRS) during tachycardia and at the first postentrainment cycle by pacing from the right ventricle for postinfaction VT ablation.
Methods: 39 consecutive VT ablation procedures in 35 patients with prior myocardial infarction were prospectively included in the study. Radiofrequency application was decided according to conventional criteria (middiastolic potentials, entrainment with concealed fusion, and postpacing interval). Prior to radiofrequency application, VT was entrained by pacing from the right ventricle and the difference between the Eg-QRS measured in the first postpacing cycle and that one measured in the second postpacing cycle (Eg-QRS-Dif) was calculated but not used to guide the ablation procedure.
Results: The Eg-QRS- Dif showed a signifficant differnece between succesful and not-successful ablation sites ($p<0.01$). A Eg-QRS Dif$<$4.5 showed 47% sensitivity and 35% specificity to predict VT termination by radiofrequency application.
Conclusions: An Eg-QRS-Dif $<$4.5 ms is a valid criteria to predict successful radiofrequency application and ablation of postinfarction VT. However, this criterion shows a medium sensitivity but low specificity. This criterion may be particularly useful for dead-end VT circuit bystander pathways.

109 Radiofrequency catheter ablation of para-hisian ventricular ectopy

A. Ardashev[1], E. Zhelyakov[2], A. Konev[1], T. Sklyarova[1], A. Shavarov[1]. *[1]Burdenko Head Clinical & Military Hospital, Interventional Cardiology Dept., Moscow, Russian Federation; [2]Moscow, Russian Federation*

Purpose: To evaluate efficiency and safety of RFA of VPB originating from His bundle area.
Material and methods: we studied 119 pts (53 female), mean age 38,7$\pm$8,2 years, with symptomatic idiopathic LBBB-shaped VPB. In 81 pts VPB originated from right ventricular outflow tract, in 12 (10%) pts in inflow right ventricular tract, in 8 (7%) pts in free wall of right ventricle and in 4 (3%) pts the source of arrhythmia was verified above pulmonary trunk valve. Para-Hisian localization of VPB was founded in 14 pts. The QRS complex of VPB originating from His bundle area characterized by normal axis in frontal plane, RI-RII-RIII-configuration, LBBB-morphology with transitional zone in V3-V4. Mean duration of QRS of VPB was 141.2$\pm$6.8 ms. All pts underwent EPS and RFA of VPB using traditional mapping technique. Ablation was considered successful when VPB was eliminated with or without isoproterinol infusion during at least 30 min after RFA. Follow up consisted of 24 hrs ECG monitoring in all pts in our hospital 2, 6 and 12 mos. after RFA without AAD. Follow up period was 10$\pm$4 mos.
Results: Optimal site for RF-application was determined near His-bundle region in all cases. Careful mapping revealed start of VPB activation from sharp (fascicular) potential preceded QRS complex by 32$\pm$3 ms in sites of effective RFA in 6 cases. Traditional slow activation during VPB with pre-QRS interval 27$\pm$5 ms was verified in 8 cases. Incremental RF-delivering were needed for safe and effective ablation at the points of interest illustrating near-the-His-bundle activation. RFA was effective in 12 cases after first RF-application. Recurrence of VPB occurred in 2 pts after first procedure through 18 and 28 hours respectively. Repeated RFA was effective in both cases.
Conclusion: Para-HisianVPB's were characterized by specific configuration of QRS complex and may be effectively and safely treated by RFA. Origin of para-Hisian VPB may be associated with structures of His-Purkinje system.

110 Ablation of ventricular tachycardia prior to implantation of cardioverter-defibrillators in coronary artery disease

A. Schaumann[1], K.-H. Kuck[1], R. Ventura[2] on behalf of VTACH study group. *[1]Asklepios Klinik St. Georg, Cardiology, Hamburg, Germany; [2]University Hospital Eppendorf, Cardiology, Hamburg, Germany*

The study was performed to evaluate the impact of ablating ventricular tachycardia (VT) in patients with coronary artery disease and stable VT scheduled for an implantable cardioverter defibrillator (ICD).
In a prospective study 110 patients were included with a prior myocardial infarction, reduced left ventricular function (LVEF$<$50%) and hemodynamic stable VT. All patients scheduled for implantation of an ICD were randomized for VT ablation prior to ICD implantation (ABL+ICD) vs. ICD implantation only (ICDonly). The primary endpoint of the study was the time from ICD implant to first VT episode. Secondary endpoints were evaluated for electrical VT storm (defined as 3 VT episodes in 24 hours) and death. Data were obtained during 2 years of follow-up (FU) on a regular scheduled outpatient contact every 3 months in 16 participating European centres.
Results: During FU of 2 years data were obtained from 50 patients assigned to ABL+ICD and 55 patients randomized to ICDonly treatment. Another 5 patients dropped out because they withdrew their consent after initial randomization. Patients clinical data (age, sex, history of myocardial infarction, revascularization, LVEF etc.) were well balanced for both groups. In ABL+ICD patients no major complications due to the ablation procedure occurred. During FU time of 2 years any VT event was seen in 33 patients (66%) ABL+ICD vs. 38 (72%) in the ICDonly group (p= 0,23). The median time from ICD implant to the first VT episode was 9,1 months for ABL+ICD vs. 5,4 months for the ICDonly patients (p=0,30). The mean number of VT events per year of FU was 9,2 for ABL+ICD patients vs. 19,6 VT events per year for the ICDonly patients. More than 2 VT events per year of FU occurred in 16 (32%) ABL+ICD vs. 27 (51%) ICDonly patients (p=0,23). The total number of VT episodes was 640 for ABL+VT patients vs. 1421 for ICDonly patients (p=0,06). VT storm occurred in 10 ABL+ICD patients vs. 15 ICDonly patients (p=0,33). In addition, data for the events of death (4 ABL+ICD vs. 3 ICDonly patients) showed no difference between treated patient groups.
The mean number of adequate ICD therapies per patient and year of FU was 12,8 in the ABL+ICD group vs. 26,8 in the ICDonly group (p=0,06) (median ICD therapy per patient and year: 0,7 ABL+ICD vs. 3,7 ICDonly).
Conclusion: Catheter ablation of VT prior to ICD implantation is able to reduce VT recurrences in patients with a history of coronary artery disease presenting with stable VT. A higher number of patients (n $>$110) is needed for significant results.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

NOVEL PERSPECTIVES ON THE METABOLIC SYNDROME

152 High Density Lipoprotein (HDL) restores impairment of endothelial progenitor cells from patients with metabolic syndrome via NAD(P)H oxidase inhibition

S.A. Sorrentino, C. Besler, F.H. Bahlmann, M. Meyer, M. Mueller, S. Flemmer, H. Haller, H. Drexler, U. Landmesser. *Hannover Medical School, Cardiology Dept, Hannover, Germany*

Purpose: Recent studies have suggested that endothelial injury in the absence of sufficient endothelial progenitor cells (EPCs) promotes progression of vascular disease. High density lipoprotein (HDL) is thought to mediate vasoprotection, however, the underlying mechanisms remain to be further characterized. Therefore, the present study examined the effect of HDL isolated from healthy subjects (HS) and patients with metabolic syndrome (MetS) on in vivo re-endothelialization capacity of EPCs and characterized underlying mechanisms.
Methods: In vivo endothelial regeneration capacity of EPCs from healthy subjects (n=10) and MetS patients (n=30) was determined by transplantation of EPCs (5x10E-5 cells) into NMRInu/nunude mice using a carotid artery injury model. R e-endothelialized area (REA) was assessed histomorphometrically 3 days after injury. The effect of HDL, isolated by ultracentrifugation, from healthy subjects and from MetS patients on re-endothelialization capacity was assessed. Furthermore, the effect of HDL on EPC superoxide ($O_2^{\bullet -}$) production, NAD(P)H oxidase activity and nitric oxide (NO) availability was analyzed by using electron spin resonance spectroscopy.
Results: Re-endothelialization capacity of EPCs from patients with MetS was markedly impaired as compared to healthy subjects (REA HS vs. MetS: 37±10 vs. 7±3%; P<0.001). Importantly, HDL from healthy subjects (REA 32±11%; P<0.001 vs. no HDL), but not HDL from MetS restored in vivo re-endothelialization capacity of EPCs from MetS. HDL from healthy subjects decreased $O_2^{\bullet -}$ production and NAD(P)H oxidase activity and increased NO availability, whereas HDL from MetS patients had little effect. The NAD(P)H oxidase inhibiting effects of healthy HDL were abolished after siRNA silencing of the lysophospholipid receptor S1P 3 in EPCs derived from MetS patients. siRNA silencing of the NAD(P)H oxidase subunit p47 phox restored in vivo re-endothelialization capacity of EPCs from MetS patients (REA 34±15%; P<0.001 vs. scrambled siRNA), suggesting that HDL improves re-endothelialization capacity of EPCs by NAD(P)H oxidase inhibition.
Conclusions: HDL from healthy subjects restores in vivo r e-endothelialization capacity of EPCs from patients with MetS, at least in part by NAD(P)H oxidase inhibition via lysophospholipid receptor $S1P_3$. Importantly, HDL from patients with MetS, however, has a markedly reduced effect, suggesting a loss of important vasoprotective properties of HDL in patients with metabolic syndrome.

153 Anti-lipolytic action of "ectopically" expressed eNOS in adipocytes

M. Eto, Y. Yamada, Y. Ito, M. Akishita, Y. Ouchi. *University of Tokyo, Geriatric Medicine, Tokyo, Japan*

Obesity/Metabolic syndrome (MetS) is a most important evolving risk factor for cardiovascular disease and circulating free fatty acids released from adipocytes through lipolysis (breakdown of stored triglycerides by adipocyte lipases such as hormone sensitive lipase (HSL)) play a pivotal role in the pathogenesis of MetS and related cardiovascular disease, because free fatty acids induce insulin resistance, endothelial dysfunction and macrophage activation. These suggest the controlled suppression of lipolysis might be a potential therapeutic strategy in this pathological condition, however, molecular mechanisms of lipolysis are not fully investigated. On the other hand, it has been recently shown that endothelial nitric oxide synthase (eNOS) is "ectopically" expressed in several types of cells including adipocytes, but the physiological and pathological functions of eNOS in adipocytes remain to be determined. Thus, the aim of this study is to investigate the role of eNOS on lipolysis in cultured adipocytes. In unstimulated 3T3-L1 preadipocytes, eNOS expression level was minimal, whereas eNOS gene and protein were dramatically upregulated (15-fold vs control) during the differentiation into mature adipocytes by adding insulin, dexamethasone and IBMX. The expression levels of iNOS were not changed during the differentiation. The inhibition of eNOS by L-NIO (10 micromol/L) and the gene knock-down of eNOS by siRNA had no effects on the process of adipocyte differentiation, assayed by oil red O staining, intracellular triglyceride content and the expression of differentiation-regulating transcription factors such as PPAR-gamma and C/EBPs. Beta receptor stimulation by isoproterenol (1 micromol/L) for 1 hour markedly induced lipolysis (8-fold vs basal level), as assayed by glycerol measurement in the medium, associated with the increase in HSL phosphorylation and in PKA activity. Isoproterenol also induced Akt phosphorylation and subsequent Akt-dependent eNOS phosphorylaiotn and NO production from 30 to 60 minutes. Both L-NIO and siRNA for eNOS gene significantly augmented lipolysis (180% and 220% vs control, respectively, n=6, P<0.01). L-NIO had no effects on isoproterenol-induced increase in HSL phosphorylation and PKA activity. These results clearly show that ectoplically expressed eNOS in adipocytes have anti-lipolytic action independently of HSL pathway. Activation of eNOS in adipocytes might be a new therapeutic strategy for MetS and obesity-related cardiovascular disease.

154 Increased high density lipoprotein cholesterol via human apolipoprotein A-I gene transfer increases adiponectin expression in abdominal adipose tissue

S. Van Linthout[1], F. Spillmann[2], C. Bucker-Gartner[1], A. Subasiguller[1], B. De Geest[3], H.-P. Schultheiss[2], C. Tschoepe[2]. *[1]Charite-Campus Benjamin Franklin, Cardiology And Pneumology, Berlin, Germany; [2]Charite - Campus Benjamin Franklin, Department of Cardiology, Berlin, Germany; [3]Center for Molecular and Vascular Biology, Department of Cardiology, Leuven, Belgium*

Purpose: High density lipoprotein (HDL) cholesterol (C) levels positively correlate with plasma adiponectin levels. However, a direct effect of HDL on adiponectin expression is unknown. To investigate the effect of increased HDL levels on adiponectin expression, gene transfer with human apolipoprotein (apo) A-I, the main apo of HDL, was performed in control mice and in lipopolysaccharide (LPS)-injected mice, associated with decreased adiponectin levels.
Methods: Eight weeks old male C57BL/6 mice were i.v. injected with 5 x 1010 total particles of the E1E3E4-deleted adenoviral vector Ad.hapoA-I, expressing human apo A-I or with the same dose of Ad.Null, containing no expression cassette. Fourteen days hereafter, mice were i.p. injected with LPS from Escherichia coli at a dose of 80 mg/kg or with saline. Mice were sacrificed 12 hours after LPS or saline injection. Human apo A-I plasma levels and mouse adiponectin plasma concentrations were determined by ELISA. mRNA expression of adiponectin and of the adipogenic transcription factor CCAAT enhancer binding protein (C\EBP) in abdominal fat was determined by real-time PCR. Abdominal fat phospho (p) and total (tot.) Akt protein levels were analyzed by Western Blot.
Results: Ad.hapoA-I GT resulted in human apo A-I expression levels of 83±4.6 mg/dl at day 14, that were associated with 1.8-fold (p<0.05) and 1.5-fold (p<0.05) higher HDL-C and adiponectin levels compared to Ad.Null mice, respectively. After LPS-injection, human apo A-I levels decreased 1.7-fold (p<0.001). Adiponectin levels in LPS-Ad.hapoA-I mice were 1.7-fold (p<0.005) lower compared to Ad.hapoA-I control mice, but 1.5-fold (p<0.01) higher compared to LPS-Ad.Null mice. On mRNA level, Ad.hapoA-I GT resulted in 8.2-fold (p<0.005) and 7.9-fold (p<0.05) higher adiponectin expression compared to control and LPS-injected Ad.Null mice, respectively. In agreement, Ad.hapoA-I GT was associated with 3.0–fold (p<0.05) and 6.0-fold (p<0.05) higher C\EBP mRNA expression in control and LPS-injected Ad.Null mice, respectively. The increased adiponectin levels in Ad.hapoA-I versus Ad.Null LPS-injected mice were associated with a 1.7–fold (p<0.05) increase in p-Akt/tot.Akt ratio.
Conclusion: In conclusion, human apo A-I GT increases adiponectin levels under normal and septic conditions involving C\EBP and Akt.

155 Deletion of cardiomyocyte PPARgamma results in cardiac insulin resistance

E. Caglayan[1], M. Kreissl[2], D. Stout[3], F. Blaschke[4], S. Rosenkranz[5], H. Schelbert[2], W.A. Hsueh[2]. *[1]University of Cologne, Department Iii For Internal Medicine, Cologne, Germany; [2]Universitaetsklinikum Wuerzburg, Nuklearmedizin, Wuerzburg, Germany; [3]UCLA, Crump Institute for Molecular Imaging, Los Angeles, United States of America; [4]Charite, Humboldt University, Cardiology, Berlin, Germany; [5]University of Cologne, Klinik III fuer Innere Medizin, Cologne, Germany*

In the diabetic heart, cardiac energy metabolism is altered towards increased free fatty acid utilization and a decrease in insulin-mediated glucose uptake. The ligand-activated nuclear receptor PPARγ is expressed in cardiomyocytes and plays a role in cardiac hypertrophy. However, the role of cardiomyocyte PPARγ regarding cardiac energy metabolism is not known.
Mice with a cardiomyocyte specific deletion of PPARγ (cPPARγ-/-) were generated using the Cre-lox P system. Littermate mice (WT) were used as controls throughout the study. Non-fasted cPPARγ-/- and WT mice (n=9-16/group) were imaged on 4 different days using small animal positron emisson tomography (microPET) technology. 18F-DG uptake was measured before and after one week of oral treatment with pioglitazone (Pio; 400 ppm), as well as with and without prior subcutaneous insulin (2 IU/kg*BW) injection. The cardiac uptake was determined after a 50-min wait period using the average of 4 small regions in the myocardial wall, normalized for body weight and injected dose.
Under conscious uptake, a significant difference was measured between WT and cPPARγ-/- mice (1.38%±0.20% vs 2.01%±0.18%; p<0.05). Insulin significantly increased cardiac 18F-DG uptake in WT (p<0.02), but not in cPPARγ-/- (1.96% ±0.09% vs. 2.12% ±0.10%). Pio enhanced cardiac 18F-DG uptake similiarly in both, WT and cPPARγ-/- (1.83%±0.23% vs. 2.58%±0.26%), indicating a cardiomyocyte PPARγ independent mechanism mediating its metabolic effect. However, insulin injection in Pio treated mice only increased 18F-DG uptake significantly in WT mice (p<0.05) (2.53%±0.14% vs. 2.73%±0.18%). There was no alteration in insulin-mediated glucose uptake in skeletal muscle, liver or brain and no difference in systemic glucose tolerance measured by oral glucose tolerance testing (OGTT). Plasma levels of glucose, insulin, free fatty acids, triglycerides and cholesterol were not significantly altered between WT and cPPARγ-/-. The observed cardiac insulin resistance in cPPARγ-/- was confirmed in isolated adult cardiomyocytes. Moreover, cPPARγ-/- hearts showed an attenuated insulin response of the glucose transporter-4 (GLUT4) translocation to the plasma membrane, although total GLUT 4 expression was not altered.
These results suggest that 1) PPARγ in the cardiomyocyte regulates insulin-mediated cardiac glucose uptake, involving mechanisms controlling the GLUT4

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

translocation to the plasma membrane.2) Pio treatment increases myocardial FDG uptake in-vivo even in the absence of PPARγ, hence a second way of action of Pio, independent of cardiomyocyte PPARγ, can be postulated.

156 Plasma adiponectin and insulin sensitivity as determinants of LV mass in healthy normotensive subjects

M. Kozakova[1], E. Muscelli[1], A. Flyvbjerg[2], J. Frystyk[1], C. Morizzo[2], E. Malshi[2], E. Ferrannini[2], C. Palombo[2]. [1]*University of Pisa, Department of Internal Medicine, Pisa, Italy;* [2]*Aarhus University Hospital, Clinical Institute and Medical Department, Aarhus, Denmark*

Background: Adiponectin is an adipocytokine expressed in fat tissue. Experimental studies have shown that adiponectin attenuates pressure-induced left ventricular (LV) hypertrophy, and that adiponectin receptors mediate the suppressive effect of adiponectin on endothelin-induced cardiomyocyte hypertrophy. Furthermore, clinical evidence suggested relationships between insulin resistance and hypoadiponectinemia, as well as between insulin resistance and LV hypertrophy. Aim of this study was to investigate the associations between plasma adiponectin, insulin resistance and LV mass in healthy normotensive individuals.
Methods: We studied 76 subjects (40 men, mean age = 43±8 years, BMI = 26±5 kg/m^2) without overt cardiovascular disease, hypertension, dyslipidemia or diabetes, who received an euglycemic hyperinsulinemic clamp (infusion of 40 mU insulin/m^2 body surface area for 2 h) to measure insulin sensitivity, and a Doppler-echocardiographic study to assess LV mass and cardiac workload.
Results: Insulin sensitivity (M-value) ranged from 12 to 81 μmol.min-^{1}.kg-^{1}, LV mass ranged from 70 to 255 g (LV mass index from 48-122 g/m^2). LV mass and mean wall thickness increased with age, male sex, body surface area, waist girth, fat-free mass, fasting plasma glucose and insulin, and stroke work (r's=0.30-0.71, p <0.01), whereas they decreased with HDL-cholesterol (r's=-0.44 and -0.40, p<0.01), M-value (r's =-0.28 and -0.23, p<0.05) and adiponectin (r=-0.46 for both; p<0.01). In multivariate analysis, independent correlates of LV mass were fat-free mass, age, adiponectin and M-value (adjusted r^2=0.67). Independent correlates of LV mean wall thickness were adiponectin and age (adjusted r^2=0.39).
Conclusions: Our results extend to normal subjects recent experimental observations on the anti-hypertrophic effect of adiponectin, and suggest a possible physiologic role for adiponectin in the control of LV mass. This hypothesis is in keeping with the inhibitory effect of adiponectin on nuclear transcription factor kappa B (NF-kB), a nuclear integrator of various signaling pathways, which appears to play a critical role in the development of myocardial hypertrophy.

157 Apelin in diabetic and hyperlipidemic cardiac dysfunction

G. Foldes[1], E. Ruzicska[1], R. Skoumal[2], M. Ilves[3], M. Toth[1], H. Ruskoaho[3]. [1]*Semmelweis University, 1St Dept of Medicine, Budapest, Hungary;* [2]*Gottsegen Hungarian Institute of Cardiology, Budapest, Hungary;* [3]*University of Oulu, Dept of Physiology, Oulu, Finland*

Long-term diabetes and dietary fatty acid intake alters the development of left ventricular hypertrophy, but the linking signaling pathways are unclear. Adipocytokine apelin and its receptor APJ have been reported to play a role in hypertrophic process. In this study, we measured left ventricular (LV) apelin and APJ receptor expressions in angiotensin II-induced pressure overload in rats with streptozotocin-induced diabetes or with randomly assigned to standard, high oil or high fat diets. As assessed by RT-PCR analysis, apelin mRNA levels were decreased 2-fold in diabetic rats (P<0.001). APJ receptor was decreased parallel with apelin, being 2.5-fold lower in diabetes (P<0.0001). Angiotensin II infusion (33 μg/kg/h, sc, 24 hrs) resulted in an additional decrease in apelin and APJ receptor mRNA levels (P<0.0001). APJ receptor mRNA levels correlated to LV weight to body weight ratio (R= -0.58, P<0.0001, n=38) and ANP mRNA levels (R=-0.61, P<0.0001, n=38). Baseline apelin and APJ receptor mRNA levels did not significantly differ in rats fed high oil or high fat from those fed standard diet. Ang II infusion markedly decreased apelin and APJ receptor mRNA levels in all three groups. In dietary fat groups, apelin mRNA levels correlated to body weight (BW: R=0.46, P<0.003, n=40), and LVW/BW ratio (R=-0.43, P<0.005, n=39). The increase in transcription factor activator protein-1 (AP-1) DNA binding activity in response to angiotensin II was higher in rats fed high oil diet compared to those fed standard diet (P<0.001). Ang II-induced increase in AP-1 DNA binding activity inversely correlated with mRNA levels of apelin (R=-0.40, P=0.014, n=38) and APJ receptor (R=-0.48, P=0.002, n=38). Infusion of apelin caused a decrease in LV AP-1 DNA binding activity in rats (P<0.01). In summary, we have shown that diabetes but not dietary fat type can attenuate the expression of apelin and APJ receptor in pressure overloaded myocardium involving distinct modulation of AP-1 signal transduction pathways.

SIGNALING IN THE HEART: FROM FUNCTION TO STRUCTURE

158 Connective tissue growth factor inhibits myocardial growth, stimulates fibrosis, but preserves myocardial function in chronic pressure overload

M.S. Ahmed[1], L. Thomas Von[2], J.A. Gravning[2], T. Edvardsen[2], O.A. Smiseth[2]. [1]*Rikshospitalet Univ. Hospital, Institute for Surgical Research, Oslo, Norway;* [2]*Rikshospitalet Univ. Hospital, Inst. for Surgical Research, Oslo, Norway*

Background: Myocardial expression of connective tissue growth factor (CTGF) is dramatically induced in heart failure (HF) of diverse etiologies. However, the physiologic and pathophysiologic roles of myocardial CTGF remain unresolved.
Methods and Results: To elucidate the actions of myocardial CTGF and its putative role in HF, transgenic mice with cardiac-restricted (a -MHC promoter) overexpression of CTGF were generated. Transgenic CTGF (Tg-CTGF) mice had slightly lower cardiac mass than that of non-transgenic littermate controls (NLC) (heart weight/tibia length of 4 months old male Tg-CTGF vs. NLC; 58.9±2.7 vs. 68.1±1.2 mg/cm, p<0.05). Consistently, echocardiography revealed slightly smaller left ventricular (LV) dimensions, including reduced end-diastolic interventricular septum thickness in Tg-CTGF vs. NLC mice. Simultaneous in vivo LV pressure-volume analysis did not disclose significant alterations of contractility and cardiac output, nor evidence of restrictive left ventricular dysfunction in Tg-CTGF vs. NLC mice. Histochemical analysis of myocardial tissue revealed subtle interstitial fibrosis in Tg-CTGF mice. This observation was corroborated by quantitation of increased myocardial hydroxyproline contents by HPLC (1.10±0.03 vs.0.82±0.05 pmol/mg dry weight in Tg-CTGF vs. NLC mice; p<0.05). Consistently, increased myocardial procollagen-α-I and -III mRNA levels in Tg-CTGF vs. NLC hearts were found. Morover, increased expression of antihypertrophic TGF-β2 and GDF-15 mRNA, and decreased expression of EGF mRNA in Tg-CTGF vs. NLC mice were detected. Tg-CTGF and NLC mice were subjected to pressure overload by abdominal aortic banding (AB) or sham-operation (SH). Four weeks after AB, significant elevations of cardiac mass were observed both in Tg-CTGF-AB and NLC-AB mice. However, cardiac hypertrophy was significantly diminished in Tg-CTGF-AB versus NLC-AB. Simultaneous PV-analysis provided evidence of cardiac dysfunction in NLC-AB mice, i.e. significantly increased LVEDD, LVEDP, and decreased stroke volume and cardiac output compared to NLC-SH mice. Strikingly, Tg-CTGF-AB revealed essentially preserved LV pressure-volume relations. Elevations of myocardial BNP mRNA leves were significantly attenuated in Tg-CTGF-AB compared to NLC-AB mice.
Conclusion: Myocardial CTGF exerts antihypertrophic effects and causes slight interstitial fibrosis, but no evidence of restrictive cardiac dysfunction. CTGF preserves left ventricular function due to pressure overload and delays onset of HF.

159 Inhibition of G protein-coupled receptor kinase-3 (GRK3) rescues cardiac dysfunction after pressure overload

J. Gravning[1], T. Von Lueder[1], T. Edvardsen[1], L. Vinge[1], O. How[2], E. Aasum[2], M.S. Ahmed[1], T.S. Larsen[2], O.A. Smiseth[1], H. Attramadal[1]. [1]*Rikshospitalet Medical Center, Univ. of Oslo, Institute For Surgical Research, Oslo, Norway;* [2]*Univ. of Tromso, Dept. of physiology, Tromso, Norway*

Background: Previous studies of transgenic mice with cardiac-restricted inhibition of GRK3 disclosed increased cardiac performance and phenotype consistent with α1-adrenergic receptor hyperresponsiveness. This is in contrast to GRK2 (β-ARK1), an isoenzyme with selectivity for β-adrenergic receptors. The aim of this study was to investigate the role of GRK3 during evolving cardiac dysfunction after pressure overload.
Methods and results: GRK3ct transgenic mice (Tg-GRK3ct) with cardiac-restricted expression of mini-gene encoding the carboxyl-terminal membrane targeting domain of GRK3 were employed. Inhibition of endogenous GRK3 was confirmed by enhanced α1-AR mediated activation of ERK1/2 in cardiac myocytes from Tg-GRK3ct as compared to non-transgenic littermate controls (NLC). Tg-GRK3ct mice characteristically displayed myocardial hypercontractility despite unaltered cardiac mass compared to NLC. Pressure overload was induced by abdominal aortic banding (AB) in weight-matched male Tg-GRK3ct (GRK3ct-AB) and NLC (NLC-AB) mice and compared with sham-operated Tg-GRK3ct (GRK3ct-SH) and NLC (NLC-SH) mice. Echocardiography revealed similar baseline cardiac dimensions among all groups. Eight and twelve weeks after AB, significant increases of cardiac mass were found in AB mice compared to sham, but no differences between GRK3ct-AB and NLC-AB were discerned. Eight weeks after AB, analysis of electrically paced, ex vivo perfused hearts at increasing filling pressures revealed preserved end-diastolic and end-systolic pressure-volume (PV) relations in Tg-GRK3ct-AB (n=10), with substantially higher cardiac output and (dP/dt)max compared to NLC-AB (n=10). Twelve weeks after AB, simultaneous in vivo PV-analysis revealed elevated end-diastolic pressure (10.6±3.1 vs. 2.7±2.2 mmHg, p<0.05) and lower cardiac output (7379±738 vs. 9847±785 μL/min, p<0.05) in NLC-AB (n=11) compared to GRK3ct-AB (n=16). Consistently, myocardial mRNA levels of B-type natriuretic peptide were substantially elevated in NLC-AB vs. GRK3ct-AB (p<0.05).
Conclusion: Inhibition of cardiac GRK3 in mice rescues cardiac dysfunction and heart failure after pressure overload.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

160 Disturbed MAPK signaling and heart failure in Impedes Mitogenic Signaling (IMP) transgenic mice

T. Seidler[1], P. Schott[2], C. Grebe[1], B. Unsoeld[1], A. Schmidt[1], H. Koegler[1], K. Guan-Schmidt[1], G. Hasenfuss[1]. *[1]Georg-August University Goettingen, Dept. Cardiology And Pneumology, Gottingen, Germany; [2]Goettingen, Germany*

Purpose: Neurohumoral activation strongly stimulates mitogen activated protein kinase (MAPK) pathways in the heart, which signal to and activate downstream effector pathways highly relevant to hypertrophy and heart failure. IMP was recently identified as an important modulator of Ras dependent activation of ERK MAPK signaling in non-cardiac cells. We identified IMP to be differentially regulated upon load induced heart failure in a proteomics study. Thus, the aim of this study was to analyse the role of IMP in myocardial hypertrophy and heart failure.
Methods: Adenoviruses for overexpression of IMP and a constitutively activated Raf mutant (Raf-BXB), were created to study the effects of IMP in vitro in isolated rat cardiac myocytes. Transgenic mice, overexpressing IMP cardiac-specifically under control of the alpha myosin heavy chain promoter were created and analysed.
Results: In both adult and neonatal rat cardiac myocytes, IMP overexpression profoundly suppressed MEK and ERK MAPK activation under baseline conditions and following Raf-BXB-stimulation. This suggests an inhibitory effect of IMP on both adaptive hypertrophy and anti-apoptotic signaling. Three independently created IMP-transgenic (TG) mouse lines in two different genetic backgrounds exhibited grossly enlarged hearts, compared to wildtype littermates (WT). Echocardiography confirmed dilation (left ventricular end-diastolic diameter 4.57±0.17 vs. 3,57±0.04 mm; $p<0.05$ IMP vs. WT; $p<0.05$; TG vs WT) and significant reduction of fractional shortening (14±3% vs. 40±0.4%; IMP TG vs. WT; $p<0.001$). Invasive hemodynamic measurements confirmed a phenotype consistent with a severe dilative cardiomyopathy. Kaplan-Maier analysis showed a significantly decreased survival with 50% of mice dying before the age of 24 weeks. In contrast to acute ectopic expression in vitro, chronic expression in mice led to counter regulation of Mek activity, activation of JNK and activation of the proapoptotic Bax protein.
Conclusions: The phenotype closely mimics that of the Raf-1 knock-out mouse suggesting an important role for IMP in maintainance of Ras/Mek vs. JNK activation balance. These data indicate that IMP can control cardiac size and function via inhibition of the Ras dependent ERK MAPK pathway.

161 Post infarction treatment with oxytocin reduces myocardial infarct size and improves left ventricular function and remodeling through phosphorylation of Akt, ERK and over expression of VEGF

H. Kobayashi[1], S. Minatoguchi[1], S. Yasuda[1], B. Narentuoya[2], M. Iwasa[1], H. Ushikoshi[1], G. Takemura[1], T. Fujiwara[3], H. Fujiwara[1]. *[1]Gifu University, Cardiology Department, Gifu, Japan; [2]Gifu University, Cardiology, Gifu, Mongolia; [3]Kyoto women University, Food Science, Kyoto, Japan*

Purpose: Oxytocin(OT) is a peptide hormone involved in the regulation of the lactation and parturition. It has been reported that both OT and OT receptors are found in the heart and that OT plays an important role in the embryonal development of the heart. Therefore, we hypothesized that OT would be beneficial to protect the heart against myocardial infarction.
Methods: Rabbits (male 2kg) underwent 30 minutes of coronary occlusion and 14 days of reperfusion. Saline (Control group) or 10mg/kg of OT (OT group) was subcutaneously injected immediately after reperfusion once/day for 5 days (total amount of 50mg/kg). Left ventricular (LV) function was measured by echocardiography. The infarct size was determined by TTC staining and expressed as a percentage of the risk area. Western blot analysis was performed to examine Akt and ERK,cell survival signals, phosphorylation and Vascular Endothelial Growth Factor (VEGF) expression.
Results: Ejection fraction, fractional shortening in the OT group (71.9±1.4%, 37.4±1.0%) were significantly greater than those in the Control group (57.8 ±2.8%, 28.2±1.9%). LV diastolic and systolic dimension in the OT group (11.9±0.5mm, 7.5±0.6mm) were significantly smaller than those in the Control group (15.4±0.5mm, 11.0±0.4mm). The infarct size was significantly reduced in the OT group (16.4±2.6%) compared with that in the Control group (23.1±2.9%). The expression of p-Akt, p-ERK and VEGF protein in the myocardium of the risk area was markedly increased 48 hours after infarction in the OT group as compared with that in the Control group.
Conclusions: Post infarction treatment with oxytocin reduces myocardial infarct size and improves LV function and remodeling. Phosphorylation of Akt and ERK and overexpression of VEGF may be involved in the beneficial effect of Oxytocin. These findings provide new insight into therapeutic strategies for ischemic heart disease.

162 Aldosterone induced IL-18 expression through Endotheline-1 and Angiotensin II via Rho, Rho-kinase and PPAR in cardiomyocytes

T. Doi, T. Sakoda, T. Akagami, T. Naka, T. Tsujino, T. Masuyama, M. Ohyanagi. *Hyogo College of Medicine, Coronary Heart Disease, Nishinomiya, Japan*

Interleukin-18 (IL-18), a member of the IL-1 family, is a proinflammatory cytokine with multiple functions. Increased levels of circulating IL-18 are thought to be one of risk factors for heart failure. We have firstly revealed that serum IL-18 concentrations increased according to worsening NYHA functional class in patients with congestive heart failure. Aldosterone is recognized as the important risk hormones for cardiovascular disease with myocardial hypertrophy and fibrosis with pathological remodeling. Endothelin-1 (ET-1) and Angiotensin-II (Ang-II) has been reported to be a potent hypertrophy-promoting factor through Rho and Rho-kinase. Aldosterone induces hypertrophic response partly by production of ET-1 and Ang-II. Pioglitazone and Bezafibrate, PPAR agonists, have shown anti-inflammatory activities in many tissues. In the present study, we examined the effect and mechanism of aldosterone on IL-18 expression in rat cardiaomyocytes (CM). Aldosterone increased IL-18 expression with dose-dependent and time-dependent manner in CM with a peak induction at 48 hours after incubation. Spironolactone and Eplerenone, mineral corticoid receptor antagonists, and Cycloheximide, a protein synthesis inhibitor, inhibited aldosterone-induced IL-18 expression. Furthermore, BQ123, an Endothelin A receptor (ETAR) antagonist and Olmesartan, an Ang-II receptor (AT-IIR) antagonist inhibited aldosterone-induced IL-18 expression. However, ETB receptor antagonist BQ788 did not inhibit this reaction. ET-1 and Ang-II induced IL-18 expression with peak inductions at 4 hours and 8 hours after incubation, respectively. These results indicate that aldosterone induces IL-18 expression intermediates ET-1 and AT-II via ETAR and AT-IIR. Furthermore, Fasudil, a Rho-kinase inhibitor and Simvastatin, a HMG-CoA reductase inhibitor led to a significant reduction in IL-18 expression. Finally, Pioglitazone and Bezafibrate attenuated aldosterone-induced IL-18 expression with dose dependent manner. Induction of IL-18 from CM by aldosterone through ET-1 and Ang-II might cause deterioration of cardiac function by autocrine and paracrine fashion. Inhibition of IL-18 expression induced by aldosterone, ET-1 or Ang-II might be one of the mechanisms of beneficial cardiovascular effects of ETAR antagonist, AT-IIR antagonist, Statin, Rho-kinase inhibitor or PPAR agonists.

163 Apoptosis in peripartum cardiomyopathy might be mediated by lack of transforming growth factor-beta1 and high levels of oxidized low density lipoprotein

O. Forster[1], D. Hilfiker-Kleiner[2], J.B. Sundstrom[3], W. Tshani[4], E. Libhaber[3], P. Nesara[3], A. Yip[3], A. Becker[3], K. Sliwa[3], A.A. Ansari[1]. *[1]University of The Witwatersrand, C. H. Baragwanath Hospital, Cardiology, Soweto, South Africa; [2]Medizinische Hochschule Hannover, Molecular Cardiology, Hannover, Germany; [3]Emory University, School of Medicine, Pathology and Laboratory Medicine, Atlanta, United States of America; [4]University of the Witwatersrand, Cardiology, Soweto, South Africa*

Purpose: Peripartum Cardiomyopathy (PPCM) is characterized by left ventricular failure that occurs in women between 1 month antepartum and 5 months postpartum. The aetiology of PPCM is unknown.
Methods: In an attempt to identify molecular pathways involved in the pathogenesis of PPCM, we measured levels of the markers of re-modeling matrix-metallo-proteinase-2 and 9 (MMP-2, MMP-9), anti-apoptotic survival factor for T-lymphocytes transforming-growth factor β-1 (TGF-β-1) and vascular endothelial growth factor (VEGF). We correlated these with the markers of apoptosis Fas/APO-1 and oxidative stress oxLDL. To set apart abnormally elevated biomarkers, we analyzed data between patients and healthy controls. To make out pathways that determine either progression or reversibility of PPCM, we analysed data between cardiac function improvers and non-improvers at baseline and after 6 months.
Results: 38 out of 43 patients completed the follow-up period of 6 months, 3 patients had died and 2 were not available for follow-up. Patients presented with a with a heart rate of 99.7±19 b.p.m., systolic blood pressure of 113.4±20.0 mmHg and a diastolic blood pressure of 75.6±13.4 mmHg. LVEF among all patients was 29.5% [13-39] with a LVESD of 4.9 mm [3.6-6.3] and a LVEDD of 5.6 mm [4.3-7.3]. Baseline serum levels of MMP-2 were higher ($p<0.0001$) among patients 368.5 ng/ml [308.2-474.9] than in healthy controls 142.2 ng/ml [111.8-184.9], while levels of MMP-9 and VEGF were not. Interestingly, TGF-β-1 was significantly ($p=0.002$) lower in PPCM patients 8.5 ng/ml [3.7-22.7] than in controls 16.4 ng/ml [9.0-30.9]. None of these markers of re-modeling differed significantly between improvers and non-improvers at baseline or over time. In the same group of PPCM patients, Fas/APO-1 was higher ($p<0.0001$) among PPCM patients 0.34 ng/ml [0.13-5.29] just as oxLDL was elevated ($p<0.0001$) in patients 16.1 IU/ml [15.3-19.4] compared to controls 8.6 IU/ml [7.5-9.3] and decreased significantly ($p<0.0001$) from 16.6±1.3 U/ml to 11.9±2.1 U/ml in improvers, but remained high among non-improvers (16.5±1.0 U/ml at baseline and 16.7±1.8 U/ml after 6 months).
Conclusions: A cellular lack of protection from increased Fas/APO-1 activity in PPCM patients could be secondary to significantly ($p=0.002$) decreased serum levels of the antiapoptotic survival factor for T-lymphocytes TGF-β1 in these patients. Additionally oxLDL sensitizes human vascular cells (smooth muscle cells

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

and endothelial cells) to Fas/APO-1 mediated apoptosis by inhibition of Fas/APO-1 degradation and therefore may further enhances apoptosis in PPCM patients.

PERCUTANEOUS CORONARY INTERVENTION FOR STEMI

189 Short-term outcomes are at least as good with drug eluting vs. bare metal stents: insights from APEX AMI

M.R. Patel[1], M.E. Pfisterer[2], A. Betriu[3], P. Widimsky[4], D.R. Holmes[5], W.W. O' Neill[6], A.L. Stebbins[2], F. Van De Werf[7], P.W. Armstrong[8], C.B. Granger[2] on behalf of APEX AMI Investigators. *[1]Duke Clinical Research Institute, Durham, United States of America; [2]University Hospital Basel, Basel, Switzerland; [3]Clinic Barcelona, Barcelona, Spain; [4]Kralovske Vinohrady University Hospital, Prague, Czech Republic; [5]Mayo Clinic, Rochester, United States of America; [6]University of Miami, Miami, United States of America; [7]University Hospital Gathuisberg, Leuven, Belgium; [8]University of Alberta, Edmonton, Canada*

Background: Recent reports have raised concerns about "off label" use of drug eluting stents (DES). There are limited randomized trial data evaluating the use of DES versus bare metal stents (BMS) in acute ST elevation myocardial infarction (AMI). Therefore, we evaluated the use and outcomes of DES in a large primary percutaneous intervention (PCI) ST elevation AMI trial.
Methods: The acute myocardial infarction pexelizumab trial (APEX-AMI) randomized 5,745 patients undergoing primary PCI to pexelizumab vs. placebo for the primary composite endpoint death, shock or heart failure. Baseline clinical and procedural variables as well as clinical outcomes were collected at 90-days and 6 months. Adjustment for clinical outcomes by stent type was performed using identified multivariable predictors of 90-day mortality (age, anterior location, total ST segment deviation, and Killip class), and time from symptom onset to PCI and post-intervention TIMI flow.
Results: Stents were deployed (according to investigator discretion) in 5,124 (89.2%) of AMI patients enrolled, with DES use in 2,221 (43.3%) and BMS use in 2,903 (56.7%) patients. Patient demographics and outcomes with DES and BMS use are in the Table. Patients receiving DES were younger and more likely from the USA. Patients treated with DES versus BMS tended to have lower adjusted recurrent MI at 6 months and lower adjusted death, heart failure, and shock at both 90-days and 6 months (see table).

	Total Stented n = 5,124	DES patients n = 2,221	BMS Patients n = 2,903
Demographics			
Age (median)	61.0 (52.0,71.0)	59.0 (50.0,69.0)	63.0 (54.0,72.0)
Male Gender	3970 (77.5%)	1735 (78.1%)	2235 (77.0%)
Killip Class > 1 at presentation	512 (10.0%)	192 (8.6%)	320 (11.0%)
USA (% region)	1515 (29.6%)	1292 (85.3%)	223 (14.7%)
Eastern Europe (% region)	1213 (23.7%)	66 (5.4%)	1147 (94.6%)
Western Europe (% region)	1601 (31.2%)	566 (35.4%)	1035 (64.6%)
Australia, NZ, Canada (% region)	795 (15.5%)	297 (37.4%)	498 (62.6%)
Clinical Outcomes (Unadjusted)			
90-day Mortality	200 (3.91%)	67 (3.02%)	133 (4.58%)
90-day Composite (Death, Shock, CHF)	467 (9.12%)	177 (7.97%)	290 (9.99%)
6 month Recurrent MI	189 (3.70%)	71 (3.19%)	118 (4.09%)
6 month Composite (Death, Shock, CHF)	487 (9.51%)	187 (8.42%)	300 (10.35%)

Adjusted Clinical Outcomes	Hazard Ratio	95% C.I.	p-value
90-day Mortality (n=5,014)	0.697	(0.476 - 1.09)	p = 0.062
90-day Composite (Death, Shock, CHF) (n=5,014)	0.862	(0.712 - 1.045)	p = 0.113
6 month Recurrent MI (n=3,393)	0.811	(0.595 - 1.106)	p = 0.186
6 month Composite (Death, Shock, CHF) (n=3,393)	0.874	(0.689 - 1.110)	p = 0.269

Conclusion: In this largest to date observational analysis of stent use in a clinical trial of 5,745 patients undergoing primary percutaneous intervention for acute myocardial infarction, DES appear as safe as BMS with similar 6-month clinical outcomes.

190 Predictors and mechanisms of early and late stent malapposition(SM) after sirolimus-eluting (SES) versus bare-metal stent (BMS) implantation in patients with ST-segment elevation myocardial infarction

B.L. Van Der Hoeven, S.S. Liem, H. Putter, J. Dijkstra, D.E. Atsma, M. Bootsma, K. Zeppenfeld, P.V. Oemrawsingh, J.W. Jukema, M.J. Schalij. *Leiden, Netherlands*

Introduction: Evidence about prevalence, predictors, mechanism and outcome of SM after primary PCI is limited. This sub-study reports on the results of the MISSION! Intervention Study, a randomized study comparing SES and BMS in 310 STEMI patients.
Methods: In 184 patients both post-procedure (post) and follow-up (fup) IVUS images were available (104 SES; 80 BMS). SM was defined as early (post), late (fup), resolved (post+, fup-), persistent (post+, fup+) and acquired (post-, fup+). Multivariate regression analysis was performed to find clinical, angiographic and procedural predictors of early, late and acquired SM. The mechanism of SM was determined by correlating delta lumen cross sectional area (CSA; fup-post) at SM sites with delta external elastic membrane (EEM) CSA (remodeling +/-) and delta plaque and media (P&M) CSA (plaque +/-).
Results: After SES or BMS implantation early SM was present in 38.5% and 33.8% (p=0.51), late SM in 37.5% and 12.5% (p<0.001) and acquired SM in 25.0% and 5.0% (p<0.001) of the patients. Early SM sites persisted more often after SES implantation (28 vs.11 BMS; p=0.04). Predictors of early SM were vessel reference diameter (SES: OR 3.49; 1.29-9.43); BMS: OR 28.8; 4.25-94.5) and maximum balloon pressure (BMS: OR 0.74; 0.58-0.94). Predictors of late SM were diabetes mellitus (SES: OR 0.16; 0.02-1.35), vessel reference diameter (BMS: OR 19.2; 2.64-139.7) and maximum balloon pressure (BMS: OR 0.74; 0.55-1.00). Predictor of acquired SM was SES implantation (OR 9.43; 2.73-32.6). Delta lumen CSA was strongly related to delta EEM CSA (R=0.73; 0.62-0.84) and weakly to delta P&M CSA (R=-0.27; -0.38- -0.16) after SES implantation and mainly to delta P&M CSA (R=-0.62; -0.77- -0.46) and less to delta EEM CSA (R=0.38; 0.23-0.54) after BMS implantation. After SES implantation, acquired SM was due to positive remodeling in 84% and plaque reduction in 16% of the SM sites.
Conclusion: Early SM was common after SES and BMS stent implantation during primary PCI and related to vessel diameter. Most early SM sites resolve in BMS patients due to neointimal growth and late SM is rare. After SES implantation, late SM is common and mainly due to acquired SM, which generally develops by positive remodeling. Plaque reduction plays a role in a minority of sites.

191 A comparison of the use of endothelial progenitor cell capture stent and a bare metal stent in the setting of acute myocardial infarction

M. Co, E. Tay, H.C. Tan, Y.T. Lim, A. Low, C.H. Lee, J. Lim, I.H. Lim. *National University Hospital, Cardiac, Singapore, Singapore*

Background: We hypothesized that the Endothelial Progenitor Cell Capture bio-engineered stent, designed to attract circulating endothelial progenitor cells (EPCs) and promote rapid healing, will lead to better clinical outcomes in patients with ST-segment myocardial infarction (STEMI) when compared with patients who received bare metal stents.
Methodology: Two hundred twenty-five patients who presented to our centers with STEMI without cardiogenic shock and received primary PCI with either Endothelial Progenitor Cell Capture stent and bare metal stent were prospectively enrolled in this study. All patients received dual anti-platelet therapy for a month; and immediate statin therapy after the procedure. The study endpoints were major adverse cardiac events (MACE) at 30 days and 6 months.
Results: A total of 131 Endothelial Progenitor Cell Capture stents and 156 bare metal stents were implanted. Baseline patient characteristics were comparable in the two groups. The mean lesion length in the 2 groups were 24.0±13.4 and 17.5±7.2mm, and the mean reference vessel diameter 2.42±1.39 and 3.16±0.66 mm respectively. The 30-day MACE were 3.4% and 6.1% for the Endothelial Progenitor Cell Capture and bare metal stent groups respectively (p=0.319).

Outcomes	Bare Metal Stent n = 116	Endothelial Progenitor Cell Capture Stent n=119	P value
MACE n (%)	7 (6.1)	4 (3.4)	0.32
Death n (%)	3 (2.58)	2 (1.7)	0.32
Myocardial infarction N (%)	1 (0.9)	0 (0)	0.15
Repeat Revascularization n (%)	3 (2.58)	2 (1.7)	0.32
Acute Thrombosis n (%)	1 (0.9)	1 (0.8)	ns
Subacute Thrombosis n (%)	1 (0.9)	1 (0.8)	ns

Conclusion: There was no significant difference in the incidence of MACE at one month between Endothelial Progenitor Cell Capturestent and Bare Metal Stent in patients with STEMI who underwent primary stenting.

192 Prospective randomized comparison of sirolimus- versus paclitaxel- eluting stents for the treatment of acute ST-elevation myocardial infarction: an intravascular ultrasound study

H.S. Kim[1], J.H. Lee[2], Y.J. Choi[2], S.H. Jo[2], J.H. Park[1], I.W. Seong[1], J.K. Chae[3], J.K. Ko[1]. *[1]Hallym University Sacred Heart Hospital, Cardiology, Anyang-Si, Korea, Republic of; [2]Chungnam National University Hospital, Cardiology, Daejeon, Korea, Republic of; [3]Chonbuk National University Hospital, Cardiology, Jeonju, Korea, Republic of*

Purpose: This study used serial intravascular ultrasound (IVUS) analysis to compare the vascular response of sirolimus- (SES) versus paclitaxel-eluting stent (PES) implantation for the treatment of acute ST-elevation myocardial infarction (STEMI).
Methods: From Jan 2004 to Jan 2006, a total of 308 patients with STEMI undergoing primary angioplasty were randomly assigned to SES or PES deployment. Among them, serial IVUS data obtained immediately after procedure and at 6-month follow-up were available in 130 patients (75 SES, 55 PES). Reference segment external elastic membrane (EEM) and lumen areas were measured over

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

a 5-mm length adjacent to each stent edge. Stent, lumen, and intimal hyperplasia (IH) areas were measured within the stented segment.
Results: The baseline characteristics were similar between 2 groups. At follow-up, in-stent IH volume in the SES was significantly lower than in the PES (37.1±16.8 mm^3 vs 55.9±27.8 mm^3, P <0.001). The overall incidence of late stent malapposition was 32.2%, which was either not different between groups. Late stent maapposition was not associated with adverse clinical events during follow-up.

Follow-up IVUS

	SES (n=75)	PES (n=55)	P value
Proximal reference EEM area, mm^2	16.1±3.6	17.2±4.2	0.15
Proximal reference lumen area, mm^2	10.5±3.0	9.7±3.4	0.21
Stented segment stent volume, mm^3	209.6±79.0	227.7±96.9	0.24
Stented segment lumenvolume, mm^3	172.5±65.9	171.7±86.3	0.95
Stented segment IH volume, mm^3	37.1±16.8	55.9±27.8	<0.001
Distal reference EEM area, mm^2	11.6±3.7	11.5±4.3	0.88
Distal reference EEM area, mm^2	8.0±2.5	7.3±3.2	0.19
Late stent malapposition	28.0%	36.4%	0.31

Conclusions: The SES significantly outperformed the PES in supressing neointimal growth in STEMI patients treated with primary stenting. Late stent malapposition was a frequent phenomenon in these groups.

193 Three-year follow-up patients with ST-segment elevation acute myocardial infarction treated with sirolimus-eluting stent and paclitaxel-eluting stent: multicenter registry in Asia

S. Nakamura[1], J.H. Bae[2], Y.H. Cahyadi[3], W. Udayachalerm[4], D. Tresukosol[5], S. Tansuphaswadikul[6]. *[1]New Tokyo Hospital, Department of Cardiology, Matsudo, Japan; [2]Konyang University Hospital, Daejeon, Korea, Republic of; [3]Husada Hospital, Jakarta, Indonesia; [4]King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [5]Her Majesty's Cardiac Center Siriraj Hospital, Bangkok, Thailand; [6]Chest Disease Institute, Bangkok, Thailand*

Background: Previous clinical study utilizing Sirolimus-eluting stent (SES) and Paclitaxel-eluting stent (PES) in simple coronary lesions demonstrated an impressive reduction in intimal hyperplasia and restenosis. However, clinical efficacy of SES and PES in treating patients with ST-segment elevation myocardial infarction (STEMI) has not been validated.
Methods: We assessed baseline clinical and angiographic characteristics, in-hospital and 12, 24 and 36-month major adverse cardiac events (MACE) in 1,838 consecutive STEMI patients who received on SES, PES or bare metal stents (BMS) without cardiogenic shock undergoing emergent PCI.
Results: The baseline clinical characteristics between 3 groups were similar. See table for the clinical results.

		BMS	SES	PES	p
Number of patients		388	843	607	–
In-hospital	Clinical success (%)	98.5	98.8	99.0	NS
	Death (%)	1.0	0.8	1.0	NS
	Stent thrombosis (%)	0.5	0	0	NS
30 days to 12 mo	Death (%)	0.5	0.2	0.3	NS
	Angiographic restenosis (%)	16.0	3.8*	4.9*	0.01
	Repeat PCI (%)	10.8	3.0*	4.9*	0.01
	Stent thrombosis (%)	0	0.2	0.3	NS
30 days to 24 mo	Death (%)	0.8	0.4	0.5	NS
	Angiographic restenosis (%)	17.5	3.8*	5.3*	0.01
	Repeat PCI (%)	11.9	3.8*	5.3*	0.01
	Stent thrombosis (%)	0	0.2	0.3	NS
30 days to 36 mo	Death (%)	0.8	0.8	0.5	NS
	Angiographic restenosis (%)	17.5	5.3*	5.9*	0.01
	Repeat PCI (%)	11.9	3.8*	5.9*	0.01
	Stent thrombosis (%)	0	1.2	0.3	NS

Conclusion: Implantation of SES and PES in STEMI patients is not associated with any risk of adverse in-hospital events, and reduced the need for repeat PCI at follow-up.

194 No improvement of outcome and no increase in stent thrombosis 2 years after PCI with PAclitaxel-eluting Stents compared to uncoated stents for ST-segment Myocardial InfarctION: the PASSION trial

M.T. Dirksen[1], M.J. Suttorp[2], M.A. Vink[1], J.G.P. Tijssen[3], B.J. Rensing[3], T. Slagboom[2], M. Patterson[2], F. Kiemeneij[2], G.J. Laarman[2] on behalf of PASSION study group. *[1]Onze Lieve Vrouwe Gasthuis, Department of Cardiology, Amsterdam, Netherlands; [2]Sint Antonius Hospital, Department of Cardiology, Nieuwegein, Netherlands; [3]Academic Medical Center, Department of Cardiology, Amsterdam, Netherlands*

Purpose: Drug-eluting coronary-artery stents have proven to decrease restenosis after percutaneous coronary intervention (PCI). The PASSION trial demonstrated that after 1 year follow-up the use of paclitaxel-eluting stent (PES) in primary PCI for acute myocardial infarction was associated with a non-significant reduction of adverse events. Recently, however, concern has arisen about the occurrence of (very) late stent thrombosis after PES implantation. Therefore, we evaluated the incidence of stent thrombosis 2 years after the use of PES or uncoated stent in patients that underwent PCI for ST-segment elevation myocardial infarction (STEMI).
Methods: We randomly assigned 619 patients presenting with a STEMI to receive either a PES or an uncoated stent. During follow-up visits up to two years after inclusion, we recorded all major adverse cardiac events (MACE). On top of the ARC criteria for stent thrombosis, three additional definitions of stent thrombosis were used: 1) angiographically proven stent thrombosis, 2) recurrent MI of the same myocardial region, and/or proven by coronary angiography or, 3) cardiac death, re-infarction of the same myocardial region, and/or proven by coronary angiography.
Results: Baseline clinical and angiographic characteristics in both groups were well matched. The total 2-year follow-up data with the occurrence of MACE of the total study population will be presented, with the emphasis on late stent thrombosis. Preliminary results of the 2-year follow-up in 465 (75% of total study population) patients showed a trend toward a lower rate of target lesion revascularization in the PES group versus the uncoated-stent group (6.3% vs. 9.3%; P = 0.19). Angiographically stent thrombosis occurred in 2% versus 1.6% (P = 0.75). The cumulative incidence of cardiac death, re-infarction of the same myocardial region, and/or proven by coronary angiography was not different after 2 years follow-up (8.8% in the PES group versus 8.6% in the uncoated stent group; Relative Risk 0.87; P = 0.85).
Conclusions: Our preliminary results of 2-year follow-up after treatment with either a PES or an uncoated stent, showed no significant differences in clinical outcome, nor is there a significant increase of (late) stent thrombosis in the PES group. However, the differences in MACE and cardiac death between DES and BMS seem less pronounced in time. Late and complete follow-up is warranted in this matter.

VULNERABLE PLAQUE: FROM A TO Z

195 Proteolytic and angiogenic activity in upstream versus downstream region of atherosclerotic plaque

I. Cicha[1], A. Yilmaz[1], D. Raaz[1], W.G. Daniel[1], M. Goppelt-Struebe[2], C.D. Garlichs[1]. *[1]Medical Clinic 2, University of Erlangen, Medical Clinic 2, Erlangen, Germany; [2]Nephrology Department, University of Erlangen, Medical Clinic 2, Erlangen, Germany*

Background: Increased incidence of plaque rupture was reported at upstream shoulder of atherosclerotic lesions. In accordance with this, a higher frequency of inflam-matory cells, chemokines, and chemokine receptors was detected in upstream plaque shoulders. As the mechanisms leading to plaque destabilization often involve increased proteinase activity and enhanced neovascularization which provides entry points for inflammatory cells, we investigated proteolytic and angiogenic protein expression along the atherosclerotic lesions.
Methods: Serial longitudinal sections of 30 human carotid specimens (AHA classification IV-VI) were immunohistochemically analyzed for the expression of mast cell chymase and cathepsin L using specific monoclonal antibodies. Antibody against von Willebrand factor (vWF) was used to detect vasa vasorum, and connective tissue growth factor (CTGF) was stained as pro-angiogenic growth factor. Immunoreactive cells were digitally counted in upstream and downstream regions of the plaques and the differences between the regions were analyzed statistically using paired t-test.
Results: Immunohistochemical analyses of the longitudinal sections of carotid plaques showed that the mean numbers of chymase-positive cells were significantly higher upstream as compared with downstream regions of the atherosclerotic carotid arteries (34.7±3.8 upstream versus 12.8±3.5 downstream, p<0.001, n=30). Similarly, the expression of cathepsin L was markedly increased in the upstream region of the plaque. With regard to pro-angiogenic growth factors, CTGF immunoreactivity was significantly higher upstream as compared with downstream region of the atherosclerotic lesions. Among the analyzed plaques, 16 specimens were undergoing active intimal neovascularization. In these plaques, the newly formed vessels accumulated particularly in upstream region, with vasa vasorum density of 2.6±0.8 per mm^2 upstream, compared with 1.1±0.5 per mm^2 downstream (p<0.01).
Conclusions: This study demonstrated that plaque instability at upstream region is related to increased expression of proteolytic and angiogenic proteins, and enhanced neovascularization. These findings underscore the close association of local hemodynamic forces with plaque composition and destabilization processes.

196 Local expression of TNF-alpha converting enzyme in ruptured plaques is related to adverse clinical outcomes in patients with AMI

M. Satoh, Y. Ishikawa, T. Akatsu, T. Itoh, Y. Minami, M. Nakamura. *Iwate Medical University, Second Deparment of Internal Medicine, Morioka, Japan*

Background: Tumor necrosis factor-α (TNF-α) converting enzyme (TACE/ADAM-17) plays an essential role in the TNF-α shedding, which could have a detrimental

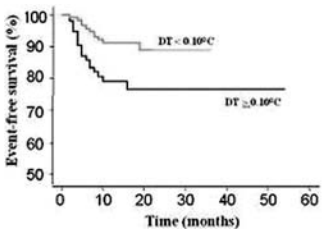
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

effect on outcome in acute myocardial infarction (AMI). However, it remains unclear whether it originates from the ruptured plaque or represents a systemic process. This study analyzed TACE-mediated TNF-α shedding at the site of ruptured plaques in AMI patients and compared them with a systemic mechanism.
Methods and results: The culprit coronary and aortic samples were obtained from 60 patients with AMI and 21 patients stable angina pectoris (AP) with using percutaneous coronary intervention with thrombus-aspiration. TACE and TNF-α levels (mRNA and protein) were higher in AMI patients than in AP patients (all $P < 0.01$). In AMI patients, TACE and TNF-α levels were higher in culprit coronary samples than in aortic samples (all $P < 0.01$). A positive correlation was seen between TACE and TNF-α levels in culprit coronary samples obtained from AMI patients (mRNA: $r = 0.69$, $P < 0.001$; MFI: $r = 0.81$, $P < 0.001$). TACE MFI was also positively correlated with plasma TNF-α levels in culprit coronary samples obtained from AMI patients ($r = 0.61$, $P < 0.001$). There were no differences in levels between coronary and aortic samples obtained from AP patients. Thrombus material removed from the ruptured plaque showed immunostainings of TACE and TNF-α in CD68-positive cell s. TACE and TNF-α levels in culprit coronarysamples were higher in AMI patients (n = 15) with in-hospital complications, which consisted of pump failure in 12, recurrent MI in 1 and cardiac death in 2, compared with those without complications (all $P < 0.01$). Univariate analysis has shown that TACE and TNF-α levels in culprit coronary samples were significantly associated with in-hospital complications. After adjusting for various clinical parameters (age, gender, peak CK, peak WBC, LVEF and culprit lesion-LAD), TACE mRNA was the strongest independent predictor of in-hospital complications in AMI patients (odds ratio = 2.60, 95%CI = 1.20 – 5.64, $P = 0.02$). In our in vitro study, PMA (an activator of TACE)-stimulated monocytes resulted in dose-dependent TACE expression and TNF-α shedding. Anti-human TACE antibody inhibited this PMA-induced TNF-α release.
Conclusions: This study demonstrates that monocytic expression of TACE is related to TNF-α shedding at the site of ruptured plaques in AMI patients. In addition, local TACE expression in ruptured plaques may play an important role in poor outcomes in patients with AMI.

197 The prognostic significance of increased atherosclerotic plaque temperature in patients submitted to percutaneous coronary intervention

E. Stefanadi[1], K. Toutouzas[2], S. Vaina[1], E. Tsiamis[1], M. Vavuranakis[1], C. Tsioufis[1], A. Androulakis[1], D. Tousoulis[1], C. Tentolouris[1], C. Stefanadis[1]. *[1]Hippokration General Hospital of Athens, First Department of Cardiology, Athens, Greece; [2]Hippokration Hospital, First Department of Cardiology, Athens, Greece*

Purpose: Local plaque inflammatory activation is detected by intracoronary thermography. The purpose of the present study was to assess the prognostic significance of increased plaque temperature in patients (pts) submitted to percutaneous coronary intervention (PCI).
Methods: We enrolled 215 pts [78 with acute coronary syndrome (ACS) and 137 with stable angina (SA)] with single vessel disease. Pts under treatment with corticosteroids or non-steroid anti-inflammatory drugs, with inflammatory disease or malignancy, and with recent myocardial infarction were excluded. The difference between the culprit lesion and the proximal healthy vessel wall was assigned as DT. After the procedure all pts underwent PCI. Clinical follow-up was scheduled at 3 and 6 months and yearly thereafter.
Results: Pts with ACS had increased DT compared with SA pts (0.16±0.10°C vs. 0.08±0.07°C, $p<0.01$). Mean follow-up period was 15.11±8.81 months. DT was greater in pts with adverse cardiac events during the follow-up period than in those without events (0.16±0.10 vs. 0.10±0.08°C, $p<0.02$). Pts with DT≥0.10°C had worse event-free survival than those with DT<0.10°C ($p< 0.001$) (Figure). Cox regression analysis after adjustment for age, treated vessels, total cholesterol, diabetes mellitus, current smoking, hypertension, left ventricular dysfunction, previous myocardial infarction, ACS, reference diameter and minimal lumen diameter revealed that DT was a strong predictor of adverse cardiac events during follow-up (OR 2.01, p=0.03).



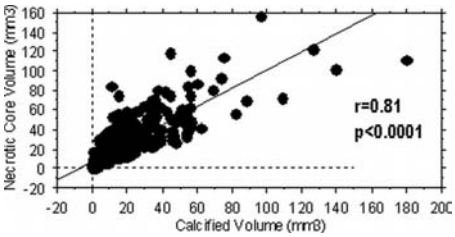
Event-free survival during follow-up

Conclusion: Increased DT is a strong predictor for an unfavourable long-term clinical outcome in pts with CAD undergoing PCI. Thus, local inflammatory activation in target lesions has important prognostic value for PCI long-term results.

198 Calcium is strongly correlated with necrotic core in human coronary arteries: insights from the multicenter VH-IVUS registry

E. Missel, G.S. Mintz, S.G. Carlier, J. Qian, K. Sano, J. Lui, R. Mehran, J.W. Moses, G.W. Stone, M.B. Leon on behalf of VF-IVUS Registry. *Cardiovascular Research Foundation, Intravascular Ultrasound Core Lab, New York, United States of America*

Background: Non-invasive detection of coronary calcification is able to predict adverse coronary events. Conversely, grayscale intravascular ultrasound (IVUS) has demonstrated only minimal calcification in lesions of patients presenting acute coronary syndromes (ACS). We used virtual histology (VH)-IVUS to study this paradox.
Methods: We performed whole pullback VH-IVUS analysis in a consecutive series of 625 pts in the multicenter VH-IVUS registry. Measurements include absolute volumes and %plaque volumes and areas containing fibrotic (FI) or fibro-fatty (FF) tissue, dense calcium (DC), and necrotic core (NC).
Results: Patients age was 62.3±11.1yrs with 75% males and 23% diabetics. Whole pullback DC volume was related to age ($r=0.25$, $p<0.0001$) and correlated with whole pullback NC volume ($r=0.81$, $p<0.0001$). Multiple regression revealed that a NC/DC ratio was positively associated to admission CRP (p=0.007) and LDL-C values (p=0.03), but not with other risk factors.



Conclusions: VH-IVUS analysis shows that "whole vessel" DC strongly correlates with "whole vessel" NC. Thus, even though calcium is not prominent within lesions of ACS patients, more calcium indicates larger and/or more numerous necrotic cores, a necessary substrate for vulnerable plaque and lesion instability. This may help to explain why a higher EBCT calcium score predicts future coronary events.

199 Characterization of the "vulnerable" coronary plaque by multi-detector computed tomography: a correlative study with intravascular ultrasound/virtual histology radiofrequency analysis

G. Sarno[1], P. Vanhoenacker[2], I. Decramer[2], J. Schuijf[3], G. Puntziute[3], M.P. Margolis[4], S. Gupta[1], J.J. Bax[3], W. Wijns[1]. *[1]Cardiovascular Center Aalst, Belgium; [2]Radiology Department Olv-Z Aalst, Belgium; [3]Department of Cardiology, Leiden University, Leiden, Netherlands; [4]Volcano Corp. Inc, Rancho Cordova, United States of America*

Purpose: To assess the incidence of different plaque characteristics by Multi-Detector Computed Tomographic Angiography in patients with known coronary artery disease and to compare these findings with those obtained with Intravascular Ultrasound/Virtual Histology radio-frequency analysis.
Methods: When assessed by Computed Tomography, lesions were classified on the basis of Hounsfield Units as non-calcified, calcified, or mixed.
By Intravascular Ultrasound/Virtual Histology analysis, plaques were classified according to the relative tissue composition (necrotic core, fibrous, fibro-fatty, calcium) and the evidence of a fibrotic cap. Vulnerable plaque was defined as either Fibroatheroma without evidence of a fibrotic cap or Thin Cap Fibroatheroma.
Results: Seventy-eight lesions were analyzed by both techniques. A higher incidence of mixed plaques was observed among lesions causing Unstable Angina and Non-ST Elevation Myocardial Infarction compared to Stable Angina (76% vs 38%, p=0.04). Plaque composition by Virtual Histology was significantly different between mixed and non-calcified plaques by Computed Tomography. The Calcium content was 5.7±4.2% vs 2.5±1.8% (p=0.001), Necrotic Core was 13.2±6.9% vs 9.5±5.6% (p=0.03) and Fibrous Tissue was 59.0±7.5% vs 63.8±5.9% (p=0.03), for mixed vs non-calcified plaques, respectively. Thin-cap Fibroatheroma was observed more often in mixed than in non-calcified plaques (41% vs 19%, p=0.07). Positive, negative predictive value and diagnostic accuracy for either type of vulnerable plaque was 77, 54 and 59% by Computed Tomography.
Conclusions: Mixed plaque by Computed Tomography correlates with plaque composition as determined by Virtual Histology analysis. Presently, the diagnostic accuracy of Computed Tomography is insufficient to consider it as the sole tool for vulnerable plaque identification.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

200 Elevation of the glycoxidation product N -carboxymethyllysine (CML) in patients presenting with acute coronary syndromes (ACS)

S. Kralev, E. Zimmerer, T. Kaelsch, M. Brueckmann, S. Lang, J. Lin, A. Rippert, M. Borggrefe, H.-P. Hammes, T. Sueselbeck. *University Hospital Mannheim, I. Med. Department, Mannheim, Germany*

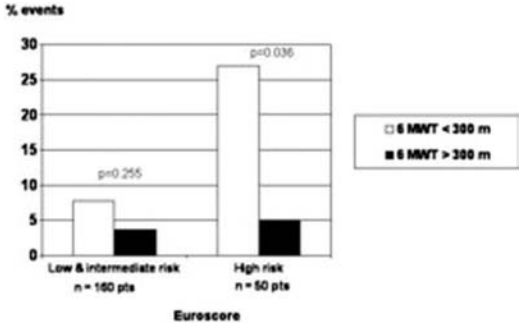
Purpose: An important role in the acceleration of vascular disease has been previously suggested for advanced glycation end products (AGE). CML is an AGE formed on protein by combined nonenzymatic glycation and oxidation (glycoxidation) reactions. Serum concentrations of CML reflect endothelial dysfunction by integrated oxidative stress and inflammation over long periods of time. Whether CML is involved in the development of ACS has not been investigated.
Methods: Within one year (2005) 70 patients (40 pat. with ACS and 30 pat. with stable coronary artery disease (CAD) as control group) were included in this study. The control group of patients with CAD was matched to the ACS patient group (17 patients with STEMI, 23 patients with NSTEMI) according to age (±1 year) and gender. All patients underwent coronary angiography. During the investigation a peripheral venous blood sample was taken for measuring serum level of CML.
Results: In comparison to the control group serum levels of CML were significantly increased in patients with ACS (17.9±10.7 vs. 6.7±2.9, P=0.0001). The receiver operating characteristic (ROC) curve for CML measurements confirmed CML as a predictor of ACS (area under the curve (AUC): 0.87; 95% CI: 0.78-0.96; P<0.001).Cut-off value CML > 9.5 derived from the ROC analysis was associated with a Relative Risc of ACS of 4.8 (95% CI: 2.3-9.9, P<0.0001), a Sensitivity of 0.85 (95% CI: 0.70-0.94) and a Specificity of 0.87 (95% CI: 0.69-0.96).
Conclusions: This is the first study showing a significant elevation of serum CML - a major advanced glycation end product in vivo - in patients presenting with ACS. CML might reflect an increased risk for ACS emphasizing the importance of endothelial dysfunction and suggesting that integrated oxidative stress and inflammation contribute to acute plaque rupture.

PREDICTORS OF OUTCOME IN VALVE DISEASE

256 Preoperative 6-minute walk test adds prognostic information to the EuroScore in patients with severe aortic stenosis undergoing aortic valve replacement

D. Perez De Arenaza[1], M. Flather[2], B. Lees[2], M. Jasinski[3], M. Lie[4], F. Nugara[2], A. Cagide[5], J. Pepper[6] on behalf of ASSERT investigators. *[1]Hospital Italiano De Buenos Aires, Buenos Aires, Argentina; [2]Royal Brompton Hospital, Clinical Trials & Evaluation Unit, London, United Kingdom; [3]University of Selisia, Cardiovascular Surgery, Katowice, Poland; [4]Ullevaal Sykehus, Cardiac Surgery, Oslo, Norway; [5]Hospital Italiano, Cardiology, Buenos Aires, Argentina; [6]Hospital Italiano, Cardiovascular Surgery, London, United Kingdom*

Background: The Euroscore is a validated tool to predict adverse cardiovascular events for patients undergoing cardiac surgery. The 6 minute walk test (6MWT) is recommended to assess prognosis and functional impairment in patients with heart failure. We investigated the additive prognostic value of the 6MWT over the Euroscore to assess the results of aortic valve replacement (AVR) in severe aortic stenosis (AS) patients.
Methods: 210 patients with severe AS had a 6MWT and were enrolled in a randomized trial (ASSERT) comparing the effect of stentless (Freestyle) and stented (Mosaic) valves on left ventricular mass regression (published). Outcome of this analysis was death or stroke at 12 months.
Results: The mean Euroscore was 3.8±2.2. The proportion of low risk patients (Euroscore 0-2) was 31%, medium risk (3-5) 45% and high risk (>6) 24%. Rate of death or stroke was 5.6% in low-medium risk patients and 18% in high risk (p=0.006). The median distance walked at basal 6MWT was 297m. The rate of death or stroke was 13.1% (n=14) in patients walking < than 300 m compared to 3.9% (n=4) in patients walking >300 m (p= 0.001). When rate of death or stroke by Euroscore risk was stratified by 6 minute walking distance, the 6MWT added prognostic information (fig). In a logistic regression model, high risk Euroscore (OR 3.34, 95% CI 1.23-9.11, p=0.018) and walking >300 m at baseline (OR 0.29, 95% CI 0.09-0.94, p=0.039) were independent predictors of death or stroke at 12 months.
Conclusion: Preoperative 6-minute walking distance adds substantial prognostic information to the Euroscore. The information obtained from this simple submaximal exercise test may be combined to the Euroscore to improve risk stratification of patients with severe AS undergoing AVR.



257 Moderate patient-prosthesis mismatch after valve replacement for isolated severe aortic stenosis has no impact on short- and long-term mortality

J. Mascherbauer, R. Rosenhek, C. Fuchs, E. Pernicka, F. Rader, U. Klaar, C. Scholten, M. Heger, G. Maurer, H. Baumgartner. *University Hospital Vienna, Cardiology Department, Vienna, Austria*

Background: The importance of moderate and even severe patient-prosthesis mismatch (PPM) for the prognosis of patients who undergo aortic valve replacement is a controversial issue. In addition, patient groups in previous studies were poorly defined.
Methods: The presence of PPM was assessed in 361 consecutive patients undergoing valve replacement for isolated severe aortic stenosis and related to perioperative and postoperative mortality. As previously proposed, prosthetic valve effective orifice areas (EOA) were obtained from data currently available in the literature specifying valve type and size and were related to the patients body surface area.
Results: Using the previously proposed cut-off of EOA ≤ 0.8 cm^2/m^2, PPM was present in 54% of patients. Patients were followed for 4.1±2.0 years (up to 8 years). Survival as estimated by Kaplan Meier analysis tended to be slightly worse in the group with PPM (1-, 3- and 5-year survival 89%, 86% and 76% vs. 92%, 88% and 82%; p=0.21). However, patients with PPM were also older (73 vs 66 years, p<0.0001), more often female (64% vs 42%, p<0.0001), more symptomatic preoperatively (NYHA class 2.4 vs 2.2, p<0.006) as well as postoperatively (NYHA class 1.7 vs 1.5, p<0.006), more often suffered from coronary artery disease (42% vs. 30%, p <0.02), triple vessel disease (10% vs 4%, p <0.04) and hypertension (75% vs 60%, p <0.03) and presented with a higher EUROscore (6.7±2.2 vs. 5.4±2.6, p<0.0001). By multivariate analysis including PPM, age, sex, EUROscore, reduced left ventricular function, coronary artery disease, additional bypass grafting, hypertension and diabetes, only diabetes, coronary artery disease and EUROscore but not PPM were independent predictors of survival.
Conclusions: Moderate PPM as currently defined is a frequent finding in patients with aortic valve prostheses. From the present data, it has no impact on perioperative and long-term survival after valve replacement for isolated severe aortic stenosis. A recommendation of more complex surgical interventions such as aortic root enlargement to avoid moderate PPM may therefore not be justified. Furthermore, it may be a major limitation of this concept to rely fully on Doppler estimates of EOA, which have been shown to markedly underestimate EOA in bileaflet prostheses.

258 Effects of aortic valve replacement for aortic stenosis on mitral regurgitation: a prospective study

P. Unger[1], D. Plein[2], G. Van Camp[3], B. Cosijns[4], O. Xhaet[3], D. De Canniere[3], P. Lancellotti[5]. *[1]ULB, Erasme Hospital, Cardiology, Brussels, Belgium; [2]Clinique Saint-Jean, Cardiology, Brussels, Belgium; [3]VUB, Akademisch Ziekenhuis, Cardiology, Brussels, Belgium; [4]Hopital de Braine L'Alleud, Cardiology, Braine L'alleud, Belgium; [5]ULG-Sart-Tilman, Cardiology, Liege, Belgium*

Purpose: Concomitant mitral regurgitation (MR) is common in patients undergoing aortic valve replacement (AVR) for aortic stenosis (AS). Its severity may decrease after AVR, but controversial results have been reported. Moreover, most studies were retrospective and grading of MR was based on color flow jet area assessment. Therefore, we aimed to assess prospectively and quantitatively the effects of AVR on MR severity.
Methods: Patients scheduled for AVR for AS were included if holosystolic MR not being considered for replacement or repair was detected. Previous mitral valve surgery; severe aortic regurgitation (vena contracta >6 mm) and poor acoustic windows were considered as exclusion criteria. Thirty-one patients (mean age 77±7 years) were studied before (median 1, range 1-41 days) and after AVR (median 7, range 4-19 days). All patients underwent a comprehensive echocardiographic examination; MR was assessed by Doppler echocardiography using color flow mapping of the regurgitant jet and the PISA method. No patient had prolapsed or flail mitral leaflet as mechanism of MR.
Results: Preoperative maximal and mean transaortic pressure gradients and aortic valve area were 74±26 mmHg, 44±16 mmHg, and 0.57±0.18 cm^2, respectively. Left ventricular (LV) ejection fraction increased from 49±16% to 55±15% after AVR (p<0.001). LV end-diastolic volume decreased from 91±32 ml to 77±30 ml (p<0.001).The ratio of MR jet to left atrial area decreased from 30±16% to 20±14% (p<0.001). MR effective regurgitant orifice (ERO) and regurgitant volume decreased from 10±5 mm^2 to 8±6 mm^2 (p=0.015) and from 19±10 ml to 11±9 ml (p<0.0001). The decrease in ERO and in regurgitant volume was similar in patients with preserved or depressed LV ejection fraction (≤ 45%) (2±3 vs 3±6 mm^2 and 7±9 vs 8±7 mm^2; p=NS, respectively).
Conclusions: Using a quantitative approach, reduction in MR severity was

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

demonstrated early after AVR for AS, mainly resulting from a decrease in regurgitant volume whereas the reduction in ERO was only modest. This suggests that reduction in systolic LV pressure was probably the main contributor to this early postoperative MR downgrading.

259 Natural history of patients with mitral valve prolapse and significant mitral regurgitation: a clinical and echocardiographic study

A. Sagie[1], H. Haim[1], M. Vaturi[1], D. Monakier[1], A. Battler[1], Y. Shapira[1], Y. Feinstein[2], D. Weisenberg[2]. *[1]rabin medical center, Petah Tikva, Israel; [2]Petah Tikva, Israel*

Background: The management of asymptomatic patients with MVP and significant MR is controversial. Some authorities advocate early operative treatment (preferably repair) while others recommend a more conservative approach.
Aim: To describe the clinical and echocardiographic natural history of patients with MVP and significant MR and look for predictors for clinical deterioration.
Methods: An observational prospective cohort study was carried out. The study group included 153 subjects (age 63+ 15; 56% F) with MVP and significant (moderate to severe or severe) MR from the database of the valvular clinic. Serial echocardiographic measures and clinical data were collected. The mean follow up period was 48±23 months (range 12-105 month). Clinical end points included change in one grade of NYHA FC, MV surgery and all cause mortality.
Results: No significant change in FC was found during the follow up period. At the end of follow-up 89% had no change in their FC and 96% were in FC I or II. There was no significant decrease in LV function as expressed by FS (41±8 to 39% + 8; p=0.09). There was a small but significant increase in LV end diastolic diameter (LVEDD); (53.8±7 to 54.5±8 mm; $p<0.05$) and in only 11% LVEDD increased more than 5 mm at the end of follow-up. There was a significant increase in LA area (29±9 to 32±10 cm^2; $p<0.001$) and in PA pressure (32.5±14 to 38±17 mmHg;$p<0.001$). The mortality rate and surgical intervention rate during follow-up was 12% (3% per year) and 22% respectively. On multivariate analysis baseline larger LA, LVEDD, PA pressure and MR severity were independent predictors for developing one of the clinical end points.
Conclusions: Patients with significant degenerative mitral regurgitation have a gradual deterioration in their clinical status, LV size and function and low mortality rate under conservative management. Baseline LA and LV size, and PA pressure predicts clinical end points.

260 Echocardiographic determinants and prognosis value of pulmonary artery pressure in organic mitral regurgitation

T. Le Tourneau, Y. Lefetz, P.H. Marboeuf, D. Huchette, A.S. Polge, S. Pouwels, N. Lamblin, H. Warembourg, C. Bauters, G. Deklunder. *Cardiology University Hospital, Lille, France*

Background: Mitral valve surgery is recommended in patients with organic mitral regurgitation (MR) and severe systolic pulmonary artery pressure (sPAP≥ 50 mmHg) at rest. We sought to evaluate the echocardiographic determinants of systolic PAP and its long-term prognosis value in organic MR.
Methods: Two-hundred twenty-eight patients (62±13 years, 148 males) with moderate to severe organic MR referred to surgery underwent a complete echocardiographic examination with pulmonary artery pressure measurement (using tricuspid regurgitation). Mitral tissue doppler imaging was performed in 134 patients to study determinants of sPAP.
Results: Mean systolic PAP was 45±13 mmHg, ranging from 25 to 105 mmHg. Sixty-seven (29%) patients had a sPAP ≥ 50 mmHg. One hundred fifty-four patients were in sinus rhythm, and 74 patients were in atrial fibrillation. In univariate analysis, echocardiographic predictive factors of sPAP were MR grade ($p<0.0001$), left atrial volume/m^2 (p=0.0001), mitral E velocity ($p<0.0001$), mitral deceleration time (p=0.0001), septal mitral E/Ea ratio ($p<0.0001$), and aortic stroke volume (p=0.0006). In multivariate analysis, left atrial volume (p=0.002), mitral deceleration time (p=0.01), mitral E velocity ($p<0.0001$), and septal mitral E/Ea ratio (p=0.0001) were independent predictors of systolic PAP. Regurgitant orifice area, left ventricular size or ejection fraction were not predictive of sPAP. Using ROC curve, a septal mitral E/Ea ratio > 16 had a sensibility of 70%, a specificity of 63%, with an accuracy of 77% in predicting a sPAP ≥ 50 mmHg. In the overall population, independent predictive factors of death in a Cox model were sex (OR 4.63, 95% CI 1.7-12.4, p=0.002), mitral valve replacement/repair (OR 3.2, 95% CI 1.5-6.8, p=0.002), age (OR 1.07, 95% CI 1.03-1.12, p=0.002) and sPAP ≥ 50 mmHg (OR 2.2, 95% CI 1.03-4.79, p=0.04). Ten year survival was 52% in patients with sPAP ≥ 50 mmHg before surgery, and 80% in patients with sPAP < 50 mmHg (p=0.0036).
Conclusion: In organic mitral regurgitation related to mitral valve prolapse, systolic PAP is associated with left atrial volume, E wave velocity, mitral deceleration time, and mitral septal E/Ea ratio. Mitral septal E/Ea > 16 is a good predictor of a systolic PAP ≥ 50 mmHg. Moreover, sPAP ≥ 50 mmHg is an independent predictive factor of late mortality after surgery for organic MR.

261 Impact of heart failure on the presentation, management and prognosis of patients with valvular heart disease

B. Iung[1], D. Detaint[1], J. Remy[1], D. Messika-Zeitoun[1], P. Tornos[2], C. Gohlke-Barwolf[3], F. Delahaye[4], G. Baron[1], A. Vahanian[1] on behalf of the Expert Committee of the Euro Heart Survey on Valvular Heart Diseases. *[1]Bichat Hospital, Cardiology, Paris, France; [2]Vall d'Hebron Hospital, Cardiology, Barcelona, Spain; [3]Heart Centre, Cardiology, Bad Krozingen, Germany; [4]Cardiology Hospital, Cardiology, Lyon, France*

Purpose: Heart failure (HF) is a severe complication of valvular heart diseases (VHD). We used the data of the Euro Heart Survey to assess the impact of HF on the presentation, management and prognosis of patients (pts) with VHD.
Methods: Of the 5001 patients included, 1149 (23%) had HF at admission (984 with native VHD and 237 with previous heart valve surgery), 3842 did not have HF and the status was unknown in 10.
Results: Patient characteristics are detailed in the Table. A decision to operate was taken in 435 (38%) pts with HF and in 1515 (39%) pts without HF (p=0.34). One-year survival was 88.4±1.0% in pts with HF vs. 95.4±3.6% in pts without HF ($p<0.0001$). Among the 1149 pts with HF, one-year survival was 90.8±1.5% when there was a decision to operate vs. 87.2±1.3% in pts who were denied surgery (p=0.002).
In multivariate analysis, the predictors of one-year mortality were older age ($p<0.001$), male gender (p=0.002), the presence of ≥1 comorbidity (p=0.0008), and a decision not to operate (Hazard ratio 0.7, 95% CI [0.50-0.99], p=0.04).

Comparison of pts with and without HF

	HF (n=1149)	No HF(n=3842)	p
Age (years)	65±14	63±14	<0.0001
Women (%)	54	48	0.0002
Previous valve surgery (%)	25	21	0.005
NYHA class IV (%)	27	3	<0.0001
Atrial fibrillation (%)	47	24	<0.0001
Diabetes (%)	18	14	0.0006
At least 1 comorbidity (%)	44	31	<0.0001
Coronary artery disease (%)	43	38	0.04
Left ventricular ejection fraction	0.49±0.15	0.58±0.12	<0.0001

Conclusions: This contemporary survey shows that pts with VHD and HF 1) Account for as many as 23% of pts with VHD. 2) Are older and have more frequent comorbidities than pts without HF. 3) Are considered candidates to surgery in only 38% of cases. 4) Have a better one-year survival after valve intervention, suggesting that surgery may be underused in these high-risk pts.

THROMBOSIS AND PLATELETS – NEW FRONTIERS

262 Combined effects of thrombosis pathway gene variants predict cardiovascular events

M. Perola, K. Auro, M. Alanne, K. Kristiansson, K. Silander, K. Kuulasmaa, V. Salomaa, L. Peltonen. *National Public Health Institute, Molecular Medicine, Helsinki, Finland*

Purpose: The genetic background of complex diseases is proposed to consist of several low-penetrance risk loci. Addressing this complexity likely requires both large sample size and simultaneous analysis of different predisposing variants. We investigated the role of four thrombosis genes, coagulation factor V (F5), intercellular adhesion molecule –1 (ICAM1), protein C (PROC), and thrombomodulin (THBD), in cardiovascular diseases: Single allelic gene variants and their pair-wise combinations were analyzed in two independently sampled population cohorts from Finland.
Methods and results: From among 14 140 FINRISK participants (FINRISK-92, n=5 999 and FINRISK-97, n=8 141) we selected for genotyping a sample of 2 222, including 549 incident cardiovascular (CVD) cases, plus random subcohorts totaling 786. We genotyped 54 single nucleotide polymorphisms (SNPs), covering all common haplotypes (>10%). Classification-tree analysis identified 11 SNPs that were further analyzed in Cox's proportional hazard model as single variants and pair-wise combinations. Multiple testing was controlled by replication in two independent cohorts and with false discovery rate. We identified several CVD risk variants: In women, the combination of F5rs7542281 x THBD rs1042580, together with 3 single F5 SNPs, associated with CVD events. Among men, PROC rs1041296, when combined witheither ICAM1 rs5030341 or F5 rs2269648 associated with total mortality. As single variant PROC rs1401296, together with F5Leiden mutation, associated with ischemic stroke events.
Conclusions: Our strategy to combine the classification-tree analysis with more traditional genetic models was successful in identifying SNPs – acting either in combinations or as single variants – predisposing to CVD, and produced replicable results in two independent cohorts. These results suggest that variants in these four thrombosis genes contribute to arterial cardiovascular events at the population level.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

263 Targeting of activated glycoprotein IIb/IIIa allows magnetic resonance imaging of activated human platelets

C. Von Zur Muehlen[1], D. Von Elverfeldt[1], J. Ender[1], C. Bode[1], K. Peter[2]. [1]*University Hospital Freiburg, Department of Cardiology and Angiology, Freiburg, Germany;* [2]*Baker Heart Research Institute, Department of Myocardial Infarction and Throm, Melbourne, Australia*

Introduction: Activated platelets as the key factor to atherothrombosis constitute an attractive target for non-invasive molecular magnetic resonance imaging (MRI). However, imaging targets on vessel walls remains challenging due to the small quantity of contrast agents delivered to areas of interests under shear stress conditions. We therefore evaluate the binding properties of a MRI contrast agent that is specific for activated human platelets via its targeting of ligand-induced binding sites (LIBS) on activated glycoprotein IIb/IIIa-receptors.
Methods and Results: MPIOs were conjugated either to single-chain antibodies targeting LIBS (LIBS-MPIO) or to an irrelevant antibody (control-MPIO). Human platelet rich thrombi were induced in vitro and exposed to three different concentrations of LIBS-MPIO or control-MPIO. Histology confirmed significant higher binding of LIBS-MPIO to platelets in a dose-dependent manner (1μg LIBS-MPIO vs. 2μg LIBS-MPIO: $p<0.01$). This result was confirmed on a 3T clinical MRI scanner. Furthermore, LIBS-MPIO and control-MPIO were perfused over a matrix of activated platelets in a flow chamber using physiological shear stress, confirming binding of LIBS-MPIO under venous and arterial flow conditions (LIBS-MPIO vs. control-MPIO; $p<0.01$).
Conclusions: LIBS-MPIO provides the opportunity to detect activated human platelets at clinically relevant MRI field strength. LIBS-MPIO binds to platelets under venous and arterial flow conditions, providing high payloads of contrast agent to a highly specific molecular epitope. These results provide proof of concept for magnetic resonance imaging of activated platelets and encourage further studies directed to the detection of thrombi/emboli and of vulnerable atherosclerotic plaques that are marked by the adhesion of activated platelets.

264 Pharmacodynamics and safety of a novel Protease Activated Receptor-1 antagonist E5555 for healthy volunteers

M. Takeuchi, M. Kageyama, S. Kitamura, R. Hagino, H. Ozawa, H. Tanaka. *Eisai Co., Ltd., Clinical Research Center, Tokyo, Japan*

Purpose: E5555 is a small molecule Protease-Activated Receptor-1(PAR-1) inhibitor and specifically binds to PAR-1 at the tethered ligand binding site on platelet membranes. We evaluated the pharmacodynamics and safety of single and repeated orally administration of E5555 in healthy volunteers in randomized, double-blind, placebo-controlled, dose-ascending clinical studies.
Methods: Forty healthy men were assigned to 5 groups (8 per group) and randomized to orally receive 20, 50, 100, 200, or 400 mg of E5555 and 24 healthy men were assigned to 3 groups (8 per group) and randomized to orally receive 50, 100, or 200 mg of E5555 or placebo once a day for 10 days. Inhibitory effect ex vivo on platelet aggregation induced by 1 and 2 units/mL of thrombin and 20 μM of ADP were assessed. Also, coagulation times (prothrombin time and activated partial thromboplastin time), bleeding time and routine laboratory tests were assessed.
Results: E5555 inhibited the thrombin-induced platelet aggregation in a dose-dependent manner with maximum effects achieved at 6 hrs after single administration. Single dose of 20 mg did not inhibit the platelet aggregation induced by 2 units/mL of thrombin although it slightly inhibited the platelet aggregation induced by 1 unit/mL of thrombin. Single dose of 50 mg or above doses inhibited more than 80% of the platelet aggregation induced by both levels of thrombin. Moreover, at 50 mg or above doses, the duration of platelet aggregation inhibition were dose-dependently prolonged with E5555 administrations. At the steady state after 100 and 200 mg repeated administration, platelet aggregation inhibition induced by 2 units/mL of thrombin achieved almost 100%, even at 24 hrs after administration. At 7 days after the completion of repeated administration, platelet aggregation was restored. On the one hand, E5555 did not affect ADP-induced platelet aggregation. There were no significant AEs and abnormalities or changes in vital sign, ECG findings, clinical laboratory tests, coagulation time and bleeding time.
Conclusion: Single oral administration (20 to 400 mg) and repeated oral administration (50 to 200 mg) of E5555 were found to be well tolerated and also inhibited the thrombin-induced platelet aggregation. In addition, E5555 affected none of the ADP-induced platelet aggregation, coagulation time, and bleeding time.

265 Cytochrome P450 2C19*2 polymorphism diminishes peri-interventional antiplatelet effect of clopidogrel in patients undergoing percutaneous coronary intervention

D. Trenk[1], W. Hochholzer[1], M.F. Fromm[2], L. Chialda[1], A. Pahl[1], F.-J. Neumann[2]. [1]*Herz-Zentrum Bad Krozingen, Abt. fuer Klinische Pharmakologie, Bad Krozingen, Germany;* [2]*Friedrich-Alexander-Universitaet, Erlangen, Germany*

The thienopyridine derivative clopidogrel is an inactive pro-drug requiring biotransformation by cytochrome P450 isoenzymes (CYP) in order to generate an active metabolite. This metabolite binds irreversibly to the platelet P2Y12 receptor and exerts thereby the antiplatelet effect. The EXCELSIOR study showed a 7-fold risk for 30-day major adverse cardiac events in patients with inadequate platelet response to loading with clopidogrel 600 mg. Studies in healthy volunteers suggest that CYP2C19 genotype may contribute to the interindividual variability in antiplatelet effect of clopidogrel.
The EXCELSIOR study enrolled 802 patients undergoing elective percutaneous coronary intervention (PCI) with stent implantation. The antiplatelet effect of a loading dose of clopidogrel 600 mg was determined by optical aggregometry (5μM ADP) before administration of clopidogrel, at the time of PCI and 24 h after PCI. CYP2C19 genotype (681G>A) was analyzed in 697 patients by real-time PCR. Antiplatelet efficacy of clopidogrel was determined for the different genotypes.
Within the subset of the EXCELSIOR cohort, 485 patients (69.6%) were CYP2C19 wild-type homozygote (*1/*1), 199 (28.6%) were CYP2C19*1/*2 and 13 (1.9%) were CYP2C19*2/*2 carrying two allelic variants encoding a deficient CYP2C19 drug-metabolizing enzyme. Residual platelet aggregation (median; inter-quartiles ranges) determined 5 minutes after addition of ADP 5μM is summarized in relation to the CYP2C19 genotypes in the Table below.

Genotype	n	Platelet aggregation (%)		
		Baseline	At PCI	24 h after PCI
CYP2C19 *1*1	485	47 (36-57)	11 (3-28)	7 (3-14)
CYP2C19 *1/*2 / CYP2C19 *2/*2	212	48 (37-60)	23 (9-38)[#]	11 (4-22)[#]

[#]$P<0.001$ by Mann-Whitney test between the different genotypes.

These results indicate that the antiplatelet response to a loading dose of clopidogrel 600 mg is substantially diminished in patients carrying at least one CYP2C19*2 allele. It seems that the CYP2C19 genotype is a major factor contributing to the observed variability in the antiplatelet effect of clopidogrel and might therefore affect clinical outcome of patients undergoing PCI.

266 CYP 2C19*2 allele contributes to low response to clopidogrel in Acute Coronary Syndrome

T. Cuisset[1], C. Frere[2], P.E. Morange[1], J. Quilici[1], L. Camoin-Jau[1], I. Juhan-Vague[1], J.L. Bonnet[1], M.C. Alessi[1]. [1]*Chu Timone, Cardiology Department, Marseille, France;* [2]*Marseille, France*

Background: Genetic polymorphisms of cytochrome P450 (CYP) isoforms genes may promote variability in platelet response to clopidogrel.
Methods: In 603 Non ST Elevation Acute Coronary Syndrome (NSTE ACS) patients, we analyzed the relationship between polymorphisms in the CYP3A4, CYP3A5 and CYP2C19 genes and clopidogrel response assessed by ADP induced platelet aggregation (ADP-Ag), VASP phosphorylation index (PRI VASP) and ADP induced P selectin expression (ADP-PS).
Results: All platelet parameters studied were correlated. The association between PRI VASP and ADP-Ag or ADP-PS ($r=0.62$ or $r=0.52$ $p<0.0001$) appeared stronger than between ADP-Ag and ADP-PS ($r=0.36$, $p<0.0001$). In stepwise linear regression models, body mass index was the only clinical correlate of ADP-Ag, PRI VASP and ADP-PS ($p<0.0001$, $p<0.0001$ and $p=0.0077$ respectively). The CYP2C19*2 polymorphism was significantly associated with ADP-Ag, PRI VASP and ADP-PS in both a recessive ($p<0.01$ $p<0.007$ and $p<0.06$ respectively) and codominant ($p<0.08$ $p<0.0001$ and $p<0.009$ respectively) models while the CYP3A4*1B and CYP3A5*3 polymorphisms were not. The CYP2C19*2 allele carriers exhibited the highest platelet indices levels in multivariate analysis ($p=0.03$). After covariates adjustment CYP2C19*2 allele was more frequent in clopidogrel non responders, defined by persistent high post treatment platelet reactivity (ADP-Ag>70%) ($p=0.03$). In addition, in a subpopulation of 243 patients undergoing coronary stenting with clinical follow-up, the CYP2C19*2 allele was marginally associated with recurrent cardiovascular event ($p=0.07$) in a recessive model.
Conclusion: We demonstrated that the CYPC19*2 alleles is involved in clopidogrel response in NSTE ACS patients.

267 Thrombin formation at the site of microvascular injury in patients treated with clopidogrel combined with aspirin and aspirin alone: effects of the PlA2 polymorphism

A. Undas[1], E. Stepien[2], A. Branicka[2], K. Zmudka[3], W. Tracz[1]. [1]*Jagiellonian University, Institute of Cardiology, Krakow, Poland;* [2]*John Paul II Hospital, Dept. of Molecular Biology, Krakow, Poland;* [3]*Jagiellonian University, Institute of Cardiology, Krakow, Poland*

It has been reported that clopidogrel does not suppress circulating blood coagulation markers, but may decrease thrombin generation triggered by vascular injury in relation to the platelet glycoprotein IIIa PlA2 polymorphism. We sought to compare the extent to which combined therapy with clopidogrel and aspirin versus aspirin alone may affect on thrombin generation and platelet activation at the site of hemostatic plug formation. We enrolled 30 men with stable coronary artery disease (CAD) receiving 75 mg/d clopidogrel, added to 75 mg/d aspirin, for at least 4 weeks and 30 well-matched patients treated with aspirin alone. We measured thrombin-antithrombin complexes (TAT), a marker of thrombin generation, while platelet activation was monitored using soluble CD40 ligand (sCD40L).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Both markers were determined in plasma and blood samples collected every 60 seconds from standard bleeding-time wounds as described (Undas A et al. Circulation 2001). The presence of the PIA2 allele was determined by using PCR. Plasma TAT and sCD40L levels in peripheral blood were similar in both groups. Bleeding time was markedly longer (by 114%, $p<0.0001$) in patients taking clopidogrel+aspirin than in those receiving only aspirin (435.2±52.3 [±SD] s). The total volume of blood collected from wounds was also much larger in the former group (medians, 434 vs 179 ml; $p<0.0001$). Formation of TAT and release of sCD40L were slower (expressed as concentration vs time) by 43% ($p<0.01$) and by 46% ($p<0.01$), respectively, in clopidogrel-treated patients on aspirin. However, total amounts of thrombin produced at the site of injury were similar in each 60-second interval and the entire bleeding time. Maximum rates for TAT (expressed as the total amounts of both parameters) did not differ significantly between the clopidogrel+aspirin (0.86±0.08 fmol/s) and aspirin groups (0.91±0.09 fmol/s; p=0.3). Corresponding values for sCD40L in bleeding-time blood showed that addition of clopidogrel to aspirin is associated with decreased maximum rate of sCD40L release by 21.2% (p=0.004) compared with the effect of aspirin alone. We found 10 heterozygous carriers of PIA2 allele in both groups. There were no differences in any variable of the coagulation model related to the PIA2 allele in either treatment group. We conclude that at the site of vascular injury, clopidogrel does not affect thrombin formation, though significantly reduce platelet activation, in CAD patients receiving low-dose aspirin, regardless of the PIA2 polymorphism.

DYSYNCHRONY: PREDICTING NEED AND RESPONSE

285 A review of the actual need and evolution of need for device therapy in a community heart failure population

H. Sulaiman, C. O'loughlin, C. Conlon, D. Mc Caffrey, M. Ledwidge, K. Mc Donald. *St Vincent's University Hospital, Heart Failure Services, Dublin, Ireland*

Background: New indications for the prophylactic use of implantable cardiac defibrillator (ICD) and the emerging use of cardiac resynchronisation therapy (CRT) have expanded the application of device therapy in heart failure (HF) with documented improvement in morbidity and mortality. The full economic impact of these changes remains unclear as the numbers suitable for these approaches remains unknown. Furthermore, the change of need over a period of time has yet to be established.
Methods and Aim: We reviewed the need for ICD and CRT in a community HF population attending an annual review clinic (ARC) at a specialised HF unit. Suitability for these interventions was determined using ESC 2005 criteria. Furthermore, the change in need over a period of time was assessed through analysis of data from the same population obtained from the HF unit database from at least one year prior to the ARC visit. Information collected included age, gender, NYHA class, ECG and left ventricular ejection fraction (LVEF) at time point one (TP1: one year prior to ARC) and time point two (TP2: ARC). The number of patients suitable for each device was assessed at each time point, numbers implanted was reviewed and the change in need between TP1 and TP2 was noted.
Results: 264 patients attended ARC from 2005 to 2006. The mean age of the sample was 70±12 years, 67% were male and 54% had ischaemic aetiology. At TP1, 30% of patients were identified as being suitable for ICD and 3% for CRT therapy. At TP2, 18% were deemed suitable for ICD and 1% for CRT therapy. 55% of the sample were neither suitable at TP1 or TP2 for ICD therapy. 9% were not suitable at TP1 but at TP2 they were deemed suitable for ICD therapy, despite the use of optimal therapy. 19% were suitable for therapy at TP1 but not at TP2. In 85% of these, the LVEF improved from 28±7% at TP1 to 44±12% at TP2 ($p<.001$), and in 34% of cases this was mainly due to optimisation of medications.
Conclusion: The expanded indications for ICD therapy have resulted in the substantial need for this intervention. However, by present indications the role for CRT is limited in this population. The determination for need for ICD/CRT should only be made after optimisation of medical therapy. These data highlight the need for regular review as the need for this therapy will evolve in a small percent of this population.

286 Incidence of new left bundle branch block in patients with chronic heart failure

A.L. Clark. *Castle Hill Hospital, Department of Cardiology, Kingston-Upon-Hull, United Kingdom*

Background: Approximately one-third of patients with chronic heart failure have left bundle branch block (LBBB) on their 12-lead ECG. Its presence is associated with inco-ordination of left ventricular contraction and an adverse prognosis. Selection for cardiac re-synchronisation therapy is largely based on QRS duration, but little is known of the incidence (rather than prevalence) of LBBB.
Methods: 1418 consecutive patients (average (SD) age 70.5 (10.4) years; 74% male) first seen in a community heart failure clinic between December 2001 and June 2006 had a 12 lead ECG. 485 (34%) had a QRS duration >119 ms. Patients with a broad QRS were older (72.2 v 69.3 years), had worse left ventricular systolic function, were on a higher daily dose of diuretic and were more likely to be on amiodarone (14.4 v 7.1%). Symptoms as rated by the New York Heart Association classification system were not different.
12 lead electrocardiogram was available for 737 patients (52%) at one year follow up. The QRS interval increased from 115.2 ms at baseline to 118.9 ($P<0.0001$). In those patients who did not have LBBB at baseline (N=477), QRS interval increased from 97.7 (12.9) ms to 102.3 (20.4) ms ($P<0.0001$). There were 52 incident cases of LBBB. an incidence of 10.9%. In this group of patients, QRS duration increased from 106.4 (14.7) ms to 136.0 (39.9) ms ($P<0.0001$). The only predictors of incident LBBB were QRS duration at baseline and amiodarone use at baseline. Starting beta adrenoceptor antagonists was not associated with prolongation of the QRS interval.
In 215 patients, a 12 lead electrocardiogram was available at 2 years and 3 years follow up. In this subgroup, QRS was 112.1 (29.2) ms at baseline, and 118.4 (37.8), 115.9 (28.9) and 118.6 (32.8) ms at 1, 2 and 3 years follow up, respectively. The proportion with LBBB increased from 34.0% at baseline to 36.7%, 37.7% and 42.3% at 1, 2 and 3 years follow up, respectively.
Baseline LBBB was associated with a worse outcome (HR 1.25 (95% CI 1.01-1.55). For those patients surviving the first year from the index ECG, new LBBB remained an independent adverse prognostic feature (HR 2.09 (95% CI 1.17 – 3.73); P=0.013).
Conclusions: The crude incidence of LBBB is 10.9% in the first year of follow up in an unselected population of ambulatory outpatients with chronic stable heart failure. A key part of the ongoing care of patients with chronic heart failure should include a regular 12 lead electrocardiogram as incident LBBB is common. the incidence (rather than prevalence) of LBBB.

287 Left ventricular dyssynchrony as only one of multiple potential mechanisms of response to CRT

C. Parsai[1], B. Bijnens[2], G.R. Sutherland[1], A. Baltabaeva[1], P. Claus[2], E. Donal[3], G. Derumeaux[4], M. Cannesson[1], L. Anderson[3]. *[1]St George's Hospital, Cardiology Dept., London, United Kingdom; [2]University of Leuven, Leuven, Belgium; [3]Hopital Pontchailloux, Cardiology, Rennes, France; [4]Hopital Louis Pradel, Cardiology, Lyon, France*

To date, attempts to predict response to CRT have been based on measurements of left ventricular (LV) dyssynchrony derived from timing of long axis events (regional velocities or strain). However, this approach assumes LV dyssynchrony to be the only mechanism to be addressed for CRT. We investigated if other mechanisms could determine response to CRT. Data from 76 pts (pre-CRT: 66±1.4 y, EF: 24±1%, QRS width >130 ms) were obtained pre- and 6 months post-CRT. Clinical response was defined as a NYHA class reduction >1 and reverse remodelling as a change in LV end-systolic volume (LVESV) ≥10%. Dyssynchrony was assessed by the radial velocity profile. Additionally, 2 established long axis Dyssynchrony Indexes (DIs) were calculated. Three different pathophysiologic subgroups, potentially responding to CRT, could be identified: 1: Intra-ventricular dyssynchrony: 36 pts (48%) had radial septal/lateral wall dyssynchrony with an early septal radial inward, immediately followed by a high outward velocity, occurring in the isovolumic contraction period (a "septal flash" (SF)). All patients who demonstrated resolution of SF with pacing were long term responders whereas persistence of SF post-CRT (6 pts) was associated with non-response. 2: Atrioventricular dyssynchrony: 15 pts (20%) had no radial LV dyssynchrony but had abnormal LV filling with either a blunted A wave due to a short A-V delay or diastolic mitral regurgitation and a partially fused E/A wave associated with a long A-V delay. 80% of these patients responded via the mechanism of AV resynchronisation alone. 3: Inter-ventricular dyssynchrony: 8 pts (11%) had neither LV dyssynchrony nor abnormal A waves, but exhibited exaggerated RV-LV interaction with abnormal passive displacement of an infarcted septum. A marked clinical improvement (NYHA <1.5±0.3) was obtained in all after RV-LV optimisation, despite the lack of LV remodelling. 4: All Others: 16 pts had none of the above response predictors and all (100%) failed to respond. Classic long axis-based DIs only predicted 75% of the actual responders and showed no correlation with the above described pathophysiological mechanisms.
Conclusions: Within the CRT population there are at least three different subgroups of responders depending on different mechanisms of response. Intraventricular dyssynchrony accounted for only 36 of 51 responders. In this series, intraventricular dyssynchrony was most easily assessed by the profile of radial (rather than longitudinal) motion.

288 Does a failing right ventricle prevent response to CRT?

C. Parsai[1], G.R. Sutherland[1], B. Bijnens[2], A. Baltabaeva[1], E. Donal[3], M. Cannesson[4], G. Derumeaux[1], L. Anderson[3]. *[1]St George's Hospital, Cardiology Dept., London, United Kingdom; [2]University of Leuven, Leuven, Belgium; [3]Hopital Pontchailloux, Cardiology, Rennes, France; [4]Hopital Louis Pradel, Cardiology, Lyon, France*

Impaired right ventricular (RV) function has important prognostic implications for heart failure patients. However it is not known whether RV function influences response to cardiac resynchronisation therapy. Data from 76 pts were assessed at baseline and 6 months after CRT (pre-CRT, 65±1y, EF: 24±1%, QRS>130 ms, 42 (55%) ischaemic aetiology). We defined two categories of response to CRT: clinical response, defined as a reduction in NYHA>1 class, and reverse remodelling, defined as a reduction in LV end-systolic volume >10%. RV function was assessed from M-mode ring excursion of the free wall and pts were subdivided into 4 groups: Normal (>20 mm), mildly reduced (15-20 mm), moderately reduced

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(10-15 mm) and severely reduced (<10 mm) RV ring excursion. As shown in table 1, 52 (68%) pts responded clinically to CRT. Reverse remodelling in addition to clinical response was seen in 39 (51%) of patients. In DCM patients, a high response rate was seen in patients with preserved RV function. However, even with advanced disease and severe RV dysfunction, the majority of DCM pts responded both clinically and echocardiographically. In ischaemic patients, no relationship was observed between overall (clinical or clinical plus remodelling) response and RV function, but the likelihood of remodelling was lower in each of the RV function groups compared to DCM and may be dictated more by the extent of viable LV myocardium.

Table 1

RV ring motion (mm)	DCM pts (n=34/76)		IHD pts (n=42/76)	
	Overall response (clinical and clinical+remodelling) n=24	Responders with LV remodelling	Overall response (clinical and clinical+remodelling) n=28	Responders with LV remodelling
>20 mm	9/10 (90%)	7/10 (70%)	3/5 (60%)	2/5 (40%)
15-20 mm	6/9 (66%)	5/9 (56%)	12/16 (75%)	9/16 (56%)
10-15 mm	7/12(58%)	7/12(58%)	10/18(55%)	6/18(33%)
<10 mm	2/3 (66%)	2/3 (66%)	3/3 (100%)	1/3 (33%)
All RV function groups	24(70%)	21(62%)	28(66%)	18(43%)

DCM: non ischaemic cardiomyopathy; IHD: ischaemic cardiomyopathy.

Conclusion: Patients can respond to CRT even in the presence of severe RV dysfunction and should not be denied CRT if they fulfil the ESC/AHA criteria. Reverse remodelling is less in ischaemic patients irrespective of the extent of RV impairment

289 Cardiac resynchronization therapy improves ventilatory perfusion coupling in patients undergoing all-day physical activity

T. Berger[1], R. Zwick[2], G. Poelzl[1], H. Hoertnagl[3], O. Pachinger[1], M. Stuehlinger[1], F.X. Roithinger[1], F. Hintringer[1]. *[1]Department of Cardiology, Medical University Innsbruck, Innsbruck, Austria; [2]Otto Wagner Hospital, Department of Respiratory and Critical Care M, Vienna, Austria; [3]Department of Sports Medicine, Medical University Innsbruck, Innsbruck, Austria*

Background: There is still little information about the cardiorespiratory effects of cardiac resynchronization therapy (CRT) in patients undergoing all-day physical activity. Aim of this study was to assess the acute effects of left ventricular and biventricular pacing on ventilatory-perfusion coupling during submaximal physical exercise.
Methods: Twenty patients underwent treadmill cardiopulmonary testing after implantation of a cardiac resynchronization therapy (CRT) pacemaker. Metabolic and hemodynamic parameters were obtained during exercise as well as during the following resting period for each single-right (RV), -left (LV) and biventricular (BiV) pacing mode as well as during the intrinsic sinus rhythm (SR) in each patient.
Results: LV and BiV pacing increased systolic (148±25 and 144±28 vs 120±29 mmHg, $p<0.05$) and mean blood pressure (109±18 and 108±19 vs 91±25 mmHg, $p<0.05$) as well as cardiac output (7.3±1 and 7.4±1 vs 6.0±1 l/min, $p<0.05$ and $p<0.01$) during exercise as compared to intrinsic SR. Simultaneously, LV and BiV pacing decreased dead space ventilation (Vde/VT; 17±3 and 16±3 vs 20±4, $p<0.01$) and the ventilatory equivalent for oxygen (30±6 and 30±4 vs 35±9; $p<0.05$) as compared to intrinsic SR. The beneficial hemodynamic effects of LV and BiV pacing (ΔCO = COpacing – COintrinsicSR) were even more enhanced during submaximal activity (1.4±0.6 l/min and 1.5±0.6 l/min) than under resting conditions (0.5±0.6 and 0.7±0.5 l/min; $p<0.05$).
Conclusion: The improvement in ventilatory efficacy during CRT, as demonstrated by the decrease in the ventilatory equivalent for oxygen, results from an increase in cardiac output and thus from a reduction in the ventilatory perfusion mismatch as indicated by a decrease in physiological dead space ventilation. When undergoing submaximal physical activity patients benefit even more from CRT than under resting conditions.

290 Predictors of left ventricular reverse remodelling in cardiac resynchronization therapy at multivariate analysis: important role of etiology

G. Boriani[1], I. Diemberger[2], M. Biffi[1], C. Martignani[1], E. Cervi[1], C. Valzania[1], M. Bertini[1], D. Saporito[1], M. Ziacchi[1], A. Branzi[1]. *[1]Institute of Cardiology, Univ. of Bologna, Cardiology Dept., Bologna, Italy; [2]Institue of Cardiology, Univ. of Bologna, Univ. of Bologna, Bologna, Italy*

Background: Cardiac resynchronization therapy (CRT) is able to induce beneficial effects on morbidity and mortality and is associated with left ventricular (LV) reverse remodelling.
Purpose: To explore possible predictors of reverse remodelling at mid term among heart failure (HF) patients undergoing CRT.
Methods: Clinical characteristics [including underlying heart disease, presence of diabetes, presence of atrial fibrillation, NYHA class and Quality of Life score (QoL)], conventional echocardiographic parameters and functional evaluation [6 minutes walking test (6MWT)] of patients with severe chronic heart HF, wide QRS and left ventricular ejection fraction (LVEF) ≤ 35% undergoing biventricular pacing implant were assessed before the procedure and after 3 months of follow-up. Patients were defined as responders to CRT if reverse remodelling [≥ 15% reduction in end-systolic volume (ESVol)] was observed at 3 months of follow up.
Results: 91 patients were implanted (71 males, with a mean age of 64±11 yrs) 78 with a CRT-D device (CRT+defibrillator capabilities) and 13 with a CRT-only device. 34 patients suffered from ischemic cardiomyopathy and 57 from dilated cardiomyopathy. NYHA functional class was II in 35% of patients, III in 57% and IV in 8% of patients. In the entire population 56 patients (61.5%) were responders to CRT in terms of LV reverse remodelling after 3 months: 15 of those with ischemic etiology (15/34 pts, 44.1%) and 41 of those with non-ischemic dilated cardiomyopathy (41/57 pts, 71.9%) p=0.008. Patients with dilated cardiomyopathy presented a higher grade of LV reverse remodeling vs. patients with ischemic cardiomyopathy (11.3±31.1 vs. 24.1±23.0 percent reduction in ESVol; p= 0.028). At the multivariate logistic regression analysis underlying non-ischemic etiology resulted to be the only independent predictor of LV reverse remodelling (OR 3.246, 95% CI:1.333-7.904), while the other clinical (NYHA class, QoL), functional (6MWT) and echo variables (baseline LVEF, baseline ESVol) were not significant predictors of LV reverse remodelling at 3 months.
Conclusions: In candidates to CRT the presence at baseline of a worse clinical or functional profile does not seem to influence the chance of a CRT-associated LV reverse remodelling at mid term. A non-ischemic etiology of HF is the only clinical and functional variable that independently predicts the occurrence of LV remodelling after CRT.

THE MULTI-FACETED ROLES OF BETA-BLOCKERS

291 Tolerability and dose-related effects of nebivolol in elderly patients with heart failure: data from the SENIORS trial

D. Dobre[1], D.J. Van Veldhuisen[1], G. Mordenti[2], M. Vintila[3], F.M. Haaijer-Ruskamp[3], A.J.S. Coats[4], P.A. Poole-Wilson[5], M.D. Flather[6]. *[1]University Medical Centre Groningen, Health Psychology, Groningen, Netherlands; [2]Menarini Recerche SpA, Clinical Research, Florence, Italy; [3]University Emergency Hospital St Pantelimon, Internal Medicine & Cardiology, Bucharest, Romania; [4]Faculty of Medicine, Sydney, Australia; [5]National Heart and Lung Institute, London, United Kingdom; [6]Royal Brompton and Harefield NHS Trust, Clinical Trials and Evaluation Unit, London, United Kingdom*

Purpose: The SENIORS trial showed that nebivolol reduces the risk of death or cardiovascular (CV) hospitalisation in elderly patients with heart failure (HF). We aimed to assess tolerability and dose-related effects of the β-blocker nebivolol in elderly patients from the SENIORS trial.
Methods: Patients assigned to nebivolol (n=1031) were classified into four groups, according to the dose achieved at the end of titration phase (maintenance dose): 0 mg, low dose (1.25 or 2.5 mg), medium dose (5 mg), and target dose (10 mg), and compared with those allocated to placebo (n=1030). The association between dose of nebivolol achieved and clinical outcomes was assessed using multivariate Cox proportional hazard models. We controlled for baseline characteristics that had an independent association with the dose achieved up to $p < 0.10$.
Results: A total of 668 (67%) patients reached the target dose, while 127 (12%), and 142 (14%) reached medium and low doses, respectively. A total of 74 (7%) patients were unable to tolerate any dose of nebivolol during up-titration. Age, gender and ejection fraction were similar between the groups, but prior myocardial infarction, coronary revascularisation and serum creatinine levels were lower in patients who achieved higher maintenance doses of nebivolol. Patients who achieved higher doses had also higher blood pressures and higher heart rates. After adjustment, all cause mortality or CV hospitalisation was significantly reduced in the target dose group compared to placebo (HR 0.75; 95% CI 0.63-0.90) which was similar to the medium dose group (HR 0.73; 95% CI 0.52-1.02). The low dose group had an apparently lower benefit (HR 0.88; 95% CI 0.64-1.20) while patients unable to tolerate any dose of nebivolol had an increased risk of death or CV hospitalisation (HR 1.95; 95% CI 1.38-2.75).
Conclusions: The benefits of nebivolol in elderly patients with HF appear to be related to the maintenance dose achieved. Patients unable to tolerate any dose have the worst prognosis.

292 The effect of heart rate reduction on survival in heart failure

J.K. Kjekshus. *Rikshospitalet, University of Oslo, Cardiology, Oslo, Norway*

Several studies have shown that elevated resting heart rate carries an increased risk for cardiovascular morbidity and mortality. Heart rate is also an independent marker of rehospitalisation due to cardiovascular disease including angina, stroke and heart failure. Drugs that reduce heart rate reduce mortality in proportion to the reduction in heart rate and independent of the initial heart rate. The mechanism is complex, but primarily due to a reduction in myocardial oxygen requirement and prolonged left ventricular diastole, which prevents mis-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

match between myocardial oxygen requirement and perfusion. Although beta-blockers induce bradycardia and reduce inotropic stimulation, which both reduce myocardial oxygen requirement, the mechanism of benefit in heart failure is not completely understood. A retrospective analysis has therefore been performed using available prospective, randomised beta-blocker trials with patients in symptomatic heart failure and EF below 35-40%. In all but one study mortality data and resting heart rate at base line and on treatment were available. Beta blocker use in these trials was propranolol (1), metoprolol tartrate (1), metoprolol succinate (1), bisoprolol (2), carvedilol (6), and metroprolol tartrate vs carvedilol (1). A total of 22618 patients were followed up from 6 to 58 months. The average heart rates for each of the trials varied from 73 to 90 beats/minute. When heart rate at baseline was related to anualised mortality a significant relationship was observed for placebo recipients but not for beta blocker users. The latter correlation line was shifted downwards, demonstrating a significant improvement for beta-blocker use in almost all studies, but with a differential in efficacy between patients with low and high heart rates. The lines converged at heart rates between 60 and 70 beats/minute, suggesting that there may be a lower limit for effect in heart failure. The reduction in average heart rates between treatment groups was significantly related to the observed risk reduction in mortality, (r=0.59, p=0.027). In conclusion, at least some of the improvement obtained with beta-blockers in heart failure is due to the reduction of heart rate. The effect is blunted at heart rates below 60-70 beats/min. At heart rates higher than 70 the slopes suggest that for each reduction of 5 beats there is a 10% reduction in mortality

293 Beta-2 adrenergic receptors gene polymorphisms influence the effects of carvedilol in the patients with heart failure

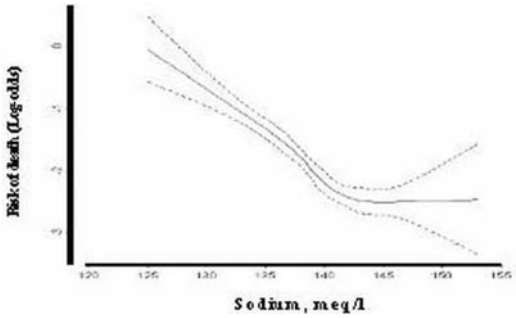
M. Metra[1], S. Nodari[2], N. Pezzali[1], L. Covolo[3], P. Milani[2], T. Bordonali[2], G. Orizio[1], U. Gelatti[1], F. Donato[1], L. Dei Cas[2]. *[1]Section of Cardiovascular Diseases, Dept. of Exp. And Appl. Medicine University, Brescia, Italy; [2]Section of Cardiovascular Diseases, Experimental and Applied Medicine, University, Brescia, Italy; [3]Hygiene, Epidemiol. Publ Health, University, Experimental and Applied Medicine, University, Brescia, Italy*

Purpose: Carvedilol is associated with highly significant improvement in left ventricular (LV) function and outcomes in patients with heart failure (HF). The individual responses to this agent are, however, heterogeneous. As it acts on both beta-1 and beta-2 adrenergic receptors (ARs), and the genes regulating beta-2 ARs expression are polymorphic, we investigated the relation of two common beta-2 AR gene polymorphism (the substitution of Arg with Gly at the position 16 and that of the Gln with Glu at the position 27) with the long-.term response to carvedilol.
Methods: 183 HF patients were studied by MUGA and right heart catheterization before and >12 months after chronic carvedilol therapy (mean dose, 34 + 20 mg/day).
Results: Thirty-one patients were homozygotes for the Arg16 polymorphism, 83 were heterozygotes and 69 were homozygotes for Gly16Gly; 27 patients were homozygotes for the Glu27 polymorphism (Glu27Glu), 66 were heterozygotes and 90 were homozygotes for the "wild-type" Gln27 polymorphism (Gln27Gln).
The Arg16Gly polymorphism had no relation with the response to carvedilol. In contrast, the patients homozygotes for the Glu27 polymorphism, associated with a reduced agonist-promoted beta-2 AR downregulation in vitro, had a greater response to carvedilol. Before carvedilol initiation, Glu27Glu patients had, compared to the others, similar LVEF (21±7 versus 21±7%), heart rate (HR, 84±14 versus 81±14 bpm), stroke volume index (SVI, 34±11 versus 31±9 ml/bt/m^2) and pulmonary wedge pressure (PWP, 16±8 versus 18±9 mmHg), with a slightly higher cardiac index (CI, 3.0±0.8 versus 2.6±0.7 L/min/m^2, $p<0.05$),. After carvedilol, Glu27Glu homozygotes showed, compared t the others, a greater change from baseline in LVEF (13±12 versus 8±10 absolute units, p=0.011), PWP (-10±10 versus –6±8 mmHg, p=.027) and SVI (13 ±9 vs 9±9 ml/bt/m^2, p=.044). LV end-diastolic volume index decreased from baseline by -17±56 ml/m^2 in Glu27Glu homozygotes versus -2± 55 ml/m^2 in the others. Significant differences were also found when comparing Glu27Glu with Gln27Gln homozygotes (LVEF, 13±12 versus 7±8 units, p=0.004; PWP, -10±10 versus -5±7 mmHg, p=0.007). Cause of HF, baseline systolic blood pressure (both $p<0.001$), the dose of carvedilol (p=0.002) and the Gln27Glu polymorphism (p=0.015) were the only variables related to LVEF changes from baseline at multivariable analysis.
Conclusion: The Glu27 gene polymorphism is associated with a greater improvement in LV function and haemodynamic variables after long-term carvedilol administration in patients with HF.

294 Effect of betablocker and ACE-inhibitor therapy on prognostic value of hyponatremia in outpatients with chronic heart failure. Data from IN-CHF database

S. Baldasseroni[1], L. Gonzini[1], R. Urso[1], F. Orso[2], V. Cirrincione[2], G. Cacciatore[2], A. De Bernardi[2], A.P. Maggioni[2] on behalf of IN-CHF Investigators. *[1]ANMCO Research Center, Florence, Italy; [2]Anmco Research Center, Florence, Italy*

Introduction: Hyponatremia has been demonstrated to predict outcomes in heart failure (HF). It has been shown that it is inversely correlated with renin–angiotensin and sympathetic nervous activity. Our aim was to confirm the prognostic value of hyponatremia and verify the capacity of betablockers (BB) and ACE-inhibitors (ACE-I) to attenuate the negative role of hyponatremia in HF.
Methods: We analyzed data from the IN-CHF Italian Registry considering all pts with sodium level recorded at entry and complete 1 year follow-up. All clinical features were registered for each patient and the value of hyponatremia, as continuous variable, has been verified in multivariate logistic model. We tested the form of the relationship between sodium levels and mortality and if it was modified by the presence of BB or ACE-I using spline cubic models.
Results: We enrolled 4670 pts, 25.6% were female, 32.2% over 70 yrs, 32.7% in NYHA III-IV class, 40.7% with ischemic etiology, 37.0% had EF <30%. Sodium concentration confirmed its prognostic value also after adjustment for all clinical and haemodynamic parameters (OR 0.87; 0.80-0.94 95% CI; p=0.0003). However the linearity of the relation was certified only for values lower or equal than 142 meq/l (Figure). The significant inverse correlation between hyponatremia and death was not modified in the group of BB (coeff.±S.E = -0.16±0.04, p=0.0008) and in the group of ACE-I users (coeff.±S.E = -0.13±0.01, p=0.001).



Conclusion: Our data confirm the prognostic value of hyponatremia, independently from BB or ACE-I. These data reinforce the hypothesis that new drugs, able to interfere with the development of hyponatremia, as vasopressin inhibitors, might become useful in the management of pts with advanced HF on top of the standardized, evidence based drug therapies.

295 Role of betablockers in patients admitted for worsening heart failure

F. Orso[1], S. Baldasseroni[2], G. Fabbri[2], L. Gonzini[2], D. Lucci[2], S. Randazzo[2], G. Lecchi[2], A.P. Maggioni[2] on behalf of Italian Survey on Acute Heart Failure. *[1]Anmco Research Center, Florence, Italy; [2]ANMCO Research Center, Florence, Italy*

Background: Several randomized clinical trials have established the capacity of beta blockers (BB) to reduce mortality in mild, moderate and severe chronic heart failure(CHF) and practice guidelines recommend their use in all pts with CHF in the absence of contraindications. Few evidence-based data are available on the usefulness of BB in patient experiencing worsening CHF and it is still debated whether these drugs should be continued or temporally withdrawn. Our aim was to analyze the role of BB therapy in reducing in-hospital outcomes in a real world setting of pts admitted to Cardiology units with a diagnosis of worsening of CHF.
Methods and Results: From 2807 pts enrolled in the Nationwide Italian Survey on Acute Heart Failure, 1572 pts hospitalized for worsening CHF have been selected. At entry 47.1% of the pts were in advanced NYHA class, 46.0% had an acute pulmonary edema and 6.9% a cardiogenic shock. Mean age was 72.4±10.5 yrs, 44.1% aged >75 yrs, 63.3% were males, 46.6% with ischemic etiology of HF, 54.0% had been hospitalized for HF in the previous year, 41.4% had history of diabetes and 66.2% hypertension. Signs of systemic and/or pulmonary congestion were observed in more than 75% of the pts. According to the presence of BB therapy before or during hospitalization we defined 4 groups of pts: Group A= no/no (n=811); Group B no/yes (n=258); Group C=yes/no (n=141); Group D= yes/yes (n=362). In the univariate analysis pts in Group B and D had a statistically significant lower in-hospital mortality with respect to the other two groups (Group B 1.2%; Group D 2.8%; Group A 10.1%, Group C 12.1%; $p<0.0001$). The association between BB use and lower mortality rate, demonstrated in univariate analysis, was confirmed by the adjusted analysis for clinical, hemodinamic and therapeutic variables. Considering Group D as the reference one we registered a higher in-hospital mortality rate in Group A and C (OR 3.24 CI 95% 1.45-7.25 p=0.004, OR 4.36 CI 95% 1.64-11.57 $p<0.0001$ respectively), while no difference was found between Group B and D (OR 0.34 CI 95% 0.06-1.79 p=0.20).
Conclusions: In pts with worsening CHF, BB use was confirmed to be associated with better patient outcomes and, interestingly, this association was demonstrated not only for pts that continued home therapy but also in those who started BB therapy during the hospitalization phase.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

296 Combined treatment with beta blockers and selective serotonin reuptake inhibitors improves survival of patients with end-stage heart failure and major depression

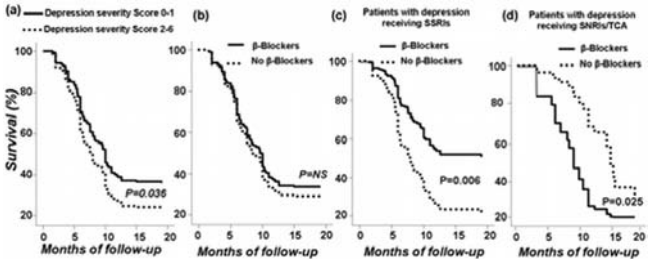
D. Tousoulis, A. Drolias, C. Antoniades, E. Vavuranakis, C. Tsioufis, C. Tentolouris, E. Stefanadi, C. Stefanadis. *Athens, Greece*

Major depression is a common feature of end-stage severe heart failure (HF). However, the impact of beta-blockers on long-term survival in patients receiving anti-depressive medication (which interferes with adrenergic signaling) is unknown.

Aim: We examined the interaction between beta-blockers and anti-depressive medication, on long-term survival of patients with end-stage severe heart failure and major depression.

Methods: The study population consisted of 250 patients with end-stage heart failure (NYHA IV). Sixty one percent of these suffered major depression and were receiving selective serotonine reuptake inhibitors (SSRIs), serotonine norepinephrine reuptake inhibitors (SNRIs) and/or tricyclic antidepressants (TCA). All patients were followed up prospectively for 18 months and the primary end-point was cardiovascular death.

Results: During the follow-up period, 167(66.8%) deaths were reported, and depression was a major predictor of cardiovascular death (HR[95%CI] 0.709[0.519-0.969], p=0.031 (Fig. a). Although β-blockers had a borderline effect on mortality in the overall population (p=0.471), (fig. b)), it had a striking beneficial effect among those patients with major depression receiving SSRIs (2.201[1.255-3.860], p=0.006 for those not receiving vs those receiving β-blockers, fig. c), while they had a negative effect on mortality in those patients receiving SNRIs/TCAs (0.190[0.044-0.814], p=0.025, fig d) and neutral effect in those not receiving any antidepressant (p=0.180).



Conclusions: Depression is a major predictor of cardiovascular death in patients with end-stage severe heart failure. Beta-blockers improve survival in patients with end-stage heart failure and depression only when they are combined with SSRIs, while their combination with SNRIs/TCAs may have the opposite effect.

RAISING HDL, IS IT A GOOD IDEA?

320 Effect of MK-0859, a potent Cholesteryl Ester Transfer Protein (CETP) inhibitor, on 24-hour ambulatory blood pressure in healthy middle-aged and elderly subjects

R. Krishna[1], B. Jin[2], J. Cote[3], F. Bieberdorf[4], D.M. Bloomfield[3], D. Miksch[1], J. Chodakewitz[4], J.A. Wagner[3]. *[1]Merck & Co., Inc., Quantitative Clinical Pharmacology, Rahway, United States of America; [2]Merck & Co., Inc, Upper Gwynedd, United States of America; [3]Merck & Co., Inc, Rahway, United States of America; [4]CEDRA Clinical Research, LLC, Austin, United States of America*

Purpose: Inhibition of CETP has been considered a potential new mechanism for the treatment of dyslipidemia and MK-0859 is a potent CETP inhibitor under development. One agent in the class (torcetrapib) was shown to increase blood pressure. Accordingly, to evaluate the possibility of a similar effect of MK-859, an ambulatory blood pressure study was performed in middle-aged and elderly healthy subjects.

Methods: A randomized, double-blind, placebo-controlled, 2-period, crossover study was conducted. Twenty-two subjects aged ≥45 and ≤75 years received either 150 mg of MK-0859 q.d. or matching placebo with a meal for 10 days in Periods 1 and 2, in a randomized sequence and a crossover manner, with at least a 14-day washout interval between the treatment periods. In addition to continuous ambulatory blood pressure monitoring conducted on Day -1 and Day 10 of each treatment period, safety was monitored throughout the study by repeated clinical and laboratory evaluation.

Results: MK-0859 was well tolerated with no serious clinical or laboratory adverse experiences reported. Treatment with MK-0859 had no statistically significant effects on ambulatory 24-hour mean systolic blood pressure or ambulatory 24-hour mean diastolic blood pressure compared to placebo (see Table).

Conclusions: MK-0859 does not increase either the 24-hour ambulatory systolic or diastolic blood pressure in healthy subjects, suggesting that the impact of torcetrapib on BP is not related to CETP inhibition itself.

24-Hour Ambulatory Blood Pressure

Test	Treatment	LS Mean on Day 10 (mm Hg)		LS Mean Difference Delta (mm Hg)		
		Value	95% CI	Value	90% CI	p-value
Systolic	150 mg MK-0859	111.82	(109.01, 114.63)	0.60	(-1.54, 2.74)	0.634
	Placebo	111.22	(108.41, 114.03)			
Diastolic	150 mg MK-0859	68.86	(66.96, 70.76)	0.47	(-0.90, 1.84)	0.561
	Placebo	68.39	(66.49, 70.29)			

321 Effect of the potent Cholesteryl Ester Transfer Protein (CETP) inhibitor, MK-0859, on lipoproteins in healthy subjects and in patients with dyslipidemia

R. Krishna[1], M.S. Anderson[2], B. Jin[3], A.J. Bergman[4], D.M. Bloomfield[2], L. Van Bortel[5], M. Gutierrez[6], J. Doherty[7], F. Bieberdorf[8], J.A. Wagner[6] on behalf of The MK-0859 001/004/011 Study Group. *[1]Merck & Co., Inc., Rahway, United States of America; [2]Merck & Co., Inc, Rahway, United States of America; [3]Merck & Co., Inc, Upper Gwynedd, United States of America; [4]Merck & Co., Inc, West Point, United States of America; [5]Ghent University Hospital, Drug Research Unit Ghent, Ghent, Belgium; [6]Comprehensive Phase One, Inc., Miramar, United States of America; [7]CEDRA Clinical Research, LLC, San Antonio, United States of America; [8]CEDRA Clinical Research, LLC, Austin, United States of America*

Purpose: CETP inhibition has been considered a potential new mechanism for dyslipidemia. MK-0859 is a CETP inhibitor under development; its effects as monotherapy on low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) concentrations were studied.

Methods: Double-blind, randomized, placebo-controlled studies were conducted. Healthy volunteers (36 active, 12 placebo), aged 18 to 45 years received MK-0859 doses of 0, 50, 100, 200, 400, and 800 mg orally once-daily for 14 days with a meal. Patients with dyslipidemia (LDL-C >100 mg/dL and <190 mg/dL) (39 active, 9 placebo), aged 18 to 75 years, received MK-0859 doses of 0, 10, 40, 150, and 300 mg orally once-daily with a meal for 28 days. Standard lipoprotein, routine laboratory safety monitoring, CETP inhibition assays and blood pressure measurements were performed.

Results: MK-0859 produced dose–dependent lipid-altering effects in both populations (see Table). Significant dose-related reductions in apolipoprotein B and increases in apolipoprotein A-I were also observed. MK-0859 was well tolerated and no changes in blood pressure were seen.

Mean % (SE) Change from Baseline

Treatment	N	HDL-C (%)	LDL-C (%)	CETP Activity (%)
Healthy Subjects				
Placebo	12	5.79 (3.05)	8.49 (3.45)	7.90 (2.37)
50 mg	6	98.30 (9.33)	-36.02 (5.41)	-39.94 (5.26)
100 mg	6	84.19 (10.56)	-45.89 (7.52)	-34.20 (3.48)
200 mg	11	118.01 (14.11)	-55.67 (4.90)	-37.90 (3.77)
400 mg	6	118.23 (14.24)	-56.66 (2.20)	-50.50 (6.86)
800 mg	6	96.93 (13.00)	-45.28 (3.58)	-60.83 (3.38)
Dyslipidemia Patients				
Placebo	9	0.37 (4.86)	3.11 (4.50)	–
10 mg	10	41.02 (5.50)	-4.99 (6.92)	–
40 mg	9	80.06 (7.62)	-31.38 (3.91)	–
150 mg	10	104.20 (8.90)	-33.66 (4.26)	–
300 mg	10	129.38 (15.05)	-37.75 (6.39)	–

Conclusions: MK-0859 produced dose-dependent inhibition of CETP activity, decreases in LDL-C and increases in HDL-C, was safe and well tolerated in this study.

322 Relationship of high-density lipoprotein cholesterol and outcomes in patients with Acute Coronary Syndromes

S. Nabais-Araujo, S. Rocha, J. Costa, P. Azevedo, J. Marques, M. Torres, M. Alvares-Pereira, A. Correia. *Hospital S. Marcos, Cardiology Dept., Braga, Portugal*

Background: Reduced high-density lipoprotein cholesterol (HDL-C) has been identified as a cardiovascular risk factor. Limited data exist regarding the prognostic impact of baseline HDL-C level in patients (pts) with acute coronary syndromes (ACS). The purpose of this study was to investigate the effect of baseline HDL-C level on outcomes of pts admitted with an ACS.

Methods: Since July 2003, 944 pts consecutively admitted to a Coronary Care Unit were included in a low HDL-C group (n=439, <40 mg/dl in men, <45 mg/dl in women, mean 33±6) or a high HDL-C group (n=505, ≥40 mg/dl in men, ≥45 mg/dl in women, mean 51±10), according to lipid measurements performed in the first 24 hours.

Results: Patients with low HDL-C more often had diabetes (30.8 vs 20.6%, p<0.001), prior myocardial infarction (20.5 vs 13.1%, p=0.003), renal insufficiency (estimated glomerular filtration rate <60 ml/min/1.73 m^2; 25.6% vs 16.9%, p<0.001), higher body mass index (p=0.018), higher triglyceride levels (165±95 vs 126±75 mg/dl, p<0.001), lower total cholesterol levels (177±46 vs 193±43 mg/dl, p<0.001), and lower low-density lipoprotein cholesterol levels (111±37 vs

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

117±38 mg/dl, p=0.012). The proportion of pts with ST-segment elevation ACS was lower in the low HDL-C group (47.6 vs 56.2%, p=0.009). There were no differences between the two groups regarding age (64±13 vs 65±13 years, p=0.26), current use of statins on admission (25.1 vs 23.0%, p=0.49), killip class, use of acute and discharge guidelines-recommended medications, cardiac catheterization (64.8 vs 66.0%, p=0.71), extent of coronary artery disease documented during angiography, and revascularization procedures. Mortality at 30 days and at 6 months were similar in the low and in the high HDL-C groups (30 days: 5.2 vs 5.8%, p=0.71; 6 months: 9.8 vs 9.6%, p=0.93, respectively). Low HDL-C at baseline was associated with increased rates of the composite end point of death, myocardial infarction, and recurrent myocardial ischemia at 6 months (24.3 vs 18.6%; OR 1.41, 95% CI 1.01-1.96, p=0.037). Multivariate analysis showed that independent predictors of major adverse cardiac events at 6 months included renal dysfunction (OR 2.32, 95% CI 1.57-3.43), age (OR 1.03, 95% CI 1.01-1.04), and left ventricular systolic dysfunction (OR 1.01, 95% CI 1.00-1.02), but not low HDL-C level.

Conclusions: Patients with low levels of HDL-C have a worse prognosis after an ACS. Further investigation is warranted to clarify this association. In addition, future efforts should be dedicated to assess the benefit of additional strategies to increase HDL-C in pts with ACS.

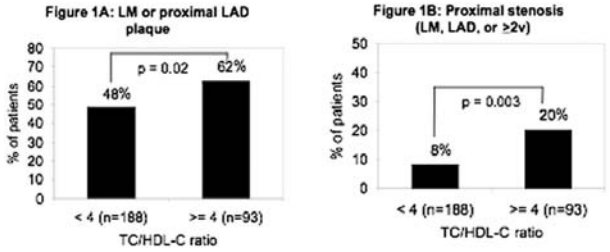
323 Total cholesterol - HDL cholesterol ratio is associated with proximal coronary artery disease

D. Nair, T.P. Carrigan, S. Kuzmiak, R.J. Curtin, P. Schoenhagen, M.Y. Desai. *Cleveland Clinic, Cardiovascular Medicine, Cleveland, United States of America*

Purpose: Elevated total cholesterol to high-density lipoprotein cholesterol (TC/HDL-C) ratio (≥ 4) is associated with increased risk of acute coronary syndromes (ACS). Most ACS occurs due to rupture of proximally located atherosclerotic plaque. Multislice computed tomography (MSCT) coronary angiography detects both obstructive and nonobstructive plaques with high accuracy, particularly in proximal vessels. We assessed the association between TC/HDL-C ratio and proximal coronary artery disease on MSCT.

Methods: Coronary MSCT angiography (40- or 64-slice) was performed on 281 individuals (39% females, mean age 54±13 years) without documented CAD, referred for coronary evaluation. TC/HDL-C ratio was calculated. Luminography was categorized for each coronary artery, with significant obstructive lesions defined as ≥ 50% stenosis in the left main (LM), proximal left anterior descending (LAD), or in ≥ 2 epicardial vessels. Proximal plaque was defined as presence of any plaque in the LM or proximal LAD and subcategorized based upon presence of calcification.

Results: Proximal plaque and significant stenoses were present in 53% and 12% of individuals, respectively. Individuals with elevated TC/HDL-C (n=93) vs. those without (n=188) had higher prevalence of proximal plaque and significant stenoses (Figure 1A and 1B). Of proximal plaques, 30% were noncalcified. On receiver operating characteristic curve, TC/HDL-C ratio was significantly associated with proximal plaque (area under curve = 0.58, p = 0.03).



Conclusions: Individuals with elevated TC/HDL-C ratio have a higher prevalence of proximal coronary plaque and significant coronary stenoses. This atherogenic lipid profile identifies a higher-risk group of individuals who could benefit from aggressive preventive strategies.

324 High HDL-C may be proatherogenic: insights from the IDEAL trial

A.G. Olsson[1], I. Holme[2], O. Faergeman[3], J.J.P. Kastelein[4], M.L. Larsen[5], M.J. Tikkanen[6], C. Lindahl[7], N.B. Cater[8], T.R. Pedersen[6] on behalf of IDEAL Study Group. *[1]Stockholm, Sweden; [2]Oslo, Norway; [3]Arhus, Denmark; [4]Amsterdam, Netherlands; [5]Copenhagen, Denmark; [6]Helsinki, Finland; [7]Taby, Sweden; [8]New York, United States of America*

Background: The relationship between cardiovascular events and very high levels of HDL-C is unclear. In reports showing relationships between cardiovascular events and HDL-C by quintle or quartile analyses, there are no indications of deviation from linearity. However, because data points at very high levels of HDL-C (>70 mg/dL, 1.8 mmol/L) is limited, we performed a posthoc analysis of the Incremental Decrease in Endpoints through Aggressive Lipid Lowering (IDEAL) trial to evaluate this relationship.

Methods: IDEAL was a 5-year prospective, randomized, open-label, blinded end point trial that compared the efficacy of atorvastatin 80mg (A80) versus simvastatin 20-40 mg (S20-40) in reducing cardiovascular events in 8888 patients with a history of myocardial infarction (MI). A80 was associated with a 11% relative risk reduciton in the primary endpoint of major coronary events (MCE: nonfatal MI, CHD death, cardiac arrest), p=0.07 and a 16% relative risk reduction in the secondary endpoint of any cardiovascular event (MCE+stroke+unstable angina+peripharal artery disease+hospitalizaiton for congestive heart failure), p<0.0001. Cox fixed covariate regression analysis was used with time to MCE after 6 months as dependent variable and age, sex, and smoking as adjustment variables. Exposure variable was the average of 3 and 6 months HDL-C levels, either as a continuous or categorized variable. Analyses were performed with or without adjustments for ApoB and ApoA-1. Deviation from linearity in HDL-C to MCE relationship was tested by a second order polynomial analysis.

Results: HDL-C measured at months 3 and 6 had a non-linear relationship to risk of MCE after 6 months (p<0.05 for test of 2nd order polynomial term). After adjustments for ApoB and ApoA-1 were made, HDL-C was a significant positive risk factor for MCE (p=0.038). Further characterization of this conditional relationship revealed that increased risk was particularly evident in patients with on-treatment HDL-C > 70 mg/dL (1.8 mmol/L), in whom the relative risk versus those with HDL-C <40 mg/dL (1.0 mmol/L) was 2.23 (95% CI: 1.17-4.24), p=0.014.

Conclusion: In CHD patients on statin therapy, there may be increased risk of MCE in those with HDL-C > 70 mg/dL (1.8 mmol/L). The explanation for this finding is unclear. Confirmation of these intriguing results by other trials is warranted.

325 The emerging anti-inflammatory role of HDL-cholesterol illustrated in cardiovascular disease free population; the ATTICA study

C. Chrysohoou[1], D.B. Panagiotakos[2], J. Skoumas[1], C. Pitsavos[1], L. Papadimitriou[1], C. Masoura[1], M. Toutouza[1], A. Zeibekis[1], N. Papaioannou[1], C. Stefanadis[1]. *[1]Glyfada, Greece; [2]Athens, Greece*

Objective: In this work we assessed the relationship between HDL-cholesterol levels and various inflammation markers status in a sample of cardiovascular disease free adult men and women from Greece.

Methods: The ATTICA study is a population -based cohort that has randomly enrolled 1128 men and 1154 women (aged > 18 years old), stratified by age – gender, from the greater area of Athens, during 2001-2002. Adherence to Mediterranean diet was assessed through a diet-score that was based on a validated food-frequency questionnaire. In this study we assessed the relationship between HDL-cholesterol levels and inflammation markers (high sensitivity C-reactive protein, interleukin-6, homocysteine and amyloid-a), after taking into account the effect of several confounders.

Results: 46% of men and 40% of women had total serum cholesterol levels >200 mg/dl, while 21% of men and 7% of women had HDL – cholesterol levels <35 mg/dl. The mean value for HDL-cholesterol was 53±14 mg/dl in females and 44±14 mg/dl in males. HDL-cholesterol levels were inversely correlated to the hs-CRP levels (b=-0.028, p=0.001) and homocysteine levels (b=-0.039, p=o.036), after adjustment for sex, age, body mass index, physical activity status, smoking, total cholesterol levels, lipid lower agents, ethanol intake and diabetes mellitus; while no statistical significance was found between HDL-cholesterol levels and interleukin-6 and serum amyloid-a.

Conclusions: In this work we evaluated the inverse relationship between HDL-cholesterol levels and inflammatory markers in a sample adult cardiovascular disease free population. This study among others illustrates the anti-inflammatory emerging role of HDL-cholesterol in reducing cardiovascular risk.

EAT YOUR HEART OUT

326 Dietary plant sterol could decrease human CRP-levels by mechanism related to reduction of oxysterols in plasma

M. Kozlowska-Wojciechowska[1], M. Naruszewicz[2]. *[1]Medical University of Warsaw, Warsaw, Poland; [2]Medical University of Warsaw, Pharmacognosy and Molecular Basis of Phytothe, Warsaw, Poland*

Background: Oxysterols in the circulation may originate from food (meat, poultry as well as milk and cereal products). In food they form spontaneously while exposed to air and/or in the course of thermal processing or storage. Oxysterols affect the structure and functions of cell membranes, and are potent regulators of cellular sterol levels and LDL receptor expression. Isolation of oxysterols from the human atherosclerotic plaque suggests that they play an active role in atherosclerotic plaque development, more potent than cholesterol itself. Dietary oxysterols are atherogenic, and elevated levels of 7 b -hydroxycholesterol are found in all coronary disease patients. The purpose of this study was to assess lipid-lowering and other effects of the diet enriched with plant sterols.

Design: Our research involved 42 healthy male students aged 22.3 ±1.6 years with a normal weight (BMI 23.7±2.5) and who during the research period (4 weeks) were subjected to a controlled regime of nutrition and physical activity. After a period of diet stabilization involving 30g butter daily in 2 servings, the subjects were randomly divided into 2 groups of 21 persons. In the first group, the butter was replaced by the same quantity of margarine with added plant sterols (2g daily), while the second group received PUFA margarine instead of butter.

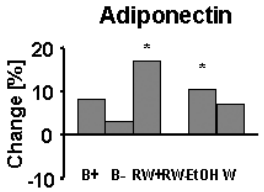
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: Serum lipid level lowering – total cholesterol by 8% ($p<0.001$), LDL cholesterol by 11% ($p<0.0001$) and oxy-LDLs by 22% ($p<0.0004$) – and hsCRP lowering by over 23% ($p<0.00001$) displayed a close interaction with dietary sterols. Furthermore, decreased serum oxysterol levels were found: 7 b - hydroxycholesterol by almost 15,8% ($p<0.00001$) and 7-ketocholesterol by 14,2% ($p<0.0002$) in the sterol-using group. In the control group except the drop in LDL cholesterol approximately 6,8% other changes are not statistic significant.
Conclusion: For the first time plant sterols were shown not only to have lipid-lowering action but also to inhibit oxysterol, maybe absorption from food, resulting in anti-inflammatory and anti-atherosclerotic effects through the mechanism of ox-LDL and CRP level lowering. On the basis of this finding, new pleiotropic action of sterols may be considered.

327 Effect of alcoholic and non-alcoholic beverages on plasma concentrations of adiponectin in healthy individuals: results of a randomised cross-over intervention study

A. Imhof[1], S. Maier[2], I. Plamper[1], G. Trischler[1], W. Koenig[1]. *[1]University of Ulm, Internal Medicine II - Cardiology, Ulm, Germany; [2]University of Ulm, Internal Medicine II - Cardiology, Ulm, Germany*

Purpose: Moderate alcohol consumption has been shown to be associated with reduced cardiovascular mortality potentially mediated by anti-inflammatory effects. Adiponectin improves insulin sensitivity and has anti-inflammatory properties. High concentrations of adiponectin were associated with lower risk of type 2 diabetes and future myocardial infarction.
Methods: Seventy-two non-smoking healthy men and women aged 22-55 years were included. After a wash-out period of two weeks they were randomly assigned to the following interventions for 3 weeks: ethanol (ETOH, concentration 12.5%), beer (B, 5.6%), or red wine (RW, 12.5%) equivalent to 30 g/d of ethanol for men and 20 g/d for women or the same amount de-alcoholised beer or red wine or pure water (W). After cross-over a second intervention for three weeks with the corresponding beverage (red wine – de-alcoholised red wine etc.) followed. Adiponectin concentrations were measured before and after intervention by sandwich ELISA (Quantikine®, R&D Systems, Wiesbaden, Germany).
Results: Among all groups except the de-alcoholised red wine group adiponectin conentrations increased after three weeks of intervention (Figure). Among those consuming alcoholic beverages the observed increase was larger compared to intervention with non-alcoholic beverages. After intervention with either ethanol solution or red wine the increase of adiponectin concentrations was statistically significant ($p<0.05$ in both groups).



Figure

Conclusions: The strongest effect on adiponectin concentrations has been observed after consumption of red wine and ethanol. Effects of moderate consumption of these beverages on adiponectin concentrations might represent a link between alcohol, inflammation and atherosclerosis. The effects seem to be mainly mediated by ethanol itself.

328 Long-term fish consumption offers cardiovascular protection in healthy people due to its anti-arrhythmic and anti-inflammatory properties; the ATTICA study

C. Chrysohoou[1], D. Panagiotakos[2], C. Pitsavos[1], J. Skoumas[1], V. Nikolaou[1], L. Papadimitriou[1], C. Paliou[1], A. Zeibekis[1], M. Toutouza[1], C. Stefanadis[1]. *[1]Glyfada, Greece; [2]Athens, Greece*

Objective: We sought to investigate whether diet enriched with fish and omega-3 fatty acids consumption is associated with changes of the electrical action potential duration as it is represented by the QT duration on a rest ECG, as well as, with levels of various inflammatory markers, related to cardiovascular disease, in a population based sample of Greek adults without any evidence of cardiovascular disease.
Methods: During 2001 – 2002 we randomly enrolled 1514 men (18-87 years old) and 1528 women (18-89 years old), stratified by age-sex distribution (census 2001) from the Attica area, Greece. We studied several demographic, anthropometric, lifestyle, dietary and bio-clinical factors of the participants. Dietary habits (including fish consumption) were evaluated using a validated food frequency questionnaire. All subjects underwent a 12-lead surface ECG, where among several other indices QT duration was measured and QTc was calculated (Bazett's rate corrected). After 12 hours fasting blood was collected by all participants under the proper conditions in order to measure among other biochemical parameters white blood cell counts and plasma levels of C-reactive protein, tumor necrosis factor – a, amyloid- A, interleukin-6 and homocysteine. The tested hypothesis was evaluated through multiple linear regression analysis, after controlling for physical activity status, sex, age, medication intake as well as several other potential confounders.
Results: 88% of men and 91% of women reported fish consumption at least once a month. Compared to non fish consumers those who consumed $>$ 300 gr/week had 13.6% shorter QTc duration (p 0.45 sec (p = 0.03). Significant results were also observed when lower quantities (150 – 300 gr/week) of fish consumed.Those findings were confirmed after adjusting for age, sex, physical activity status, BMI, smoking habits, nuts intake and other confounders.
Conclusion: Long-term consumption of fish is independently associated with shorter QTc interval and with lower inflammatory markers levels, among healthy adults.in free eating people without any evidence for cardiovascular disease. Thus, fish intake seems to provoke antiarrhythmic and anti-inflammatory cardiovascular protection at population level.

329 Methionine-loading induces endothelial dysfunction by activating endothelin-1 pathway in hypertensive patients

G. Bouras[1], D. Tousoulis[1], C. Antoniades[2], C. Vasiliadou[1], K. Marinou[1], N. Papageorgiou[1], E. Stefanadi[1], G. Siasos[1], C. Stefanadis[1]. *[1]Athens, Greece; [2]University of Oxford, Cardiovascular Medicine Dept, Lab 3, Oxford, United Kingdom*

Endothelin-1 (ET-1) is a key regulator of arterial blood pressure in humans. Although ET-1 expression is redox-sensitive, it is unclear whether in hypertensives, conditions associated with increased oxidative stress (such as homocysteinemia) may affect ET-1 levels.
Aim: We examined the impact of acute homocysteinemia on endothelial function in hypertensive patients and healthy individuals. Also, we examined the potential role of ET-1 and oxidative stress in homocysteine-induced endothelial dysfunction in both groups.
Methods: In this double-blind placebo controlled study, 35 hypertensive subjects and 30 healthy volunteers underwent methionine-loading (100mg met/kg BW) after they received vitamins C (2g) plus E (800IU) (16 hypertensives (HTN+vit) and 15 healthy (C+vit)) or placebo (18 hypertensives (HTN+placebo) and 15 healthy (C+placebo)). Endothelial function was evaluated by gauge-strain plethysmography (to determine endothelium dependent dilation (EDD)), at baseline and 4 hours post loading (4hPML). ET-1 and lipid hydroperoxides (per-ox) levels were measured by ELISA.
Results: Homocysteine was similarly increased in both hypertensives (by $22.2\pm1.26\mu M$ $p<0.0001$) and healthy controls (by 23.2 ± 2.22 μM, $p<0.0001$), and was not affected by pre-treatment with antioxidants. EDD was significantly decreased in HTN+placebo (75.4±11.5 to 51.6±7.3%, $p<0.05$) and C+placebo (96.7±9.6 to 52.2±6.5%, $p<0.0001$), while antioxidant treatment did not prevent this effect in either HTN+vit (76.4±8.8 to 53.7±7.8%, $p<0.01$) or C+vit(86.6±10.5 to 41.1±6.3%, $p<0.001$). Importantly, ET-1 was increased 4hPMLonly in hypertensive individuals (HTN+placebo: 1.09±0.3 to 1.40±0.4pg/ml, $p<0.05$) an effect not prevented by antioxidants (HTN+vit: 0.82±0.08 to 1.1±0.09pg/ml $p<0.01$). Per-ox were significantly decreased in the HTN+vit (170[65-368] to 148[98-372]pg/ml, $p<0.05$) but not in the HTN-placebo (170[65-268] to 148[98-372]pg/ml, p=NS). No effect of methionone-loading was observed on ET-1 levels in healthy individuals (C+placebo: 1.96±0.84 to 1.87±0.77pg/ml and C+vit: 3.59±1.35 to 2.84±1.15pg/ml, p=NS).
Conclusions: Experimental homocysteinemia rapidly blunts endothelial function in both hypertensive subjects and healthy individuals. The rapid elevation of ET-1 levels observed only in hypertensives, suggests that the ET-1 may be the key mediator of homocysteine-induced endothelial dysfunction in this group of patients, independently of oxidative stress status.

330 Canola oil, but not sunflower oil, decreases cholesterol and improves endothelial function in patients with peripheral arterial occlusive disease: a double-blind, randomized interventional study

H. Stricker, F. Duchini, M. Facchini, G. Mombelli. *Ospedale La Carita, Medicine, Locarno, Switzerland*

Introduction: Dietary supplementation with omega-3 polyunsaturated fatty acids (PUFAs) has been shown to reduce cardiovascular morbidity and mortality, but the results have recently been challenged. The biological effects of omega-3 PUFAs are not fully understood, but may impact atherothrombosis, endothelial function, lipid levels, and heart rate variability.
Methods: Forty patients with peripheral arterial occlusive disease supplemented their usual diet with 2 tablespoons/day of canola oil (n = 20) or sunflower oil (n = 20) for 8 weeks. Skin perfusion, measured by laser Doppler flux (LDF), was assessed at rest and during reactive hyperemia. Parameters of heart rate variability were calculated using a 24-hour ECG. Measurements included markers of plasmatic coagulation (F1+2, TAT), fibrinolysis (DD, tPA, PAI-1), platelet activation (sCD40L), inflammation (hsCRP), and lipid and homocysteine levels.
Results: LDL-cholesterol decreased (from 2.74±0.73 to 2.42 ±0.65 mmol/L, p = 0.007) with canola oil but not with sunflower oil, whereas triglycerides and HDL-cholesterol did not change. The difference in the percent increase of LDF after ischemic challenge increased with canola oil from 108±98 to 179±88% (p =

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

0.012) but not with sunflower oil (from 190±138 to 246±172%, p = 0.22). Markers of haemostasis, fibrinolysis, platelet activation, inflammation, homocysteine, and heart rate variability did not change.
Conclusions: Canola oil containing omega-3 PUFAs may confer cardiovascular protection by improving endothelial function and lowering LDL-cholesterol.

331 Is green tea better than black tea in ameliorating endothelial function?

N. Jochmann[1], M. Lorenz[1], A. Von Krosigk[1], P. Martus[1], V. Boehm[2], G. Baumann[1], K. Stangl[1], V. Stangl[1]. *[1]Charite, Universitaetsmedizin Berlin, Med Klinik Kardiologie und Angiologie, Berlin, Germany; [2]Friedrich-Schiller-Universitaet Jena, Institut fuer Ernaehrungswissenschaften, Berlin, Germany*

Objective: A positive correlation between endothelial function and the consumption of green and black tea has been established. It is assumed that catechins are the tea ingredients responsible for these beneficial effects. In black tea, catechin concentrations are significantly lower than in green tea. This study was designed to compare green and black tea with regard to amelioration of endothelial function.
Methods: Endothelial function in response to green and black tea was assessed in bovine aortic endothelial cells (BAEC) and rat aortic rings. To elucidate whether these findings are also applicable to humans, endothelial-dependent vasodilation (flow-mediated dilation, FMD) and endothelial-independent vasodilation (nitro-mediated dilation, NMD) were assessed by high-resolution ultrasound in 21 healthy women before and two hours after consumption of green and black tea, in comparison to control (water) in a cross-over design.
Results: In BAEC, green and black tea significantly increased eNOS activity to the same extent. Similarly, both teas induced comparable endothelial-dependent vasodilation in rat aortic rings. These effects were completely prevented by nitric oxide synthase (NOS) inhibition. In humans, ingestion of green and black tea led to significant ($p<0.01$; n=21) increase of FMD: from 5.4±2.3% to 10.2±3%, and from 5±2.6% to 9.1±3.6%, respectively. The increase in FMD was not significantly different between the two tea preparations. NMD did not vary between any of the groups.
Conclusions: Green and black tea are equally effective in improving endothelial function in vitro and in vivo. These results suggest that both teas may provide comparable cardiovascular health effects.

WHAT IS NEW IN NUCLEAR CARDIOLOGY IN 2007

332 Integrated SPECT/CT for the assessment of clinically significant coronary artery lesions in patients hospitalized for acute coronary syndromes

S. Rispler, Z. Keidar, S. Abadi, A. Roguin, E. Ghersin, R. Beyar, O. Israel, D. Aronson. *Rabmam Medical Center, Cardiology Department, Haifa, Israel*

Background: Early and accurate triage of patients with acute coronary syndromes (ACS) is frequently based of clinical risk scores, with patients at high risk referred to coronary catheterization without further diagnostic testing. CT coronary angiography (CTCA) may be useful in reducing the number of patients with ACS referred for coronary catheterization. However, the hemodynamic consequences of coronary stenoses detected by CTCA may be equivocal. We studied the clinical usefulness of a SPECT/CTCA hybrid imaging device in patients with ACS.
Methods: Fifty-seven patients presenting with unstable angina or non-ST-elevation infarction underwent a single-session SPECT-myocardial perfusion imaging and CTCA with the hybrid device (General Electric, Milwaukee, USA). The Thrombolysis in Myocardial Infarction (TIMI) risk score for patients with unstable angina/non-ST-elevation myocardial infarction was used to classify patients as low- or high-risk (≥3 risk factors). Fused SPECT/CTCA images were used to detect clinically significant lesions (potentially requiring catheterization), defined as >50% stenosis by CTCA and reversible perfusion defects in the same territory.
Results: Based on the TIMI risk score, 30 patients (52.6%) were defined as high risk. CTCA demonstrated at least 1 lesion with >50% stenosis in 21 of these patients (70%). However, only 9 of these patients (30%) had clinically significant lesions. Of the 27 patients with low-risk TIMI score, 9 had at least 1 lesion with >50% stenosis (33.3%) by CTCA, and only 4 patients (14.8%) had clinically significant lesions. Perfusion SPECT imaging was negative in all patients with negative CTCA regardless of TIMI risk score. The TIMI risk score had a moderate sensitivity (69%) and low specificity (48%) for detecting clinically significant lesions. Considering all patients with either high TIMI score or positive CTCA as high-risk patients, increased the sensitivity to 100% but the specificity remained unsatisfactory (59%).
Conclusion: The results of the present study suggest that patients with ACS and a negative CTCA may be managed conservatively regardless of TIMI risk score. However, a positive CTCA has a low specificity even in patients with high-risk TIMI score. Hybrid SPECT/CTCA imaging may play a potentially important role in the risk stratification of patients with ACS providing an objective decision making tool regarding the need for invasive procedures.

333 Sympathetic innervation and risk of ventricular tachycardia in genotyped patients with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC-9)

M. Paul, M. Schafers, P. Kies, E. Schulze-Bahr, O. Schober, G. Breithardt, T. Wichter. *Hospital of the University of Muenster, Cardiology and Angiology, Muenster, Germany*

Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically heterogeneous myocardial disease accounting for ventricular tachycardia and sudden cardiac death in a young population. Mutations in the gene encoding for plakophilin-2 (PKP2) have recently been reported by our group as the most common cause of autosomal-dominant ARVC (ARVC-9). In this study, we investigated the potential role of adrenergic dysfunction on the arrhythmia profile in patients (pts) with or without PKP2 mutations with the help of 123I-meta-iodobenzylguanidin scintigraphy (MIBG-SPECT). MIBG, as a norepinephrine analogue, is a marker of presynaptic sympathetic innervation (uptake-1).
Methods: Forty two pts with definite ARVC were divided into those with (PKP2-positive; 17 pts) and without a PKP2 mutation (PKP2-negative; 25 pts). MIBG-SPECT was performed in all pts and compared to results obtained from 10 control subjects (n=10) without identifiable structural heart disease. There were no differences in age or gender between the groups. MIBG images were acquired four hours post injection and analysed for regional 123I-MIBG uptake in a standardized 33-segment bull's eye scheme.
Results: Overall, an abnormal tracer uptake was detected in 25 pts with ARVC (59%). There was no difference between PKP2-pos (n=11; 65%) and PKP2-neg (n=14; 56%) pts. During long-term follow-up (9.1±3.8 years), ventricular tachyarrhythmias occurred in 27 pts. However, ARVC pts with an abnormal MIBG-SPECT experienced more often sustained VT when compared to those with a normal sympathetic innervation ($P<0.01$). PKP2-pos pts with a reduced MIBG uptake showed a trend to more frequent recurrences of sustained VT than those PKP2-neg pts (P=0.051).
Conclusions: An impairment of adrenergic innervation appears to account for a higher risk for VT recurrences in pts with ARVC, and seemingly even more so in pts with a PKP2 mutation. These results indicate a possible role of MIBG-SPECT in terms of an individualized future risk stratification in pts with ARVC.

334 Prognostic value of myocardial perfusion and function as assessed by quantitative gated SPECT in the elderly patients with known or suspected coronary artery disease: results of the Q-PROVE study

S. Hida, T. Chikamori, T. Nagao, Y. Igarashi, H. Tanaka, Y. Usui, T. Hatano, A. Yamashina. *Tokyo Medical University, Second Department of Internal Medicine, Tokyo, Japan*

Background: Although ECG-gated SPECT may be useful in risk stratification particularly for elderly patients with CAD, few studies have prospectively evaluated the prognostic value of gated SPECT in this patient population.
Methods: A total of 175 elderly patients aged 75 years or more with known or suspected CAD were prospectively evaluated by stress gated SPECT using a 20-segment model and an automatic functional analysis. Patients with AMI or unstable angina within the previous 3 months, and those who underwent coronary revascularization within 3 months after the SPECT study were excluded. Outcome assessment included prespecified cardiac events and noncardiac deaths.
Results: During a mean follow-up of 3.4 years, 17 had cardiac events: 2 cardiac deaths, 1 nonfatal myocardial infarction, 3 coronary artery bypass grafting, 5 percutaneous coronary intervention, 1 unstable angina, 3 heart failure, and 2 malignant arrhythmias. The incidence of cardiac events was higher in the highest quartile for a summed stress score (SSS>14), summed rest score (SRS>12), end-diastolic volume (EDV>68 ml) and end-systolic volume (ESV>42 ml), and the lowest quartile for ejection fraction (EF<57%) than in the remaining quartiles. Kaplan-Meier survival estimation indicated event-free survival rates at 3 years of 78%, 83%, 78%, 76% and 80%, respectively in patients with SSS>14, SRS>12, EDV>68 ml, ESV>42 ml and EF<57%, but 95%, 94%, 95%, 96% and 95%, respectively in those in the remaining quartiles (p=0.0003, p=0.026, p=0.0005, p=0.00001 and p=0.016; respectively). Multivariate analysis using the Cox proportional hazard model demonstrated that an SSS>14 (OR=5.9, $p<0.02$) and the ESV>42 ml (OR=8.8, $p<0.05$) were independent predictors for subsequent cardiac events.
Conclusions: These results indicate that not only myocardial perfusion but also myocardial volumetric measurements derived from gated SPECT predicts cardiac events in elderly patients aged 75 years or more with known or suspected CAD, and may have a role in risk stratification for this patient population.

335 Which is the best predictor of event-free survival in patients with chronic ischemic heart disease?

A. Gimelli[1], P. Landi[1], P. Marzullo[1], P. Marraccini[1], A. L'abbate[2], D. Rovai[1]. *[1]CNR Clinical Physiology, Department of Nuclear Medicine, Pisa, Italy; [2]Scuola Superiore Sant'Anna, Department of Medicine, Pisa, Italy*

Purpose: To predict the outcome of patients with chronic ischemic heart disease using clinical data, 12-lead ECG at rest and on effort, routine laboratory exami-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

nation, two-dimensional echocardiography, gated SPECT and coronary arteriography.
Methods: From 2001 to 2006 a group of 687 consecutive patients with known or suspected ischemic heart disease, without evidence of acute or recent myocardial infarction or previous coronary artery bypass surgery, was prospectively studied. Patients were followed-up for 35±16 months. The predictive value of the different variables was tested by Cox proportional hazard regression analysis.
Results: During follow-up, 27 (3.9%) patients died for cardiac causes and 18 (2.6%) had a non-fatal myocardial infarction. The prediction of event-free survival at the different steps of patient care are shown in the Table. Patient age was the only cardiovascular risk factor independently associated with event-free survival. A previous myocardial infarction and the history of angina at stress were the clinical variables independently associated with event-free survival. The body mass index, serum creatinine and HDL cholesterol levels were the only biometric and laboratory variables associated with event-free survival. The maximal work load at exercise stress test was also associated with survival. Of the examined echocardiographic variables, left ventricular ejection fraction was an independent predictor of survival. Summed rest and stress score were the gated SPECT variables independently associated with survival. Finally, the number of major coronary arteries with a >50% luminal diameter reduction was independently associated with event-free survival. Considering all the independent variables together, only summed rest and stress score were the final independent predictors of event-free survival (chi-square 38.5, $p < 0.0001$).

Predictors of event-free survival

Predictors	Risk factors	Clinical history	Biometrics	Laboratory examinations	ECG	2D-Echo	SPECT	Coronary angiography
Chi Square	3.9	18.0	3.1	14.4	4.0	29.4	38.5	18.3
p value	<.005	<.0001	<.01	<.001	<.05	<.0001	<.0001	<.0001

Conclusion: In patients with chronic ischemic heart disease, myocardial perfusion abnormalities at rest and after stress allow event-free survival to be predicted more accurately and independently of clinical, electrocardiographic, laboratory, echocardiographic and angiographic data.

337 Rest and low-dose dobutamine Tc-99m-mibi gated SPECT for early prediction of left ventricular remodeling in patients with a first STEMI treated by PCI

L. Ernande[1], F. Cachin[2], S. Monzy[1], N. Durel[1], L. Boyer[3], J. Ponsonnaille[2], J. Maublant[3], J. Lipiecki[2]. *[1]Department of Cardiology, University Hospital, Clermont Ferrand, France; [2]Jean Perrin Cancer Center, Clermont Ferrand, France; [3]Departement of Radiology, University Hospital, Clermont Ferrand, France*

Background: Left ventricular (LV) remodeling occurs in about 30% of patients (pts) treated successfully by PCI in the acute phase of myocardial infarction (MI) but cannot be predicted by simple clinical, biological or angiographic parameters.
Aim of the study: To test the value of rest and low-dose dobutamine (LDD) Tc-99m-mibi SPECT for early prediction of LV remodeling in pts treated by PCI in the acute phase of a first ST-elevation MI.
Patients and methods: 40 pts (8 females, 32 males, mean age: 58.6 years) were prospectively included in this study. Each pt underwent a rest and LDD Tc-99m-mibi gated SPECT 5±2 days after the acute event. Mean tracer uptake in the infarct related artery (IRA) territory was calculated quantitatively and regional thickening was analysed using a 3-point scoring system (0=normal, 1=diminished and 2=absent). LV volumes were assessed by MRI studies which were performed within the 24 hours from SPECT and repeated 6 months later. LV remodeling was defined as 20% increase in LV end diastolic volume between the acute phase and 6-month follow up.
Results: LV remodeling was observed in 27.5% of pts (11/40). Mean tracer uptake on the rest study in the IRA territory in pts with remodeling was 50.1% while it was 58.4% in pts without (p=0.07). A cut off value of 47% separated in the best fashion pts with and without remodeling (PPV = 60% and NPV = 83%). Presence of residual thickening in the IRA territory (mean score ≤ 1.0) in patients with tracer uptake < 47% further improved PPV to 75% without altering the NPV. On the LDD study a cut off value of 43% of mean tracer uptake separated in the best fashion pts with and without remodeling (PPV = 83% and NPV = 82%). The analysis of regional thickening did not further improve the value of this test.
Conclusion: LDD gated SPECT performed 5 days after a first STEMI treated by PCI allows prediction of LV remodeling observed at 6 months with high accuracy.

NEW FRONTIERS IN CARDIAC COMPUTED TOMOGRAPHY

338 Cardiac dual-source computed tomography in unselected patients with severe coronary calcifications and a high prevalence of coronary artery disease

C. Burgstahler[1], A. Reimann[2], M. Heuschmid[2], I. Tsiflikas[2], H. Brodoefel[2], A.F. Kopp[2], S. Schroeder[1]. *[1]Eberhard-Karls-University, Department of Cardiology, Tuebingen, Germany; [2]University of Tuebingen, Diagnostic Radiology, Tuebingen, Germany*

Background: Cardiac multi-detector computed tomography (MDCT) with retrospective ECG-gating permits the visualization of coronary artery stenosis. However, in patients with severe coronary calcifications, higher heart rates and arrhythmia MDCT was found to have limitations due to insufficient temporal and spatial resolution. Thus, the aim of the present study was to evaluate the diagnostic accuracy of a new dual-source computed tomography (DSCT) scanner generation with 83 ms temporal resolution in cardiac imaging, especially in patients with high calcium scores and a high prevalence of coronary artery disease.
Methods: Out of 82 unselected consecutive patients scheduled for invasive coronary angiography (ICA) because of suspected or known coronary artery disease (CAD), 41 persons were identified to have severe coronary calcifications (Agatston score > 350, 35 male, mean age 66.2±8.4 years, median 68 years, number of risk factors 3.5±1.3). All patients were examined with DSCT (Somatom Definition™, Siemens). Beside assessment of total calcium score all coronary segments were analyzed after intravenous injection of contrast media with regard to the presence of coronary artery lesions. Image data were reconstructed with a slice thickness of 0.75mm and a reconstruction increment of 0.4mm. The findings were compared to ICA in a blinded fashion.
Results: During CT examination, mean heart rate was 64±14 bpm, median 59 bmp. 16/41 patients (39%) had non sinus rhythm. Mean Agatston score equivalent (ASE) was 1391, median 1146, ranging from 358 to 3898 ASE. Prevalence of CAD was 98% (40/41). Based on a coronary segment model sensitivity was 91%, specificity 84%, positive predictive value 70%, and negative predictive value 96% for the detection of significant lesions (≥50% diameter stenosis). The main reason for false positive results was an overestimation of mild lesions by DSCT. Vessels with false positive results had significantly higher ASE-values compared to coronaries without false positive results (median 319.1 vs. 143.3, p<0.001).
Conclusion: In unselected patients with severe coronary calcifications, a very high prevalence of CAD and a remarkable number with heart rhythm irregularities, our data indicate that the accuracy of DSCT with 83ms temporal resolution, even with a stabilized image quality, is limited in clinical routine. The overestimation of stenosis, mostly in severely calcified segments, remains a limitation of the method.

339 Radiation dose of the new dual source CT in multislice computed tomography of the coronaries

G. Conradi[1], J. Rixe[1], A. Rolf[1], A. Deetjen[2], C.H.R. Hamm[2], T. Dill[2]. *[1]Kerckhoff-Heart-Center, Department of Cardiology - Cardiac Imaging, Bad Nauheim, Germany; [2]Katharinen-Hospital, Department of Cardiology, Stuttgart, Germany*

With the introduction of the Dual-Source Computed Tomography system (DSCT) a reduction of radiation dose exposure compared to the existing systems was promised. Examination numbers are increasing and no data comparing radiation dose of the DSCT for coronary CTA with other Multislice CT scanners (MSCT) and invasive angiography exist. The aim of this study was to provide data for radiation exposure of the MSCT in comparison to MSCT.
Patients and methods: Retrospective analysis of radiation exposure in 210 patients (pts) was performed: MSCT 16 slices in 56 pts (Age 68± 8; 49 men; Body surface area (BSA) of 1.94±0.13 m ^{2}, 64 ±11 bpm), MSCT 64 slices in 47 pts (Age 57±10; 25 men; BSA 1.85 ±0.18 m ^{2}, 55±6 bpm), and DSCT in 107 pts (Age 62± 14; 75 men; BSA 1.99±0.20 m ^{2}, 64±13 bpm). DSCT or MSCT of the coronaries, respectively, was done for clinical reasons. No beta-blockers were used in the DSCT group. The effective dose (ED) was chosen as comparison parameter and was calculated from the dose length product and a conversion factor k (chest with a value of 0.017 mSv x mGy-1 x cm-1) according to the guidelines of the European work community for quality criteria in computed tomography.
Results: For MSCT with the 16 slice scanner the ED was 9.76± 1.84 mSv, with the 64 slice scanner 13.58±2.80, and with the DSCT 13.40 ±6.83. There was no statistically significant difference between groups with respect to BSA and heart rate (16-slice: 64 bpm; 64-slice: 55 bpm; DSCT:64 bpm; p=0.8).
Conclusion: The new DSCT does not show a reduction of radiation dose exposure compared to 16-and 64-slice MSCT scanners at similar heart rates. However, the theoretical advantage of DSCT due to its high temporal resolution is a reduction of radiation exposure at higher heart rates.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

340 Plaque characterization using different x-ray energy by dual source computed tomography and comparison with histology

S. Komatsu, A. Kuhlmann, V. Campean, D. Ropers, U. Ropers, M. Wechsel, W.G. Daniel, K.U. Amann, S. Achenbach. *University of Erlangen-Nuernberg, Department of Cardiology, Erlangen, Germany*

Background: In addition to high spatial (0.4 mm) and temporal resolution (83 ms), Dual Source CT (DSCT) allows simultaneous imaging with two different x-ray energies. This may be beneficial for tissue characterization. Objectives. To determine the accuracy of ex vivo atherosclerotic plaque characterization with DSCT and to assess the CT attenuation of various plaque components depending on X-ray energy.
Materials and Methods: 18 atherosclerotic vessels of coronary, carotid and iliac arteries obatined from autopsy were analyzed by DSCT. Each lumen of the vessels was filled with contrast media (30X Imeron 350). The collimation was 2X64X0.6 mm, rotation time was 330 msec., temporal resolution was 83 msec. Data sets were obtained using a tube voltage of 80, 100, 120, and 140 kV. The x.-ray attenuation of lipid-rich plaque, fibrous plaque, calcified plaque and contrast-enhanced lumen were determined for all x-ray energies by comparison to histology at 25 sites. In addition, cross-sectional images were reconstructed with 0.75 mm slice thickness and 0.4 mm increment. 26 slices at 10 mm interval were analyzed by comprehensive color-coding according to CT number.
Results: There were significant differences among CT attenuations of lipid-rich, fibrous and calcified plaque using 80, 100, 120, and 140 kV (Table, $p<0.01$), respectively. The averaged ratio of CT attenuation of lipid-rich, fibrous plaque, and calcified plaque to the Contrast-enhanced lumen for 80kV and 140kV were -16%, 11%, 14%, respectively ($p<0.05$).

The Attenuation on Different Energy

Energy	Contrast-enhanced lumen	Calcified plaque		Fibrous plaque		Lipid rich plaque	
		Absolute	Relative to lumen	Absolute	Relative to lumen	Absolute	Relative to lumen
80 kV	632±12 HU	618±12 HU	98%	369±43 HU	57%	130±43 HU	21%
100 kV	423±27 HU	508±19 HU	120%	285±33 HU	67%	76±15 HU	18%
120 kV	315±31 HU	423±20 HU	134%	161±25 HU	38%	52±20 HU	17%
140 kV	276±17 HU	316±13 HU	114%	127±24 HU	46%	18±24 HU	7%

Conclusions: The relationships between lumen enhancement and each plaque component, such as lipid-rich, fibrous plaque and calcified plaque were different as changing the x-ray energy level. Through the use of varying x-ray energy, DSCT may facilitate detection of atherosclerotic plaque and characterization of plaque components.

341 Prevalence of coronary artery disease demonstrated by 64 slice coronary CT angiography in asymptomatic patients with type 2 diabetes mellitus

I. Dobrecky-Mery[1], T. Gaspar[1], M. Azencot[1], B.S. Lewis[1], N. Peled[1], N. Yaniv[2], L. Slezak[1], M. Sabbah[1], T. Margolis[1], D.A. Halon[2]. *[1]Lady Davis Carmel Medical Center, Cardiology, Haifa, Israel; [2]Clalit Community Health Services, Haifa, Israel*

Background and aims: In patients with type 2 diabetes mellitus (DM) coronary artery disease (CAD) may be advanced by the time of clinical presentation. Diagnosis prior to clinical presentation may allow better preventive therapy whereas non-invasive stress testing and perfusion imaging reveal only disease severe enough to limit coronary blood flow.
We examined the prevalence of coronary plaque with 64 slice coronary CT angiography (CTA) in asymptomatic pts with DM and no history of CAD enrolled in an ongoing prospective outcomes study.
Methods: CTA was performed in 119 pts (63.4±5.6 yrs, 64% women) with DM (mean duration 11.9±8.0 yrs) and no history of CAD. A third (42, 35%) were receiving insulin.
Results: Risk factors included current smoking (14.0%), past smoking (30.8%) and hypertension (66.4%). Baseline therapy included statins in 69.2% and angiotensin converting enzyme inhibitors or receptor blockers in 58%. Only 27 pts (22.7%) had no coronary artery plaque and multivessel plaque was common irrespective of calcium score (Table). Independent predictors of multivessel coronary plaques were duration of DM (OR 1.1/yr, p=0.005), smoking (OR 1.03/pkyr, p=0.023), age (OR 1.1/yr, p=0.09) and total cholesterol/HDL-C ratio (OR 1.6, p=0.09). Gender, hypertension, hemoglobin A1C, albuminuria, ankle/brachial pressure ratio, serum C-reactive protein and insulin therapy were not predictors of multivessel plaque.

Prevalence of coronary plaque

Patients	Any plaque N (%pts)	Multivessel plaque N (%pts)	Stenosis (>50%) N (%pts)	Multivessel stenosis N (%pts)
All (N=119)	92 (77.3)	67 (56.3)	32 (26.9)	8 (12.3)
Ca score<100 (N=65)	22 (33.8)	16 (24.6)	8 (12.3)	1 (1.5)
Ca score=0 (N=28)	4 (14.3)	4 (14.3)	1 (3.6)	0

Conclusions: In asymptomatic pts with DM and no history of CAD undergoing 64 slice CTA: 1. Non-obstructive multivessel coronary plaque was found in more than half the pts and obstructive narrowing in one quarter. 2. Multivessel plaque was common in pts with low calcium scores. 3. Duration of DM and total cigarettes smoked were the most prominent independent predictors of prevalent multivessel coronary disease.

342 Discrepancy between MSCT, conventional coronary angiography and intravascular ultrasound versus myocardial perfusion

J.D. Schuijf[1], J.M. Van Werkhoven[2], G. Pundziute[1], J.W. Jukema[1], I. Decramer[3], M.J. Schalij[2], J.H.C. Reiber[2], E.E. Van Der Wall[2], W. Wijns[1], J.J. Bax[2]. *[1]Leiden University Medical Center, Cardiology, C5-P, Leiden, Netherlands; [2]Leiden University Medical Center, Cardiology, Leiden, Netherlands; [3]Cardiovascular Center Aalst, Cardiology, Aalst, Belgium*

Purpose: Multi-slice computed tomography (MSCT) is a new technique that allows non-invasive detection of coronary artery disease (CAD) through direct visualization of atherosclerosis. How these observations should be interpreted is however not fully understood. The purpose of the present study therefore was to evaluate the severity of CAD as determined by MSCT, conventional coronary angiography and intravascular ultrasound (IVUS) imaging in relation to functional assessment by means of myocardial perfusion imaging (MPI).
Methods: A total of 45 patients underwent both conventional coronary angiography (in combination with IVUS) and MPI in addition to MSCT. Quantitative coronary angiography (QCA) and IVUS measurements were performed of the severest lesion, while MSCT studies were classified as normal, non-obstructive (<50%) CAD and obstructive (≥50%) CAD. Stress-rest gated MPI was performed to evaluate myocardial perfusion.
Results: Normal perfusion was observed in 31 (69%) patients, in which MSCT showed respectively at least 1 significant stenosis in 14 (45%), non-obstructive CAD in 13 (42%) and no CAD in only 4 (13%) patients. QCA however showed an average percentage stenosis of 26.5%. Similarly, percentage diameter stenosis on IVUS was 28.3% with an average minimal lumen area of 5.7 mm^2. Nonetheless, average plaque area and burden were still considerable, respectively 9.0 mm^2 and 63% in patients with abnormal MSCT versus 3.7 mm^2 and 27% in patients with a normal MSCT ($P<0.05$).
Conclusion: Initially contradictory findings were obtained. In patients with normal MPI, abnormal MSCT was frequently observed despite only mild stenosis on conventional coronary angiography. IVUS imaging however confirmed the presence of considerable plaque burden without luminal compromise. Accordingly, the current findings underline the complementary nature of MSCT and MPI.

343 Prognosis of patients with suspected coronary artery disease and normal computed tomography

M. Gilard, G. Le Gal, J.C. Cornily, U. Vinsonneau, C. Joret, P.Y. Pennec, J. Mansourati, J. Boschat. *Chu La Cavale Blanche, Department of Cardiology, Brest Cedex, France*

Background: The current gold-standard test for the diagnosis of coronary artery disease (CAD) is conventional coronary angiography (C-CAG). Lately, multi-slice computed tomography (MSCT-CAG) demonstrated very high sensitivity and negative predictive value for CAD primary diagnosis when compared to C-CAG. The aim of our study is to prospectively assess the safety of ruling out CAD on the sole basis of a normal MSCT-CAG.
Methods: From June 2004 to January 2006, consecutive patients initially scheduled for C-CAG for primary diagnosis of CAD underwent MSCT-CAG instead. Patients with a highly calcified coronary network or with an abnormal or non-interpretable MSCT-CAG underwent secondary C-CAG and were excluded from the study. We included patients whose diagnosis of CAD was ruled out by a normal MSCT-CAG; in those cases, C-CAG was not performed. All patients underwent further follow-up with clinical endpoints (death, subsequent C-CAG, myocardial infarction).
Results: In 141 patients, MSCT was considered as normal. During the 14.7 months follow-up those patients experienced a 0.0% mortality rate, a 3.6% rate of subsequent coronary angiography and a 0.7% rate of myocardial infarction. The risk of subsequent death, coronary events or new referral for C-CAG compares favourably with the one following a normal conventional artery angiography.
Conclusion: MSCT coronary angiography safely rules out coronary artery disease in suspected patients and allows patients to be managed less invasively, by reducing the number in whom conventional coronary angiography has to be performed.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

POSTER SESSION 1

MODERATED POSTERS 1:
CARDIAC SURGERY: RECENT ADVANCES IN CORONARY ARTERY SURGERY AND HEART TRANSPLANTATION

P366 Statin withdrawal is associated with an increase in cardiac events after vascular surgery

O. Schouten[1], S.E. Hoeks[1], G.J.M.J. Welten[1], J.J.P. Kastelein[2], H.H.H. Feringa[2], R.T. Van Domburg[2], R. Vidakovic[2], M. Dunkelgrun[2], J.J. Bax[3], D. Poldermans[2]. *[1]Erasmus MC, Vascular Surgery, Rotterdam, Netherlands; [2]AMC, Vascular Medicine, Amsterdam, Netherlands; [3]LUMC, Cardiology, Leiden, Netherlands*

Background: Discontinuation of statin therapy in patients with an acute coronary syndrome has been associated with an increase of adverse coronary events. Patients undergoing major vascular surgery frequently are not able to take oral medication shortly after surgery. Since there is no intravenous formula for statins, interruption of statins in the postoperative period is a serious concern. The objective of this study was to assess the effect of perioperative statin withdrawal on postoperative cardiac outcome. Also, the association between outcome and type of statin was studied.
Methods: In 298 consecutive statin users (100 fluvastatin extended release, 86 simvastatin, 35 pravastatin, and 77 atorvastatin) undergoing major vascular surgery a detailed cardiac history was obtained and medication use was noted. Postoperatively troponin levels were measured on day 1,3,7,30 and whenever clinically indicated by ECG changes. Endpoints were postoperative troponin release, myocardial infarction, and a combination of non-fatal myocardial infarction and cardiovascular death. Multivariable analyses and propensity score analyses were performed to assess the influence of type of statin and discontinuation of statins for these endpoints.
Results: Statin discontinuation was associated with an increased risk for postoperative troponin release (HR 4.6, 95%CI 2.2-9.6), and the combination of myocardial infarction and cardiovascular death (HR 7.5, 95% CI 2.8-20.1). Importantly, fluvastatin extended release was associated with less perioperative troponin release compared to simvastatin (HR 2.7, 95% CI 1.1-6.5), pravastatin (HR 6.6, 95% CI 2.2-19.6), and atorvastatin (HR 4.2, 95% CI 1.7-10.4). Also for the endpoint of myocardial infarction and cardiovascular death fluvastatin was associated with less events as compared to simvastatin (HR 4.1, 95% CI 1.1-14.8), pravastatin (HR 5.7 95% CI 1.2-26.8), and atorvastatin (HR 1.3, 95% CI 1.3-16.3).
Conclusion: This study showed that statin withdrawal in the perioperative period is associated with an increased risk for perioperative adverse cardiac events. Furthermore there seems to be a better outcome in patients who received statins with an extended release formula.

P367 Acute coronary syndrome-like ECG findings in patients with acute aortic syndrome: frequency, determinants and clinical relevance, including potential for misdiagnosis

E. Biagini, C. Lofiego, G. Rocchi, R. Fattori, M. Ferlito, M. Graziosi, L. Lovato, L. Di Diodoro, A. Branzi, C. Rapezzi. *University Hospital S. Orsola-Malpighi, Dept. of Cardiology, Bologna, Italy*

Purpose: Patients with acute aortic syndrome (AAS) can present with acute coronary syndrome-like (ACS-like) ECGs. We assessed frequency/characteristics of ACS-like ECG profiles among patients with a final diagnosis of AAS, and explored pathophysiologic determinants and prognostic relevance within each Stanford subtype.
Methods: Blind review of presentation ECG of consecutive patients (n=233, period 1990–2005) with final diagnosis of AAS (164 Stanford type A) was performed.
Results: Prevalence of ACS-like ECG was 27%: type A 26% (42/164); type B 29% (20/69). ACS-like ECG were more often non-STEMI-like: in type A 83% (35/42); type B 85% (17/20). Patients with ACS-like ECG more often had coronary ostia involvement (p=0.002), pleural effusion (p=0.02), significant aortic regurgitation (p=0.01), and troponin positivity (p=0.001). Multivariate analyses were appropriate for patients with type A disease. Predictors of ACS-like ECG profile appeared to be significant aortic regurgitation (OR 2.36, 95% CI 1.04–5.35) and coronary ostia involvement (OR 3.22, 95% CI 0.96–10.79). Regarding prognosis, ACS-like ECG profile predicted in-hospital mortality as did age, dyspnea at presentation and no surgical intervention (table 1).
Conclusions: About a quarter of AAS patients presented with ACS-like ECG patterns–often with non-STEMI characteristics–which could cause misdiagnosis. ACS-like ECG was associated with more complicated disease, and in type A disease was an independent predictor of in-hospital mortality.

Table 1

	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Age (each incremental 10-yr)	1.65 (1.21–2.27)	0.002	1.46 (1.03 – 2.07)	0.035
Male gender	0.66 (0.33–1.31)	0.232		
History of systemic hypertension	1.23 (0.61–2.50)	0.563		
Dyspnea at presentation	3.02 (1.14–7.99)	0.026	3.10 (1.06 – 9.07)	0.039
Syncope	3.14 (1.35–7.32)	0.008	2.40 (0.89 – 6.46)	0.084
ACS-like ECG profile	2.20 (1.06–4.59)	0.035	2.51 (1.07 – 5.92)	0.035
Shock	2.54 (1.15–5.64)	0.022		
Pericardial effusion	2.45 (1.21–4.96)	0.013		
Pleural effusion	3.41 (1.21–4.96)	0.015		
Aortic insufficiency	1.24 (0.62–2.50)	0.545		
No surgical intervention	5.56 (2.56–12.50)	<0.001	4.76 (2.04 – 11.11)	<0.001

P368 3D-Rapid Prototyping of cardiac structures for guidance in heart surgery

S. Jacobs, V. Falk, F.W. Mohr. *Heartcenter Leipzig, Cardiothoracic Surgery, Leipzig, Germany*

Background: Aim of the study was to create an anatomical correct 3D R apid Prototyping Model (RPT) for patients with complex heart disease and altered geometry of the atria or ventricles to facilitate planning and execution of the surgical procedure.
Methods: Based on computer tomography (CT) - and magnetic resonance imaging (MRI) images, regions of interests were segmented using the Mimics 9.0 software (Materialise, Leuven, Belgium). The segmented regions were the target volume (left ventricular aneurysm or tumor), and structures at risk (left anterior descending artery, papillary muscles); in addition segmentation was used to discriminate functional from non-functional tissue (viable myocardium versus scar). After the segmented area of the original patient dataset was transferred into an STL-file (Stereo Lithography file), the file was sent to the 3D printer Z ä 510 (4D Concepts, Gross-Gerau, Germany) to print out a 3D plaster model. The patient individual 3D printed RPT-models were used to guide the resection of a left ventricular aneurysm and right ventricular tumor.
Results: The comparison of the 3D heart model with the native heart during the surgical procedure facilitated these operations. The surgeon was able to identify risk structures, assess the ideal resection lines and determine the residual shape after a reconstructive procedure (LV remodelling, infiltrating tumor resection). Using a 3D-print of the LV-aneurysm reshaping of the left ventricle ensuring sufficient LV volume was easily accomplished.
Conclusion: The use of the 3D Rapid Prototyping Model (RPT-model) during resection of ventricular aneurysm and malignant cardiac tumors may facilitate the surgical procedure due to better planning and improved orientation.

P369 Long-term follow-up of elderly patients with permanent AF who underwent radiofrequency modified Maze and concomitant cardiac surgery

H. Sen, H.T. Sie, W.P. Beukema, A.R. Ramdat Misier, A. Elvan. *Isala Klinieken, Cardiology, Zwolle, Netherlands*

Purpose: Of patients scheduled for elective open heart surgery up to 50% have preoperative atrial fibrillation (AF). The "cut and sew" Maze procedure abolishes AF in 45-95% during intermediate-term follow-up. Limited long-term follow-up data are available.
Methods: From Nov 1995 to Nov 2003, 258 patients (pts) with structural heart diseases and permanent AF for at least 12 months were scheduled for elective cardiac surgery and included in a registry. They underwent a radiofrequency (RF) modified Maze procedure as an adjunct to the open heart operation. In all pts either an irrigated, customized unipolar RF probe was used or a commercially available irrigated unipolar RF ablation pen. Pts were followed in the outpatient clinic. We sought to assess whether SR during follow-up would be a prognostic factor for all cause mortality, cardiac mortality and stroke using multivariate analysis.
Results: 258 pts, mean age 68±9.5 years with permanent AF, underwent a total of 655 cardiac surgical procedures and concomitant RF Maze surgery. Mean duration of permanent AF was 66±69 months (range 12-396). Preoperatively 82.9% of pts were in NYHA class 3 and 5.0% in class 4. In-hospital mortality was 4.2% (12 pts) and during a mean follow-up of 36.5±23.6 months (range 12-114) 75 pts died (26.3%). LV EF was normal (50-60%) in 49.3%, moderate (30-50%) in 37.3% and poor (<30%) in 13.4% of pts. Sustained SR, including atrial rhythm was present in 59% of pts at 1 year, in 54.4% at 3 years, in 53.4% at 5 years and in 57.1% of pts at the latest follow-up. Stroke was reported in 6 pts (2.1%).
Conclusions: Long term follow up after RF modified Maze shows an AF recurrence rate of 43%. In these pts postoperative rhythm was neither predictive of all cause mortality, cardiac mortality and stroke. The stroke rate was very low.

P370 Solid malignancies after cardiac transplantation: final results of the German Heart Transplantation Tumor Registry

H.-U. Stempfle[1], S. Schulze-Schleithof[2], N. Hiemann[3], C. Bara[4], T. Dengler[5], T. Stadlbauer[6], A. Rahmel[7], U. Franke[8], K. Pethig[7] on behalf of German Working Group on Heart Transplantation. *[1]Kardiologie, Bad Toelz, Germany; [2]Kardiologie, Bad Oeynhausen, Germany; [3]Berlin, Germany; [4]Hannover, Germany; [5]Heidelberg, Germany; [6]Kardiologie, Giessen, Germany; [7]Kardiologie, Leipzig, Germany; [8]Kardiologie, Jena, Germany*

Purpose: The high incidence of neoplasm after cardiac transplantation (HTx) is

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

a well-established complication which limits long-term survival. However, little is known about type and time course of the malignant disease, a potential relation to various immunosuppressive therapies, pattern of organ involvement and the impact on surveillance strategies.
Methods: Recently the German Working Group on Heart Transplantation completed an internet based Tumor Data Base survey which was started in 2004 and included each transplanted recipient of 8 participating centers.
Results: 3803 patients (pts) with a mean follow up of 11.0± 5.1 years after HTx (670 female, 3133 male; mean age 60±14 years) were evaluated in the registry. Underlying disease before HTx was dilated CMP in 2241 pts (59%), ischemic CMP in 1292 pts (34%) and other in 270 (7%) pts. A total of 2263 pts. were treated with an antibody induction therapy early after transplantation. Immunosuppressive therapy was administered in form of Cyclosporine in 68%, Tacrolimus in 15%, Sirolimus/Everolimus in 3%, Azathioprine in 44%, Mycophenolate Mofetil in 17%, and Steroids in 65% of pts. In 750 (19,7%) out of 3803 pts. 1094 solid malignancies were observed. The most common malignancies were skin cancers (52%), followed by lymphomas (15%), lung cancers (11%), urogenital- (9%) gastrointestinal cancers (8%) and others (5%). Solid malignancies comprised 37% of all deaths after HTx.
Conclusions: In contrast to the Cincinnati Transplant Tumor Registry, the striking findings of the German Tumor Data Base were the prominence of skin cancers followed by lymphomas and by a high percentage of lung cancers. In contrast to previously described inversed ratio of squamous to basal cell carcinoma, German transplant recipients showed a ratio (1:11) which was comparable with the general population. Further analysis of the registry is aimed towards potential association to immunosuppressive therapy and new surveillance strategies.

P371 Successful allogenic re-transplantation of long-term preserved beating donor hearts

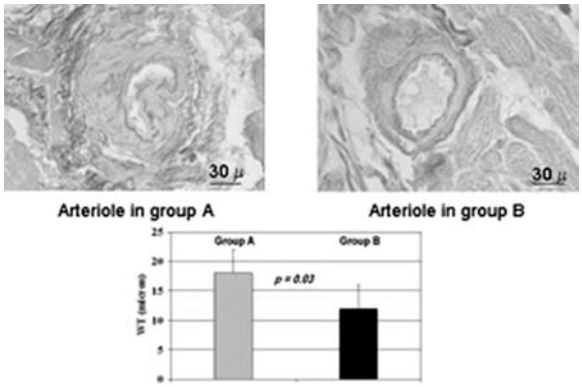
J. Garbade[1], T. Kuntze[1], C. Ullmann[1], H. Aupperle[2], S. Jacobs[2], T. Walther[2], F. Falk[2], S. Dhein[2], F.W. Mohr[2]. *[1]Heart Center Leipzig, Dept. of Cardiac Surgery, Leipzig, Germany; [2]Dept. of Veterinary Pathology, Leipzig, Germany*

Objective: Innovative techniques of donor heart preservation may permit extended storage and remote procurement of organs. The aim of the study is the allogenic re-transplantation of extracorporeal long-term preserved beating donor hearts using a newly developed extracorporeal preservation technique.
Methods: Hearts of six pigs (40-50kg) were explanted in a beating heart manner using a newly developed double-lumen cannula followed by immediately connection to a modified circulating constant pressure Langendorff-system (40-50mmHg) consisting of an oxygenator and a centrifugal pump. The perfusate consisted of a modified Tyrode solution with 1000 ml leukocyte depleted donor blood and supplements. Left atrial and aortic root pressures were kept constant. Contractility and metabolic functions were monitored continuously. For pH and electrolyte regulation a haemofiltration was carried out. Left ventricular biopsies were taken in situ, within 12 hours of perfusion and after re-transplantation, fixed in glutaraldehyde and prepared for transmission electronmicroscopy.
Results: After 12 hours of beating heart preservation and constant low pressure perfusion the donor organs were arrested using HTK-Bretschneider solution. Subsequently the hearts were re-transplanted in a recipient animal in a biatrial technique followed by one hour of reperfusion. Ischemia-time was about 35 minutes (±12). To prevent rejection the recipients received urbasone (500mg) and cyclosporine (1mg/kg). At one hour of reperfusion left ventricular developed pressure was similar to the initial in-situ measurement. All animals were successful weaned from ECC. But inotropic support was necessary in all animals. Electron microscopy showed moderate lesions of cardiomyocytes, whereas capillary endothelia were predominantly intact.
Conclusion: This new technique of heart explantation and preservation extends the current accepted preservation limit and improves the time dependent viability and myocardial function. Thereby, the successful re-transplantation of these extracorporeal preserved hearts is feasible.

P372 Impaired coronary flow reserve in heart transplant patients with normal coronary angiograms: predictive role of interstitial fibrosis and medial thickening of intramyocardial coronary arteries

F. Tona[1], A. Angelini[1], A.L.P. Caforio[1], C. Castellani[1], R. Montisci[2], A. Gambino[2], A. Ramondo[2], G. Gerosa[2], G. Thiene[2], S. Iliceto[2]. *[1]University of Padova, Cardiology, Padova, Italy; [2]University of Cagliari, Cardiology, Cagliari, Italy*

In heart transplantation (HT), coronary flow reserve (CFR) may be impaired despite a normal coronary angiogram. Aim of this study was to assess myocardial and microvascular alterations at endomyocardial biopsy (EMB) as potential markers of CFR impairment.
Methods: Coronary flow velocity in the anterior descending coronary artery was detected at rest and during i.v. adenosine by transthoracic echocardiography. CFR was the ratio of hyperaemic diastolic mean velocity (DMV) to resting DMV. CFR <2.5 was considered abnormal. We studied 17 patients (pts) with normal coronary angiogram (13 M, age at HT 50±12 years) at 7± 4 years from HT. CFR was abnormal in 7 (group A) and normal in 10 (group B).At 1st year EMB, interstizial fibrosis volume fraction (FV), vessel luminal area (VA), and medial area (MA) were determined by quantitative morphometry. Average medial wall thickness (WT) of intramyocardial arterioles (20-150 μm) was calculated as $[(VA+MA)/\pi]^{\frac{1}{2}} - (VA/\pi)^{\frac{1}{2}}$.
Results: CFR was lower in group A (1.7±0.2 vs 4.2±0.4, p<0.0001), WT was higher in group A (18±4 vs 12±4 μm, p=0.03) (Figure) and FV tended to be higher in group A (34±8 vs 26±10%, p=0.09). Time from HT, diabetes, hypertension, hypertrophy and rejection episodes were similar in the two groups. CFR was inversely related to WT (r=-0.595, p=0.01). At multivariable analysis, adjusted for time from HT, diabetes, hypertension and hypertrophy, only WT was independently related to CFR (beta =-0.762, p=0.01).



Figure

Conclusion: Structural remodeling of the intramyocardial arterioles, and not fibrosis, was independently related to a reduced CFR, in HT pts with normal coronary angiograms. These findings indicate hystopathological and physiological evidence of allograft vasculopathy without epicardial artery stenoses.

P373 Intermediate-term results of bipolar irrigated radiofrequency modified Maze procedure in 200 patients with concomitant cardiac surgery

H. Sen, H.T. Sie, W.P. Beukema, A.R. Ramdat Misier, A. Elvan. *Isala Klinieken, cardiology, Zwolle, Netherlands*

Purpose: The Cox's Maze procedure is considered as an effective surgical treatment of atrial fibrillation (AF) in patients. Radiofrequency (RF) energy is an alternative to the complex surgical maze procedure. This study evaluated the medium-term results of a novel ablation technique to eliminate AF by means of an irrigated bipolar RF ablation device.
Methods: Lines of conduction block was produced, similar to the bi-atrial lesion pattern as used in the modified "cut and sew" Maze surgery. All lesions were made with this RF clamp, which has a self-regulating ablation protocol based on an impedance feedback system. This bi-atrial procedure can safely be performed partially on beating heart.
Results: From Oct 2003 to Dec 2006, 200 patients with structural heart diseases and permanent AF underwent bipolar irrigated RF ablation with concomitant cardiac surgery. Mean age was 68±11 yrs (range 31-87) euro score 6.4±2.8 (1-16), duration of AF 57.1±57.8 months (range 4-360) and LA dimension 48.3±7.8 mm (range 31-85). All patients were treated according to bi-atrial Maze pattern. Mean cardiopulmonary bypass (CPB) and cross-clamp durations were 238.7±85.3 min and 119.3± 50 min respectively. Mean ablation time was 236.9±64.4 secs. Concomitant procedures included mitral valve (MV) plasty (n=111), MV replacement (n=23), aortic valve replacement (n=50), aortic root replacement (n=4), tricuspid valve plasty (n=156) and CABG (n=86). During mean follow-up of 19±11 months (range 1- 40) the in-hospital mortality was 3.0% (n=6). SR, atrial rhythm or atrial based paced rhythm was present in 73% at 12 months and in 73% at 24 months.
Conclusion: This novel bipolar irrigated RF modified MAZE technique is effective in eliminating AF with promising intermediate-term results.

MODERATED POSTERS 2: ACUTE CARDIAC CARE, OTHER

P375 Is there a Relative Adrenal Insufficiency (RAI) in patients with Cardiogenic Shock (CS)?

B. Fellner[1], P. Smetana[1], I. Tentzeris[1], A. Fuernkranz[1], T. Hoechtl[1], G. Zorn[1], O. Wagner[2], K. Huber[2], A. Geppert[2]. *[1]Wilhelminenhospital, Cardiology Department, Vienna, Austria; [2]Medical University, Medical and Chemical Laboratory Diagnostics, Vienna, Austria*

Purpose: It is well known that patients (pts) with septic shock exhibit RAI and cortisol substitution has been shown to improve blood pressure and outcome.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Because inflammation plays an important role in the development and outcome of CS, we investigated, whether pts with CS have inadequate adrenal reserve too.
Methods: We measured serum cortisol levels before and 60 minutes after a 0,25mg corticotropin stimulation test in 15 pts with CS following acute myocardial infarction (MI) and in a control group of 8 pts with uncomplicated MI at day 0, 1, 2, 3, 5, and 7 after onset of shock/MI. RAI was defined by an increase in serum cortisol levels in response to corticotropin of less than 9μg/dl. Data were correlated to vasopressor-need and interleukin (IL) levels (IL1,IL6,IL8,IL10).
Results: Baseline cortisol levels in pts with CS were significantly higher than in control pts especially on day 0 (35±22 vs 15±9, p=0.006). In 5 CS-pts the test-series were stopped at day 1 to 3 because the physician in charge started a therapy-trial with hydrocortisone due to increasing vasopressor need. Three other pts died within the seven day period. RAI was observed only at day 0 in 5 of the 15 CS-pts but in none of the control pts (p=0.06). These CS pts with RAI had higher Il-6 and IL-10 levels at baseline (249.7pg/ml [31.5-504.9] and 16.4pg/ml [8.8-183.4]) than CS pts without RAI (8.4pg/ml [2.7-43.1] and 0 [0-3.5], p= 0.045 and p= 0.007, respectively), but the vasopressor need (average dose per hour over the first day and vasopressor need on study inclusion) was not significantly higher. In the following days all CS-pts - except one CS patient at day 3 - responded adequately to the corticotropin test. Of note 4 of these 5 pts with RAI received cortisol substitution therapy based on clinical suspicion only.
Conclusion: A subgroup of pts with CS exhibit RAI on day 0 of shock. This subgroup of pts might be identified based on higher IL-6 and IL10 levels. Whether cortisol substitution is warranted in this subgroup of CS pts remains to be analysed.

P376 Microcirculatory changes due to Cooling therapy in patients with cardiogenic shock

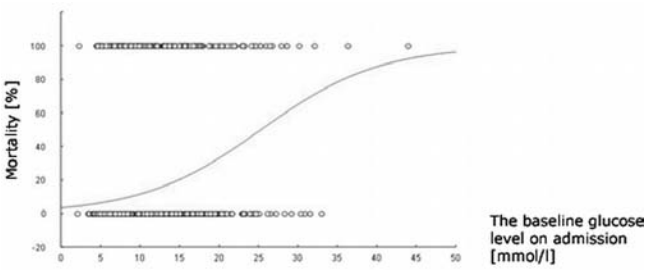
R. Wimmer, M. Janusch, H. Lemm, A. Christoph, M. Winkler, K. Werdan, M. Buerke. *Martin-Luther-University, Dept. of Medicine III, Halle/Saale, Germany*

Background: OPS vessel microscopy (orthogonal polarized spectral imaging) is a new method to visualize microcirculation.
Methods: In this study 20 Patients with cardiogenic shock after cardiac arrest and cooling therapy caused by a myocardial infarction were followed after their PCI. Five areas in the oral vestibule were recorded and averaged each 24 hours for three days. Data were transferred on a PC and analysed: the average of diameters, of flow and the cell blood velocity (CBV) were recorded. In this way, we compared all data recorded at temperatures lower than 34 °C to data recorded at higher temperatures (more than 38°C) and to data recorded at normal temperatures from 36-38 °C.
Results: At temperatures below 36°C we found lower CBV (295,5μm/s vs. 527,6μm/s; p= 0,0027) and flow (308 x 10^{-9}ml/s vs. 740 x 10^{-9}ml/s; p=0,018) in patients with cardiogenic shock and cooling therapy compared to normal temperatures. It is remarkable, that medium vessel diameter is relatively constant and independent from temperature changes (32,5μm vs. 31,9μm vs. 31,1μm; p= 0,96 und 0,83). The biggest flow and CBV were found at normal temperatures.
Discussion: This data may suggest a decrease of organ perfusion under hypothermia. It shows that OPS technology is a useful tool to follow heart patients on the intensive care unit in order to estimate influences of cooling therapy on microcirculation.

P377 Influence of baseline glucose level on 12-month mortality in patients with cardiogenic shock treated with percutaneous coronary intervention for ST-segment elevation myocardial infarction

M. Gasior, D. Pres, G. Stasik - Pres, P. Lech, P. Buchta, M. Gierlotka, M. Hawranek, A. Lekston, Z. Kalarus, L. Polonski. *Silesian Center for Heart Disease, Cardiology Dept., Zabrze, Poland*

The cardiogenic shock (CS) is the main cause of mortality in patients with ST-segment elevation myocardial infarction (STEMI). The prognostic significance of blood glucose abnormalities in acute phase of myocardial infarction has also been suggested as a risk factor. There are not many evidences that baseline glucose level affects mortality in patients with STEMI complicated by CS.
Aim: The aim of this analysis was to assess whether baseline glucose level affect 12-month mortality in patients with CS treated with PCI for STEMI.
Methods: Consecutive patients with cardiogenic shock on admission treated with PCI for STEMI were included in the analysis. We took into account patients with and without diabetes. The baseline glucose level had been measured on admission before coronary angiography was performed. We analyzed the influence of the baseline glucose level and various risk factors on 12-month mortality.
Results: A total of 207 patients with STEMI complicated by CS were included in the analysis. The incidence of diabetes was 29,9%. The mean 12-month mortality in the analyzed group was 42,5%. The 1 mmol/L increase of the baseline glucose level among various risk factors (anterior wall myocardial infarction, hypertension, final patency in the infarct coronary artery) was the independent prognostic factor of higher 12-month mortality (HR=1,05;95%CI(1,02-1,08), p=0,0035). Interestingly, the diabetes was not the independent prognostic factor (HR=1,12;95%CI(0,68-1,85), p=0,65).In the figure 1. 12-month mortality according to the baseline glucose level was presented.



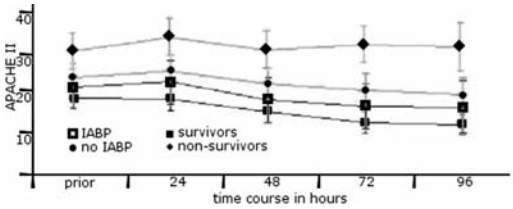
12-month mortality.

Conclusion: The higher baseline glucose level, but not diabetes is associated with the higher 12-month mortality in patients with ST-segment elevation myocardial infarction complicated by cardiogenic shock.

P378 A prospective, randomised evaluation of intraaortic balloon counterpulsation on the prevention of multiorgan-dysfunction-syndrome in patients with cardiogenic shock after acute myocardial infarction

H. Lemm, R. Prondzinsky, M. Swyter, N. Wegener, S. Unverzagt, A. Schlitt, A. Christoph, M. Russ, K. Werdan, M. Buerke. *Martin-Luther-University Halle-Wittenberg, Department of Internal Medicine 3, Halle, Germany*

Objectives: In patients with cardiogenic shock following myocardial infarction (MI-CS) the use of IABP is a recommended part of the standard regimen. Yet, no randomised clinical trial could prove the beneficial effect of IABP on the unfavourable prognosis determined not only by deterioration of cardiac function but also by development of multiorgan dysfunction syndrome (MODS).
In this monocentric, randomised and prospective trial with two arms and parallel design the role of IABP on the prevention or reduction of MODS in PCI-treated patients with MI-CS was examined.
Primary end point of the study was the decrease of the APACHE II score - a severity of disease score - from day 0 to day 4 indicating improvement of MODS.
Methods: 40 patients with MI-CS within 12 h of onset of hemodynamic instability were included in the study (31 males, 9 female, mean age 64± 1,9 yrs., 28- day survivors 27/40; CI day 0: 2,52±0,15 l/min/m^2, day 4: 3,17±0,39 l/min/m^2;
total IABP-on-pump-time: 44±8,2h). The APACHE II score was taken initially, 24, 48, 72 and 96 hours after randomisation.
Results: Initial and serial APACHE II scoring were prospectively identified as valuable prognostic markers with a strong decrease of APACHE II score from day 0 to day 4 in survivors indicating a favourable prognosis (survivors: Δ -4,2; non-survivors: Δ +0,7). Only minor differences could be observed in the study groups (IABP: Δ –2,8; non-IABP: Δ -2,5).



Conclusions: The use of IABP did not show a beneficial effect on the severity of disease (MODS) in patients with MI-CS during the first 4 days. Consequently no beneficial effect of IABP on development and progression of MODS could be documented. However, the APACHE-II-score taken during the first 48 hours was strongly predictive for survivors and non-survivors of CS.

P379 Incidence and clinical course of the patients with transient left ventricular apical ballooning during long term follow-up

T. Pawlowski, M. Mlotek, J. Rzezak, H. Rdzanek, R.J. Gil. *Klinika Kardiologii Inwazyjnej, Csk Mswia (Central Hospital), Warsaw, Poland*

Background: Transient left ventricular apical ballooning (TLVAB) is being diagnosed in the increasing number of patients. The aim of the study is to assess incidence and clinical course of TLVAB patients during long term follow-up.
Methods: Out of the population of 2658 patients with the acute coronary syndromes in 2001-2006, the 45 (1.69%) patients with TLVAB were selected. The diagnosis was made based on the presence of typical balloon-like left ventriculography abnormalities and other signs (ECG changes, chest pain and the history of triggering factor). During follow-up the control echocardiography scan to assess left (LV) and right (RV) ventricles, was performed. The end diastolic and systolic volumes (LVEsV, LVEdV) were calculated as well as ejection fraction (EF). The right ventricle was assessed by it's ejection fraction (EF). The clinical 3 years follow-up was performed.
Results: During hospitalisation, there were 2 cases (4.4%) of pulmonary edema

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

and 1 case (2.2%) of cardiogenic shock. The RV function was depressed in 10 cases (22.2%) and all mentioned cases with hemodynamic instability. The mean RV EF was 25±8% in patients with it's depression and 47±10% in patients with normal RV function. The LV EF was depressed at index hospitalization, but during follow-up at 6±2 months in all patients LV contractility abnormalities disappeared as well as in RV (Table 1). During 2 years follow-up (completed by 77.7% patients), there were 2 cases of TLVAB recurrence and during 3 years follow-up (completed by 46% of patients), there was another one case of TLVAB recurrence. There were no cases of deaths or myocardial infarction during follow-up.

Table 1

	Baseline	Follow-up	p
Left EF (%) by Angio	53±11	69±14	<0.05
Left EF (%) by Echo	41±10	62±10	<0.05
Left LVEdV (mm^3) by Echo	125±52	119±54	NS
Right EF (%) by Echo	37±11	43±11	NS

Conclusions: The TLVAB is quite common across patients with the suspicion of acute coronary syndrome. Global improvement in both LV and RV function is observed during follow-up. The recurrence rate of the disease is low.

P380 Prevalence of tako-tsubo cardiomiopathy in subjects with acute coronary syndrome

M. Dominici, C. Milici, D. Formigli, C. Bock, D. Forlani, D. Bovelli, M. Bazzucchi, G. Rasetti. *Cardiology Department, Santa Maria Hospital, Terni, Umbria, Italy*

Purpose: Tako-Tsubo cardiomyopathy or apical ballooning syndrome or stress-induced myocardial stunning represent an reversible left ventricular dysfunction with a ballooning of the left ventricular apical myocardium without significant coronary artery disease. Ethyology and prevalence of this disease is yet unclear. The aim of this retrospective study is to assess the prevalence of Tako-Tsubo cardiomyopathy among patients undergoing urgent coronary angiography for suspected acute coronary syndrome in our institute.
Methods: we retrospectively reviewed, for Tako-Tsubo cardiomiopaty, 558 consecutive patients underwent coronary angiography in our catheter laboratory for suspected acute coronary syndrome (myocardial infarction or unstable angina) in year 2006.
Results: seven patients (all female, mean age 63±10 years) fulfilled the diagnostic criteria for Tako-Tsubo cardiomiopaty (chest pain induced by emotional stress, ST-T abnormalities at electrocardiography, reversible balloon-like wall motion abnormality with absence of significant coronary stenosis). Hypertension was present in 57% of them, hypercholesterolemia in 29%, smoking in 14%. Familiarity for coronary artery disease was present in 29%. One patient had persistent atrial fibrillation. A preceding emotional stress was present in all patients. One patient had an episode of ventricular fibrillation on onset of chest pain. ST segment elevation was present in 43% patients while the remaining 57% had T-wave inversion on their admission electrocardiograms. At 2D echocardiogram the mean value of eiection fraction on admission was 46±9%. One patient presented a reversible dynamic left ventricular outflow obstruction associated with moderate mitral regurgitation. All patients presented an elevation of myocardial enzymes (mean peak Troponin I: 8.3±7 ng/ml, mean peak CK-MB: 22±8 UI/L) and had normal vessels (without significative stenosis) at coronary angiography.
The mean hospidalization time was 6±2 days. Discharge echocardiography control showed an improvement of myocardial kinesis with mean ejection fraction 60±4%. A complete resolution of electrocardiography and echocardiography alterations showed in all patients after some weeks.
Conclusions: in our cath-lab the prevalence of Tako-Tsubo cardiomiopaty among patients undergoing coronary angiography for suspected acute coronary syndrome (myocardial infarction or unstable angina) was 1,25% (7/558); in female population was 4,1% (7/171).

P381 Is transient left ventricular apical ballooning a benign disease? Comparison with anterior myocardial infarction

B. Schneider, K. Peters, S. Koch, J. Stein. *Sana Kliniken, Klinik Fuer Kardiologie, Luebeck, Germany*

Background: Transient left ventricular (LV) apical ballooning (AB) is characterized by chest pain, ECG changes and LV apical akinesia mimicking anterior myocardial infarction (AMI) in the absence of coronary artery disease. Since LV function returns to normal within days, prognosis of AB is believed to be excellent.
Methods and Results: Among 2086 patients with an acute coronary syndrome (ACS) undergoing coronary angiography over a 6.5-year period, 33 patients (1.6%) with apical ballooning (AB) were identified (29 f, 4 m, age 72±11 years). Prevalence of AB was 4.1% in females and 0.3% in males with ACS. Patients with AB were compared to 28 consecutive age and sex matched AMI patients undergoing PCI of the LAD with similar findings on LV angiography. Chest pain at presentation was more frequent in AMI (28/28 vs 24/33) whereas 24% of AB patients complained about dyspnea (p<0.01). A triggering event was present in 1/28 AMI vs 31/33 AB patients (p<0.001) consisting of emotional (n=20) and/or physical stress (n=23). There was no significant difference regarding the number of patients with ST-segment elevation or T-wave inversion between both groups. In AB levels of CK (273±297 vs 2076±1706 U/l) and troponin I (7.5±6.9 vs 238±241 ng/ml) were significantly lower than in AMI (p<0.001). Ejection fraction was similar (54±15 vs 55±13%) but LVEDP (25±9 vs 31±9 mm Hg) was higher in AMI (p<0.02). Complications occurred in 17/33 (51%) AB vs 5/28 (18%) AMI patients (p<0.01). One patient in each group died from cardiogenic shock. One AMI patient had reinfarction due to stent thrombosis. Ventricular tachycardia was observed only in AMI (4/28 vs 0/33, p<0.05). Other complications were seen only in AB: pulmonary edema (6/33 vs 0/28, p<0.05), atrial fibrillation (n=5), transient LV pressure gradient (n=5), LV thrombus and/or stroke (n=4), RV apical involvement (n=3). Normalization of LV function (within 24±21 days) and ECG normalization (within 91±108 days) occurred in all AB but in only 1/28 AMI patients (p<0.001).
Conclusion: Despite similar symptoms, ECG changes, ejection fraction and a lower level of cardiac markers, AB patients have a significantly higher rate of severe complications compared to AMI patients undergoing successful PCI. Although LV function and ECG changes return to normal within days to weeks, the initial clinical presentation of AB is not at all benign, and careful monitoring during in the acute phase is required.

P382 Midventricular ballooning syndrome in patients with acute myocardial infarction: clinical findings, prognosis and comparison with apical ballooning syndrome

M. Previtali, A. Repetto, R. Camporotondo, S. Panigada, E. Chieffo, L. Tavazzi. *IRCCS Policlinico S.Matteo, Cardiology, Pavia, Italy*

Background: Midventricular ballooning syndrome (MVBS) has been recently described as a variant of left ventricular apical ballooning syndrome (ABS).The aim of the study was to assess the prevalence and clinical characteristics of MVBS and to compare it with ABS in a population with acute myocardial infarction (AMI).
Methods and Results: In a population of 1491 consecutive pts with ST- or non-ST elevation AMI who underwent coronary angiography within 36 hours from symptom onset 7 pts (0.4%) fulfilled the diagnostic criteria for MVBS including akinesia of mid-LV segments with normal basal and apical segments and normal coronary arteries or ≤ 50% stenosis and 23 (1.5%) those for ABS; all had serial 2-D echo and were followed up for 25±11 months; 22/30 underwent dobutamine echo for evaluation of LV dynamic obstruction. The clinical characteristics of MVBS and ABS are compared in the Table.

	MVBS	ABS	p value
Mean age (years)	58±9	72±9	<.005
Sex (men/women)	0/7	0/23	ns
Triggering event (%)	28	48	ns
ECG: ST elevation/negative T wave (%)	43/57	43/57	ns
Acute Ejection Fraction (%)	48±11	46±9	ns
Discharge Ejection Fraction (%)	53±5	54±9	ns
Acute Wall motion score index	1.6±.1	1.6±.1	ns
Discharge Wall motion score index	1.3±.1	1.3±.2	ns
Abnormal (>27) TIMI Frame Count on LAD/Cx/RCA (%)	27/42/42	30/52/34	ns
Dobutamine-induced LV obstruction (%)	0	22	ns
Death/Major complications/minor complications (%)	0/0/28	0/0/13	ns
Recurrences (%)	0	8	ns

LAD: Left anterior descending coronary artery; Cx: Left circumflex artery; RCA: Right coronary artery.

Conclusions: 1) In a population with AMI studied within 36 hours the prevalence of MVBS is 0.4% compared to 1.5% of ABS; both affects post-menopausal women. 2) Prognosis of MVBS is good, with recovery of regional function and no death, major complication or recurrences. 3) Pts with MVBS are younger and have a lower prevalence of dynamic obstruction than pts with ABS, but the other clinical and angiographic characteristics and the prognosis are similar.

CARDIAC SURGERY: RECENT ADVANCES IN CORONARY ARTERY SURGERY AND HEART TRANSPLANTATION

P384 No proarrhythmia found testing skeletal myoblast implants in the healthy swine heart at short term

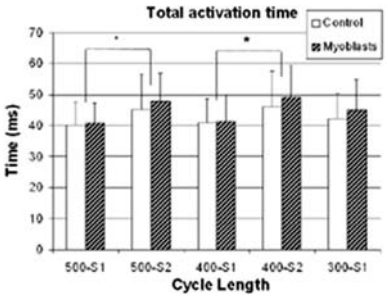
J. Moreno Planas[1], J. Perez-Villacastin[2], J.L. Rojo[1], N. Perez-Castellano[1], E. Usandizaga[1], S. Garraza[1], C. Macaya[1]. *[1]Hospital Clinico San Carlos, Cardiology Dept, Unidad Arritmias. 2N, Madrid, Spain; [2]Madrid, Spain*

It remains controversial whether skeletal myoblasts implants facilitate ventricular tachyarrhyhmias. We sought to determine in the healthy pig heart whether implants promote ventricular arrhythmias at electrophisiologic study (EPS) and to evaluate epicardial wavefront propagation over implanted and control areas in isolated hearts.
Methods: from 8 pigs, 30-40kg, myoblasts were isolated and incubated from biopsy samples of the sternohyoid muscle. A mean of 125±37 million cells were subepicardially implanted, 1-month later, over a ~1 cm^2 area of the mid anterolateral aspect of the LV. After 3-4 weeks, an EPS was performed, pacing epicardially

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

on the LV at 500, 400 and 300 ms using one (n=6) or up to two (n=2) extrastimuli, to test for ventricular arrhythmias. Hearts were then excised and, on a Langendorff setup, optical mapping (Di-4ANEPPS) of the implanted and an adjacent control epicardial (3x3cm^2)surfaces of the LV was performed. Movies recorded wavefront propagation, pacing at the left upper corner of each field of view at 500, 400 and 300ms and after one extraestimulus (S2) close to refractoriness at the formers.

Results: at EPS no ventricular tachyarrhythmia was induced in any in-vivo heart. In the isolated hearts, wavefronts propagated homogeneously in both type of surfaces, with no significant slow propagation zones. No arrhythmia was induced in this setting either.The figure shows the time required for the paced wavefront (S1 or S2) to depolarize the whole field of view. S2 wavefronts were significantly slower than S1. No significant difference was found comparing myoblasts and control zones.



Total activation time

Conclusion: an isolated myoblasts implant do not seem to slow local conduction significantly enough to facilitate ventricular tachyarrhthmias due to reentry.

P385 Crucial role of heart cell Ca 2+ handling in initiation, sustaining and termination of lethal arrhythmias

N. Tribulova[1], S. Seki[2], P. Kaplan[3], E. Babusikova[1], V. Knezl[4], S. Mochizuki[5], M. Manoach[6]. *[1]Institute For Heart Research Sas, Bratislava, Slovak Republic; [2]Division of Cardiol, Jikei Univ,, Tokyo, Japan; [3]Dept. Biochem. Fac Med, Comenius Univ., Martin, Slovak Republic; [4]Inst.Exper.Pharmacol, SAS, Bratislava, Slovak Republic; [5]Division of Cardiol, Jikei Univ, Tokyo, Japan; [6]Dept. Physiology, Tel Aviv Univ,, Tel Aviv, Israel*

Sudden cytosolic free Ca^{2+} ($[Ca^{2+}]i$) disturbances triggers VF, particularly due to spontaneous Ca^{2+} oscillations and Ca^{2+} overload induced gap junction channels uncoupling. We hypothesize, therefore, that prevention of Ca^{2+} overload and/or decrease of elevated $[Ca^{2+}]i$ should be associated with prevention and/or termination of VF and sinus rhythm restoration. The aim of the study was 1) to monitor myocardial $[Ca^{2+}]i$ levels during the development and persistence of VF as well as during its conversion to sinus rhythm. 2) to detect cell-to-cell gap junction coupling alterations prior occurrence and immediately after termination of VF when sinus rhythm appeared. 3) to analyse as whether susceptibility of guinea pig heart to electrically-induced VF is associated with the activity of main myocardial Ca^{2+} cycling system, i.e. SERCA2a.

Methods: $[Ca^{2+}]i$ was continuously monitored using Fura2, optical fibre probe and analysing system in isolated guinea pig heart subjected to K^+ deficient perfusion to induce sustained VF followed by perfusion with standard solution containing antiarrhythmic drug stobadine (10^{-6}M) to restore sinus rhythm as indicated ECG recordings. Ca^{2+} overload-related cardiomyocyte injury and impairment of intercellular coupling and synchronisation were revealed by ultrastructure examination. Sarcoplasmic reticulum Ca^{2+} ATPase activity (SERCA2a) was analysed by biochemical method. Results showed that elevation of diastolic $[Ca^{2+}]i$ reached 180% of baseline level prior occurrence of VF that was associated with an impairment of gap junction mediated cell-to-cell coupling, whereby VF sustaining lead to further $[Ca^{2+}]i$ increase and aggravated cell-to-cell synchronisation. While VF conversion to sinus rhythm was dependent on the restoration of basal $[Ca^{2+}]i$ levels facilitated by stobadine and it was linked with attenuation of cell-to-cell coupling disorders. SERCA2a activity was significantly decreased in old guinea pig hearts that were susceptible to electrically-induced VF in comparison to young hearts that were rather resistant. The latter developed Ca^{2+} overload-induced cardiomyocyte injury inlcuing marked impairment of cell-to cell coupling only after prolonged repetitive electrical stimulations different to old guinea pig hearts that developed these changes after a few electrical stimuli. Collectively these findings indicate that modulation of Ca^{2+} handling may be critical in development, sustaining and termination of VF. It appears that prevention of Ca^{2+} overload in diseased heart by enhancement of SERCA2a activity can protect against malignant arrhythmias.

P386 Role of intracellular calcium waves in triggered arrhythmias -simultaneous confocal recording of single-cell membrane potentials and calcium dynamics in the rat heart-

H. Tanaka, K. Fujiwara, H. Mani, T. Nakagami, M. Oyamada, T. Takamatsu. *Kyoto Prefectural University of Medicine, Pathology And Cell Regulation, Kyoto, Japan*

Intracellular calcium (Ca) waves have been regarded as an important substrate for arrhythmias. Previous studies in isolated myocytes revealed that Ca waves generate membrane depolarization by Na-Ca exchange current and other Ca-activated currents, leading to triggered activity. However, it is unknown whether Ca waves in the individual myocytes really contribute to triggered arrhythmias in the heart in situ. To obtain the direct relationship between Ca waves of individual myocytes and the corresponding membrane potentials (Vm) in the heart, we established a method for detecting intracellular Ca (Ca(i)) dynamics and Vm simultaneously with dual-rapid confocal microscopy (x40 objective lens, 3.7 ms/frame, 192 x 128 pixels) equipped with an image splitting module. Langendorff-perfused rat hearts loaded with both the Ca(i) indicator Fluo4/AM and voltage-sensitive dye RH237 were applied to the microscopy under perfusion with bicarbonate-buffered solution added with cytochalasin D (40 μM) at room temperature. Optical signals for Ca(i) and Vm were obtained simultaneously from the subepicardial myocardium excited by Argon/Krypton (488/568nm) laser. The dual, non-overlapping signals for fluo3 and RH237, obtained by splitting the emitted light with a dichroic filter (565nm) and the respective emission filters of 535/40 nm and $>$ 650 nm, were detected by a high-speed CCD camera. During sinus rhythm the myocytes exhibited spatially uniform Ca transients with simultaneous action potentials among individual cells. In contrast, under perfusion with low K (2.7 mM) solution with isoproterenol (20 nM), myocytes exhibited Ca waves sporadically and asynchronously in between the Ca transients, where no discernible membrane fluctuation was detected during diastole. Cessation of high-frequency pacing from the apex ($\sim$ 5 Hz) was followed by triggered beats and subsequent synchronous Ca waves among individual cells that were accompanied by fluctuations of Vm. Detailed observations of the Ca(i)- and Vm-signals revealed that Ca waves precede the membrane depolarization. In addition application of ryanodine (1 μM) abolished both the triggered activity and subsequent fluctuation of Vm in association with disappearance of Ca waves, indicating a causative role of Ca release from the sarcoplasmic reticulum for membrane depolarization. In conclusion, our present observations provide a direct clue for arrhythmogenic potentials of Ca waves in the heart in situ. While sporadic and asynchronous Ca waves are not electrogenic, the waves can contribute to triggered arrhythmias when they emerge synchronously and prevalently within the heart.

P387 Reduction of repolarization reserve unmasks the role of late sodium current in rabbit isolated hearts

L. Wu[1], S. Rajamani[2], H. Li[2], J.C. Shryock[2], L. Belardinelli[2]. *[1]Cv Therapeutics, Inc., Pharmacological Sciences Dept., Palo Alto, United States of America; [2]CV Therapeutics, Palo Alto, United States of America*

Background: The amplitude of the late sodium current (I_{NaL}) is normally small. However, when the delayed rectifier K^+ current (I_{Kr}) is reduced and repolarization reserve is decreased, the contribution of I_{NaL} to ventricular repolarization could be unmasked. To test this hypothesis, the effects of tetrodotoxin (TTX) and ranolazine, known I_{NaL} inhibitors, on ventricular repolarization were determined in the presence of the I_{Kr} inhibitor, E-4031.

Methods: Female rabbit hearts were isolated and paced at 1 Hz and exposed to E-4031 (1-60 nM) in the absence and presence of TTX (0.1-1 μM) and ranolazine (5-30 μM). Monophasic action potentials (MAP) from both epicardium and endocardium, and 12-lead ECG signals were recorded continuously.

Results: E-4031 concentration-dependently prolonged the epicardial MAP ($MAPD_{90}$) ms from 180$\pm$3 to 254$\pm$6 ms (n=21, $p<0.001$), and increased transmural MAPD dispersion from 18$\pm$4 to 90$\pm$10ms (n=21, $p<0.001$). Spontaneous or 3-sec pause triggered polymorphic ventricular tachycardia (TdP) occurred in 19 out of 21 hearts. Ranolazine concentration-dependently prolonged epicardial $MAPD_{90}$ by 32$\pm$4% (n=7, $p<0.01$) with no effect on transmural dispersion of $MAPD_{90}$, consistent with its effect to reduce I_{Kr}. TTX alone had no effects on $MAPD_{90}$ or transmural dispersion of $MAPD_{90}$ (n=5, $p>0.05$). In the presence of 60 nM E-4031, ranolazine (10 μM) shortened the $MAPD_{90}$ and decreased transmural dispersion by 19$\pm$5 and 40$\pm$9 ms, respectively (n=9, $p<0.01$). TTX (1 μM) shortened the $MAPD_{90}$ and decreased transmural dispersion by 33$\pm$8 and 47$\pm$11 ms, respectively (n=10, $p<0.05$). E-4031 (60 nM)-induced spontaneous and pause-triggered TdP were completely abolished by ranolazine (10-30 μM, n=11) and TTX (1 μM, n=12). Ranolazine and TTX caused no or minimal changes in QRS interval, hence, their effects are unlikely to be due to the inhibition of peak $I_{Na.}$

Conclusion: Inhibition of I_{NaL} can reverse the prolongation of APD and arrhythmogenesis caused by a pure I_{Kr} blocker. This finding could explain the observations that sodium channel blockers are effective in reducing proarrhythmic risk when repolarization reserve is reduced.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P388 In vivo assessment of Tpeak to tend interval as an index of global dispersion of ventricular repolarization during right and left ventricular pacing: a monophasic action potential mapping in swine

Y. Xia[1], O. Kongstad[2], P. Platonov[2], M. Holm[3], B. Olsson[3], S. Yuan[3]. *[1]Lund, Sweden; [2]Lund University, Dept of Cardiology, Lund, Sweden; [3]Johnson and Johnson Inc, Biosense Webster, Brussel, Belgium*

Introduction: The peak to the end of the T wave (Tp-Te) has been suggested to be an index of transmural dispersion of ventricular repolarization (DVR) in ventricular wedge preparations. However, recent in vivo studies suggested that Tp-Te interval is highly correlated with the global DVR, but not transmural DVR. In this study we try to analyze the relationship between global DVR and Tp-Te interval under different pacing protocols.
Methods: Using the CARTO mapping system, global monophasic action potential (MAP) mapping of the left and right ventricular endocardium in total 120±24 sites were performed during RA pacing, RV apical endocardial (RVEndo) and LV lateral epicardial (LVEpi) pacing in 10 healthy pigs. Local MAP duration and end-of-repolarization (EOR) time were measured and 3D maps of the EOR were constructed. Global dispersion of EOR times was calculated as the maximal difference of the EOR times in each map. ECG was simultaneously recorded during MAP mapping, from which Tp-Te intervals were acquired.
Results: 1) The global dispersion of EOR times during LVEpi pacing (93±18 ms) is significantly greater than those during RA (59±11 ms, p0.05) 2) Tp-Te intervals during LVEpi pacing (71±8 ms) is also significantly greater than those during RA (58±8 ms, p 0.05). 3) The global DVR correlate well with the Tp-e intervals ($p<0.05$; $r = 0.78$) in all the pigs, though the magnitude of the latter underestimated global DVR by about 23% during LVEpi pacing.
Conclusions: Tp-Te interval is highly correlated with the global DVR either during normal ventricular activation sequence, or during different pacing protocols. These findings suggest that Tp-Te interval might be served as a non-invasive estimation of global DVR

P389 Right ventricular endocardial mapping in Brugada syndrome patients reveals prolonged activation and increased electrogram fragmentation

P.G. Postema, P.F.H.M. Van Dessel, J.M.T. De Bakker, L.R.C. Dekker, A.C. Linnenbank, A.A.M. Wilde, H.L. Tan. *Amsterdam Medical Centre, Cardiology, Amsterdam, Netherlands*

Purpose: Brugada syndrome (BS) is characterised by specific ST segment elevation (type 1) in the right precordial ECG leads, which may be unmasked by Na-channel blockers, in the absence of apparent structural changes. The pathophysiology of the specific ECG and ventricular tachyarrhythmias remains debated but is thought to arise from depolarisation or repolarisation heterogeneity in the right ventricle (RV). We aimed to study whether RV activation in BS patients is impaired using endocardial catheter mapping.
Methods: CARTO mapping of the RV during sinus rhythm in 6 BS patients referred for electrophysiologic study (age 48±9 years) was compared to 3 controls referred for AV nodal re-entrant tachycardia ablation (n=2) or atrial tachycardia ablation (n=1) (46±13 years). In 2 BS patients with a type 2 ECG at baseline, a re-map was made after ajmaline had induced a type 1 ECG.
Results: Of the BS patients, 2 had aborted sudden cardiac death (SCD) or syncope, 4 a type 1 ECG at baseline, 2 an ajmaline-induced type 1 ECG, 4 an SCN5A mutation and 3 a family history of SCD or BS. BS patients with a type 1 ECG (at baseline or ajmaline-induced) had longer RV activation times, more fragmentation (expressed as mean number of intrinsic deflections per electrogram), and longer PQ and QRS intervals than controls (see table).

Brugada syndrome patients vs. controls

	RV activation time (ms)	Fragmentation	PQ (ms)	QRS (ms)
Brugada syndrome (BS)	94±19	1.42±0.14	225±42	125±30
Controls	66±9	1.13±0.03	141±11	79±4
p (BS vs. controls)	0.048	0.01	0.01	0.04

Conclusions: In BS patients with a type 1 ECG, endocardial RV activation is prolonged and electrograms are more fragmented compared to controls. This may be a sign of asynchronous and slowed impulse transmission, caused by structural derangements (e.g., fibrosis) which remain undetected by routine cardiac imaging. Ultrastructural derangements which cause conduction slowing (e.g., fibrosis) may be an important contributor to the ECG features and ventricular tachyarrhythmias in BS.

P390 Effects of a selective phosphodiesterase Type III inhibitor on the defibrillation efficacy

N. Chattipakorn[1], N. Kanlop[2], K. Shinlapawittayatorn[1], S. Chattipakorn[1], N. Lailerd[1]. *[1]Cardic Ep Research And Training Center, Dept. of Physiology, Faculty of Medicine, Chiang Mai, Thailand; [2]Cardiac EP Research and Training Center, Chiang Mai, Thailand*

Cilostazol, a new potent cyclic nucleotide phosphodiesterase type-III inhibitor, is primarily used as a strong antiplatelet agent. Cilostazol has also been shown to diminish the action potential notch and suppress the substrate and trigger for ventricular tachycardia/fibrillation (VT/VF), leading to an increasing use of cilostazol for reducing episodes of VF in the Brugada syndrome patients. However, the effect of cilostazol on defibrillation efficacy has never been investigated. We sought to test the hypothesis that intravenous administration of cilostazol can significantly decrease the defibrillation threshold (DFT).
Methods and Results: A total of 18 pigs (20- 30 kg) were randomly assigned into 3 groups. In each pig, the DFT was determined at the beginning of the study using a three-reversal up/down protocol. Each shock (RV-SVC, biphasic) was delivered after 10 seconds of VF. After a control DFT was obtained, a solution containing 200-mg cilostazol (group I, n=8) was injected intravenously at the rate of 2 mL/min over 50 minutes. The DFT (drug-DFT) was determined again after the drug administration. In group II (n=5) and group III (n=5), 100-mg cilostazol and 100-mL saline were infused, respectively, and the DFT was determined similar to that in group I. In group I, the drug-DFT was significantly lower than the control DFT (Table). This accounts for the reduction of ~13% by peak voltage, and ~25% by total energy. In groups II and III, the drug (or saline) DFT was not different than the control DFT (Table).

Parameters	Group I (n=8)		Group II (n=5)		Group III (n=5)	
	Control	200-mg Cilostazol	Control	100-mg Cilostazol	Control	100-mL saline
Peak voltage (V)	486±65	421±48*	516±65	488±68	407±54	407±51
Total energy (J)	16±4	12±3*	18±5	16±4	12±3	12±4
Systolic pressure (mmHg)	93±15	91±12	115±22	116±15	102±7	101±8
Heart rate (beats/min)	86±20	82±17	85±22	99±4	110±11	112±11

Conclusion: 200-mg cilostazol infusion significantly decreases the DFT. This finding indicates that cilostazol could increase the defibrillation efficacy by reducing the defibrillation threshold.

P391 Fish oil likewise atorvastatin decrease susceptibility of hypetriglycerolemic rat hearts to ventricular fibrillation

N. Tribulova[1], V. Knezl[2], M. Fialova[3], K. Dlugosova[1], L. Okruhlicova[1]. *[1]Institute For Heart Research Sas, Bratislava, Slovak Republic; [2]Institute of Exper. Pharmacol Sas, Bratislava, Slovak Republic; [3]Institute for Heart Research Sas, Bratislava, Slovak Republic*

We have shown previously that rats suffering from hereditary hypertriglycerolemia (hHTG) are characterised by structural and gap junction channel, connexin-43 (Cx43), remodelling that may account for their increased susceptibility to ventricular fibrillation (VF). Since fish oil rich in n-3 polyunsaturated fatty acids (PUFA) as well as lipid-lowering drugs, such as statins were shown to possess antiarrhythmic potential, the aim of this work was to examine their effects on distribution and/or expression of Cx43, integrity of cardiomyocytes and their junctions as well as on threshold for VF.
Methods: 3 month-old male hHTG and age-matched Wistar rats were divided to six groups: 1) Wistar rats untreated 2) Wistar rats feed with PUFA (40mg/100g of body weight) for 2 month. 3) Wistar rats treated with Atorvastatin (0.05mg/100g of body weight) for 2 month. 4) hHTG rats untreated. 5) hHTG rats fed with PUFA (40mg/100g of body weight) for 2 month. 6) hHTG rats treated with Atorvastatin (0.05mg/100g of body weight) for 2 month. Isolated perfused heart model was used to test VF threshold.Ventricular tissues of additional rats from each group were processed for in situ immunolabelling of Cx43 and electron microscopy examination. Results showed that VF threshold of hHTG rat hearts was less than in normal Wistar rats, i.e. 15mA vs 25mA. While PUFA supplementation and Atorvastatin treatment resulted in a significant increase of VF threshold to 40mA and 45mA respectively, in hHTG rat hearts. Moreover, in 3 PUFA fed hHTG rats only transient VF could be induced using repetitive 45mA test stimulus. Immunolabelling of Cx43 revealed pronounced changes in distribution of gap junctions, i.e. increased number of Cx43-positive gap junctions on lateral surfaces of the cardiomyocytes, in addition to typical intercalated disc related gap junctions. In parallel, electron microscopy revealed neo-formation of lateral ("side-to-side") gap junctions as well as cytoplasmic annular profiles of the gap junctions in the vicinity of intercalated discs. These changes, i.e. "lateralisation" and "internalisation" of Cx43 containing gap junctions were not affected either by PUFA or Atorvastatin. However, integrity of the cardiomyocytes and their junctions were better preserved in hHTG rat hearts upon treatment. It is concluded that PUFA likewise Atorvastatin exert significant antifibrillating effects in hHTG rat hearts. Although myocardial structural and gap junction Cx43 remodelling was not eliminated by the treatment its beneficial effect on Cx43 channel conductivity can not be ruled out rather examined by further electrophysiological studies.

P392 Ischemia-induced electrotonic uncoupling facilitates twa in animals susceptible to ventricular fibrillation

C.L. Del Rio, M. Kukielka, B.D. Clymer, G.E. Billman. *The Ohio State University, Anesthesiology, Columbus, United States of America*

Background: Repolarization heterogeneities, reflected as T-wave alternans (TWA), have been linked to increased vulnerability to ventricular fibrillation (VF) in different settings, including myocardial ischemia. However, the mechanisms underlying TWA and VF-vulnerability remain largely unknown. Evidence

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

suggests that ischemia-induced TWA in the surface ECG arise from oscillations in action potential duration (APD). Interestingly, it has been shown that electrotonic (passive) loading, resulting from heterogeneities in the ventricle, triggers the remodelling of the Ito current and changes in APD. Similarly, structural barriers between neighbouring regions of myocardium are known to facilitate TWA development. Hence, it is possible that ischemia-induced electrotonic uncoupling may enhance TWA and lead to malignant arrhythmias.

Materials and Methods: To test this hypothesis, dogs with healed anterolateral (LAD) infarction (MI), were chronically instrumented with myocardial electrical impedance (MEI) electrodes, for measurements of electrotonic-coupling in the left-circumflex (LCX) distribution. After recovery, 2-minute LCX coronary artery occlusions (CAO) were made at rest, and, during the last minute of submaximal exercise (in order to test VF-susceptibility); 10 animals developed VF (susceptible, S) and 10 did not (resistant, R). TWA were quantified by power spectral analysis of the ECG (15s-epochs). Data are presented as mean±SEM and were analyzed using two-way ANOVA (w/Tukey test, $P<0.05$).

Results: No TWA amplitude differences were observed early (30s) during CAO (S: 6.6±1.9mV vs. R: 6.9±1.4mV, N.S.). However, after 90s of CAO, alternans increased significantly in susceptible animals (S: 24.4±5.9mV vs. R: 11.1±2.1mV, $P<0.05$), despite similar degrees of CAO-induced electrotonic uncoupling (S: +21±4Ω vs. R: +17±4Ω, N.S.). Furthermore, in susceptible animals, TWA were linearly correlated (R=0.71, $P<0.05$) with the degree of uncoupling (MEI changes).

Conclusion: Together, these data suggest that ischemia-induced electrotonic uncoupling facilitates the development of ventricular electrical oscillation (such as TWA) in of post-MI animals susceptible to malignant arrhythmias and sudden death.

P393 Methadone maintenance therapy for opiate addiction and prolongation of QT interval

A. Pathak, A. Perrin-Terrin, J.L. Montatstruc, M. Lapeyre-Mestre.
Medical Univ. of Toulouse, Dept. of Pharmacology, Toulouse, France

Purpose: Recent case series have suggested the role of synthetic opioïd methadone in QT prolongation and Torsades de Pointes (TdP) ventricular arrhythmia. Prolonged QT and TdP can occur over a wide range of dosages including those usually recommended for opiate maintenance. Methadone coprescription with drugs known to cause Tdp or with drugs known to interfere with the metabolism of methadone will enhance the cardiac toxicity of methadone. This study assessed frequency of interval QT prolongation and QT dispersion in a population of patients treated by methadone and associated factors.

Methods: In a first step, the study was a retrieval and retrospective analysis of reports of adverse effects associated with Methadone voluntary reported to the French Pharmacovigilance data base from 1985 to 2005. Then, the study design was a cross-sectionnal observational study. Patients were recruited from specialized methadone centres and from hospital units. We measured QT interval, QT dispersion and simultaneous serum methadone levels. QT was corrected from heart rate using Bazett's method. Data concerning methadone treatment, coprescribed licit or illicit psychoactive drugs, medical history, and other clinical and biological data were collected from patient's interview and from medical files.

Results: Among the 550 methadone related reports in the French Pharmacovigilance database, we found 4 cases of QT prolongation (2 with TdP) and 4 cases of sudden death. All patients were treated with oral methadone, with a median daily dose of 62.5mg (range 40-80mg). In parallel, we included 42 methadone treated patients during 6 months (December 2004-May 2005) for whom a standard 12-lead electrocardiogram was performed. The value of QTc interval was 412±32 ms [range 320-485] and QTc dispersion was 54±33ms [range 15-145]. A prolonged QTc and QTc dispersion were respectively observed in 7% and 12% of cases. A multiple linear regression found a significant relationship between QTc or QTc dispersion and history of cardiac disease, methadone dose, recent increase in methadone dose, use of cocaïne and use of CYP 450 inhibitors.

Conclusion: Methadone can prolong the QTc interval at a dose usually recommended for addiction maintenance treatment, especially when it is coprescribed with other drugs such as CYP 450 inhibitors. Eventhough no case of ventricular arrhythmia or TdP were observed in this sample of patients, a systematic ECG, in patients with cardiac history or treated with CYP450 inhibitors or with drug known to prolong the QT interval, could be useful during methadone treatment.

P394 Supplementation of old hypertensive rats with n-3 polyunsaturated fatty acids (PUFA) results in protection againts ventricular fibrillation

M. Fialova[1], K. Dlugosova[1], L. Okruhlicova[1], V. Knezl[2], J. Drimal[2], N. Tribulova[1]. *[1]Institute for Heart Research, Bratislava, Slovak Republic; [2]Institute of Experinental Pharmacology, Bratislava, Slovak Republic*

Clinical trials have shown that consumption of fish oil, rich in PUFA reduces incidence of cardiovascular disease and sudden cardiac death, while experimental studies suggest their antiarrhythmic effects. However, cardioprotective mechanisms of PUFA are not fully elucidated. We have shown previously that hypertension-related myocardial remodelling and defective connexin-43 (Cx43) gap junction channels are involved in the development of malignant arrhythmias, such as ventricular fibrillation (VF), which can be facilitated by aging. Aim of the study was, therefore, to examine effects of PUFA on gap junction Cx43 expression and cell-to-cell communication as well as susceptibility of aged spontaneously hypertensive rats (SHR) to VF. Male and female 14 moth-old SHR with and without PUFA feeding (20 mg/day for 2 months) were used. In situ myocardial Cx43 was detected by immunofluorescence technique using mouse monoclonal antibodies and ultrastructure examination was performed to detect impairment of gap junction channel mediated intercellular communication. PUFA supplementation resulted in significant blood pressure and heart rate reduction in both male and female SHR. All untreated SHR hearts were prone to develop sustained VF already after first or a few repetitive electrical stimuli, in isolated heart preparation. In contrast, the number of stimuli was increased and incidence of VF was suppressed by 57% and 67% in PUFA-treated male and female SHR. Notably, PUFA supplementation led to clear anti-fibrillating effects despite myocardial remodelling, i.e. fibrosis and hypertrophy were not eliminated. Immunolabelling of Cx43 showed besides end-to-end type (intercalated disc-related) enhanced expression of lateral (side-to-side type) of Cx43-positive gap junctions. Neither this pattern of distribution nor Cx43 density was significantly affected by PUFA. However, cardiomyocyte ultrastructure and intercellular gap junction integrity of PUFA-treated SHR heart resistant to VF were better preserved compared to untreated SHR vulnerable to VF. Preservation of cell-to-cell communication resulted in maintenance of synchronised myocardial contraction as indicated by uniform patterns of sarcomere shortening in majority of cardiomyocytes. Thus, PUFA exert clear antifibrillating effects in aged SHR, whereby protection of Cx43 mediated cell-to-cell coupling likely, due to preservation of cell membrane integrity, may be involved in.

P395 Effects of inflammation in alimentary lipemia in patients with a history of ventricular fibrillation during acute myocardial infarction

T. Kaelsch[1], E. Elmas[1], X.D. Nguyen[2], T. Sueselbeck[2], C.E. Dempfle[2], M. Borggrefe[2]. *[1]University Hospital Mannheim, 1st Department of Medicine, Mannheim, Germany; [2]Institute of Transfusion Medicine, Mannheim, Germany*

Aims: Acute myocardial infarction, often occurring postprandially, can be complicated by ventricular fibrillation. The role of acute alimentary lipemia and inflammation in the occurrence of ventricular arrhythmias in acute myocardial infarction have not been described yet.

Methods and Results: Before and two hours after consumption of a defined fatty meal, blood samples of 27 patients with a history of acute myocardial infarction (AMI) were incubated with lipopolysaccharide (LPS). In 10 patients, AMI was complicated by ventricular fibrillation (VF), in 17 patients, AMI occurred without VF. CD40-ligand and CD62P expression on platelets, tissue-factor binding on monocytes and platelet-monocyte aggregates were measured with flow cytometry. Soluble CD40-ligand plasma levels were measured with an ELISA.

With the meal, serum triglyceride levels increased from 211.85±94.60 mg/dl to 273.59±122.52 mg/dl (p=0.0002). LPS stimulation before the meal showed a non-significant tendency to increase platelet-monocyte aggregates and tissue factor on monocytes in both patient groups. LPS stimulation in acute alimentary lipemia significantly increased tissue factor expression on monocytes in both patient groups and platelet-monocyte aggregates in patients with VF. Baseline plasma levels of soluble CD40L did not differ significantly between both groups. Acute alimentary lipemia significantly decreased total plasma levels of sCD40L, leading to a significantly lower level of sCD40L in patients with a history of VF.

Demographic Characteristics

	With VF (n=10)	Without VF (n=17)	p-value
Mean age [yr]	62.8±11.9	61.9±9.2	n.s.
Male sex [%]	80.0	64.7	n.s.
Smoking [%]	30.0	35.2	n.s.
Hyperlipidemia [%]	80.0	64.7	n.s.
Hypertension [%]	40.0	29.4	n.s.
Diabetes [%]	20.0	17.6	n.s.
Medication:			
Beta-blockers [%]	80	94.1	n.s.
ACE-Inhibitors [%]	70.0	82.4	n.s.
Aspirin [%]	100	94.1	n.s.
Statins [%]	90.0	100.0	n.s.
Ejection fraction [%]	59.5	59.6	n.s.

Conclusions: Alimentary lipemia enhances procoagulatory effects of inflammatory stimulation in patients with a history of AMI complicated by ventricular fibrillation. These observations might reveal a mechanism for an increased risk of VF in acute coronary syndromes in a postprandial state.

P396 IKr blocker induces spiral wave-type of ventricular tachycardia via an increment of on APD dispersion between ventricles but IKs blocker does not

K. Kamiya[1], Z. Lu[2], H. Nakagawa[1], M. Yamamoto[1], R. Niwa[1], H. Honjo[1], I. Kodama[1]. *[1]Nagoya University, Res Inst Environmen Med, Nagoya, Japan; [2]Nagoya, Japan*

Regional heterogeneity of action potential duration (APD) leads to inappropriate dispersion of repolarization in the ventricle and may predispose to cardiac arrhyth-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

mias. Heterogeneous distribution in delayed rectifier potassium channels (IKr and IKs) were reported among epi-, endo- and mid myocardium (dog: Liu et al., 1995) and between base and apex of LV (rabbit: Cheng et al., 1999). Distribution of IKr and IKs between RV and LV was not fully understood. We investigated the the effects of E-4031 (IKr blocker) and chromanol 293B (IKs blocker) on APD dispersion between ventricles and probability of proarrhythmias in rabbit ventricles.
Methods: APD mappings were recorded by a multi-channel optical recording system. IKr and IKs were recorded from single rabbit ventricular myocytes by using the whole-cell patch clamp method.
Results: E-4031 increased APD dispersion between ventricles by a more APD prolongation in RV than in LV. Chromanol 293B produced a similar extent of APD prolongation between ventricles and did not increase APD dispersion between ventricles. IKr blocker led to spiral wave-type polymorphic ventricular tachycardia (VT) in 5 of 8 rabbit ventricles. However, IKs blocker induced no arrhythmias in all 7 ventricles. IKs blocker did not improve the VT inducibility in duced by IKr blocker, while IKr blocker increased the VT inducibility based on IKs blockade. Amplitude of IKr was not significantly different between RV and LV, while IKs was smaller in RV than in LV.
Conclusion: in rabbit hearts, larger IKs in LV than in RV give rise to a substantial difference of repolarization reserve in the two ventricles. This inhomogenous distribution of repolarization reserve underlies the potential proarrhythmic action by Class III antiarrhythmic drugs through IKr blockade.

P397 Intronic branch point mutations, affecting splicing, can cause the Long QT Syndrome

L. Crotti[1], R. Insolia[1], M.A. Lewandowska[2], M. Pedrazzini[1], L. Tosin[1], G. Celano[1], F. Dagradi[1], G.M. De Ferrari[1], F. Pagani[2], P.J. Schwartz[1]. *[1]Fondazione IRCCS Policlinico San Matteo, Cardiology, Pavia, Italy; [2]International Centre for Genetic Engineering, Trieste, Italy*

Background: Mutations in Long QT Syndrome (LQTS) genes are found in approximately 70% of the affected probands but 30% of the patients with clear clinical diagnosis remain genotype negative. Genotyping strategy has so far focused mainly on non-synonymous exonic nucleotide changes or substitutions at canonical splice sites (intron-exon boundaries), overlooking the fact that any intronic variant could lead to profound splicing abnormalities. To define which intronic variants are disease-causing represents a technical and diagnostic challenge. We report our findings in a three-generation LQTS family, in which traditional molecular screening was negative.
Methods and Results: The proband (25 yr) died suddenly in the post-partum period at the telephone ring. Nine family members had a clear QTc prolongation with notched T waves while 7 were asymptomatic with normal QTc. Molecular screening was negative in the coding sequences of the KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2 genes. However, a novel A to G branch point substitution in KCNH2 intron 9 (IVS9-28A/G) was identified. The variant, absent in 400 reference alleles, perfectly co-segregated within the family with the clinical phenotype, suggesting its pathological role. Hybrid minigene splicing assay demonstrated that the mutation induced intron retention, in association with a weak consensus sequence of the polypyrimidine track, in the 3'-acceptor splice-site of intron 9.
Conclusion: This is the first demonstration of a branch point mutation in KCNH2, inducing intron retention and causing a typical form of LQTS type 2. This finding represents the proof of concept that intronic mutations may be responsible for some LQTS cases, negative at molecular screening. Accordingly, genomic investigation of non-canonical splice sequences, can represent a strategy to reduce the number of genotype-negative cases.

P398 Expanding the phenotype of sudden cardiac death

J. De Backer[1], K. Van Beeumen[2], M. Duytschaever[1]. *[1]University Hospital Ghent, Department of Cardiology, 8K12, Ghent, Belgium; [2]Ghent, Belgium*

Background: Familial occurrence of sudden cardiac death (SCD) is related to a variety of clinical conditions, which can be delineated in up to 40% of families through a combination of cardiovascular examination and genetic studies. Genetic testing in these families facilitates the identification of asymptomatic carriers. Patients with Lamin A/C gene mutations are at increased risk for SCD, but "laminopathies" are not included into clinical algorithms of SCD.
Here we present a family with SCD, in the absence of cardiomyopathy related to a Lamin A/C mutation, suggesting that this entity should be added to the list of diseases underlying familial SCD.
Materials and Results: The 40 y old male proband was diagnosed with 2nd degree AV block, type Wenkebach. Electrophysiological study revealed non-sustained VT and a conservative strategy was proposed. The proband died during a badminton game 2 years later. His one year older brother was subsequently also diagnosed with AV block. NSVT was induced on the EP study. An ICD was implanted and successful termination of tachyarrhytmias was documented on 2 occasions. Both brothers had normal echocardiographic findings. Reportedly, their mother had died from a cardiac cause at the age of 70. Their maternal grandfather and a maternal nephew had died suddenly during a sports game at the age of 60 and 37years respectively.
Mutation analysis in the proband's brother revealed the presence of a nonsense mutation in the Lamin A/C gene (p.E358X).
This enabled us to identify the asymptomatic affected son of the proband at the age of 18 years. Electrophysiologic study in him showed suprahissian conduction pathology with prolongation of the HV interval.
Conclusion: SCD associated with AV-block can be related to Lamin A/C mutations, even in the absence of dilated cardiomyopathy and should therefore be included in the clinical algorithm of SCD. Primary prevention with an ICD should be considered in these patients, even in the absence of inducible ventricular arrhythmias

P399 Clinical presentation and evolution of the Brugada syndrome in the elderly

V. Probst[1], J. Mansourati[2], P. Mabo[3], S. Abbey[4], F. Sacher[5], D. Babuty[6], B. Petit[7], J. Albuisson[4], P. Bru[8], H. Le Marec[5]. *[1]Chu Nantes, Cardiology Dept., Nantes, France; [2]Brest, France; [3]Rennes, France; [4]Nantes, France; [5]Bordeaux, France; [6]Tours, France; [7]La Reunion, France; [8]La Rochelle, France*

Introduction: Brugada syndrome (BrS) is an arrhythmogenic disease characterized by an ECG pattern of ST-segment elevation in the right precordial leads and an increased risk of sudden cardiac death. The clinical presentation and evolution of the disease in the elderly is poorly known. The aim of this study was to compare the clinical presentation and evolution of BrS in patients before (young group; YG) and after 65 year-old (elderly group, EG).
Method and result: Patients were considered to be affected by the BrS only if their ECG displayed a type I pattern before or after the sodium blocker challenge. We identified 458 patients (327 males, 71%) younger than 65 and 46 patients (33 males, 71%) older than 65 affected by the BrS. In the YG the mean age at diagnosis was 42±13 years vs 71±6 years in the EG. The diagnosis of BrS was performed in 120 (26%) cases after syncope in the YG and in 10 (21%) in the EG (NS). In the YG, 332 (72%) were index patients and 34 (74%) in the EG (NS). The PR interval 187±33 vs 175±31 ms (p=0.02) and the QRS duration 111±23 vs 103±16 ms (p=0.003) were longer in the EG. A spontaneous type I EKG was found in 213 (46%) patients in the YG and 23 (50%) patients in the EG (NS). A genetic screening for SCN5A mutation was performed in 303 (66%) patients in the YG and 28 (60%) in the EG (NS) and was positive in 92 (30%) and 4 (14%) respectively (NS). An electrophysiological study (EPS) was performed in 220 (34%) patients in the YG and 16 (34%) in the EG (NS). The EPS induced severe ventricular arrhythmias in 89 (40%) in the YG and 7 (43%) in the EG (NS). An ICD was implanted in 164 (36%) patients in the YG and 18 (39%) in the EG (NS). During a mean follow-up of 37±26 months in the YG and 39±21 months in the EG, 13 (3%) in the YG experienced symptoms whereas none of the EG experienced symptoms (NS).
Conclusion: This study demonstrates that the identification of a BrS is not rare in the elderly. The clinical presentation of the BrS is not different before and after 65 year-old even if the clinical evolution in the elderly population seems to be better.

P400 Are there differences in baseline characteristics between genders that could explain the better long-term prognosis of women with a Brugada syndrome?

V. Bertault-Valls[1], R. Carlioz[2], M. Lerecouvreux[3], A. Leenhardt[4], N. Sadoul[5], V. Probst[6], J. Clementy[7], J.M. Davy[8], R. Frank[9], J.J. Blanc[3]. *[1]CHU de Brest, Brest, France; [2]Toulon, France; [3]Hopital Percy, Clamart, France; [4]Hopital Lariboisiere, Paris, France; [5]CHU de Nancy, Nancy, France; [6]CHU de Nantes, Nantes, France; [7]CHU de Bordeaux, Pessac, France; [8]CHU de Montpellier, Montpellier, France; [9]Hopital de la Pitie Salpetriere, Paris, France*

Background and objectives: The Brugada syndrome (BS) is an inherited autosomic dominant disease. But if males and females are genetically equally affected women have been reported to carry a much better long-term prognosis than men. However it has not been precisely evaluated if this discrepancy could be explained by baseline differences between genders in risk factors for subsequent ventricular tachyarrhythmias.
Methods: Before been included in the multicenter French COBRA (Collective Observatory for BRugadA syndrome) registry, ECG of patients suspected to have BS were systematically reviewed and classified by at least 2 blinded experts. Parameters on which risk stratification is currently based were particularly assessed: basal ECG, history of syncope or sudden resuscitated cardiac death, and inducibility of ventricular tachyarrhythmias.
Results: Among the 388 patients included in the COBRA registry, 301 were males and 87 females. Their mean ages were not statistically different (46±18 and 43±12 years). When compared to men, women had or were: 1) more frequently diagnosed during familial screening (46% vs 14%, $p<0.0001$), had more baseline ECG classified out of the Wilde classification at review (53% vs 19% $p<0,0001$), drug challenge (87% vs 59%,$p<0,03$) 2) less aborted sudden death (0%vs 5% $p<0,03$), coved type (30% vs 51%,$p<0,03$) or type 2 WILDE classification (9% vs 19%,$p<0,02$), induction of ventricular fibrillation during electrophysiological test (13% vs 44%, $p<0,001$) 3) a similar proportion of syncope (14% vs 20%) or presyncope (21%vs 13%), familial history of sudden death (40% vs 33%), induction of coved type during drug challenge (68% vs 62%), induction of sustained ventricular tachycardia (14% vs 11%).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusion: Results drawn from this large cohort of patients with a BS suggest that women have more benign baseline characteristics than men. As most of these characteristics are risk factors for subsequent sudden death it seems logical that women with BS have better outcomes than men.

P401 Identification of Long-QT syndrome genetic variants in Sudden Infant Death Syndrome: a prospective study

P. Chevalier[1], G. Millat[1], B. Kugener[1], P. Bouvagnet[1], M. Chahine[2], R. Rousson[1], L. Fayol[1], C. Rodriguez-Lafrasse[1]. [1]*Hospices Civils de Lyon, Lyon, France;* [2]*Laval University, Laval, Canada*

Purpose: To evaluate the prevalence of Long QT syndrome (LQTS) in Sudden Infant Death Syndrome (SIDS).
Methods: We prospectively investigated 60 unrelated cases of SIDS. Once analysed using a standardized autopsy protocol, 37 patients were classified as SIDS and their genomic DNA were subsequently screened by denaturing high-performance liquid chromatography (DHPLC) analysis of the KCNQ1, KCNH2, SCN5A, KCNE1, and KCNE2 genes.
Results: 55% of the infants were males. The peak of death was between the first and fourth months. Six infants (16%) were found to have LQTS variants that could be directly involved in SIDS. Two of them were carriers of two LQTS genetic variants whereas the 4 others cases contained only one mutation.Among the 8 LQTS identified gene variants that could be associated with SIDS, half of them were located on the SCN5A gene (p.S524Y, p.Q692K, p.R975W, p.S1333Y). The other variants were located either on the KCNH2 gene (p.R148W, p.D259N), on KCNQ1 gene (p.G626S), or on the KCNE1 gene (p.T20I). In the family members neither history of sudden cardiac death nor a mutation was identified.
Conclusions: Our results 1) are in agreement with previous studies and confirm that some cases of SIDS could be caused by long-QT syndrome 2) suggest that an ECG would probably identify most infants at risk for sudden death due to LQTS.

P402 Clinical presentation and evolution of the Brugada syndrome associated with a short QT interval

V. Probst[1], F. Sacher[2], D. Babuty[3], P. Mabo[4], J. Mansourati[5], G. Lande[6], F. Kyndt[3], J.J. Schott[3], L. Jesel[7], H. Le Marec[3]. [1]*Chu Nantes, Cardiology Dept., Nantes, France;* [2]*Bordeaux, France;* [3]*Tours, France;* [4]*Rennes, France;* [5]*Brest, France;* [6]*Nantes, France;* [7]*Strasbourg, France*

Introduction: Brugada syndrome (BrS) is an arrhythmogenic disease characterized by an ECG pattern of ST-segment elevation in the right precordial leads and an increased risk of sudden cardiac death. A novel clinical entity characterized by the association of a short QT syndrome (Qtc<360 ms) and a BrS has been described. This syndrome has been link to mutation in the cardiac calcium channel. The aim of this study was to compare the clinical presentation and evolution of BrS in patients in whom the QTc was under 360 ms (short QT group; SG) and patients in whom the QTc was above 360 ms (normal QT group, NG).
Method and result: Patients were considered to be affected by the BrS only if their ECG displayed a type I pattern before or after the sodium blocker challenge. We identified 29 patients in the SG and 463 patients in the NG. The proportion of male patients 26 males, 89% was higher in the SG than in the NG 336 males, 72%, p=0.03. In the SG, the mean age at diagnosis was 44±15 years vs 44±15 years in the NG. The diagnosis of BrS was performed in 10 (34%) cases after syncope in the SG and in 117 (25%) in the NG (p=0.06). In the SG, 26 (89%) were index patients and 332 (71%) in the NG (p=0.03). The PR interval 176±33 vs 176±31 ms (NS) was similar in both groups but the QRS duration 97±12 vs 103±17 ms (p=0.003) and the QTc duration 351±9 vs 416±36 ms (p<0.00001) were shorter in the SG. A spontaneous type I ECG was found in 17 (59%) patients in the SG and 215 (46%) patients in the NG (p=0.06). A genetic screening for SCN5A mutation was performed in 21 (72%) patients in the SG and 304 (65%) in the NG (NS) and was positive in 5 (24%) and 89 (29%) respectively (NS). An electrophysiological study (EPS) was performed in 18 (62%) patients in the YG and 228 (49%) in the EG (p=0.059). The EPS induced VF in 10 (55%) in the SG and 94 (41%) in the NG (p=0.07). An ICD was implanted in 15 (51%) patients in the SG and 164 (35%) in the NG (p=0.06). During a mean follow-up of 35±37 months in the SG and 37±25 months in the NG, 1 (3%) in the SG and 12 (3%) in the EG had appropriated shock (NS).
Conclusion: This study demonstrates that short QT interval is rare (5%) in patients affected by a BrS. The clinical presentation of the BrS with a QTc<360 ms seems to be more severe with a higher proportion of symptomatic and spontaneous type I ECG patients. The frequency of SCN5A mutation is identical in both groups and in this relatively small population, the evolution of this two population seems to be similar. The evaluation of the proportion of patients carrier of a calcium channel mutation is under progress.

P403 Sudden death in the young in Greece: the unknown cause cases and the hidden cardiac diseases

A. Anastasakis[1], N. Protonotarios[1], V. Rentoumi[1], E. Sevdalis[1], A. Miliou[1], M.X. Kotta[1], C. Kotsiopoulou[1], W. Mckenna[2], C.H. Spiliopoulou[1], C. Stefanadis[1]. [1]*University of Athens, A' Dpt of Cardiology, Athens, Greece;* [2]*University of London, Dpt of Cardiology- Heart Hospital, London, United Kingdom*

Purpose: Aim of the study was to investigate the causes of sudden death (SD) in the young in a representative Greek population, and to further evaluate the families of the "unknown cause" cases.
Methods: We recorded consecutive cases of SD in children and young adults (1-35 years), in the region of Attica and Cyclades, during a 8-year and 6 months period and identified the cause of death according to pathological examination. Then we screened clinically and/or genetically families from the unkown cause cases.
Results: We recorded 349 consecutive cases of SD. 242 (69%) were males (mean age: 26.9yrs) and 107 (31%) females (mean age: 22.9yrs). At age range 1-20, SD occurred in 97 (28%) cases, while in age between 21-35 years, 252 (72%) cases died suddenly. The monthly SD mortality rate was 3.4. SD was of cardiovascular origin in 226 (65%) of cases. In age group 1-20, the most frequent cardiac cause of SD was hypertrophic cardiomyopathy (HCM) (15 cases – 15%) and congenital heart diseases (15 cases – 15%). In age group 21-35, atherosclerotic coronary artery disease (CAD) was the leading cause of SD (73 cases – 29%). In 63 (18%) cases (44 males, 19 females), mean age 24.6yrs, the histopathological evaluation did not reveal the cause of SD. We further investigated clinically 20 out of the 63 consecutive unknown cause SD families and identified an inherited cardiovascular disease in 5 out of the 20 families (20%). In detail, it was found arrhythmogenic right ventricular cardiomyopathy (ARVC) (2 families), hypertrophic cardiomyopathy (1 family), longQT syndrome (1 family) and catecholaminergic polymorphic ventricular tachycardia (1 family).
Molecular genetic analysis was performed in 4 out of 5 families and the causative mutation was identified in all of them. Analysis of extracted DNA from paraffin blocks of heart tissue revealed pathogenic PKP2 mutations in 2 ARVC cases that had been given the diagnosis of "unknown cause SD" on postmortem.
Conclusions: SD in children and young adults is of cardiovascular origin in the majority of cases. A considerable number of SD cases in the young remain of unknown cause on postmortem; however, in a significant number of such cases, family screening unmasked a genetic arrhythmic disorder. Juvenile SD of unknown cause prompt specialized histopathological evaluation of the heart as well as clinical and molecular genetic evaluation of family members.

P404 The nonsense-mutation R413X in the plakophilin-2 gene causes a severe inherited form of arrhythmogenic right ventricular cardiomyopathy (ARVC) in a large family

B. Unsoeld[1], C. Pfeiffer[1], S. Gunkel[1], C. Noack[1], A. Schmidt[1], D. Lossnitzer[2], B. Wollnik[3], E. Schulze-Bahr[4], G. Hasenfuss[2], R. Knoell[2]. [1]*University of Goettingen, Cardiology and Pneumology, Goettingen, Germany;* [2]*University of Heidelberg, Cardiology and Angiology and Pneumology, Heidelberg, Germany;* [3]*University of Cologne, Human genetics, Cologne, Germany;* [4]*University of Muenster, Medizinische Klinik und Poliklinik C, Muenster, Germany*

Inherited forms of ARVC are often caused by mutations in desmosomal proteins. Mutations in the gene for plakophilin-2 (PKP2) have been described as the most frequent underlying mutations. We identified a large family with an inherited form of ARVC due to a nonsense-mutation (C1237T, R413X) of the PKP2 gene. On the basis of the modified consensus criteria for the diagnosis of ARVC we identified 8 affected patients (6 male, 2 female) in this family. 5 of these 8 patients (4 male, 1 female) have died of sudden cardiac death at ages from 14 to 29 years. Occurrence of SCD was often linked to physical activity in these patients. Kaplan-Meier analysis revealed that SCD occurred at significantly younger age in these patients than in a previously published collective of ARVC patients (mean survival 21 vs. 33.4 years; p=0.0005). Similarly the arrhythmia free survival in the affected patients was significantly lower than that of a previously published collective of ARVC patients with other underlying PKP2 mutations (24.8 vs. 32.5 years; p=0.013). The affected patients show typical signs of ARVC such as dilation and reduced contractility of the right ventricle, T-inversions in the precordial ECG leads often reaching to V4 or V5, frequent ventricular ectopies and occurrence of ventricular tachycardia. Further genetic testing in the family revealed the mutation in 6 previously asymptomatic or mildly symptomatic patients that have not been diagnosed with ARVC sofar (3 female, 3 male) and 3 family members (all female) have been identified as obligate carriers of the mutation. Clinical examination of these patients is currently being performed. MRI studies on two of the male carriers showed signs suggestive of ARVC and in one of them syncope accompanied by tachycardia has occurred some years ago. Analysis of mRNA isolated from peripheral blood of an affected carrier showed that the mutated allele is transcribed. A transgenic mouse model overexpressing the mutated allele has been successfully established. The mice from these lines show robust overexpression of the truncated PKP2. Echocardiography at 3 months of age revealed normal global heart function. More detailed phenotyping of the mice is currently being performed. In conclusion this data shows that the R413X mutation leads to

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

a severe form of ARVC. Genetic testing of relatives can lead to the identification of previosly undiagnosed relatives with early stages of the disease. A transgenic mouse model will presumably provide important new informations for the comprehension of the pathophysiology of ARVC.

P405 Prevalence of channelopathies in newborns suspected by the electrocardiogram: role of ethnic origin

J. Marti Almor, R. Berrueco, O. Garcia Algar, A. Mur, L. Recasens, V. Bazan, J. Perez Rodon, J. Bruguera. *Hospital del Mar, Cardiology, Barcelona, Spain*

Background: Prevalence of long QT syndrome (LQTS) in newborns is well established in some European countries like Italy. Prevalence of LQTS and others channelopathies as Brugada syndrome (BS) or short QT syndrome (SQTS) are unknown in others countries, specially in newborns from different ethnic origins.
Aim: To know the prevalence of channelopathies that can be detected by a single electrocardiogram (EKG) recording as LQTS, BS and SQTS in newborns in a multiethnic Mediterranean city.
Methods: From November 2005 to November 2006 we obtained an EKG from all newborns in Hospital del Mar (Barcelona), during the first 48 hours of life. The EKGs were read by two senior cardiologists in order to avoid interobserver variability as guidelines recommend. PR, QT, and QT corrected (QTc) intervals by heart rate using Bazzet formula, were measured in lead II. Other variables included: weight, sex, Apgar score, hydroelectrolites abnormalities or drugs taken by the mother and ethnic origin of both parents.
Results: We included 1309 newborns, 674 males (51.5%). 10 different ethnics origins were detected, being the large ones the Spanish group (n=496), Center and South America (n=201), Magreb and Near East group (n=119), and Indian-Pakistan group (n=78). Median heart rate was 133.15 (18.34) bpm, PR interval 109.27 (9.76) msec, QTc 417.79 (28.47) msec. No difference by sex or others variables were found. No BS pattern or SQTS (QTc defined as shorter than 300 msec) were found. QTc longer than 440 msec was present in 240 newborns (18.33%). Comparing by ethnic origin we found 17.9% pathologic QTc in the Spanish group in front of 27.7% in the Magreb and Near East groups (p=0.016) or Indian-Pakistan group 28.2% (p=0.033). If we defined pathologic QTc values in the Spanish group as over percentile 97.5 (QTc $>$ 470.38), 59 newborns (4.52%) had pathologic values, and ethnic differences between those groups were still maintained.
Conclusions: Median QTc is slightly longer in our study compared with the Italian study. QTc interval can be different attending to ethnic origin due to genetic differences, without implying abnormal clinical significance. Following the accepted standard values (440 msec), neonatal routine EKG and follow up (EKG at 1 and 12 months) in these ethnic subgroups are warranted because of the theoretical risk of sudden death. Other channelopathies out of LQTS are very rare in newborns, and maybe EKG must be performed later on to rule out this possibility.

VENTRICULAR TACHYCARDIA

P407 Bailout catheter ablation for end-stage electrical storm

C. Carbucicchio[1], M. Santamaria[2], N. Trevisi[2], G. Maccabelli[2], M. Moltrasio[2], F. Giraldi[2], P. Della Bella[2]. *[1]Centro Cardiologico Monzino, Univ. of Milan, Arrhythmia and EP Spt., Milan, Italy; [2]Catholic Univ. of the Sacred Heart, Cardiovascular Dpt., Campobasso, Italy*

Purpose: Electrical storm (ES) is an acute life-threatening condition due to recurrent ventricular tachyarrhythmias causing numerous device discharges in implantable cardioverter-defibrillator (ICD) patients (pts). Iterative ventricular tachycardia (VT) episodes not responsive to medical treatment represent the most frightening scenario and frequently lead to cardiogenic shock. Acute and long-term efficacy of catheter ablation (CA) for end-stage ES was investigated.
Methods: Fifty consecutive pts (48 M; age 65$\pm$12yrs), (coronary artery disease, 40; idiopathic dilated cardiomyopathy, 7; arrhythmogenic right ventricular dysplasia, 3) undergoing CA for intractable VT episodes ($>$20 shocks/day) were prospectively evaluated: all pts had been admitted to the Intensive Care Unit and required an emergency CA (8$\pm$5 hours from admission) due to the absolute refractoriness to medical treatment and to the development of acute heart failure. Electroanatomical mapping was applied in 33 pts, non–contact mapping in 10, both methods in 5; percutaneous cardiopulmonary support was provided in 10 pts. Acute efficacy was defined by in-hospital outcome and by programmed electrical stimulation; long-term follow up focused on ES recurrences and on sudden cardiac death.
Results: After 1–3 procedures, ES was suppressed in all pts, with no ES recurrence during the pre-discharge period ($\geq$1 week). Induction of the clinical VT(s) was prevented in 42/50 pts (84%). No major complications occurred. At a 22$\pm$13 month follow up, ES recurred in 8/8 pts having clinical VT(s) still inducible after CA, and caused sudden death in 4 and acute surgical treatment in 4 (cardiac transplant, 2; left ventricular aneurismectomy, 2). All remaining pts (42 pts, 84%) were free from ES. Four pts died due to chronic heart failure.
Conclusions: Advanced strategies of CA as bailout therapy in pts with end-stage ES are effective in the arrhythmia acute control. Despite short–term clinical benefit, the treatment of all clinical VT(s) is required aiming at the prevention of long-term recurrences and of sudden cardiac death. Alternative options of therapy should be considered after a failed CA.

P408 Primary prevention of sudden death by prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy and no prior sustained ventricular tachyarrhythmias

D. Corrado[1], H. Calkins[2], W.J. Mckenna[3], M. Link[4], T. Wichter[5], S. Favale[6], L. Leoni[3], G. Buja[3], G. Thiene[7], S. Iliceto[4]. *[1]Division of Cardiology, University of Padova, Dept of Cardiac, Thoracic And Vasc. Sciences, Padova, Italy; [2]Johns Hopkins Hospital, Baltimore, United States of America; [3]Heart Hospital, University College, London, United Kingdom; [4]New England Medical Center, Boston, United States of America; [5]Division of Cardiology, University Hospital, Munster, Germany; [6]Division of Cardiology, University of Bari, Bari, Italy; [7]Cardiovascular Pathology,University of Padova, Padova, Italy*

Patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) who survived an episode of arrhythmic cardiac arrest have a risk of recurrent ventricular tachycardia or ventricular fibrillation so high as to justify implantable defibrillator (ICD) therapy. The arrhythmic risk stratification with regard to prophylactic ICD in patients with a diagnosis of ARVC/D but without a previous documentation of sustained ventricular tachyarrhythmias is an unsolved issue. The present International Multicenter study investigated the incidence of appropriate ICD shocks in a cohort of ARVC/D patients who received an ICD for primary prevention of sudden death. The study population comprised 106 consecutive patients who fulfilled Task Force diagnostic criteria for ARVC/D (62 men and 44 women; mean age 33$\pm$18 years) who received a prophylactic ICD with electrogram storage capability. The predominant clinical reasons for ICD implantation were unexplained syncope in 42, asymptomatic nonsustained ventricular tachycardia (NSVT) on either Holter or exercise testingin 40 and a family history of sudden death in 24; no patients previously experienced either spontaneous sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). During a mean follow-up of 59$\pm$34 months, 25 of 106 patients (24%) experienced appropriate ICD interventions against a first episode of life-threatening ventricular tachyarrhythmia.The mean time to first event was 9$\pm$3 months. Eight patients had VT and 17 had VF. Young age (p=0.01), unexplained syncope (p$<$0.001), NSVT (0.02), and left ventricular involvement (p=0.04) were significantly associated with the appropriate ICD intervention. On multivariate analysis, unexplained syncope was the only significant independent predictor of arrhythmic risk (RR=7.69, 95% CI. 3.2-19.8; p$<$0.001); NSVT was associated with a trend toward higher arrhythmic risk (RR= 3.15, 95% CI 1.2-10.7; p=0.08). Programmed ventricular stimulation was of limited value in predicting appropriate ICD discharge (positive predictive value 35%, negative predictive value 66%, and test accuracy 48%). In conclusion, during a long term follow-up one fourth of patients with ARVC/D and no previous history of sustained ventricular tachyarrhythmias experienced a first episode of VT or VF that was successfully treated by ICD therapy. Unexplained syncope was the only independent predictor of life-threatening ventricular arrhythmias. The low predictive value of programmed ventricular stimulation makes its application in ARVC/D risk stratification questionable.

P409 Sarcoidosis as a primary cause of life-threatening ventricular tachyarrhythmias

P. Raatikainen[1], P. Uusimaa[1], E. Paakko[1], K. Ylitalo[1], T. Kerola[2], O. Anttonen[1], V. Virtanen[3]. *[1]University of Oulu, Division of Cardiology, Oulu, Finland; [2]Paijat-Hame Central Hospital, Lahti, Finland; [3]University of Tampere, Heart Center, Tampere, Finland*

Aims: Sarcoidosis is a multisystem, granulomatous disease with occasional cardiac manifestations. The clinical course of patients with ventricular tachyarrhythmias as a primary presentation of sarcoidosis has not been duly studied.
Methods: The patient population consisted of 9 consecutive patients (4 males and 5 females) who were admitted to our institutions during years 1998-2006 for evaluation of malign ventricular arrhythmias. The age of the patients was 53$\pm$10 years (range 33-68). All patients underwent through non-invasive cardiologic examinations including careful history and clinical examination, laboratory tests, repeated ECG recording, chest X-ray and echocardiography. Magnetic resonance imaging (MRI) was done in 5 patients. In one patient MRI was hampered by ventricular ectopy, whereas it could not be performed in 3 patients because of the ICD. Coronary angiography was done in all patients and left ventricle kineangiography in 7 patients. Right ventricular endomyocardial biopsies were taken from all patients.
Results: The presenting symptoms of the patients varied from occasional palpitations to cardiac arrest. The clinical arrhythmias included non-sustained and sustained ventricular tachycardia (VT), incessant VT and ventricular fibrillation. The disease was diagnosed by endomyocardial biopsy in 8 patients and mediastinoscopic lymph node biopsy in one patient. In all cases, the granulomas occurred in the absence of any other identifiable cause (e.g., tuberculosis). Chest X-ray and coronary angiography was normal in all patients, but local abnormalities in the ventricular wall were observed in 5 patients. All patients received implantable cardioverter defibrillator (ICD) and antiarrhythmic medication. High-dose steroid treatment was used in 8 cases. During the follow-up (50$\pm$34 months) appropriate ICD therapies occurred in 5 patients and non-sustained VT episodes were

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

detected in 4 patient. Two patients developed incessant VT which was treated by catheter ablation. One patient was referred for heart transplantation despite all other therapies.
Conclusionss: Our data indicate that sarcoidosis can manifest as malignant VT without any detectable systemic findings. This makes sarcoidosis an important diagnostic consideration in patients with VT of unknown origin. Arrhythmia control in cardiac sarcoidosis is difficult and in many cases all modern treatments including high-dose steroids, antiarrhythmic drugs, ICD and catheter ablation are needed to suppress the arrhythmias.

P410 Effects of ischemic stroke laterality on cardiac ventricular arrhythmias

G. Polak[1], Z. Orzalkiewicz[2], R. Przybyl[1]. [1]*Municipal Hospital, Cardiology Department, Bydgoszcz, Poland;* [2]*Fado, Bydgoszcz, Poland*

Background: The neurogenic heart syndrome refers to the microstructural damage to the heart resulting from lesions of the central nervous system, leading to electrocardiographic changes, cardiac arrhythmias and unexpected sudden death.
Purpose: To evaluate the differential effects of laterality of ischemic hemispheric stroke on occurrence of cardiac ventricular arrhythmias.
Methods: We studied 42 right-handed patients (24 women, 18 men, aged 68±15) with the acute ischemic hemispheric stroke confirmed by computerized tomography. 24-hour electrocardiographic Holter recordings were performed on the 1st day of stroke. Then the patients were divided into 2 groups depending on lateralization: 23 patients with the right-sided and 19 patients with the left-sided hemispheric stroke. Differences between groups were evaluated by chi-squared test. Differences were considered statistically significant at $p<0.05$.
Results: Results are presented in the table.

Cardiac arrhythmias in ischemic stroke

Cardiac arrhythmia	Right stroke n=23	Left stroke n=19
single PVCs	16 (69%)[#]	18 (95%)[#]
multiform PVCs	5 (22%)[##]	14 (74%)[##]
couplets of PVCs	6 (26%)	9 (47%)
nonsustained VT	1 (4%)[#]	6 (32%)[#]

PVCs - premature ventricular complexes; VT - ventricular tachycardia; [#]$p<0.05$, [##]$p<0.01$ - the comparison between the right and the left stroke patients.

Conclusions: The ventricular arrhythmias are significantly more frequent in the left-sided than in the right-sided acute ischemic hemispheric stroke of the right-handed patients.

P411 Catheter ablation of ventricular tachycardia in arrhythmogenic right ventricular dysplasia: A 24 year experience

J. Lacotte, G. Fontaine, J. Tonet, G. Duthoit, F. Hidden-Lucet, Y. Gallais, R. Frank. *Hopital de la Pitie-Salpetriere, Institut de Cardiologie, Paris, France*

Background: Catheter ablation using direct current fulguration (DCF) or radiofrequency (RF) has been used to treat ventricular tachycardia (VT) in patients with an arrhythmogenic right ventricular dysplasia (ARVD). We report our experience and the results of a long term follow-up.
Materials and methods: all the patients presenting with an ARVD (WHF criterions) and referred to our center between 1983 and 2006 for a CA of a drug refractory VT were included. From Aug 1983 to Feb 1992, CA was performed using DCF with stiff catheters. After Feb 1992, RF and DCF were used in first and second intention respectively, using 4 mm tip steerable catheters before Oct 1999 and 8 mm or irrigated tip catheters afterwards.
Results: 69 patients (79% male, mean age=45±15 years, range 17 to 76) underwent CA in our department for a drug refractory VT. Mean LVEF was 59±10% (LVEF $\leq$ 45% in 4 individuals). Sustained spontaneous VTs had multiple patterns in a majority of patients (1, 2, $\geq$3 morphologies in 44%, 30% and 26% respectively, range 1 to 11). ICD was present before CA in 4 patients and 5 others had a prior anti-arrhythmic surgery. DCF was used alone in 27 (38%) first consecutive patients, RF in first intention in the remaining 45 (62%) patients but DCF was required in 54% of cases after RF because of ablation failure. Several procedures were needed because of primary CA failure ± early VT recurrences (1, 2 or 3 CA interventions in 50, 33 and 17% respectively, mean 1.68, range 1 to 4). Immediate success rate (clinical VT not inducible) was 81% and 93% with DCF alone and RF±DCF (p=NS). Major CA complications occurred in 7 (14%) patients and one death was reported, only when using DCF during the first period. After a mean follow-up of 5.8 years, no recurrence of VTs ablated was recorded in 89% of patients (81% after DCF alone, 96% after RF±DCF).
Conclusion: We report a high success rate of CA in ARVD patients with drug refractory VT during a long term follow-up.

P412 Impact of radiofrequency catheter ablation on quality of life in patients with frequent premature ventricular beats with respect to an arrhythmia origin in the RVOT or LVOT and neurohumoral activation

M.Z. Erkal, A. Berkowitsch, H.J. Schneider, M. Kuniss, S. Zaltsberg, H.F. Pitschner, C. Hamm, K. Kurzidim. *Kerckhoff-Klinik, Cardiology, Bad Nauheim, Germany*

PVB can adversely affect quality of life (QOL), but relatively little is known about clinical predictors of reduced QOL. RFCA has been proven to be curative for patients suffering from PVB originating either in the RVOT or LVOT. Aim of this study was to determine whether improvement in quality of life (QOL) is related to arrhythmia origin and neurohumeral activation as evaluated by serum levels of NT-pro-BNP. Patient referred for radiofrequency catheter ablation (RFCA) due to symptomatic isolated PVB were studied. LVEF measurements were performed before RFCA and 3 months afterwards. Absolute numbers of PVB were determined from Holter 1 day before, and again after 3 months. Levels of NT-pro-BNP were determined coinciding with the end of each Holter. Success of RFCA was defined by complete disappearance of target PVB and lack of arrhythmia related symptoms after 3 months. Quality of life was assessed using two derived from Short-Form 36 (SF36) questionnaire parameters: Physical component Score (PCS) and Mental component Score (MCS). Since Jan. 2004, 44 of 47 patients have been successfully treated by RFCA either in the RVOT (n=20, women 17, age: 41 (33-54), Median (IQR)) or the LVOT (n=24, men 14, age: 66 (58-71), Median (IQR)). In RVOT patients, the Median (M) number of PVB during 24 h Holter could be reduced from n=11176 to 130 after 3 months, respectively ($p< 0,001$); in LVOT patients from 17194 to 203, resp. ($p<0,001$). NT-pro-BNP levels in RVOT patients (125 pg/ml, M, to 68, resp. $p<0,001$) and in LVOT patients (410 pg/ml to 167, (88-388)), resp. $p<0,01$) showed a decline at 3 months. RVOT patients had few co-morbidities (hypertension (HT), n=2, non-ischemic CAD (CAD)=1), in contrary to LVOT patients (HT, n=17, CAD=8). 9 LVOT patients showed an EF 40 (30-45). After 3 months, EF in this 9 patients raised to 48 (45-55), resp. p=0,043. Before RFCA were PCS and MCS 39 (35-42) and 43 (35-47) (RVOT); 42 (33-45) and 34 (28-42) (LVOT). After 3 months, increased both score in RVOT patients (PCS: 51 (46-55), MCS: 51 (46-55) ($p<.001$ for both)) and in LVOT patients (PCS; 48 (39-57), MCS: 48 (41-54) ($p<.01$ for both)). Quality of life can be improved in both RVOT and LVOT patients by successful RFCA. Striking differences in baseline characteristics, ejection fraction and NT-pro-BNP levels between RVOT and LVOT patients, however indicate differences both regarding etiology and response to frequent PVB. RFCA seems similar effective to RVOT and LVOT patients in improving QOL. Improvement in EF and NT-pro-BNP levels, more frequently observed in LVOT patients may indicate prognostic benefits of RFCA.

P413 Life-threatening post-ischemic arrhythmic storm: is there a place for arrhythmic surgery?

J.-L. Pasquie[1], R. Demaria[2], B. Albat[1], J.M. Davy[1], F. Leclercq[1], J.M. Frapier[1]. [1]*C.H.U. De Villeneuve, Service De Cardiologie A, Montpellier Cedex 05, France;* [2]*Chu Montpellier, France*

Background: A late surgical approach is effective in patients with left ventricular (LV) aneurism and stable ventricular tachycardia (VT). However, arrhythmic storm due to refractory ventricular fibrillation (VF) is a rare but potentially lethal complication of acute myocardial infarction (AMI). Recent studies suggest a role for catheter ablation of ectopies initiating VF in these patients. The aim of our study was to assess the short and long-term efficacy of early post-infarct aneurismectomy with encircling cryoablation in patients with ischemic VF storm refractory to medical treatment.
Methods/Results: From 1985 to 1999, 60 patients underwent post-infarct aneurismectomy with encircling cryoablation at our institution. Most of them had stable VT with LV aneurism late after MI. Five of these patients (4M, 63±12 yo) presented with ischemic VF storm refractory to maximal medical treatment early after AMI. MI was anterior in all pts. None had had efficient revascularization (failed thrombolysis in all with no access to rescue PTCA). Evolution was associated with the early development of LV aneurism with symptoms of congestive heart failure in all pts. All pts had occlusion of the LAD and only one had bitroncular lesions. Mean LV ejection fraction was 30±7%. Arrhythmic storm occurred 17.1±6.6 days after AMI and consisted in recurrent VF in all 5 patients. VF was initiated by short coupling ventricular ectopies in all of them. As maximal medical treatment as well as general anesthesia failed to stop VF storm, large encircling cryoablation without mapping along with aneurysmectomy appeared as the only therapeutic alternative to save patients life and was realized in all patients. Surgery was successfully performed in all patients, 30.3±9.8 days after AMI. Post-operative LV ejection fraction was significantly improved in all pts. Post-operative EP study (2 weeks after surgery or before hospital discharge; RV apex and RVOT, 600 to 400 ms basic cycle length and up to 3 ES down to 200 ms) was negative in all pts. As no arrhythmia was inducible and as postoperative LV EF was $>$ 35% in all patients, none of these patients was implanted with an ICD. On a follow-up of 7.8±5.1 year, the 5 patients are alive and no pt had recurrence of ventricular arrhythmia.
Conclusion: Post-ischemic VF storm is a rare complication of acute MI occurring in the first month following MI. Post-infarct aneurismectomy with encircling cryoablation without mapping appeared to be an efficient therapeutic alternative

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

to save patients life in emergency and prevented further ventricular arrhythmia recurrence on the long-term.

P414 Evidence of increased cardiac sympathetic nerve innervation in patients with premature ventricular complex and structurally normal heart: assessment with 123-I-metaiodobenzylguanidine imaging

D.H. Kim, D.G. Shin, J.S. Park. *Yeungnam Univ. Hospital, Cardiovascular Division and Nuclear medicine, Daegu, Korea, Republic of*

Background and Objectives: Premature ventricular complex(PVC) is one of the most common arrhythmia encountered in clinic and an important factor for the genesis of life threatening ventricular arrhythmia in cardiac diseases. However, the pathophysiology of PVC is not well understood. The object of this study is to evaluate relationship between cardiac sympathetic nerve activity by using MIBG and PVC in patients with structurally normal heart.
Methods and Results: Thirty-four patients(12 men, mean age 61.6± 12.8 years) with echocardiography proven structurally normal heart were studied and divided into 2 groups with Holter monitor documented PVC(group A; 22 patients) and without PVC(group B; 12 patients). Echocardiography, 24-hour Holter monitoring and 123 I-MIBG were performed in all patients. The early(15min) and delayed(3hours) uptake, heart to mediastinum uptake(H/M) ratio, global washout ratio (WOR: defined as [early H - delayed H]/early H ' 100) were measured on 123 I-MIBG. Polar map of LV myocardium were divided into 5 segment(anterior, septum, lateral, inferior and apex) and calculated regional uptake and WOR. The clinical variables, echocardiographic parameters and 123-I-MIBG derived parameters were compared between the 2 groups.
Results: Average of PVC count was 5,198/day in group A patients. There were no significant difference in age, LVEF(60.4±8.6% vs 61.4 ±9.7%, p=NS), LVESD and LVEDD between the 2 groups. Group A patients had higher early(2.75±0.36 vs 2.62±0.61, p=0.349), delayed H/M ratio(2.64±0.47 vs 2.27±0.57, p=0.130) and lower average WOR than that of group B(0.24±0.11 vs 0.27±0.11, p=0.407), though the difference was not statistically significant. The delayed inferior wall H/M ratio increased significantly in group A (2.69±0.45 vs 2.26± 0.54, p=0.044), and early inferior wall H/M ratio has a tendency to be higher in group A(2.81±0.37 vs 2.62±0.63, p=0.087).
Conclusion: The occurrence of PVC in structurally normal heart may be related to increased cardiac sympathetic nerve innervation, especially of inferior wall. These results might partially explain the role of sympathetic nervous system in the genesis of PVC.

P415 Effect of endurance exercise training on ischemically induced changes in the T-wave and susceptibility to ventricular fibrillation

G.E. Billman, M. Kukielka, C.A. Carnes. *The Ohio State University, Dept of Physiology, Columbus, United States of America*

Background: Myocardial ischemia provokes a dispersion of repolarization that can induce ventricular fibrillation. As the transmural dispersion of repolarization is associated with changes in the descending portion of the T wave (Tpeak-Tend), T wave changes may precede ventricular fibrillation onset. We previously demonstrated that endurance exercise training protected against ventricular fibrillaiton. We hypothesized that exercise training protected against ventricular fibrillation through the reversal of ischemic abnormalities in repolarization (i.e., smaller ischemic T wave changes after training).
Methods: To test this hypothesis, T wave changes were recorded when ischemia was induced by a 2 min occlusion of the left circumflex artery during the last min of an exercise test in dogs with healed myocardial infarctions: 20 had ventricular fibrillation (susceptible) and 13 did not (resistant). These dogs were then randomly assigned to either 10-wk exercise training (treadmill runnning - 1st wk 20 min at 4.8 kph/0% grade, 10th wk 90 min at 6.4 kph/14% grade; susceptible n = 9, resistant n = 8) or an equivalent sedentary period (susceptible n = 11, resistant n = 5). The exercise plus ischemia test was then repeated at the end of this 10-wk period.
Results: Before training, ischemia induced significantly (ANOVA, $P<0.01$) greater increases in Tpeak-Tend in the susceptible dogs (Pre-occlusion 41. 5±3.7 ms; Occlusion 60.7±4.4 ms) compared to resistant dogs (Pre-occlusion 38.3±4.2 ms; Occlusion 45.1±3.0 ms). Post-training, ischemia failed to produce T wave changes in either group (Susceptible, Pre-occlusion 39.3±3.4 ms; Occlusion 40.4±3.1 ms versus Resistant, Pre-occlusion 39.9±5.0 ms; Occlusion 42.9±4.2 ms) and did not provoke ventricular fibrillation. In contrast, in the sedentary susceptible dogs ischemia still provoked ventricular fibrillation and T wave increases (Pre-occlusion 48.7 ±8.4 ms, Occlusion 62±9.2 ms).
Conclusion: These data suggest that endurance exercise training can reduce ischemically induced inhomogeneities in repolarization and thereby could protect against ventricular fibrillation.

P416 Prevalence of Brugada-type changes during health check-up ECG registration

D. Duplyakov[1], V.L. Gluckova[2], Z.I. Vozhdaeva[2], S.V. Maximova[2], I.V. Starostina[2], E.N. Vasilyeva[2], E.V. Sysuenkova[2], L.P. Svetlakova[2], S.V. Goleva[2], T.T. Sorokina[2]. *[1]Samara Region Cardiology Center, Samara, Russian Federation; [2]VAZ Medical Center, Cardiology Department, Togliatti, Russian Federation*

Background: The Brugada syndrome has been associated with sudden death in subjects without structural heart disease. It is well known that the prevalence of Brugada-type ECG varies among populations. Nothing is known about its prevalence in Russia. The aim of this study was to evaluate the prevalence of Brugada-type ECG in Russian adult population.
Methods: Prevalence of Brugada-type ECG was studied among subjects who underwent ECG registration during annual health checkup.
Results: 42,779 subjects, aged 22-68 years, underwent rest ECG during annual health check-up (01/05/2005 - 01/05/2006). The Brugada-type ECG was observed in 20 of them (0.047%). The classical Brugada-type (type 1) was found in four subjects only, while others had type 2 of Brugada syndrome. The prevalence for male subjects was 90%. Three subjects had a family history of sudden death but all cases had occurred in males older than 45 years. Four subjects had a history of syncope but all were considered as neurocardiogenic in origin by clinical features. Nonsustained ventricular tachycardia was observed on Holter ECG during night hours in one subject. Both tredmill test and echocardiography were out of value. No death or syncope occurred during the study.
Conclusions: We can conclude that i n our population the prevalence of Brugada-type ECG is rare. These findings are in line with previous studies performed in European population.

P417 Ventricular fibrillation and tachycardia during acute myocardial infarction: incidence, predictors, mortality and treatment

L. Lazarov[1], V. Kotevski[2], A. Georgievski[1], E. Lazarova[1], D. Projevska[1], H. Pejkov[1], S. Tosev[1], M. Boshev[1], A. Veljanovska[1], S. Caeva[1]. *[1]Institute of Heart Disseases, Coronary Artery Dissease Department, Skopje, Macedonia, The Former Yugoslav Republic of; [2]Institute for Heart Diseases, CCU, Skopje, Macedonia, The Former Yugoslav Republic of*

Purpose: (1) To evaluate the in-hospital incidence and mortality of patients (pts) with acute myocardial infarction (AMI) complicated by rapid polymorphic ventricular tachycardia (VT) and/or primary/secondary ventricular fibrillation (VF), (2) to identify the independent predictors of inhospital VT/PVF and (3) to verify the most appropriate treatment of AMI.
Methods: Total of 10.212 pts with AMI admitted in the CCU was included in the study. The study period was January 1994 to December 2006. We have analyzed separately the data of subgroup of pts with AMI+VF/VT treated in the period 1999-2006 (6781 pts with AMI, 393 with VF/VT) because of predominant use of PCI and Thrombolysis.
Results: In-hospital incidence of VF/VT in total group was 5.9% (605 pts) with total mortality of 41.0%. In the subgroup the incidence of VF/VT was 5.8% with mortality rate of 38.7%. VF occurred in 247/393 pts, with mortality rate of 38.5% in primary VF pts and 51% in secondary VF pts. VT occurred in 146/393 pts with mortality rate of 14.4%. The mortality rate in the first hour was 30.8%, in the first 24 hours 57.7%, in the first 72 hours 80.8%.
Independent predictors of higher in-hospital VF/VT incidence were: male gender (75% pts), anterior wall AMI (67% pts), higher ST-segment elevation on admission ECG, lomger time to PCI/thrombolysis (>3 hours), acute heart failure (21% pts) and larger enzymatic infarct size. VT/VF was not associated with: history of prior infarction, hypertension, smoking, diabetes mellitus and lower serum potassium. After initial cardioversion, thrombolytics (Streptokinase, rTPA) were used in 18.1% pts and PCI was performed in 24.7% pts. The 3rd group of pts was treated with LMWH + Amiodarone or beta blockers. The mortality rate in PCI group was 23.7%, in thrombolytic group 26.8% and in the 3rd group (no PCI/fibrinolysis) 43.5%. Patients admitted for AMI+VT/VF were less often submitted to revascularization procedures during hospital stay (42.9%) compared to non VT/VF pts (82%).
Conclusions: AMI complicated with VT/VF occurred mostly in man, with anterior wall AMI, higher ST-segment elevation, higher enzymes at admission and lower blood pressure. The inhospital mortality rate was higher for patients with early (<24 hours after enrollment) versus late (>24 hours) ventricular arrhythmias. Primary PCI and thrombolysis have significant effect ($p<0.05$) on lowering the mortality rate of AMI+VT/VF. Despite the improvement in the treatment of AMI, the onset of VT/VF is still associated with poor prognosis.

P418 Ventricular tachycardia substrate characteristics in relation to tachycardia cycle length: different location of middiastolic electrograms in scar

L. Atea[1], A. Arenal Maiz[2], T. Datino[2], E. Torrecilla[2], F. Atienza[2], J. Almendral[2], A. Esteve[2], L. Castilla[2], F. Fernandez Aviles[2]. *[1]HGU Gregorio Maranon, Cardiology, Madrid, Spain; [2]Madrid, Spain*

Background: Definition of ventricular tachycardia (VT) substrate in relation to the

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

cycle length could facilitate ablation of unmappable tachycardias. The purpose of this study was to define the relation to the scar border of Fast (F) and Slow (SL) VT middiastolic electrograms (MDE) and to define the electrogram characteristics of these sites during right ventricular apex pacing (RVAP) on sinus rhythm.
Methods/Results: 3-Dimensional left ventricle electro-anatomical maps were obtained during RVAP in 23 patients with chronic myocardial infarction referred for VT ablation. Voltage maps were displayed using 0.50/0.51mV as lower and upper limits of the voltage color range. Three zones were delimited: 1) Exterior border: from the border line to 1cm around, 2) Interior border: from the border to 1cm inside and 3) Scar center: the remaining central part of the scar. MDE were recorded in 26 monomorphic VTs, 9 TVs had aVTCL$\leq$300 ms (FVT) (277$\pm$21 ms), the remaining 17 were considered SLVT (396$\pm$65 ms). In the FVT group none MDE site was recorded in the center of the scar, 3 sites were in the interior and 6 in the exterior border, in the SLVT group 9 MDE were recorded in the center of the scar, 4 in the interior and 4 exterior border ($p<$. 02). Electrograms with delayed component (E-DC) were recorded during sinus rhythm at all MDE sites but FVT related electrograms had: 1) shorter activation time of the latest component (173$\pm$10 vs. 217$\pm$29 ms, $p<$. 0001, 2) shorter duration (82$\pm$34 vs. 140$\pm$28 ms, $p<$. 001) and 3) lower incidence of an isoelectric interval $\geq$ 50 ms separating electrogram components (1/9 vs. 16/17, $p<$ 0.001).
Conclusion: Location and E-DC characteristics differentiate F and SLVT substrate. This information could be useful to guide ablation of unmappable VTs.

P419 Ventricular tachycardia involving the left bundle Purkinje system in patients with structural heart disease. Identification of slow conduction during sinus rhythm

M. Ulbrich, A. Hahnefeld, C. Reithmann, G. Steinbeck. *Klinikum Grosshadern, Cardiology Department, Munich, Germany*

Introduction: Ablation at sites with abnormal diastolic potentials (DPs) during sinus rhythm within the posterior Purkinje network can eliminate idiopathic left ventricular tachycardia. The purpose of this study was to determine whether such abnormal DPs can also be recorded in patients with structural heart disease and ventricular tachycardias (VTs) involving the left bundle Purkinje system.
Methods and Results: Eight patients (mean age 67$\pm$11 years, 5 with non-ischemic cardiomyopathy, 3 after myocardial infarction) with VTs involving the left bundle Purkinje system (mean cycle length 376$\pm$45 ms) and were referred to catheter ablation. Abnormal isolated DPs of low amplitude with a QRS - earliest DP interval of 374$\pm$86 ms could be found in all patients during sinus rhythm in the mid or inferior left ventricular septum in areas with Purkinje potentials. Three types of VT were observed: interfascicular VT with participation of both left bundle fascicles (3 patients), scar-related VT with Purkinje fibers as part of the reentrant circuit associated with ischemic cardiomyopathy (3 patients) and fascicular VT involving the left posterior fascicle (2 patients). Due to hemodynamic intolerance or poor reproducibility, ablation was performed during sinus rhythm in 7 patients. Abnormal DPs during sinus rhythm coincided or were in proximity to DPs during VT in 6 patients. Ablation at sites with the earliest abnormal DPs during sinus rhythm eliminated the VT in 6 of 7 patients. 6 of 8 patients were free of VTs during follow-up of 11$\pm$5 months.
Conclusions: In patients with structral heart disease and VTs involving the left bundle Purkinje system, isolated DPs during sinus rhythm were found in the posterior Purkinje network. Abnormal DPs during sinus rhythm apparently represent slow conduction critical for the reentrant circuit within diseased Purkinje network and can be used to guide successful catheter ablation.

P420 Primary ventricular fibrillation in overt and concealed Wolf-Parkinson-White syndrome

L.J. Szumowski, M. Orczykowski, E. Szufladowicz, P. Derejko, P. Urbanek, R. Bodalski, R. Kepski, A. Biederman, K. Bieganowska, F. Walczak. *Institute of Cardiology, Warsaw, Poland*

Sudden cardiac death can be the first presenting symptom of WPW Risk factors for VF in pts with WPW are still under investigation. The aim of this study was to analyze clinical and electrophysiological data of pts with WPW and a history of primary VF, in order to define risk factors of SCD. Patients in whom the first documented arrhythmia degenerated into VF were also analyzed. Group and Methods: The group consisted of 802 pts who underwent ablation or operation of WPW. 54 (7,22%) pts (14F, 41 M, age 1$-$70) had documented VF. 19 (2,3%) pts (14M, 5F) had VF as an end point of the first arrhythmia episode. Pts with no documented arrhythmia prior to aborted SCD were considered primary VF.
Results: 15 pts (3F, 12M, mean age 23,4 years) had primary VF. 3 pts (20%) had 2 AP, 1pt (6,5%) 3 AP. 1 pt (6,5%) had wide AP. In 12 pts VF episode occurred during exertion combined with stress, in 2 during normal activity, in 1 pts while sleeping. In remaining pts with VF as an end point of the first arrhythmia, in 2 pts VF occurred after iv administration of an antiarrhythmics (AA) and in 2 pts during transesophageal atrial pacing. The mean age of pts with primary VF was significantly lower than pts with history of AVRT and/or AF, 24, vs. 36 and 38 yrs. respectively. In the whole group of pts with aborted SCD in 25pts (46%) VF occurred after i.v. administration of an antiarrhythmics (AA). In the whole study group refractory periods of accessory pathway and A$-$V node were short. The mean ejection fraction was 60%
Conclusions: – In 26% pts with history of aborted SCD, no arrhythmia preceded VF
– Patients with primary VF are young, and significantly younger than patients with non primary VF.

SUDDEN CARDIAC DEATH AND RESUSCITATION

P421 Can we predict cardiac arrest in aortic stenosis?

E.H. Orlowska-Baranowska[1], R.B. Baranowski[2], J.S. Stepinska[1]. *[1]Institute of Cardiology, Valvular Heart Diseases, Warszawa, Poland; [2]Warsaw, Poland*

Syncope [SE] and cardiac arrest [CA] are well-recognized complications of aortic stenosis [AS]. The aim of the study was to investigate the history of CA and SE in pts with AS and analysis if simple clinical, ecg and echo parameters could be possible markers of CA pts with AS.
Methods: The group consisted of 954 pts (age 61$\pm$10 yrs) with isolated AS, who underwent clinical examination before valve replacement [VR] between 1997-2003. The incidence of SE and CA before VR and its correlation with clinical (age, sex, NYHA, coronary artery disease [CAD]), Echo (maximal aortic gradient [MAG], LV hypertrophy: mass index [LVMI], wall thickness [WT], ejection fraction [EF]); standard ECG: heart rate [HR], QRS duration, QT duration [QTc],and dispersion [QTd] and ventricular arrhythmia (VA) in 24h ECG were assessed.
Results: CA was present in 26 pts (2,6%). The mechanism was VF in 25 and AV3st block in one. Syncope was detected in 267 pts (28%). The results are shown in table. Results of the univariate logistic regression analysis: NYHA p=0,014, age-NS, gender-NS, QRS p=0,02, QTc p=0,0001, QTd p=0,04, LVMI p=0,0001, EF p=0,0001, MGA – NS, VA p=0,01. In the multivariate analysis LVMI (p=0,003), NYHA (p=0,025) and QTd (0,035) were selected.

Parameter	SE	CA	no CA/SE	ANOVA or Kruskall-Wallis test
QRS(ms)	100$\pm$20	111$\pm$22	101$\pm$17	0,015
QTd(ms)	60$\pm$22	72$\pm$29	59$\pm$24	NS
HR(b/min)	72$\pm$14	76$\pm$15	70$\pm$13	NS
QTc(ms)	451$\pm$36	478$\pm$48	458$\pm$40	0,007
MGA(mmHg)	96$\pm$30	89$\pm$27	100$\pm$30	NS
EF(%)	61$\pm$16	50$\pm$20	63$\pm$14	0,005
LVMI(g/m^2)	218$\pm$68	274$\pm$121	214$\pm$64	0,0001
WT(mm)	29$\pm$5	28$\pm$4	28$\pm$4	NS
VA (n/24h)	331$\pm$1253	885$\pm$2430	532$\pm$2117	0,009
CAD(%pts)	22	22	16	NS
NYHA IV (%pts)	31	65	34	0,03

Conclusions: The prevalence of CA in pts with AS is higher in decompensated course of disease. Risk stratification is possible by simple clinical and noninvasive methods: ecg, 24h ecg and echo.

P422 Sudden cardiac death at patients with ischemic heart disease and ethanol consumption

S. Galyavich[1], N. Nigmatullin[2], A. Chromova[2], A. Shaidoullina[1]. *[1]Kazan State Medical University, Faculty Therapy, Kazan, Russian Federation; [2]State Medical Examiner Office, Kazan, Russian Federation*

There are same data that the moderate consumption of alcohol is associated with low risk of sudden cardiac death (SCD).
Purpose: to define a level of ethanol at suddenly died persons for reasons of ischemic heart disease (IHD).
Methods: 279 men and women (55.45$\pm$10 and 61.92$\pm$16.2 years old respectively) owing to IHD without signs of myocardial infarction are studied by autopsy. Presence of changes of IHD was established by typical histological criteria. The level of ethanol in blood was defined by a method of a gas chromatography. Depending on a level of ethanol all patients have been divided into 4 groups - an moderate, average, strong, heavy degree of alcoholic intoxication (0-1.5‰, 1.5-2.5 ‰, 2.5-3 ‰, more 3 ‰ respectively).
Results: From 279 person died suddenly the raised level of ethanol in blood has been found out in 44.4%: the moderate degree - at 12.1% (at 10% of men and 2.1% of women), the average degree - at 7.1% (at 6.4% of men and 0.7% of women), the strong degree - at 4.5% (at 3.5% of men and 1% of women), the heavy degree - at 20.7% (at 16.4% of men and 4.3% of women).
Conclusions: The raised level of ethanol in blood is a risk factor of development of sudden cardiac death at persons with morphological signs of ischemic heart disease.

P423 Effect of high glycemic index diet on ST segment elevation in Brugada syndrome

P.M.A. Makarawate, S.S.A. Sangwatanaroj. *Chulalongkorn University, Department of Medicine, Bangkok, Thailand*

Background: Previous studies suggested that glucose-induce insulin secretion is one of the contributing factors of fluctuation of ST segments elevation

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

in Brugada syndrome patients. However, the effect of high glycemic index diets on ST segment elevation in both asymptomatic and symptomatic patients has not been studied.
Objectives: To evaluate the ST segment elevation post Thai regular diet and high glycemic index diet in symptomatic and asymptomatic Brugada syndrome patient.
Methods: Eighteen patients with type-1 Brugada ECG pattern in right precordial leads were enrolled. Eight were asymptomatic (male:female = 5:3) and ten were symptomatic (male:female = 8:2).The 48-hour Holter continous-3-right precordial-lead-ECG monitoring started at one hour before breakfast of day 1 and finished before breakfast of day 3. All patients took three Thai regular diet on day1 and three high glycemic index diet on day2. The maximum J point elevation (mV) in one right precordial lead at 0,30,60,120 and 180 minutes after each meals were measured.
Results: Among the malepatients, the difference of maximal J point elevation at 0 and 60 minutes after high glycemic index diet were significantly higher than those after regular diet (0.27±0.24 vs 0.23±0.2 mV, p= 0.01), (total meals of each diet, n= 39) but no difference in female patients (0.26±0.14 vs 0.25±0.17, p = 0.99).
Conclusion: This is the first report on the effect of high glycemic index diet on increasing the ST segment elevation in male Brugada syndrome patients compared with regular diet. This finding may help to elucidate the pathogenesis of dynamic ST-T changes in Brugada syndrome.

P424 CPR using simultaneous chest and abdominal compression. Summary of a 5 year study

T.K. Petelenz[1], P. Chrusciel[2], J. Wolkowski[3]. [1]*Silesian School of Medicine, Cardiology Foundation, Katowice, Poland;* [2]*City Hospital, Cardiology, Nowy Targ, Poland;* [3]*City Hospital, Cardiology, Dabrowa Gornicza, Poland*

Background: Chest compression cardiopulmonary resuscitation (CC-CPR) is a resuscitative procedure of choice in Sudden Cardiac Arrest (SCA). It is, however, effective in only 5-10% of patients due to insufficient arterial pressure generated by chest compressions alone. Complications are common and are usually attributed to excessive compressive forces and prolonged brain ischemia. Based on hemodynamic studies that show low efficacy of CC-CPR in generating arterial pressure required for adequate brain perfusion, a modified CPR procedure using simultaneous abdominal compressions (SAC-CPR) was proposed. In a 5-year SAC-CPR we have demonstrated a 100% increase in SCA survival rate as compared to the treatment using standard chest compression procedure.
Aim of the study: The objective of the study was to compare safety and efficacy of the SAC-CPR method with the results of standard CC-CPR.
Methods: During this prospective 5-year trial (2002-2006), unconscious SCA victims (207 patients, 71±10 yrs) were treated using the SAC-CPR method and the clinical outcomes were compared with the retrospective 2-year (2000-2001), (138 patients, 69±12yrs) CC-CPR records in the same hospitals. Return of spontaneous circulation (ROSC) and of consciousness, as well as hospital discharge were classified as "success".
Results: (Table 1) Overall ROSC reached 38% in SAC-CPR vs. 16% in CC-CPR group ($p<0.05$), with hospital discharge rate of 24% vs. 10%, respectively ($p<0.01$), independent of the SCA mechanism (VF or asystole). Incidence of complications was lower in the SAC-CPR group and no adverse effects related to abdominal compressions were observed. Overall morbidity in the study group did not differ from that in the aged-matched control group.

Table 1. Results summary

Method	N	SCAMechanism		Success Rate			
		VF/VT	ASY	Total	VF/VT	ASY	HospitalDischarge
CC-CPR	138	112 (81%	26 (19%)	22 (16%)	19 (17%)	3 (12%)	14(10%)
SAC-CPR	207	143 (69%)	64 (31%)	79 (38%)	54 (38%)	25 (37%)	50(24%)

Conclusions: In the 5-year study of the SAC-CPR use in patients with SCA of cardiogenic origin the survival rate was significantly higher as compared to that in the retrospective standard CC-CPR group. This modified CPR treatment can be considered a safe and effective enhancement of the traditional CPR and should become an element of the ACLS training.

P425 Endovascular versus external cooling to induce therapeutic mild hypothermia after out-of-hospital cardiac arrest

I. Andrade Ferreira, M. Schutte, E. Oosterloo, B.W. Mooi, A.W.J. Van 'T Hof, J.H.E. Dambrink. *Isala Klinieken, cardiology, Zwolle, Netherlands*

Purpose: Therapeutic mild hypothermia has been recommended for post-cardiac arrest coma. However, no study has evaluated which cooling technique is more effective in this setting in improving neurological outcome or survival.
Methods: A retrospective study was conducted in a fourteen bed Critical Care Unit in a tertiary centre. We evaluated 70 consecutive comatose patients presenting with an out-of-hospital cardiac arrest (OHCA) due to ventricular fibrillation and nonventricular fibrillation rhythms (asystole/pulseless electrical activity). We compared 25 patients who were treated with external or surface cooling during the period of October 2005-February 2006 with 19 patients who received endovascular cooling in the period March 2006-September 2006. Twenty-six patients admitted between January 2005-September 2005 treated with standard (post-)resuscitation measures served as controls. Mild hypothermia was defined as a central target temperature of 33°C. Efficacy and outcome at hospital discharge were assessed.
Results: No significant differences in baseline characteristics were present between the groups. The mean time to reach hypothermia and normothermia by endovascular approach was shorter compared to an external approach (1.9±1.0h vs 4.5±2.0h, P=0.002 and 5.5±1.3h vs 8.5±2.5h, $P<0.0001$ respectively). The hypothermic period by endovascular cooling was more stable. Endovascular cooling resulted in better neurological outcome (3.82 [0.95-15.36], $P<0.05$) and survival (0.59 [0.34-0.97], $P<0.05$) as compared to surface or external cooling versus standard therapy.
Conclusions: Both endovascular and surface cooling compare favourably to conservative therapy after OHCA in terms of outcome. However, therapeutic hypothermia by an endovascular approach was more rapidly and stable compared to conservative measures. This may have additional benefit in terms of clinical outcome.

P426 A successful defibrillation may be blunted by a precocious chest compression in out-of-hospital cardiac arrest

A. Capucci, D. Aschieri, M.S. Pisati, C. Armentano, M.F. Piepoli, A. Rosi, S. Ferraro, E. Bonibaldoni, G.Q. Villani. *Hospital G. da Saliceto, Cardiology, Piacenza, Italy*

Purpose: The aim of this study was 1) to determine survival rate after out-of-hospital cardiac arrest in a first aid system of lay responders trained to only defibrillate and 2) to determine the relationship between chest compression (CC) and recurrent ventricular fibrillation (rVF).
Methods: AEDs were provided to Progetto Vita lay volunteers (PV-AED) in the city of Piacenza, Italy. PV-AED and emergency medical rescue (EMS) were simultaneously deployed to possible cardiac arrests. Time to first defibrillation and survival rate were compared in PV-AED vs EMS. ECGs of patients (pts) with rVF after first shock were examined. rVF were classify as spontaneous or CC-related and were assessed for association with either asystole or spontaneous rhythm (SR).
Results: 1) Among 1516 paired dispatches pts the time from 1-1-8 call to defibrillation was 5.20±1.20 min for PV-AED vs 7.30±2.40 min for EMS ($p = 0.0012$). PV-AED arrived first in 57% of calls. VF was present in 175/1516 pts (11%): 88/175 in group PV/AED, 87/175 in group EMS. A 29.7% survival rate (52/175 pts) was observed. Survival rate was higher in group PV-AED (39.8%) than in group EMS (18%) ($p < 0.005$). 89% of the initial rhythms were nonshockable, reducing the absolute survival to 3.4% (PV-AED, 4.0%; EMS, 2.4%, $p < 0.05$). 2) 59 pts had a good quality ECG for VF analysis. VF recurred in 33/59 pts (55.9%): 29/33 pts (87,9%) experienced at least one CC- related VF. 119 rVF were calculated: 84/119 rVF (70.5%) were CC-related and 35/119 (29.5%) were spontaneous. A SR was present before CC in 63/84 episodes (75%) while asystolia was present in only 21/84 episodes (25%) (Table 1).

Table 1. r VF causes and the preceeding rhythm

	CC-related rVF	Spontaneous rVF
r VF	84/119 (70,5%)	35/119 (29,5%)
SR preceeding - rVF	63/84 (75%)	31/35 (88.5%)
Asystolia preceeding - rVF	21/84 (25%)	4/35 (11.5%)

see text.

Conclusions: Lay responders trained to only defibrillate reduced response times to defibrillation and improved survival rate more than twice compared to EMS group. CC is related to rVF in 70.5% of cases, in particular when a SR is restored. The beginning of CC should be delayed when a SR is recoverd.

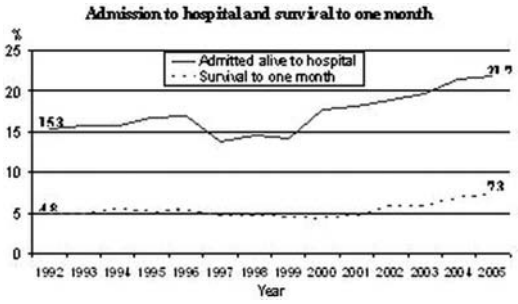
P427 Increased survival after out-of-hospital cardiac arrest in Sweden

J. Hollenberg[1], J. Herlitz[2], J. Lindqvist[2], M. Rosenqvist[1], L. Svensson[1]. [1]*Karolinska Institute, South Hospital, Dept of Cardiology, Stockholm, Sweden;* [2]*University of Goteborg, Sahlgrenska Hospital, Dept of Cardiology, Goteborg, Sweden*

Aim: To describe one month survival after out-of-hospital cardiac arrest when cardiopulmonary resuscitation (CPR) was attempted in Sweden during the last 14 years.
Methods: All patients suffering from out-of-hospital cardiac arrest in whom CPR was attempted between 1992 and 2005, who were included in the Swedish Cardiac Arrest Registry were included in the study.
Results: In all, 38 646 patients were included in the survey. There was an increase in the proportion of patients who were admitted alive to a hospital from 15.3% in 1992 to 21.7% in 2005 ($p<0.0001$). The corresponding value for the proportion of patients being alive after 1 month was 4.8% and 7.3% respectively ($p<0.0001$).
The increase in one month survival was particularly marked among patients who were found in a shockable rhythm (increase from 10.7% in 1992 to 18.6% in 2005 ($p<0.0001$). The corresponding change among patients found in a non shockable rhythm was 1.0% in 1992 to 1.9% in 2005 (NS).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Possible contributory factors to the increase in survival were an increase in bystander CPR from 31% in 1992 to 49% in 2005 ($p<0.0001$) and an increase in crew-witnessed cases from 10% in 1992 to 24% in 2005 ($p<0.0001$). Logistic regression analyses demonstrated that crew-witnessed cases was the only variable with clear and direct effect on total survival; after correction for crew-witnessed arrests, the increase in total survival no longer reached significance.



Conclusion: We have found a significant increase in survival after out-of-hospital cardiac arrest in Sweden over the last 14 years. The increase was particularly marked among patients found in a shockable rhythm. Two probable contributory factors to this increase in survival are an increase in bystander CPR and a remarkable increase in the proportion of crew-witnessed cases.

P428 Out-of-hospital cardiac arrest outcome after early defibrillation. A 24-months retrospective analysis

P. Terranova, B. Severgnini, P. Valli, S. Dell'orto, E.M. Greco. *U.O. Cardiologia,Presidio Ospedaliero"Uboldo", Cernusco S/N, Milano, Italy*

Introduction: Cardiovascular disease remains the most common cause of death in the United States and most other Western nations. Among these deaths, sudden, out-of-hospital cardiac arrest claims approximately 1000 lives each day in the United States alone. Most of these cardiac arrests are due to ventricular fibrillation. Though highly reversible with the rapid application of a defibrillator, ventricular fibrillation is otherwise fatal within minutes, even when cardiopulmonary resuscitation is provided immediately. The overall survival rate in the United States is estimated to be less than 5 percent. Recent developments in automated-external-defibrillator technology have provided a means of increasing the rate of prompt defibrillation after out-of-hospital cardiac arrest. After minimal training, also nonmedical personnel (e.g., flight attendants and casino workers) are able to use defibrillators in the workplace, with lifesaving effects. Nonetheless, such programs have involved designated personnel whose job description includes assisting persons who have had sudden cardiac arrest. Data are still lacking on the success of programs in which automated external defibrillators have been installed in public places to be used by persons who have no specific training or duty to act.
Materials and Methods: All patients who had an out-of-hospital cardiac arrest between January 2003 and December 2004 and who received early defibrillation for ventricular fibrillation were included. We conducted a 24 months retrospective population–based analysis of the outcome in our population.
Results: Over a 24 month period, 446 people had non–traumatic cardiac arrest, and in all of them it was observed a ventricular fibrillation. In a very few cases, the defibrillator operators were good Samaritans, acting voluntarily. Eighty–nine patients (about 19%) with ventricular fibrillation were successfully resuscitated, including eighteen who regained consciousness before hospital admission.
Conclusions: Automated external defibrillators deployed in readily accessible, well-marked areas, is really very effective in assisting patients with cardiac arrest. However, it's quite true that, in the cases of survivors, most of our users had good prior training in the use of these devices.

P429 Efficacy of administration of Nifekalant in patients with out-of-hospital ventricular fibrillation from Utestein style records

M. Igarashi[1], Y. Miyake[2], S. Ishimatsu[1], S. Sakamoto[1], Y. Tawara[1], Y. Tokuyasu[1], A. Saito[1], S. Kanesaka[1], S. Hori[1], K. Nagao[1] on behalf of SOS-KANTO Investigators. *[1]SOS-KANTO Investigators, Critical Care Center, Tokyo, Japan; [2]Tokyo, Japan*

Purpose: A survey of survivors after cardiac arrest in KANTO area (SOS-KANTO) was conducted in 58 communities and involved emergency medical service in Japan. The purpose our study is to evaluate intravenous administration of Nifekalant (NF) as Class III antiarrhythmic agent affect defibrillation effects and discharge rate from Utestein style records.
Method: 9592 patients who were found as cardiopulmonary arrest since July 2002 to December 2003 were enrolled in this study. Subjects were finally 1044 patients (mean age=62 years old, Male=839) with out-of-hospital VF excluded restored heart beats. The patients were divided into two groups; group N, in which they intravenously administered NF, and group C, in which conventional therapies were performed. The independent predictors of admission to intensive care unit and discharge of hospital, including age, sex, the presence of witness, administering vasopressin, lidocaine, NF, were examined using multiple logistic-analysis.
Result: 100 patients were in Group N, and 944 patients in Group C. 50 patients (50%) admitted to Intensive Care Unit (ICU) in Group N, in contrast 169 patients (17.9%) also admitted to ICU. Additionally, 11 patients (11%) in Group N, and 42 patients (4.4%) were able to discharge hospital. Administering NF was the independent predictor with an adjusted odds ratio of 0.27 (p=0.0002), and vasopressin was also of 0.44 (p=0.012). There was no significance with discharge from hospital on these factors.
Conclusion: NF and vasopressin are contributed to admission, but all factors are not related with discharge ratio.

IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

P430 5-year follow-up on ICD patients with electrical storm: a single center experience

T. Becker, T. Kleemann, M. Vater, K. Doenges, J. Senges, K. Seidl. *Herzzentrum, Ludwigshafen, Germany*

Background: In 10 to 30% of all ICD patients (pts) the phenomenon of electrical storm (ES) occurs. This denotes a temporal clustering of ventricular tachyarrhythmia with consecutive therapy by the ICD. Pts suffering ES and the clinical concomitants of this condition are poorly described.
Methods: Analysis of the pts in our prospective ICD registry who suffered ES (definition: $>$ 2 episodes of ventricular tachycardia/fibrillation within 24 hours, end of ES is defined as freedom from arrhythmia for 14 consecutive days)
Results: Of the pts consecutively included in our ICD registry since 1991, 171 pts (12%) suffered ES. Clinical characteristics are shown in Table1.
In these pts 253 episodes of ES occured (1.5$\pm$0.9 episodes of ES per pt). In 43 of 253 episodes of ES (17%) secondary causes were present (hypokalemia, rapid atrioventricular conduction of atrial fibrillation, discontinuation of antiarrhythmic drugs). A mean of 1.6$\pm$0.7 antiarrhythmic drugs per pt were used to treat ES. 66 pts (39%) died during a mean follow-up period of 1858$\pm$1273 days. In pts who died, time from first ES to death was 605$\pm$681 days.

Table 1

Female gender	38 pts (22%)
Age (ICD first implanted)	62$\pm$11 y
CAD	113 pts (66%)
Dilative cardiomyopathy	39 pts (23%)
Isolated electrical disease	8 pts (5%)
EF $<$ 40%	134 pts (78%)
ICD for primary prophylaxis	14 pts (8%)
Time from ICD implantation to first ES	940$\pm$1067 d

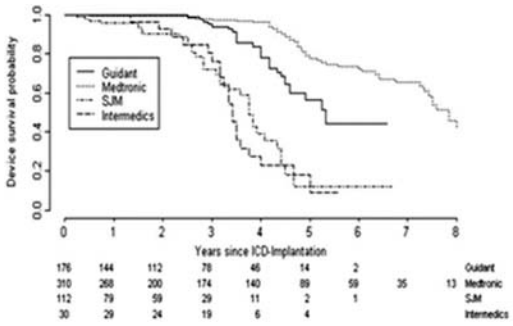
Summary: 1. Mortality rate for ICD pts with electrical storm was 40% over a period of 5 years 2. ICD pts with ES were middle aged, 80% of them had a low EF and two thirds suffered from CAD 3. In pts with ES mean time from ICD implantation to first ES was 2.6 years 4. Secondary causes were present in every sixth episode of ES 5. ICD was implanted for primary prophylaxis in 1/10 of pts with ES.

P431 Marked differences in ICD longevity between different manufacturers

B.A. Schaer, L. Joerg, C. Sticherling, S. Osswald. *University Hospital, Cardiology, Basel, Switzerland*

Background: Device safety, inappropriate shocks, longevity and battery replacement ahead of schedule are of major concern for ICD patients (pts). There is very limited industry-independent data on true device longevity and time to replacement, most of them with small numbers of pts.
Methods: Inclusion of all 679 devices implanted in 533 pts 3/94-12/06. Documentation of manufacturers, devices and pacing mode and averaged shocks per ICD. 17 ICDs exchanged for other reasons than ERI (9 recalls, 5 infections, 3 others) and thus excluded.
Results: The survey consists of 629 ICDs (311 Medtronic, 112 St. Jude, 176 Guidant and 29 Intermedics). Of the 526 pts, 415 had just one device implanted, 85 had two, 25 three and 1 four, respectively. 426 were VVI, 134 DDD, 87 CRT. Kaplan-Meier curve of the longevity in different manufacturers is shown in fig 1. There was no difference between VVI and DDD modes, CRT devices were replaced significantly (mean 2 y) earlier. Number of shocks (without DFT-testing/auto-cap reform) per ICD were: Medtronic 2.9$\pm$15.2; Intermedics 2.1$\pm$4.6; Guidant 0.7$\pm$3.4; St.Jude 0.3$\pm$0.9 and thus cannot be responsible for the marked longevity difference. 131 ICD were replaced (Medtronic 49, St.Jude 34, Guidant 27 and Intermedics 21) after mean 48$\pm$19 months (range 3-96): Medtronic after 61$\pm$19, Guidant after 47$\pm$9, Intermedics after 35$\pm$9 and St.Jude after 26$\pm$13 months. 59 Medtronic ICDs (19%), 3 Guidant (2%) and 1 St.Jude (1%) are in service for $>$ 5 and 18 Medtronic ICDs for $>$ 8 years.
Conclusions: There are marked differences in device longevity between manufacturers which can't be explained by different number of shocks. Further con-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020



ICD longevity in different manufacturers

founders as different rates of pacing need and threshold values must be investigated. CRT devices have a much lower longevity than VVI or DDD devices.

P432 Appropriate and inappropriate therapy occurrence in ICD patients from a "real world" French registry

P. Defaye[1], A. Duparc[2], N. Delarche[3], O. Bizeau[4], J.M. Dupuis[5], J.L. Pasquie[6], R. Azoui[7], C. Braban[3], A. Leenhardt[8] on behalf of OPERA study group. *[1]University Hospital, Grenoble, France; [2]University Hospital, Toulouse, France; [3]General Hospital, Pau, France; [4]General Hospital, Orleans, France; [5]University Hospital, Angers, France; [6]University Hospital, Montpellier, France; [7]Guidant France, Rueil Malmaison, France; [8]University Hospital, Lariboisiere, France*

Introduction: Few data are available about the time of occurrence and the determinants of inappropriate therapy in pts with ICD. The prospective multicenter OPERA study was designed to analyze the time and causes of delivery of the first appropriate (FAT) and inappropriate therapy (FIAT) in pts with a primary (PP) or secondary prevention (SP) indication.
Methods and results: 655 patients (88% males, 62±13.6 years, 28.7% for PP) were implanted with a single/dual chamber ICD with or without ventricular resynchronization. During a mean follow-up (FU) of 20.2± 8 months, 217 pts (33%) received a first therapy: 182 pts had a FAT (27.4%), 57 pts had a FIT (8.6%) and among them, 22 pts had both. Demographic data of the population are shown in the table.
The FAT were preferentially delivered in pts implanted for a PP indication (19.9% vs 30.6%, p<0.01) but there was no difference for the FIT (6.8% vs 9.3% p=NS). The mean time occurrence between FAT and FIT was 7.8± 6.9 vs 6.9±6.6 months (NS). Among the FIT, 25 (44%) could have been avoided by optimizing the programming, including a higher cut-off zone, an appropriate atrial blanking, detection algorithm turned on, and sustained rate duration algorithm turned off.

	FAT	FIT	P
Male (%)	90.7	91.3	NS
Age (years)	64.4±13	60.6±15	P<0.05
SVT history (%)	31.7	34.8	NS
LVEF (%)	36.6±14.4	35.6±14.9	NS
NYHA > or = II (%)	73	77	NS
Ischemic CM (%)	66	68	NS
AA drug Tx (%)	88	80	P<0.01
P P indication	20.3	22.8	NS
Single chamber ICD	36.3	42.1	NS

CM:cardiomyopathy; AA drug Tx: anti-arrhythmic drug therapy.

Conclusion: During a mean FU of 20 months, 33% of pts received a therapy. The delivery of a FAT was significantly higher in the population implanted for a secondary prevention indication. Age and anti-arrhythmic drug were associated to FAT and FIAT deliveries. Optimization of ICD programming may decrease by 44% the rate of inappropriate therapies. These results will be confirmed during the 2-year overall duration of the study.

P433 Automatic remote transmission of intracardiac electrograms after tachyarrhythmia detection enables improvements in ICD therapy

C. Perings[1], W. Bauer[2], H. Bondke[3], C. Mewis[4], J. Schwab[5], P. Broadhurst[6], M. James[7], G. Mentz[8], K. Wallbrueck[9], H.J. Trappe[5] on behalf of RIONI investigator group. *[1]Herne, Germany; [2]Wuerzburg, Germany; [3]Berlin, Germany; [4]Homburg/Saar, Germany; [5]Bonn, Germany; [6]Aberdeen, United Kingdom; [7]Taunton, United Kingdom; [8]Wiesbaden, Germany; [9]Erlangen, Germany*

Purpose: Appropriate and inappropriate therapies by an implantable cardioverter defibrillator (ICD) have a major impact on mortality and quality of life in ICD patients (pts). Intracardiac electrograms (IEGM) enable the analysis of episodes and subsequent therapies. Recently, IEGMs have become available via remote transmission, i.e. episode evaluation is possible without the patients having to see their cardiologists. We present first data on reliability and clinical utility of this feature.
Methods: Patients indicated for ICD implantation according to the guidelines receive single or dual chamber ICD, or CRT-D home monitoring device, and are followed for 12 months. IEGM messages are analyzed immediately after notification and are compared to the conclusions drawn at the next follow-up from the IEGMs stored in the ICDs.
Results: 523 pts have been enrolled (78 f; mean age ± SD: 63±12 years; LVEF: 36±14%; 53% secondary prevention; 64% ischemic etiology; 328 single chamber, 154 dual chamber ICD, and 41 CRT-D). Mean follow-up was 303±116 days. 198 pts (38%) experienced 4263 arrhythmias, including 488 ventricular fibrillation (VF) and 1998 ventricular tachycardia (VT1, VT2) episodes. Remote IEGM was successfully transmitted for 1310 episodes for 190 pts. Mean IEGM coverage, i.e. percentage of episodes with remote IEGM available, was 79% for VT1, 65% for VT2, and 76% for VF. For 58% of the pts every VT1 episode was accompanied by a remote IEGM, and for 69% every VF episode could be analyzed with an IEGM. Clustering of episodes, i.e. 3 or more episodes within 24 hours, resulted in a worse coverage. For cluster-free patients, mean coverage was 91% for VT1, 78% for VT2, and 81% for VF. In 81% of these pts, IEGM was available for every VT1, in 79% for every VF episode.
93% of the transmitted IEGMs could be interpreted by the attending physician, 7% were indeterminable, mainly due to the missing atrial channel (single chamber ICD), or the missing IEGM for termination. For 12% of the interpretable IEGM, the physician concluded that the ICD therapy was inappropriate (due to supraventricular tachycardia, T-wave oversensing, lead problems, or noise).
Conclusion: Our investigation shows that the automatic remote transmission of intracardiac electrograms after tachyarrhythmia is technically feasible and clinically useful: IEGM transmission enables with high reliability an immediate analysis of tachyarrhythmia by the attending physician, without the patient having to visit the ICD clinic. For a significant portion of the detected episodes, the transmitted data reveal the necessity of optimization in ICD therapy.

P435 Prevalence of severely impaired ejection fraction after percutaneous coronary intervention

L. Joerg[1], B. Schaer[2], T. Dieterle[2], S. Osswald[2], C. Sticherling[2]. *[1]University Hospital Basel, Cardiology, Basel, Switzerland; [2]University Hospital Basel/Cardiology, Cardiology, Basel, Switzerland*

Prevalence of severely impaired ejection fraction after percutaneous coronary intervention for acute myocardial infarction
Background: Several studies (MADIT-II, SCD-HeFT) showed that post myocardial infarction (MI) patients with an ejection fraction (EF) below 35% benefit from primary prophylactic implantation of a cardioverter defibrillator (ICD) to prevent sudden cardiac death (SCD). Frequently, the question arises when to implant the ICD, since implantation 6-40 days post-MI proved not to be beneficial in the DINAMIT study.
Purpose: To determinate the incidence of potential ICD-candidates in consecutive patients with acute myocardial infarction (AMI) treated with percutaneous coronary intervention (PCI) at a single centre and to follow the recovery of EF over time.
Methods: 292 consecutive patients undergoing PCI for an acute myocardial infarction (243 STEMI, 49 NSTEMI) between 1.1.2006 and 31.8.2006 at a single center were identified. EF was determined by echocardiography, gated myocardial perfusion imaging, or ventriculography. We aimed to obtain a follow-up EF in all patients by consulting the general practitioner or performing EF studies in house.
Results: The prevalence of an EF below 35% early after AMI was 13% (39/292 patients). Of those, 34 (87%) patients suffered from STEMI and 5 (13%) from NSTEMI (p=0.47). 8 of 39 patients (21%) died (5 infarct related deaths, 3 not infarct related). In 7 (18%) patients, no follow-up EF was obtained. In the remaining 24 (62%) patients EF at a median follow-up of 60 days (range: 40-306 days) after AMI recovered from 34±7% to 40±8% (p=0,002). Four weeks or later after AMI, a persistent low EF <35% was found in 4/24 patients (16%) resulting in an overall rate of AMI survivors with an EF<35% of 1.3%.
Conclusions: In our population, the prevalence of an EF <35% immediately after PCI was only 13%. Four weeks after PCI for myocardial infarction, the EF improved to over 35% in the vast majority of patients with initially depressed LV-Function. Thus, only very few patients finally fulfilled the criteria for primary prophylactic implantation of an ICD. These findings may help to explain why the DINAMT study showed no benefit of ICD implantation early post-MI.

P436 Clinical outcomes of implantable cardioverter defibrillator patients according to the implant testing procedure from a multicenter prospective study (Leader)

N. Sadoul[1], P. Defaye[2], O. Bizeau[3], J.M. Dupuis[4], A. Lazarus[5], J.M. Davy[6], N. Delarche[7], E. Mouton[8], P. Guesdon[4] on behalf of Leader study group. *[1]University Hospital, Nancy, France; [2]University Hospital, Grenoble, France; [3]General Hospital, Orleans, France; [4]University Hospital, Angers, France; [5]Clinic Bizet, Paris, France; [6]University Hospital, Montpellier, France; [7]General Hospital, Pau, France; [8]Guidant France, Rueil Malmaison, France*

Introduction: Intra-operative defibrillation testing (DFT) is currently performed (+)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

during the implantation of cardioverter defibrillator (ICD). Recently, many investigators have raised questions about DFT usefulness. The aim of this work was to assess the clinical outcomes of patients (pts) with or without DFT at implant.
Methods: Among 388 pts enrolled in 36 French centers, implanted with an ICD with or without cardiac resynchronization (CRT), DFT was not performed (-) in 44 pts (11.3%). The demographic data were as follow: mean age = 62.9 ±12.9 years (83.9% men), mean LVEF = 31.9±13.6%, ischemic cardiomyopathy = 64.5%, prophylactic indication (PI) = 54%, history of supraventricular tachycardia = 28.8%. The demographic data did not differ between the 2 populations (DFT - vs DFT +) except for PI (80 vs 51%, p<0.001), NYHA Class III+IV (77 vs 40%, p<0.001), LVEF (24±7 vs 33±14%, p<0.001), QRS (148±38 vs 128±39 mm, p<0.01), CRT-D (73 vs 42%, p<0.001), rate of the VF zone (205±12 vs 213±16 min-1, p<0.01).
Results: The table summarises the main events that occured during a mean follow-up (F.U) of 5.1±5.0 months. Two patients in the DFT + group died from sudden cardiac death (SCD), one from VF and one from myocardial infarction.

Clinical outcome

	Pts with A.Tx N (%)	Pts with I.Tx N (%)	HF hospitalisation N	SCD N	ICD lead repositioning N
DFT - (n=44)	2 (4.5)	2 (4.5)	0	0	0
DFT + (n=344)	45 (13.1)	13 (3.8)	11 (3.2)	2 (0.6)	5 (1.5)
p	NS	NS	NS	NS	NS

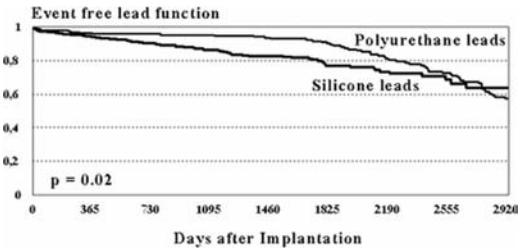
A.Tx: ≥1 appropriate therapy; I.Tx: ≥1 inappropriate therapy; HF: heart failure.

Conclusions: These preliminary data indicate that there are no difference between the clinical outcomes in the FU of ICD pts with or without DFT at implant. A longer FU is mandatory to confirm these data.

P437 Defibrillation lead failure in polyurethane leads compared to silicone leads

T. Kleemann, T. Becker, M. Vater, K. Doenges, S. Schneider, J. Senges, K. Seidl. *Herzzentrum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany*

Introduction: Coaxial polyurethane insulated leads are known to be prone to insulation failure. Newer lead models have a multilumen design and are insulated by silicone rubber. However, the rate of lead failure in newer models is not well known. Aim of the study was to compare the rate of transvenous defibrillation lead defects in polyurethane leads compared to silicone leads.
Methods: From 1991 to 2005, 243 (21%) polyurethane insulated right ventricular defibrillation leads and 895 (79%) silicone leads were implanted. Median follow-up time was 934 (368/1870) days. Lead defect was defined as a lead malfunction which needed surgical correction.
Results: Lead failure occurred in 69 (28%) polyurethane leads and in 108 (12%) silicone leads. During the first 5 years the failure rate of silicone leads was more than doubled compared to polyurethane leads (23% vs. 10% at 5 years, p < 0,05). At 8 years lead survival rates were similar between both groups (57% in polyurethane leads and 63% in silicone leads, p = n.s.). The major lead complications in both models were insulation failure (55% in polyurethane versus 40% in silicone leads). Ninety percent of insulation failure in polyurethane leads occurred later than 5 years after implantation whereas in silicone leads insulation failure occurred at any time after implantation.



Event free lead function

Conclusions: 1. The failure rate of silicone leads was more than doubled during the first 5 years compared to polyurethane leads. 2. However, a difference of lead survival rate was no more observed after 8 years. 3. Insulation failure remained the major lead complication in both types of leads. 4. In polyurethane leads insulation failure was a late lead complication whereas in silicone leads insulation failure occurred at any time after implantation.

P438 Prevalence of MADIT II criteria in a consecutive post-myocardial infarction population

C. Holmgren, B. Nystrom, N. Edvardsson. *Sahlgrenska University Hospital, Goteborg, Sweden*

A low ejection fraction after myocardial infarction is an accepted criterion for prophylactic ICD implantation following MADIT II. It is not well-known what the consequences would be if the MADIT II criteria were applied. We present prospectively collected data in a consecutive post-myocardial infarction population at a university hospital with high activity in thrombolysis and PCI.
Patients: 586 patients were identified and myocardial infarction was confirmed by ECG and/or enzymes. Seventy percent were males. One hundred fifty one patients had had at least one previous myocardial infarction. During the hospital stay 83 patients received thrombolysis, 259 underwent PCI and 62 CABG. 42 patients received more than one of these treatments.
Results: The two-year all-cause mortality was 21.7%. Thirty-seven patients (6.3%) died <1 week, fourteen (2.4%) between 1 week and 1 month and another 76 patients (13%) between 1 month and 2 years. In 79 of 545 patients who survived the first month echocardiography was not performed during the hospitalization. Twenty of those who died between 1 month and 2 years had no echocardiography, 14 had EF <0.30, 18 an EF 0.31-0.40 and 24 an EF >0.41. Of all patients who survived for >2 years, 5,8% of patients had an EF <0.30, 12.3% had an EF 0.31-0.40 and 83% an EF >0.40.
As many as 79% of the patients who survived for >2 years had no previous myocardial infarction, as compared to 54% of those who died between 1 month and 2 years. A history of atrial fibrillation was present in 28% of those who died between 1 month and 2 years, respectively, as compared with 8,1% in survivors >2y.
Conclusion: EF<0.30 was present in 33 of the patients alive at one month and was associated with a a 25% mortality between 1 month and 2 years. Cardiac death occurred in 46 patients >1 month - 2 years, 12 of which were arrhythmic. Of patients who had an EF <30% only 3 died an arrhythmic death between 1 month and 2 years.

PHARMACOLOGIC THERAPY

P439 Role of nuclear factor-kappaB in the left ventricular remodeling of diabetic heart exposed to repetitive hypoxic stress

T. Hayashi[1], C. Yamashita[2], T. Mori[1], C. Matsumoto[2], C. Kwak[2], Y. Okada[1], N. Fukuda[1], M. Miyamura[1], Y. Matsumura[2], Y. Kitaura[1].
[1]*Osaka Medical College, Third Department of Medicine, Takatsuki, Japan;*
[2]*Osaka University of Pharmaceutical Sciences, Takatsuki, Japan*

Purpose: Diabetes is a major cause of cardiovascular disease and premature death. Recently, intermittent hypoxia was reported to activate inflammatory pathways including nuclear factor-kappaB (NF-kB) in patients with sleep apnea syndrome. The aim of this study was to examine the role of NF-kB in the development of left ventricular (LV) remodeling in diabetic heart exposed to intermittent hypoxia.
Methods: Male OLETF rats at 9 weeks of age were kept under intermittent hypoxia (oxygen, 10.0±0.5% for 8 hours per day) or normoxia for 3 weeks. Rats exposed to intermittent hypoxia were treated with vehicle or 80 mg/kg/day of NF-kB inhibitor pyrrolidine dithiocarbamate (PDTC). Fine structure of the LV myocardium and percent fibrosis (%Fibrosis) in the interstitium were evaluated, and oxidative stress in the LV myocardium was assessed by immunohistochemical expression of 4-hydroxy-2-nonenal protein (4-HNE). The NF-kB binding activity and the mRNA expression of TGF-beta were examined by electrophoretic mobility shift assay and RT-PCR, respectively.
Results: Intermittent hypoxia significantly increased hypertrophy of cardiomyocytes and %Fibrosis (Figure). Moreover, TGF-beta expression, NF-kB binding activity and 4-HNE expressions were increased by intermittent hypoxia. Treatment with PDTC significantly reduced mean diameter of cardiomyocytes and %Fibrosis via suppressing TGF-beta expression, NF-kB binding activity and 4-HNE expressions.

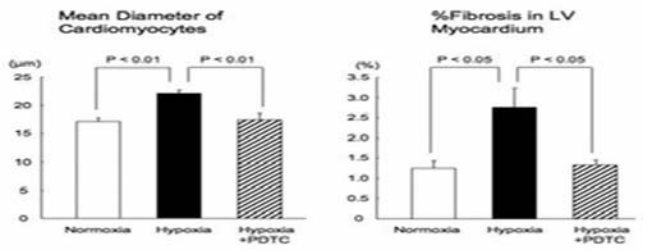


Figure. Effect of PDTC on diabetic heart

Conclusions: PDTC inhibits NF-kB binding activity and exerted cardioprotection in diabetic rats exposed to intermittent hypoxia. This study suggests that NF-kB activation might contribute to the development of LV remodeling in diabetic patients with the sleep apnea syndrome.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P440 Tranilast attenuates structural and functional aspects of diabetic cardiomyopathy in the transgenic (mRen-2) 27 rat

K.A. Connelly[1], D.J. Kelly[2], Y. Zhang[2], R.E. Gilbert[2]. *[1]St Vincent's Hospital,University of Melbourne, Department of Medicine And Cardiology, Fitzroy, Australia; [2]University of Melbourne, Medicine, Melbourne, Australia*

Objective: Diastolic dysfunction is an increasingly recognised complication of diabetes that develops in relatively young patients as a result of diabetic cardiomyopathy (DCM). With recent advances in echocardiographic technology now permitting the reliable assessment of diastolic function the rat, we examined cardiac function and structure in diabetic rodents and assessed the effects of intervening with tranilast, an anti-fibrotic compound that has been shown to attenuate the actions of transforming growth factor-β (TGF-β) in cardiac fibroblasts. We also sought to examine the mechanism whereby tranilast inhibits the actions of TGF-β.
Methods: Six week old heterozygous (mRen-2)27 rats were randomized to receive either streptozotocin or citrate buffer then further randomized to receive either tranilast (400 mg/kg/day by twice daily gavage) or vehicle for another eight weeks. Cell signalling was examined in neonatal cardiac fibroblasts.
Results: At 16 weeks of age, diabetic animals demonstrated impaired diastolic function with reduced "E/A" ratio (1.5±0.27 v 1.04± 0.05) and prolonged deceleration time (35.7±2.6 v 55.7±1.97 ms) when compared to control ($p<0.05$). Tranilast treatment was associated with improved diastolic function as evidenced by a change in the "E/A" ratio (1.04±0.05 v 1.48±0.5) and reduced deceleration time (55.7± 1.97 v 42.9±1.18ms, $p<0.05$). Furthermore, tranilast treated animals demonstrated a reduction in collagen types I and III along with a reduction in cardiomyocyte diameter and reduced cellular apoptosis ($p<0.01$). While tranilast did not affect Smad phosphorylation it significantly attenuated TGF-β induced p44/42 mitogen activated protein kinase (MAPK) phosphorylation.
Conclusion: Tranilast inhibits TGF-β induced p44/42 MAPK activation and prevents the functional and structural manifestations of diabetic cardiomyopathy in (mRen-2)27 rats.

P441 Improvement in mechanical alternans as shown by Doppler in patients with severe heart failure: levosimendan versus dobutamine

M.B. Yilmaz, F. Karadas, A. Erdem, I. Tandogan. *Cumhuriyet University School of Medicine, Cardiology, Sivas, Turkey*

Mechanical alternans (MA), an ominous sign of terminal systolic heart failure(HF), could be indirectly shown by Doppler analysis. We searched the effect of L versus dobutamin (D) onto Doppler alternans in patients with systolic HF. 22 consecutive patients with systolic HF and MA were randomized to either L or D infusion. Pulsed wave Doppler analysis of left ventricular outflow tract (LVOT) was performed. Minimum and maximum velocities were measured. Doppler alternans of the LVOT velocities was expressed as the percent change in the velocity during ten cycles both before and after the infusion (Vc: [maximum-minimum velocity]/maximum velocity x 100). DVc was expressed as percent improvement from the basal Vc to the Vc after the infusion.
Before the infusions, all patients had pulsus alternans, noticeable at bedside as mechanical alternans (MA). Mean EF in the whole group before infusions was 20.1±2.8%, and increased significantly to 25.1±3.8% ($p<0.001$). Mean Vc1 was 35.7±8.5% before the infusions and decreased significantly to 28.5±9.7% (Vc2, $p<0.001$) after therapy. Two patients in L and four patients in D groups, those with relatively minor change in Vc and with almost unchanged symptomatic status, had MA at bedside after the infusion. Those with persisting alternans at bedside had also significant improvement, though minor, in the EF (22.3±2.2% versus 26.6±2.4%, p=0.004), though, they did not have any improvement in the DVc (38.8±4.8% versus 38.3±5.6%, p=0.852). Percent change in the EF was expressed as DEF, and calculated as EF1 (before the infusion)-EF2 (after the infusion)/EF1 x 100. Patients in both groups were not different in used drugs, EF before and after infusions, basal VC. Vc significantly improved in the L group (35.7±8.7% and 23.4±7%, $p<0.001$), whereas not in the D group (35.2±9.3% and 33.5±9.5%, p=0.383), though both had significant improvements in the EF ($p<0.001$ for both). DVc was negatively correlated with DEF in patients with L (r= -0.676, p=0.022), whereas there was no significant correlation of DVc with DEF in patients with D. On the other hand, those who stated moderate-marked improvements in their symptoms (dyspnea) in both groups following infusion were those with more significant improvement in their DVc compared to those who stated not (28.9±12.8% versus 11.3±19.1, p=0.017) despite no difference in DEF compared to those who stated not (26.1±15.4% versus 23.9±11.7%, p=0.730).
Conclusion: Levosimendan improves beta-to-beat alteration in patients with systolic HF, demonstrated by pulsed Doppler compared to dobutamin.

P442 Ivabradin versus bisoprolol influence on functional mitral regurgitation in patients with postinfarction heart failure

K.G. Adamyan, A.L. Chilingaryan, A.V. Astvatsatryan, T.R. Astvatsatryan, S.I. Vardanian. *Institute of Cardiology, Acute myocardial infarction, Yerevan, Armenia*

Functional mitral regurgitation (FMR) is one of the major contributors of clinical course and prognosis of heart failure. Induced by apical and posterior displacement of papillary muscles due to local LV remodeling and myocardial asynchronism in the presence of reduced contractility it changes its severity during exercise depending on changes of myocardial contractility leading to dyspnoea and fatigue. We assumed that β-blockers might increase exercise FMR grade in contrast to ivabradin (I) which does not influence on inotropy.
Methods: 107 pts (67 women) aged 57±8 yrs in sinus rhythm with postinfarction heart failure (PHF) due to systolic dysfunction (EF < 35%) and mild, moderate or severe exercise augmented FMR on ACEI, diuretics, digoxin as a standard therapy were evenly (according to exercise FMR severity) distributed in two groups in order to receive bisoprolol (B) titrated to 10 mg/day, n = 54; or I titrated to 7.5 gm BID, n = 53. Maximal symptom-limited (dyspnoea or fatigue) exercise stress test (EST) was performed after 1 month follow up. Mitral regurgitant volume (RV) and effective regurgitant orifice (ERO) were measured before and after ET.
Results: After 1 month follow up RV and ERO were decreased, unchanged, or worsen in B 32%, 35%, 33% pts compare to I in 34%, 43%*, 23%* pts respectively (*$p < 0.005$). RV and ERO changes at peak ET were worse in B compare to I (RV: 17±6 ml vs 12±5 ml, $p < 0.03$; ERO: 13±3 mm^2 vs 11±2 mm^2; $p < 0.05$). HR did not differ significantly in groups at rest and peak ET, but exercise time (ET) were greater in I compare to B: (457±15 sec vs 415±20 sec, $p < 0.05$). Thus, I is better tolerated than B in PHF with FMR, probably due to lack of negative inotropy which increases FMR through coaptation force reduction. Further follow up is needed to study long-term effects of both drugs on FMR.

P443 Role of digitalis in the contemporary management of systolic heart failure

J.K. Ghali[1], S.W. Tam[2], J.E. Mitchell[3], M. Worcel[1], M.L. Sabolinski[1]. *[1]Wayne State University, Medicine, Detroit, United States of America; [2]NitroMed, Inc., Clinical Development, Lexington, United States of America; [3]SUNY Downstate Medical Center, Medicine, Brooklyn, United States of America*

Purpose: The effects of digitalis in patients with systolic heart failure (SHF) have not been evaluated in the era of contemporary medical therapy including the use of beta blockers. In the African-American Heart Failure Trial (A-HeFT), the fixed-dose combination of isosorbide dinitrate/hydralazine (FDC I/H) decreased mortality and morbidity and improved patient reported functional status in self-identified black patients with SHF stabilized on contemporary heart failure (HF) therapy. We investigated the effect of digitalis in A-HeFT.
Methods: A pre-specified Kaplan-Meier survival analysis was performed to determine the effect of FDC I/H compared to placebo with or without the use of digitalis in A-HeFT (n=1050). Analogous retrospective analyses within the FDC I/H and placebo groups were performed.
Results: In A-HeFT, 62% of patients received digitalis at baseline. Patients receiving digitalis had lower systolic BP (125 vs. 128 mmHg), diastolic BP (76 vs. 78 mmHg), and qualifying LV ejection fraction (23.3 vs. 25.6%). Concomitant medications were comparable for either ACEI or ARB (93%) and beta blockers (87%). Digitalis users had significantly higher use of diuretics (94 vs. 89%) and spironolactone (45 vs. 29%). Compared to placebo, FDC I/H was associated with 53% improvement in survival ($p<0.01$), and a 32% decrease in death or first HF hospitalization ($p<0.01$) in patients treated with digitalis. There was a trend for an increase in all-cause mortality in patients receiving digitalis (see Table) that was noted primarily in the placebo group (HR=1.65; 95% CI 0.91-2.76, p=0.102) and not the FDC I/H group (HR=1.02; 95% CI 0.50-2.10, p=0.96). Digitalis use was also associated with a significant increase in the risk of mortality or first heart failure hospitalization.

Digitalis on outcomes in all patients

Outcome	Hazard Ratio	95% CI	Risk increase	p value
Death	1.38	0.88-2.11	38%	0.166
Death or 1st HF Hospitalization	1.38	1.06-1.74	38%	0.015

Conclusions: Within the limitations of sub-group analysis, our data indicate that the use of digitalis was not associated with beneficial effects on morbidity and mortality in patients with SHF receiving contemporary therapy. FDC I/H improved outcomes in patients with HF independent of the use of digitalis.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P444 Structural and electrophysiological effects on cardiac remodeling by ivabradine

C. Ceconi[1], L. Comini[2], S. Suffredini[3], E. Cerbai[1], R. Ferrari[3], M. Bouly[4], A. Mugelli[1]. [1]*University of Ferrara, Chair of Cardiology, Ferrara, Italy;* [2]*Foundation Salvatore Maugeri IRCCS, Core Laboratory, Gussago, Italy;* [3]*CIMMBA University of Florence, Florence, Italy;* [4]*Servier Laboratories, Courbevoie, France*

Rationale: Left ventricular (LV) remodeling plays a major role in progression of heart failure (HF) after myocardial infarction (MI). Drugs able to modulate preload and afterload have a favorable impact on LV remodeling. We have investigated the hypothesis that heart rate reduction per se, obtained by chronic treatment of ivabradine (IVA), the first selective and specific inhibitor of the pacemaker current If with no effect contractility, is able to modulate electrophysiological and structural remodeling processes in post-MI rats.
Methods: IVA was orally given at 10 mg/kg/day for 90 days to Wistar rats subjected to left descending coronary artery ligation (MI) 7 days after surgery. Sham operated rats (SH) were used as control group and sham rats treated with IVA only for electrophysiology evaluation. 32 MI animals were randomly allocated to IVA or vehicle. End-systolic (ESV) and end-diastolic (EDV) volumes and ejection fraction (EF) were evaluated by echocardiography. Long term IVA effect on transient potassium outward current (Ito) was also evaluated by using single left ventricular cardiomyocyte (LVM) enzimatically isolated from MI and SH. Ito was recorded in the whole-cell configuration by applying steps from the holding potential (-70 mV) to -30/+60 mV using a pre-step to inactivate sodium and calcium currents.
Results: Echocardiography: At 3 months, IVA significantly reduced heart rate (-11%), ESV (-31%) and improved EF (13%) in MI rats (table).
Electrophysiology: IVA did not change peak Ito density measured at +50 mV in LVMs from SH (9.3±1.1pA/pF; n=21; 9.5±1.7 pA/pF, n=20, treated vs non treated). Peak Ito was significantly reduced in LVMs from MI non-treated rats (5.1±0.7 pA/pF, n=30 $p<0.01$ vs SH) and partially restored in LVMs from MI treated rats (7.3±0.8 pA/pF, n=28) ($p<0.05$).

	SH (n=15)	MI (n=15)	MI+IVA (n=17)
Heart rate (beats/min)	228±5	235±4	208±5†
ESV (ml)	0.41±0.03	0.78±0.10**	0.54±0.08†
EDV (ml)	1.22±0.07	1.69±0.18	1.39±0.15
EF (%)	66.2±1.3	54.7±2.3**	62.8±1.7†

†$p<0.05$ vs. MI; **$p<0.01$ vs. SH.

Conclusions: These data indicate a beneficial effect of ivabradine on electrophysiological and structural remodeling in post-MI rats supporting its use in treatment of heart failure.

P445 A restrictive pattern of left ventricular filling and its changes after beta adrenergic blockade with Carvedilol in heart failure patients

J. Nessler[1], B. Nessler[1], M. Kitlinski[2], N. El Massri[1], W. Piwowarska[1]. [1]*Institute of Cardiology, Dpt of Coronary Disease, Cracow, Poland;* [2]*University Hospital, Dpt of Cardiology, Malmoe, Sweden*

Background: Restrictive mitral filling pattern (r-MFP) significantly modifies the clinical course of congestive heart failure (CHF). Aim: To assess the influence of chronic Carvedilol therapy on selected clinical parameters depending on the pattern of left ventricular filling.
Material and Methods: 86 pts aged 56±9.19 years with symptomatic systolic heart failure, EF below 40% and NYHA class II/III. They were divided into rMFP group-36 pts (E/A over 2 or E/A between 1 and 2 and deceleration time E-DT<140ms) and nrMFP group -50 pts not meeting the criteria above. The following parameters were analyzed at baseline, 3 and 12 months after Carvedilol was introduced: parameters of systolic and diastolic function, concentrations of ET-1, BNP, inflammatory markers and CPX parameters.
Results: At baseline there was a positive correlation between heart rate at rest (HRs) and E/A (r=0.55; p=0.049). The table nr 1summarizes the parameters that differed significantly between groups at baseline. At 3 months after Carvedilol the frequency of rMFP was reduced in 19% of patients, and at 12 months rMFP was present only in 14% of patients. At 12 months in 60.8% of patients in rMFP group the filling pattern changed to nonrestrictive. In nrMFP group the nonrestrictive pattern changed to restrictive only in 6 pts (12%) at 12 months. At 12 months the frequency of rMFP significantly reduced from 36.1% to 20%;p=0.04. The E/A ratio significantly reduced from 2.9±1.2 to 1.4±0.9; p=0.003. In both groups there was a significant increase in LVEF, whereas ET-1 and BNP decreased. In rMFP group VO2peak significantly increased from 12.5 to 14.5±3.1ml/kg/min, p=0.04; in contrast to nrMFP group.

Table 1

	NYHA	HR (l/min)	LVEF (%)	LA (mm)	ET-1 (pg/ml)	BNP (pg/ml)	VO2peak (ml/kg/min)
rMFP	2.9±0.4	91.3±17.4	26.6±5.8	48.1±6.6	65.7±27.5	541.5±206.7	12.5±3.7
nrMFP	2.5±0.5	83.4±7.3	30.0±6.2	43.0±6.1	37.0±24.8	412.6±207.2	16.5±4.7
p	0.001	0.04	0.03	0.01	0.03	0.009	0.001

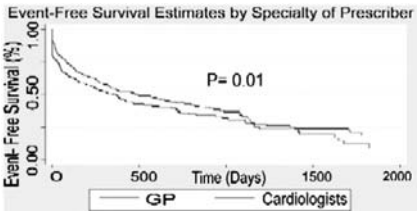
Significant differences between study groups at baseline.

Conclusions: 1.The presence of rMFP in CHF patients is associated with significantly increased ET-1 and BNP, higher NYHA class and lower VO2 peak as compared with nrMFP patients. 2.Chronic beta-adrenergic blockade significantly improves diastolic function in 60.8% of patients with rMFP and improves exercise capacity. 3.A change from restrictive to nonrestrictive filling pattern suggests its reversibility after Carvedilol.

P446 Beta-blockers in heart failure: the influence of the specialty of the prescriber on clinical outcomes

M. Bernier[1], M. Dorais[1], A. Rakel[1], O. Sheehy[1], J.F. Boivin[2], J. Lelorier[2]. [1]*Universite de Montreal, Pharmacoepidemiology Center, Montreal, Canada;* [2]*McGill University, Department of Epidemiology, Montreal, Canada*

Background: Beta-blockers (BB) have been to shown to reduce mortality and morbidity in heart failure patients. This has been demonstrated in large randomized trials and with different molecules. However, real life experience with the introduction of BB for that indication is not well described. We sought to investigate the effect of the prescriber specialty on mortality and hospitalization in heart failure patients treated with different BB.
Methods: From July 1997 to October 2005, we studied a cohort of patients aged 65 or older with a diagnosis of heart failure covered by the Quebec Health Insurance Plan. Inclusion criteria were treatment with an ACE inhibitor or an angiotensin receptor blocker and initiation of BB therapy (Metoprolol, Bisoprolol, Carvedilol) by a cardiologist or general practitioner (GP). All cause mortality and hospitalization for heart failure were recorded. Multivariate survival analysis using Cox Proportional Hazard models were performed. Comorbidity adjusted Hazard Ratio with their 95% CI are reported.
Results: A total of 7675 patients were included. Multivariate analysis showed significant lower mortality and hospitalization rate for heart failure in the carvedilol group if prescription and follow up was performed by a cardiologist as compared to a GP with a Hazard Ratio of 0.61 (95%CI 0.37 – 0.98) and 0.82 (95%CI 0.67 – 1.00) respectively. These differences were not found in the metoprolol or bisoprolol group.



Event Free Survival in carvedilol group

Conclusion: Our study suggest that prescription of carvedilol by a cardiologist in heart failure patient leads to lower mortality and hospitalization rate when compared to GP. This is possibly due to the particular pharmacodynamic of carvedilol (Beta and alpha blocking properties) and may justify specialized care for its prescription in this population.

P447 Utility of levosimendan in patients with infarct-related cardiogenic shock under IABP exposure

M. Greif[1], L. Zwermann[1], C. Reithmann[1], M. Weis[2]. [1]*Munich, Germany;* [2]*University Hospital Munich-Grosshadern, Medizinische Klinik Und Poliklinik I, Munchen, Germany*

The calcium sensitizer levosimendan may provide a promising alternative/additive to conventional inotropes for patients with acutely decompensated heart failure. Data on the use of levosimendan in patients with infarct-related cardiogenic shock already under inotropes and intra-aortic balloon pump (IABP) are limited.
Methods: 6 patients with refractory cardiogenic shock after ST-elevation myocardial infarction, multi organ failure and under maximal intensive care (inotropes, IABP) were treatd with levosimendan (Bolus 12 μg/kg i.v., thereafter 0.1-0.2 μg/kg over 24 h). Hemodynamic effects were registered invasively and monitored over 72h post infusionem. Inotropes therapy was triggered for a mean arterial pressure > 70mmHg and systemic vascular resistance at 800-1000 dyn x sec/cm-5.
Results: Therapy with levosimendan rapidly and significantly reduced required epinephrine concentrations (1.9±0.9 mg/h before levosimendan; 1.6mg/h after 12h, 1.3 mg/h after 24h, 0.3±0.4mg/h after 72h; $p< 0.001$ vs baseline). Norepinephrine infusion had to be adjusted during the first 12h of levosimendan infusion (+75%; $p<0.01$), but was significantly reduced after ≥72h compared to baseline (0.6±0.7 vs 0.3±0.2 mg/h after 72h; $p< 0.05$). Cardiac output increased significantly during levosimendan infusion (baseline 2.1±0.5 l/min versus 3.2±0.4 l/min > 48h after infusion; $p<0.05$).
IABP therapy could be weaned in all patients during 5 days after infusion and all patients survived the cardiogenic shock.
Conclusion: Levosimendan therapy was associated with a rapid and consistent stabilization of patients with severe cardiogenic shock and multiorgan failure even under IABP therapy.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P448 Tulobuterol tape, an adhesive patch of beta-2 adrenergic agonist, is a novel cardioprotective parenteral inotrope for heart failure

K. Komamura[1], H. Asanuma[1], A. Hirata[2], M. Wakeno[1], H. Takahama[1], T. Nakatani[1], M. Kitakaze[1]. *[1]National Cardiovascular Center, Department of Cardiology, Suita, Japan; [2]Osaka Police Hospital, Dept. of Cardiology, Osaka, Japan*

Purpose: Intravenous inotropic agents for chronic heart failure (CHF) require long-term hospitalization, higher medical cost and lower quality of life. Since beta-2 adrenergic agonist has inotropic and anti-apoptotic effects on myocardium, we tried to develop an adhesive patch of beta-2 agonist as a new inotropic agent for CHF patients.
Methods: 1) Tulobuterol, a beta-2 agonist, was administered to lewis rats (1.0mg/kg, n=6) for a month. Concomitantly, rats were given doxorubicin (15mg/kg) to induce left heart failure. After a month, LV ejection fraction (LVEF) was determined by echocardiography, which was compared to placebo group (saline, n=6). LV tissue was stained with sirius red and TUNEL to determine fibrotic area and number of apoptotic cells. In the separate set of 10 animals, mortality was observed over two months. 2) Tulobuterol was administered to wister rats, to which monochrotaline (60mg/kg) was given to induce right heart failure. After a month, right ventricular pressure was measured, and LV tissue was stained with sirius red. In the separate set of 10 animals, mortality was observed over two months. 3) Tulobuterol tape (1.0mg/kg) was attached for two hours to anesthetized beagle dogs (n=6) with myocardial infarction. LVEF was determined by echocardiography, and cardiac output was determined by thermodilution method.
Results: 1) After a month, LVEF was higher in the tulobuterol group than in the placebo group (97±2 vs. 82±4%, $p<0.05$). Fibrotic area and number of TUNEL positive cells were smaller and fewer in the tulobuterol group than in the placebo group (5.7±1.5 vs. 10.1±2.0%, $p<0.05$; 6±3 vs. 20±9/10^2 cells, $p<0.05$). There was no difference in mortality over two months. 2) Right ventricular pressure was lower in the tulobuterol group than in the placebo group (71±6 vs. 46±6 mmHg, $p<0.05$). Fibrotic area was smaller in the tulobuterol group than in the placebo group (1.5±0.9 vs. 3.6±1.0%, $p<0.05$). Kaplan-Meier analysis showed lower mortality in the tulobuterol group than in the placebo group ($p<0.01$). 3) Without significant changes in heart rate and blood pressure, LVEF and cardiac output increased (45±4 to 58±7%, $p<0.05$; 1.4±0.2 to 1.7±0.2L/min, $p<0.05$), and LV end-diastolic pressure decreased (26.0±4.8 to 19.2±1.9mmHg, $p<0.05$), compared with the baseline.
Conclusions: Tulobuterol may have a potential of inotropic and cardioprotective action on chronic heart failure. Tulobuterol tape may provide an alternative strategy for intravenous inotropes.

P449 Increase of coronary flow after levosimendan infusion is associated with improvement in cardiac performance in patients with decompensated heart failure

I. Ikonomidis, I. Parissis, I. Paraskevaidis, K. Kourea, G. Filippatos, D. Kremastinos. *University of Athens, Attikon Hospital, 2nd Cardiology Department, Athens, Greece*

Levosimendan is a novel calcium sensitizer which improves cardiac contractility without increasing myocardial oxygen demand. We examined the effects of levosimendan infusion on coronary flow and the relation between changes in coronary flow and the reciprocal changes in BNP, in echocardiographic and clinical indices of cardiac performance after levosimendan infusion in patients with decompensated heart failure.
Methods: We studied 42 patients, of mean age 62±12 years, with chronic decompensated heart failure (NYHA III-IV) refractory to conventional therapy and LV ejection fraction (EF) 22±16%. Patients were randomized to receive levosimendan 0.1 μg/kg/min (n=21) or placebo (n=21) for 24 hours. Before and 48h after each treatment patients underwent: A) assessment of max, mean and time integral (VTI) of the coronary flow velocity (CFV) in LAD using a 7MHZ transducer during colour-guided Doppler echocardiography, of RV systolic pressure (RVSP) by means of Doppler echocardiography, of E/E' ratio using Doppler imaging of mitral inflow velocity and tissue Doppler imaging of the mitral annulus and of LVEF B) measurement of plasma BNP levels.

Levosimendan	Max-CFV (m/sec)	VTI-CFV (m/sec)	RVSP (mmHg)	E/E'	EF (%)	BNP (pg/ml)
BASELINE	0.29±0.1	10.3±2.6	59±8	26±21	25±7	1115±611
48h POST	0.43±0.2	16.3±6	51±7	13±5	33±4	588±471
p	0.017	0.002	0.002	0.014	<0.01	<0.01

Results: There were no differences in baseline characteristics between patients receiving levosimendan or placebo. ANOVA showed that there was a greater increase in max, mean and VTI –CFV, and decrease in BNP levels, RVSP and E/E' after levosimendan than after placebo (table, $p<0.05$) Compared to baseline, increasing VTI-CFV was related to an improvement in EF, E/E', BNP after treatment in patients receiving levosimendan (r=0.69, r=-0.41and r=-0.80 $p<0.05$ respectively) Conclusion: Short-term levosimendan therapy improves coronary flow in parallel with improvement in cardiac function parameters in patients with heart failure

P450 Effects of aldosterone blockers on left ventricular function and remodeling in patients with mild-moderate chronic heart failure and optimized therapy

S. Nodari, M. Metra, G. Milesi, D. Fumagalli, A. Manerba, P. Rocca, D. Maffeo, L. Dei Cas. *University of Brescia, Brescia, Italy*

Background: In Chronic Heart Failure (CHF) Aldosterone Blockers (AB) are actually indicated only for patients (pts) in III/IV NYHA class. Nevertheless this therapy could be effective also in pts in a earlier stage of desease. There are many evidences, indeed, about the escape of aldosterone during ACE-I/ARB chronic therapy, and about its important role in myocardic hypertrophy and fibrosis. Aim. To assess the effects of AB treatment on left ventricular (LV) function and remodeling in pts with mild-moderate CHF (II NYHA class) and optimized therapy, during a 6 months follow-up.
Methods: Among 170 CHF consecutive pts, referred to our Institution, 122 pts fulfilling the inclusion/esclusion criteria were randomized to placebo or active treatment (spironolactone or potassium canrenoate), in a simple-blind design. The dose of AB has been established considering the clinical and laboratory analysis at the entry of the study and during a follow-up. Both before starting therapy and after a 6 months follow-up, all pts underwent clinical evaluation, ECG, ECHO, GATED-SPECT scintigraphy, and lab analysis (bun, creatinine, electrolytes).
Results: The drug administration was stopped in thirteen pts (21%) because of side effects. Ejection Fraction (EF) significantly increased in treatment group vs control group, while endiastolic volume (EDV), endsystolic volume (ESV), and LV mass (LVM) decreased significantly as well (table). Pts with previous severe diastolic dysfunction (restrictive pattern) showed a significant improvement in all echo parameters.

	EDV (ml)		ESV (ml)		EF %		LVM (g)	
	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy
Baseline	192±50	197±58	120±37	115±40	35,4±10	34,5±10	269±74	274±80
6 month	185±48	170±49*	118±33	98±32*	34,6±10	38,7±10*	260±70	242±73*
	E wave (cm/s)		A wave (cm/s)		E/A Ratio		DT (cm/s)	
Baseline	48±24	97±27	59±33	31±13	0,8	3,2	249±45	152±43
6 months	35±11	35±8§	63±37	72±13§	0,5	0,4	274±56	323±27§

*$p<0.05$; §$p<0.001$.

Conclusions: AB therapy of CHF pts, added to standard one, can produce a further decrease of LV remodeling, and consequently a considerable improvement both of systolic and diastolic function. The positive effects, observed in severely affected pts, are recorded also in pts with mild-moderate HF.

P451 Nebivolol compared to Metoprolol-Succinate improves endothelial function, endothelial progenitor cell mobilization, left ventricular remodeling and dysfunction early after myocardial infarction

S.A. Sorrentino, C. Doerries, W. Mohmand, R. Akbar, C. Besler, A. Schaefer, H. Drexler, U. Landmesser. *Hannover Medical School, Cardiology Dept, Hannover, Germany*

Purpose: A protective role of endothelial nitric oxide synthase (eNOS)-dependent nitric oxide (NO) production on left ventricular (LV) remodeling and dysfunction after myocardial infarction (MI) has been suggested by recent studies. Hence, we hypothesized that the effect of Nebivolol, due its NO-releasing properties, may be superior to Metoprolol-Succinate post-MI with regard to improvement of endothelium-dependent, NO-mediated vasodilatation, cardiomyocyte hypertrophy, interstitial fibrosis and LV-dysfunction.
Methods and Results: Mice with extensive anterior myocardial infarction (n=30) were randomized to treatment with Nebivolol (10 mg/kg/d), Metoprolol-Succinate (20 mg/kg/d), or placebo via gavage for 30 days starting on day 1 after surgery. Infarct size was similar among groups and both β-adrenergic receptor antagonist agents caused similar decreases in heart rate. Nebivolol improved endothelium-dependent, acetylcholine-induced vasorelaxation of thoracic aortic ring segments 4 weeks post-MI (Nebivolol vs. placebo 55±7 vs. 21±4%; $P<0.05$), whereas Metoprolol-Succinate had no effect (Metoprolol 21±1%; Metoprolol vs. placebo: P=n.s.). Nebivolol improved LV-dysfunction post-MI as assessed by echocardiography, while Metoprolol-Succinate had no significant effect (LV-ejection fraction: Nebivolol vs. Metoprolol vs. placebo 26±3 vs. 18±3 vs. 15±2; nebivolol vs. placebo: $P<0.05$). Nebivolol treatment, but not Metoprolol-Succinate, caused an increased EPC mobilization (Nebivolol vs. Metoprolol-Succinate vs. placebo: 260±32 vs. 142±44 vs. 145±25 cells per hpf; $P<0.05$ Nebivolol vs. Metoprolol-Succinate & placebo). In addition, Nebivolol had a more pronounced effect on cardiomyocyte hypertrophy and interstitial fibrosis as assessed by histomorphometric analysis. Moreover, Nebivolol, but not Metoprolol-Sucinate, improved post-MI survival as compared to placebo.
Conclusions: In conclusion, the present findings suggest that Nebivolol improves endothelium-dependent vasodilatation in mice post-MI, whereas Metoprolol-Succinate had no effect. Moreover, at equivalent myocardial β-adrenergic receptor blocking doses, Nebivolol had a more pronounced effect on cardiomyocyte hypertrophy, interstitial fibrosis and LV-dysfunction post-MI, compatible with the notion that Nebivolol may exert beneficial effects post-MI beyond β-adrenergic receptor blockade.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P452 Discharge medication in acute heart failure patients with respect to left ventricular function

K. Siirila-Waris[1], J.P.E. Lassus[1], J. Melin[2], K. Peuhkurinen[3], M.S. Nieminen[1], V.-P. Harjola[1] on behalf of FINN-AKVA study group. *[1]Helsinki, Finland; [2]Jyvaskyla, Finland; [3]Kuopio, Finland*

Purpose: To investigate the implementation of heart failure (HF) medication according to ESC chronic HF guidelines in acute HF patients with systolic HF (SHF), compared with diastolic HF (DHF).
Methods: HF medication at discharge was assessed from patients discharged (n=573) after hospitalization for acute HF in the FINN-AKVA study. Patients were also categorized into SHF (LVEF <45%) and DHF (LVEF ≥ 45%). Achieved dosages in relation to target dosages in ESC guidelines (expressed as percentages of maximum target dose) were evaluated in patients discharged with the specified medication.
Results: Patients mean age was 74.8 years, half had de novo HF and 9% had chronic renal insufficiency. LVEF was known in 68%, and 50% of these had SHF. Use of furosemide and beta-blockers (BB) was similar in both groups, whereas agents inhibiting renin-angiotensin system were more frequently prescribed in SHF (Table 1). Discharge dosages as percentages from target dose: BB 53%, ACE-inhibitors 58% (ACEI), angiotensin receptor blockers (ARB) 56% and spironolactone 59%. In SHF group percentages were respectively 50, 54, 56 and 47, whereas in the DHF group 55, 63, 59 and 66.

Use of HF medication at discharge

	ALL (%) (n=573)	LVEF<45% (%) (n=193)	LVEF≥45% (%) (n=197)	p-value
BB	86.0	91.7	86.8	0.118
ACEI/ARB	76.6	85.0	73.6	0.006
Spironolactone	19.7	28.5	15.7	0.002
Furosemide	88.8	90.7	85.8	0.135
ACEI/ARB+BB	67.2	78.2	65.0	0.004
ACE/ARB+BB+spironolactone	14.1	21.8	11.2	0.005

Conclusion: Use of spironolactone, ACEI/ARB and their combinations were significantly better implemented in SHF patients to whom the evidence based guidelines are targeted. In BB users there was no significant difference. Use of BB and ACEI/ARB was surprisingly high in the DHF group. Triple therapy (ACE/ARB, BB, and spironolactone) was rather infrequent even in patients with SHF. Target doses were halfway implemented by hospital discharge, and titration indeed is needed during early follow-up. However, in this real-life aged population with coexistent conditions, the realistic and optimal goal is often lower than the maximum guideline doses.

P453 Carvedilol effect on the right ventricular function in chronic heart failure

A. Bennis[1], G. Benhayoun[2], M. Zahraoui[1], H. Bougtab[1], M. Bennani[1]. *[1]Centre De Cardiologie, Casablanca, Morocco; [2]Centre de cardiologie, Centre de cardiologie, Casablanca, Morocco*

Beta-blocker use improves left ventricular ejection fraction (LVEF) in patients with heart failure. A similar effect of b blockers on right ventricular function has been proposed, although the effect of carvedilol on right ventricular function has not been assessed.
This study investigated the short-term effect of carvedilol on right ventricular function in chronic heart failure patients. A cohort of 60 heart failure patients who were not taking b blockers at baseline was studied prospectively. Right ventricular ejection fraction (RVEF) and LVEF were measured at both baseline and 6 months by echocardiography. Various parameters of the right ventricular function were measured: Simpson RVEF, surface shortening fraction, right ventricular outflow tract (RVOT%), TAPSE (mm), S' wave with tissue Doppler (S' dti cm/s), and the Tei index. The threshold of significativity was fixed at 5%.Carvedilol was up-titrated during four monthly visits by a preestablished protocol to a target dose of 50 mg/d. The dose of vasodilators was not changed. Quality of life and brain natriuretic peptide level were assessed.
Mean age was 65.7±16.3 years. Baseline RVEF was 25.6±5.2% and baseline LVEF was 20.8±6.4%. Mean carvedilol dose reached was 25±12.5 mg daily. At 6 months, RVEF significantly increased by 7.5% (95% confidence interval, 3.9-10.2; p=0.0001) and LVEF also increased significantly by 9.5% (95% confidence interval, 4.0%-11.9%; p=0.0003). All the parameters of the right ventricular function improved.
Quality-of-life score improved from 42.8 to 30.8 (p=0.047). No correlation was found between brain natriuretic peptide levels and RVEF. Carvedilol treatment for 6 months resulted in a significant improvement of RVEF, which paralleled the improvement of LVEF.

P454 Bisoprolol compare to verapamil improves diastolic function and reduces NT-pro-BNP levels in patients with diastolic heart failure

K.G. Adamyan, A.L. Chilingaryan, A.V. Astvatsatryan, T.R. Astvatsatryan, S.I. Vardanian. *Institute of Cardiology, Acute myocardial infarction, Yerevan, Armenia*

β-blockers improves clinical course of diastolic heart failure (DHF) through HR reduction thereby LV filling time prolongation and myocardial oxygen demand reduction, regression of left ventricular hypertrophy, and direct inhibition of renin release. Data of β-blockers influence on LV remodeling, contractility and cardiac peptides levels in DHF are scarce. We study effects of bisoprolol on diastolic function, contractility and NT-pro-BNP levels in DHF. Metods: 185 pts (62 women) with DHF (E/A 240 msec) NYHA III and EF ≥50% aged 58±11 years on ACEI/ARB and (if necessary) diuretics were randomized to two groups to receive bisoprolol (B) titrated to 10 mg/day (n = 92) or verapamil (V) titrated to 240 mg/day (n = 93). Total ischemic burden (TIB) as total time of ST segment depressions ≥ 1 mm and ≥1 min duration was measured by 24 hour monitoring. Midwall fractional shortening (MFS), E/Em of LV lateral mitral annulus, transmitral E wave deceleration time (EDT), E/A, NT-pro-BNP were measured by EchoCG in 30, 90, 180 day and 1 year follow up by experts unaware of the study aims.
Results: In 30 day all parameters did not reach statistical significance between groups. In 90 day TIB was less in B compared to V (24±7 min vs 35±9 min, $p < 0.03$) and MFS, E/A, EDT were better in B (MFS: 13±4% vs 9±2%, $p < 0.05$; E/A: 0.7±0.2 vs 0.5±0.2, $p < 0.05$; EDT: 305±25 msec vs 325±20 msec, $p < 0.05$). In 180 day in addition to further improvement of TIB (14±5 min vs 32±7 min, $p < 0.001$), MFS (18±5% vs 11±3%, $p < 0.01$), E/A (1.2±0.5 vs 0.7±0.4, $p < 0.01$) and EDT (296±12 msec vs 310±14 msec, $p < 0.01$) in B also observed improvement of E/Em and NT-pro-BMP level. (E/Em: 9.6±6.7 vs 13.2±5.8, $p < 0.03$; NT-pro-BMP: 92.3±5.5 pg/ml vs 125±8.4 pg/ml, $p < 0.003$) After 1 year follow up differences in parameters between groups remain unchanged. Fewer hospitalizations was observed in B (10 pts vs 23 pts, $p < 0.01$).
Thus B reduces hospitalization rate, improves diastolic function and reduces ischemia in pts with DHF NYHA III, and probably thereby declines levels of NT-pro-BNP toward normal.

P455 Inhibition of inducible nitric oxide synthase attenuates functional deterioration and myocyte hypertrophy in pacing-induced heart failure

S. Aker, K. Klein, I. Konietzka, A. Van De Sand, G. Heusch, R. Schulz. *University of Essen, Essen, Germany*

Background: In failing hearts, independent of the underlying cause - ie. dilated or ischemic cardiomyopathy -, the expression of inducible nitric oxide synthase (iNOS) is increased. Experimental and preliminary clinical studies in scenarios of increased iNOS expression such as sepsis demonstrated enhanced survival when iNOS was inhibited. We therefore investigated the effects of iNOS-inhibition with 1400W on left ventricular (LV) function and morphology in rabbits with pacing-induced heart failure.
Methods: HF was induced by LV pacing (400 bpm) for 3 weeks; 7 rabbits received 1400W (1mg/kg/d sc) at the onset of pacing and 7 rabbits received placebo. Sixteen sham-operated rabbits served as controls; 8 received 1400W and 8 received placebo.
Results: In sham rabbits treated with 1400W or placebo, LV end-diastolic diameter (LVEDD, echocardiography), systolic fractional shortening (FS) and morphology remained unchanged. In HF rabbits treated with placebo, LVEDD increased (16.9±0.3 to 20.0±0.5mm) and FS was reduced from 30.2±0.7 to 11.1±1.4% (both $p<0.001$) after 3 weeks of pacing. In HF rabbits treated with placebo, the cardiomyocyte iNOS protein expression was increased (1151±29 vs. 531±22 AU, $p<0.05$, confocal microscopy), and this increase was prevented by 1400W. In HF rabbits treated with 1400W, FS after 3 weeks of pacing was better preserved than in HF rabbits treated with placebo (15.1±1.6 vs. 11.1±1.4%, $p<0.05$), whereas LVEDD was increased to the same extent. The extent of myocardial fibrosis (10.6±0.5 vs. 14.1±1.4% per field of view) and the increase in myocyte cross-sectional area (255±10 vs. 314±9μm^2) were significantly less in HF rabbits treated with 1400W compared to placebo. In contrast, the number of TUNEL-positive cardiomyocytes was increased to a comparable extent in both HF groups.
Conclusion: Inhibition of iNOS improves LV systolic function and attenuates fibrosis and myocyte hypertrophy in pacing-induced HF in rabbits.

P456 Electrophysiological effects of levosimendan administration in patients with advanced heart failure secondary to ischemic or dilated cardiomyopathy

H.E. Mavrakis, E.M. Kanoupakis, E.M. Kallergis, E.P. Koutalas, C.E. Lathourakis, E.G. Nyktari, E.G. Manios, P.E. Vardas. *Heraklion University Hospital, Cardiology Department, Heraklion, Greece*

Purpose: Levosimendan administration exerts favourable effects on systolic and diastolic cardiac function, as well as on neurohormonal and inflammatory activation of pts with CHF. However, this calcium sensitizer inotrope may have proarrhythmic effects. The purpose of the present study was to evaluate the effects of levosimendan infusion, on human cardiac electrophysiological properties.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Methods: In 11 stable pts (68±4.5 years) with left ventricular dysfunction (EF<30%), due either to CAD (n=5) or to dilated cardiomyopathy (n=6) two electrophysiological studies were performed, before and 24 hours after the infusion of levosimendan (0.1 μg/kg/min). All pts were in sinus rhythm and were free of antiarrhythmic drugs. Before and after the infusion of levosimendan, we measured AH and HV intervals, corrected SNRT and the Wenckebach point. Atrial and ventricular effective refractory period (ERP) at 3 cycle lengths (CL: 600,500,400ms), as well as inducibility of ventricular tachycardia, were also tested in both studies. Holter recordings were obtained before and after the infusion.
Results: After the infusion of levosimendan AH and HV intervals, corrected SNRT, Wenckebach point and atrial ERP were unaffected. Ventricular ERP showed a non-statistically significant reduction. Sustained ventricular arrhythmias were inducible in 8 of the 11 pts, at baseline. A monomorphic VT was inducible in 5 pts, a rapid polymorphic VT was inducible in 3 pts. Only 1 pt was inducible with 2 extrastimuli. In another 7 pts, ventricular arrhythmias were inducible by the third premature stimulus. The mean values for 2 and 3 premature beats that induced ventricular tachyarrhythmias were 226±21 ms and 203±19 ms, respectively. After infusion of levosimendan, sustained ventricular arrhythmias were still inducible in these 8 pts, although a less aggressive stimulation protocol was required. (Five pts were inducible with one extrastimulus and 3 pts with 2. The mean values for one and two premature beats that induced ventricular tachyarrhythmias were 244±20 ms and 221±23 ms, respectively). In 2 other pts sustained VT not present at baseline study was induced after levosimendan administration. The mean number of ventricular extrasystoles and non-sustained VT episodes increased significantly after levosimendan administration.
Conclusions: Short-term levosimendan infusion increases myocardial excitability. This is reflected by complex ventricular arrhythmogenesis in Holter recordings and the increased susceptibility for sustained ventricular tachyarrhythmias.

P457 Heart failure therapy improves in octogenarians enrolled in Euro Heart Failure Survey II

M. Komajda[1], O. Hanon[2], M. Hochadel[3], J.L. Lopez-Sendon[4], L. Tavazzi[5], F. Follath[6], P. Ponikowski[7], H. Drexler[8], K. Dickstein[9], M. Nieminen[10]. *[1]Chu Pitie Salpetriere, Cardiology Dept., Paris, France; [2]Hopital Broca, Gerontology, Paris, France; [3]Stifftung Institut fur Herzinfarktforschung, Cardiology, Ludwigshafen Am Rhein, Germany; [4]Hospital General Gregorio Maranon, Cardiology, Madrid, Spain; [5]Policlinico San Matteo, IRCCS, Cardiology, Pavia, Italy; [6]University Hospital, Cardiology, Zurich, Switzerland; [7]Klinika Kardiologii, Cardiology, Wroclaw, Poland; [8]Zentrum Innere Medizin, Cardiology, Hannover, Germany; [9]University of Bergen, Cardiology, Stavanger, Norway; [10]Helsinki University - Central Hospital, Cardiology, Helsinki, Finland*

Background: Chronic heart failure (HF) is common in elderly patients. Data of Euro Heart Failure Survey I (performed in 2000-2001) indicated an under use of HF recommended therapy (use of ACE inhibitors=50%, use of beta-blockers=24% (Eur Heart J. 2006 Dec 21).
Objectives: We compared the modalities of HF therapy received by 741 octogenarians (median age = 84y) and 2836 younger patients (median age = 68y) admitted for HF in 133 hospitals in 30 European countries, between October 2004 and August 2005, participating in the Euro Heart Failure Survey II.
Results: At admission, the use of ACE inhibitors (50% vs 56%, p<0.01) and spironolactone (20% vs 30%, p<0.0001) was significantly reduced in octogenarians compared to younger people, whereas calcium channel blockers were more often prescribed in older subjects (23% vs 17%, p<0.001). Prescriptions of beta blockers (41% vs 44%, p=0.20), diuretics (73.5% vs 71%, p=0.12), nitrates (29% vs 27%, p=0.38) and digitalis (27.5% vs 26%, p=0.52) were similar in both groups. At discharge the use of HF recommended therapy increased in both groups, but this increase was less important in the octogenarians group compared to younger patients (ACE inhibitors 65% vs 73%, p<0.0001, beta blockers 53% vs 63%, p<0.0001). After 1 year of follow up, the rate of prescription of ACE inhibitors in survivors was similar in both groups (71% vs 71%, p=0.97) and the use of beta blockers (58% vs 70%, p<0.0001) or spironolactone (35% vs 44%, p<0.01) was reduced in octogenarians, whereas digitalis (32% vs 25%, p<0.05), nitrates (38% vs 27%, p<0.001) and diuretics (92% vs 84%) were more commonly prescribed in older people.
Conclusions: These results indicate an improvement in the prescription rate of recommended HF therapy in older subjects compared to previous studies. Particularly, the use of ACE inhibitors was similar in octogenarians and younger people after 1 year of follow up. However, octogenarians are less likely to receive beta blocker therapy and more likely to receive symptom relieving drugs (diuretics, digitalis, nitrates) than younger HF patients.

P458 Adequacy of diagnosis and treatment of chronic heart failure in Primary Care Medicine in Sweden

U.G. Dahlstrom[1], J. Hakansson[2], K. Swedberg[3], A. Waldenstrom[4]. *[1]University Hospital, Cardiology, Linkoping, Sweden; [2]Krokom Primary Care Center, Primary Health Care, Krokom, Sweden; [3]Sahlgrenska University Hospital/Ostra, Medicine, Gothenburg, Sweden; [4]University Hospital, Cardiology, Umea, Sweden*

Design: Non-interventional, retrospective, observational multicentre study. Historical and current data of diagnosis and treatment of the 10-15 latest subjects diagnosed with chronic heart failure (CHF) were collected from each centre (The OBS-study).
Purpose: To obtain an overview of the diagnostic tools and treatments currently used in patients with CHF in Primary Health care (PHC) in Sweden in relation to official guidelines.
Methods: We collected data from 2093 patients in 158 randomly selected PHC centers, which the patients had visited between January 2004 to January 2006.
Results: The mean age was 79 yrs (F 81 and M 78). The dominating etiology to the CHF was Hypertension and Ischemic Heart Disease. 19% were in NYHA class I, 42% in class II, 25% in class III and 7% in class IV. 69% had their diagnosis based on symptoms and/or ECG and/or Chest X-ray (79% of the females). Thus only 31% (21% of the females) were fulfilling the diagnostic ESC criteria for CHF. The patients had at least two concomitant diseases on an average. 32% suffered from a severe somatic disease and 8% from a severe psychiatric disease and/or dementia. Common symptoms/signs were dyspnea (60%), fatigue (49%) and peripheral oedema (36%). Mean systolic blood pressure was 135/76 mm Hg, mean heart rate was 73 bpm (37% had > 75 bpm), mean serum-creatinine was 105 umol/L and mean Hemoglobin was 135 g/L.
74% (69% of the females) were on treatment with ACE-inhibitors and/or AII-antagonists, but only 37% had > 50% of the recommended target dose. 68% were on treatment with beta blockers but only 31% had > 50% of the recommended target dose. Only 42% were on treatment with both ACE-inhibitors and/or AII-antagonists and beta blockers and only 20% had > 50% of the recommended target dose.
Conclusions: Only about 30% of the patients were fulfilling the diagnostic ESC criteria for CHF, including investigation with echocardiography. Compared to official guidelines both used agents and dosages of the recommended drugs were generally lower. This may reflect underutilization but may also partially be related to the patients high age and other severe concomitant diseases.

P459 Increased mortality and cardiovascular risk associated with non-selective non-steroidal anti-inflammatory drugs and selective cyclooxygenase-2 inhibitors in chronic heart failure

G.H. Gislason[1], J.N. Rasmussen[2], S.Z. Abildstrom[1], T.K. Schramm[3], M.L. Hansen[1], F. Folke[1], S. Rasmussen[3], L. Kober[4], M. Madsen[3], C. Torp-Pedersen[1]. *[1]Gentofte University Hospital, Department of Cardiology, Hellerup, Denmark; [2]National Institute of Public Health, Copenhagen, Denmark; [3]Bispebjerg University Hospital, Department of Cardiology, Copenhagen, Denmark; [4]Rigshospitalet Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark*

Purpose: To study risk associated with non-steroidal anti-inflammatory drugs (NSAIDs) (non-selective NSAIDs and selective cyclooxygenase-2 (COX-2) inhibitors) among unselected cohort of patients with chronic heart failure (HF).
Methods: The study population comprised 107,092 patients surviving first HF hospitalization in Denmark 1995-2004, identified from the nationwide Danish Patient Registry. The relationship between NSAID use and death or re-hospitalisation for either acute myocardial infarction (MI) or HF was analysed by multivariable time-dependent Cox proportional-hazard models.
Results: The mean observation period was 2.6 years (SD 2.4); 60,974 (56.9%) patients died, and 8,970 (8.4%) and 39,984 (37.5%) were re-hospitalized for MI and HF, respectively. NSAID treatment was initiated in 37,574 (35.1%) patients at some point after discharge. Selective COX-2 inhibitors as well as non-selective NSAIDs were associated with increased risk of death, and re-hospitalisation for MI or HF, with a dose-dependent response in risk (Table), although partial effect of unmeasured confounders cannot be excluded.

Drug	Death		Re-hospitalization for HF		Re-hospitalization for MI	
	HR	95% CI	HR	95% CI	HR	95% CI
Rofecoxib ≤ 25 mg/d	1.50	1.38-1.62	1.36	1.22-1.52	1.29	1.04-1.60
Rofecoxib > 25 mg/d	3.73	3.28-4.23	1.89	1.50-2.40	1.61	0.98-2.64
Celecoxib ≤ 200 mg/d	1.41	1.28-1.56	1.26	1.11-1.43	1.36	1.07-1.73
Celecoxib > 200 mg/d	2.82	2.54-3.13	1.27	1.05-1.54	1.52	1.09-2.13
Ibuprofen ≤ 1200 mg/d	0.99	0.94-1.05	1.16	1.09-1.24	1.31	1.16-1.49
Ibuprofen > 1200 mg/d	2.85	2.67-3.05	1.19	1.05-1.34	1.50	1.17-1.93
Diclofenac ≤ 100 mg/d	1.33	1.22-1.44	1.34	1.22-1.49	1.15	0.92-1.44
Diclofenac > 100 mg/d	5.59	5.14-6.09	1.43	1.18-1.74	2.46	1.76-3.44
Naproxen ≤ 1000 mg/d	1.04	0.90-1.21	1.19	1.00-1.42	1.50	1.09-2.06
Naproxen > 1000 mg/d	3.62	2.76-4.73	1.11	0.63-1.96	1.79	0.66-4.84
Other NSAID	1.55	1.48-1.63	1.23	1.15-1.32	1.29	1.12-1.48

Adjusted hazard ratios (HR) for death, re-hospitalization for acute myocardial infarction (MI) or heart failure (HF) associated with NSAID treatment in chronic HF.

Conclusion: Non-selective NSAIDs and selective COX-2 inhibitors seem to be associated with increased mortality and cardiovascular risk, and should be used with caution in chronic HF.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P460 The impact of sildenafil use in acute reduction of pulmonary arterial hypertension in advanced heart failure patients

A. Freitas Jr, F. Bacal, L.F.P. Moreira, A.I. Fiorelli, R. Honorato, J.L. Oliveira Jr, C.P. Silva, G.V. Guimaraes, N.A.G. Stolf, E.A. Bocchi.
Heart Institute, University of Sao Paulo, Sao Paulo, Brazil

Introduction: Pulmonary arterial hypertension (PAH) due to chronic and severe left ventricular dysfunction is an incapacitating disease associated to quality of life worsening and mortality rates increase before and after heart transplantation. A vasodilator challenge should be administered in all heart transplant (HT) candidates with advanced PAH and it is, traditionally, performed by using sodium nitroprusside during right heart catheterization. That is a direct arterial vasodilator with limited usefulness due to important side effects like hypotension.
Objective: To compare two different protocols (sildenafil citrate vs. sodium nitroprusside) efficacy in the acute reduction of PAH in HT candidates.
Material and Methods: 20 patients (mean age: 42±15 years, 12 men) with advanced heart failure (mean EF: 27±9%, NYHA III–IV) and PAH (mean sPAP 60±9 mmHg) were submitted to right heart catheterization and basal hemodynamic pulmonary pressures study during routine evaluation to HT. They were randomized in two different groups to receive sildenafil citrate (100mg sublingual single dose) or intravenous sodium nitroprusside titrated from 0,5–10ucg/kg/min up to the limit determined by systolic blood pressure 85mmHg. The second pulmonary hemodynamic parameters evaluation was done within 60 and 15 minutes after initial drugs administration to sildenafil and sodium nitroprusside group, respectively. The data of both groups during the two measurements was obtained by ANOVA.
Results: Both sildenafil and sodium nitroprusside groups, comparing to basal measurements, showed respectively significant reduction of sPAP (58.8±11 vs. 49.8±19.15 mmHg and 64.5±8.34 vs. 56.8±21.11 mmHg, CI=95%, $p<0.05$) and PVR (5.8±3.41 vs. 2.81±1.22 Wood units and 6.5±2.05 vs. 3.96±1.63 Wood units, CI=95%, $p<0.05$). When analyzing comparatively the results of both, we noticed that sildenafil group was superior to sodium nitroprusside considering PVR reduction (2.81±1.22 vs. 3.96±1.63 Wood units, CI=95%, $p<0.05$) without significant reduction in mean arterial blood pressure (90,3±8,01 vs. 82,9±15 mmHg, CI=95%, p=0,3 and 89,3±10,04 vs. 73,06±26,75 mmHg, CI=95%, $p<0,05$).
Conclusion: Sildenafil citrate is an efficacy alternative drug to acute reduction of pulmonary arterial hypertension in heart transplant candidates. It was superior to sodium nitroprusside in PVR reduction without significant systemic hypotension.

P461 Candesartan use in hypertrophic and non-obstructive cardiomyopathy estate (the CHANCE): a double-blind, placebo-controlled, randomized, multicenter study

M. Penicka[1], J. Krupicka[2], R. Kerekes[3], D. Marek[4], P. Gregor[5] on behalf of This study was supported partly by AstraZeneca and partly by research grant IGA NR 9164-3 awarded by the Czech Ministry of Health..
[1]Third Facutly of Medicine, Charles University, Cardiocenter, Praha 10, Czech Republic; [2]Na Homolce Hospital, Prague, Czech Republic; [3]Associated Medical Institution, Krnov, Czech Republic; [4]University Hospital, Olomouc, Czech Republic; [5]Third Facutly of Medicine, Charles University, Prague, Czech Republic

Background: Magnitude of left ventricular (LV) hypertrophy is one of the major determinants of symptoms and prognosis in hypertrophic cardiomyopathy (HCM). In a double-blind, placebo-controlled, randomized study, we tested the effects of angiotensin II type 1 receptor antagonist candesartan on LV hypertrophy in patients with non obstructive HCM.
Methods: Twenty-four consecutive genetically independent adult patients (age 43±13 yrs; 46% males) with non obstructive HCM were randomly assigned in 1:1 ratio either to candesartan or placebo. At baseline, patients underwent mutational analysis, bicycle ergometry and echocardiography. Ergometry and echocardiography was repeated 12 months after the maintenance dose of study drug was reached.
Results: No patient developed LV outflow tract obstruction or any other side effects during up-titration of study drug and follow-up. Target dose of study drug (32 mg daily) was reached in 8 (67%) and 9 (75%) patients in candesartan and placebo group, respectively (ns). At 12-month follow-up, patients on candesartan showed significant reduction of LV mass as compared to patients recieving placebo (-15.4% vs. -0.05%. p=0.04) with the greatest effect in carries of β-myosin heavy chain mutation (Table 1). Furthermore, candesartan use was associated, with significant increase in peak mitral annular systolic (Sa) and diastolic (Ea) velocity (+34,4% and +45,4%, respectively), decrease (-31,1%) in LV filling pressures (E/Ea) and increase (+30,8%) in total exercise time between baseline and follow-up (all $p<0.01$). In contrast, no significant improvement in these parameters was observed in placebo group.
Conclusions: In non obstructive HCM, candesartan induced significant regression of LV hypertrophy, improvement of LV function and exercise tolerance with no side effects.

Table 1. Mean Δ of LV mass in candesartan group

	Mean LV mass change, g (%)
β-MHC (n=5)	- 113 (-23)
cMYBPC (n=3)	- 47 (-14)
Other genotyped patients (n=4)	- 28 (-7)
p value (ANOVA)	< 0.001

P462 FT-011, a novel anti-fibrotic drug, reduced cardiac fibrosis and improved cardiac function in an experiemental model of myocardial infarction

M. Elsik[1], Y. Zhang[1], B. Wang[2], A. Adrahtas[1], R. Gilbert[2], H. Krum[2], D. Kelly[2]. *[1]St Vincents Hospital, University of Melbourne, Epidemiology and Preventive Medicine, Melbourne, Australia; [2]Dept of Epidemiology & Preventative Medicine, Epidemiology and Preentive Medicine, Monash University, Melbourne, Australia*

Introduction: Myocardial fibrosis, is a hallmark feature of chronic heart failure. Following myocardial infarction (MI), reactive fibrosis distal to the site of the infarct, results from pathological deposition of excess collagen and has adverse effects on cardiac function. We tested the hypothesis that preventing reactive fibrosis, using a novel antifibrotic drug, FT-011, would preserve cardiac function.
Methods: 10 week old Sprague Dawley rats underwent ligation of the left anterior descending artery to induce MI (or sham procedure) and were treated for 4 weeks with FT-011 or vehicle beginning 1 week post surgery. Left ventricular(LV) function was assessed with echocardiography (day 2 and 35) and with cardiac catheterization (day 35). Total collagen (TC) deposition was assessed with picrosirius red staining, and collagen subtypes I and III (C-I, C-III) using immunohistochemistry. In cell culture experiments, isolated neonatal rat cardiac fibroblasts (NCF) were stimulated with angiotensin II (AII) or TGF-β, to assess whether FT-011 had a direct effect on collagen synthesis assessed by proline incorporation.
Results: A summary of results is reported in the table. MIs were of comparable size (18.94% of LV) in FT-011 and (16.43%) in vehicle treated group. Treatment with FT-011 significantly reduced pathological deposition of TC (as well as C-I and C-III) in the myocardium, resulting in improved LV systolic function, normalization of diastolic function parameters and improvement in heart failure. Lung weight/body weight ratio was significantly lower with FT-011 ($p<0.05$) treatment further supporting improved LV function with FT-011. Cell culture experiments demonstrated a direct dose dependent reduction of collagen with FT-011 in response to both AII and TGF-β stimulation ($p<0.01$).
Conclusion: Treatment with FT-011 post MI prevented heart failure by reducing the pathological remodeling of collagen in the ventricle.

P463 Digoxin and reduction in early mortality in chronic heart failure: insights into the lack of late mortality reduction in the digitalis investigation group trial

A. Ahmed[1], F. Zannad[2], J.B. Young[3], F. Waagstein[4], M. White[5], S.R. Rahimtoola[6]. *[1]Univ of Ala. At Birmingham & V A Med. Center, Medicine Dept., Birmingham, United States of America; [2]University of Nancy, Cardiology, Nancy, France; [3]Cleveland Clinic Foundation, Cardiology, Cleveland, Ohio, United States of America; [4]Sahlgrenska University, Cardiology, Goteborg, Sweden; [5]University of Montreal, Cardiology, Montreal, Canada; [6]University of Southern California, Cardiology, Los Angeles, California, United States of America*

Background: Post hoc analyses of the Digitalis Investigation Group (DIG) trial suggest that digoxin may reduce mortality at low (0.5-0.9 ng/ml) serum digoxin concentrations (SDC) in heart failure (HF) and that low dose (≤0.125 mg/day) digoxin is a strong predictor of low SDC. SDC was not accounted for in the DIG trial that showed no effect of digoxin on mortality. SDC 0.8-2.5 ng/ml, now considered harmful, was considered therapeutic in the DIG trial, and was used to determine digoxin dose. We hypothesize that chronic use of high-dose digoxin may have cancelled an early survival benefit of digoxin in the DIG trial.
Methods: Ambulatory chronic HF patients (n=7788; 6800 had ejection fraction <45%) with normal sinus rhythm, and receiving ACE inhibitors and diuretics, were randomized to receive placebo (n=3899) or digoxin (n=3889) at 302 centers in the United States and Canada.
Results: All-cause mortality occurred in 11.5% patients receiving placebo (rate, 102 deaths/10,000 person-years) and 10.1% patients receiving digoxin (rate, 89 deaths/10,000 person-years) during the first year of follow up (hazard ratio, 0.87, 95% confidence interval, 0.76-0.995; p=0.043). Kaplan-Meier plots for mortality are displayed in Figure 1. Over 80% of patients were receiving ≥0.25 mg/day of digoxin.

Abstract P462 – Table 1. Data - 35 days post MI. Mean(SEM)

	FAC %	LVEDVol (ml)	LVESVol (ml)	LVEDDiam (cm)	LVESDiam (cm)	E:A ratio	Deceleration time (ms)	PRSW slope (mmHg)	TC %	Lung/body wt ratio
Sham + Vehicle	66.40(1.52)	0.43(0.04)	0.08(0.01)	0.83(0.02)	0.46(0.03)	2.45(0.17)	34.75(1.49)	72.77(6.70)	1.03(0.08)	0.27(0.05)
MI + Vehicle	27.56(1.18)**	0.90(0.08)#	0.48(0.04)**	0.99(0.03)#	0.81(0.03)**	3.46(0.52)	50.09(1.78)#	53.49(4.66)	2.23(0.24)#	0.39(0.02)
MI + FT-011	42.69(2.27)**	0.53(0.04)#	0.15(0.02)**	0.92(0.03)	0.70(0.03)*	2.00(0.26)*	38.64(1.18)**	65.15(3.04)*	1.5(0.18)#	0.33(0.01)#

*$p<0.05$, #$p<0.01$, **$p<0.0001$. (MI + Vehicle compared to Sham + Vehicle and MI + FT-011 compared to MI + Vehicle). FAC = fractional area change, PRSW = preload recruitable stroke work, LVES = LV end systole, LVED = LV end diastole.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

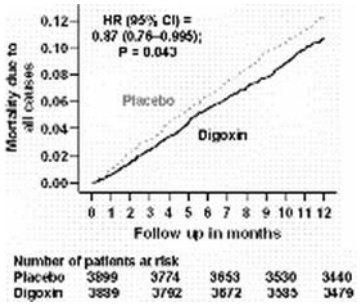


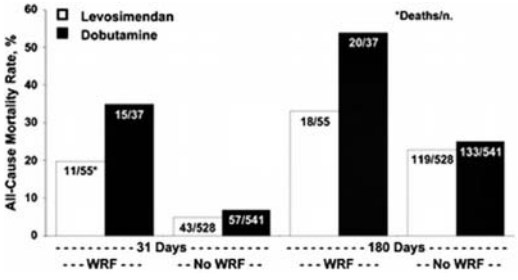
Figure 1. Kaplan-Meier plots for all-cause mortality during the first year of follow up in the Digitalis Investigation Group trial.

Conclusions: Digoxin (regardless of SDC) reduced early all-cause mortality in HF, which was eliminated in later years, likely due to continued use of high-dose digoxin. Digoxin should be used in low doses in HF patients who are symptomatic despite therapy with ACE inhibitors and beta-blockers, or who cannot tolerate or afford these drugs. The effect of low-dose digoxin in chronic HF patients receiving ACE inhibitors, beta-blockers and aldosterone antagonists should be examined in a prospective randomized clinical trial.

P464 Levosimendan compared to dobutamine does not adversely impact mortality in patients with transient worsening renal function: SURVIVE

A. Cohen-Solal[1], R. Thakkar[2], L. Delgado-Herrera[1], R.J. Padley[1], A. Mebazaa[2]. *[1]Hospital Lariboisiere, Paris, France; [2]Abbott, Abbott Park, United States of America*

Purpose: Worsening renal function (WRF) during treatment of acute heart failure (AHF) has been associated with increased mortality risk. The association of WRF with mortality was assessed in SURVIVE, which compared levosimendan, a vasodilator and enhancer of cardiac contractility, to dobutamine in 1327 patients with AHF.
Methods: The primary endpoint was 180-day all-cause mortality (ACM). Post-hoc analyses examined the relationship between WRF, defined as increases in serum creatinine (Cr) $\geq$0.5 mg/dL or 25% above baseline, and ACM.
Results: Hazard ratios (HR: levosimendan vs dobutamine) from pre-specified analyses of 31- and 180-day ACM (ITT population) were 0.85 (95% CI, 0.63-1.15; p=0.29) and 0.91 (95% CI, 0.74-1.13; p=0.40). Baseline Cr and mean change in Cr from baseline through 31 days were similar between treatment groups. The proportion of patients with WRF trended higher in the levosimendan group at 24 hours [9% (55) vs 6% (37), p=0.064], but not at any other time point. In patients with WRF at 24 hours, the total number of deaths was numerically lower at all time points for the levosimendan group than for the dobutamine group, even though there were an increased number of patients with WRF at 24 hours in the levosimendan group. For those with WRF at 24 hours, hypotensive events in the first 24 hours occurred with similar frequency for both treatments [18% (10/55) for levosimendan vs. 19% (7/37) for dobutamine].



Conclusion: Even though the incidence of WRF trended higher only at 24 hours for the levosimendan group, there were fewer total deaths at all time points evaluated for patients with WRF following treatment with levosimendan compared to dobutamine.

P465 Endothelial vasodilatation reserve assessment for brachial artery using paired test with hyperemia

L. Polonetsky, L. Gul, E. Shantsila, L. Lakhanko, S. Yasinskaya, I. Polonetsky. *Scientific-Practical Centre "Cardiology", Dept of Urgent Cardiology, Minsk, Belarus*

Purpose: Endothelial vasomotor function (VF) state assessment for brachial artery (BA) by impedancemetry in performing paired tests (PT) with reactive hyperemia (RH)
Methods: 157 coronary heart disease (CHD) patients with class II-III stable angina and 19 healthy volunteers were observed. The mean age was 53$\pm$4.7 years for patients and 45$\pm$3.2 years for healthy persons.104 patients with positive dynamics for endothelial vasomotor function indices in paired test with hyperemia were included into group I. 53 patients with impaired endothelial function were included into group II. Endothelial vasomotor function state was assessed by computer impedancemetry of brachium. Relative change in maximal blood filling velocity dz/dt was calculated by formula:
D dz/D dt = $((dz/dt_{1'} - dz/dt_{baseline})/dz/dt_{baseline}) \times 100\%$, where $dz/dt_{baseline}$ and $dz/dt_{1'}$ are maximal blood filling velocities at rest and in 1 minute after decompression, accordingly. If D dz/D dt $>$ 12%, endothelial VF is unaltered. Test was carried out with 5-7 minute interval between investigations.
Results: Highly significant ($p<0.00001$) improvement in endothelial vasomotor function at 1st minute of test (2.18$\pm$2.06 versus 21.14$\pm$2.10%) was detected in patients of group I. Significant impairment ($p<0.0001$) of endothelial state in performing the second test was observed in group II (6.42$\pm$3.45% versus –0.76$\pm$2.90%). Patients from group I received ACE inhibitors within 6 months before investigation, mainly perindopril. Coronary stenting with subsequent administration of perindopril was performed in 26 patients (25%) of this group. Patients from group II did not receive regular therapy with ACE inhibitors. Significant ($p<0.003$) improvement in endothelial vasomotor function was noted in group of healthy volunteers in comparing first and second test results (22.36$\pm$3.63% versus 35.78$\pm$4.42%).
Conclusions: The performance of subsequent paired tests with reactive hyperemia in CHD patients allows to reveal endothelial vasodilatation reserves or their deterioration and to improve the efficacy of treatment.

P466 Evaluation of the management of heart failure in primary care in the United Kingdom

M. Calvert, A. Shankar, R. Mcmanus, R. Ryan, N. Freemantle. *University of Birmingham, Birmingham, United Kingdom*

Objective: Heart failure is a common chronic disease often managed in primary care. The extent to which guidelines for the treatment of heart failure are followed is unclear. This study aims to evaluate the prevalence and management of patients with heart failure in UK general practice.
Methods: Population based study, using data from 163 UK general practices contributing to the DIN-LINK database over a five year period until December 2006. Patients with definite or probable heart failure were identified based on Read Codes, prescribing data and diagnostic test results. The proportion of patients prescribed ACE inhibitors/ARBs, beta-blockers and loop diuretics and treatment to ESC guideline target doses were assessed.
Results: From a patient population of nearly 1.43 million, 15183 patients with definite or probable heart failure were identified (mean age 76 years (SD 12)) giving an estimated prevalence of 1.1%. Of these 11785 (78%) were prescribed a loop diuretic, 11282 (74%) were prescribed an ACE inhibitor or ARB, 5843 (38%) were prescribed a beta-blocker and but only 4716 (31%) were prescribed an ACEI or ARB and a beta-blocker in combination. Thirty-five percent of patients prescribed ACEI and 9% of those prescribed beta-blockers met ESC guideline target doses. Patient characteristics that predict whether a patient with evidence of heart failure receives a beta-blocker or ACE inhibitor will be described.
Conclusions: These data suggest that while most patients with heart failure in primary care receive an ACEI/ARB, few are titrated to target dose and many do not receive a beta-blocker.

P467 Evidence based drug therapy: are optimal doses and multiple medication therapies realistic in patients with chronic heart failure?

A. Driscoll[1], L. Worrall-Carter[1], D.L. Hare[2], P.M. Davidson[3], B. Riegel[4], A. Tonkin[5], S. Stewart[6]. *[1]Deakin University, Melbourne, Australia; [2]University of Melbourne, Melbourne, Australia; [3]University of Western Sydney, Sydney, Australia; [4]University of Pennsylvania, Pennsylvania, United States of America; [5]Monash University, Melbourne, Australia; [6]Baker Institute, Melbourne, Australia*

Background: Chronic Heart Failure (CHF) has a high mortality and morbidity. Large scale randomised controlled trials have proven the benefits of beta blockade and ACE inhibitors in reducing mortality in patients with CHF and expert guidelines mandate their use. In spite of these recommendations, important therapies are under-prescribed and under-utilised.
Method: 1015 consecutive patients enrolled in CHF management programs across Australia were surveyed during 2005-2006 to determine prescribing patterns in heart failure medications. These patients were followed-up for a period of 6 months.
Results: The survey revealed that beta blockers were prescribed to 80% of patients (more than 85% were on sub-optimal doses) and 70% were prescribed Angiotensin converting enzyme (ACE) inhibitors (approximately 50% were on sub-optimal dose). 19% of patients were prescribed Angiotensin receptor blockers (ARBs). By 6 months $<$25% of the patients who were on sub-optimal dose beta blockers or ACE inhibitors at baseline, had been up-titrated to maximum dose ($p<0.0001$). In CHF programs, were nurses were able to titrate medications, 75% of patients reached optimal dose of beta blockers compared to those programs with no nurse-led medication titration, where only 25% of patients reached

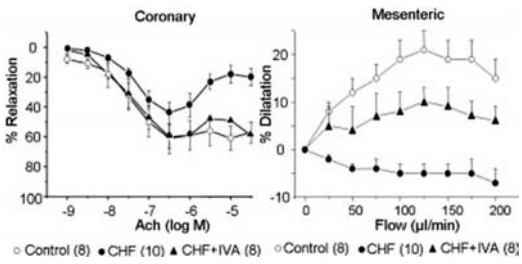
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

optimal dose ($p<0.004$). When examining optimal dosage for any two of these mandatory medications, less patients were on optimal therapy. Beta blockers and ACE inhibitors, were both prescribed in combination in 60% of patients. While beta blockers and ARBs were prescribed to 15% of patients.
Conclusion: Whilst prescribing rates for a single medication strategy of beta blockers, or ACE inhibitors were greater than 70%, an increase in dosage of these medications and utilisation of proven combination therapy of these medications was poor. It is suggested that clinical outcomes for this cohort of patients could be further improved by adherence to evidence-based practice, ESC guidelines, and optimisation of these medications by heart failure nurses in a CHF program. On the basis of these findings and in the absence of ready access to a polypill, focussing on evidence-based practice to increase utilisation and optimal dosage of combination medication therapy is critical.

P468 Protection of Endothelial Function by long term heart rate reduction induced by ivabradine in a rat model of chronic heart failure

M. Vercauteren, J. Favre, P. Mulder, F. Mahlberg-Gaudin, C. Thuillez, V. Richard. *Inserm U644, Rouen, France*

We have shown previously that long-term selective heart rate reduction (HRR) with the I_f inhibitor ivabradine (IVA) improves cardiac function and remodeling in rat chronic heart failure (CHF), but whether HRR also affects endothelial function in CHF is unknown.
Thus, CHF rats (coronary ligation) were untreated or treated for 3 months with IVA (10 mg/kg/d in diet). Interventricular coronary arteries were mounted in a wire myograph (responses to acetylcholine, Ach), while small mesenteric resistance arteries were canulated to evaluate flow-mediated dilatation (FMD).
Figure shows that IVA improved endothelial dysfunction in coronary and peripheral (mesenteric) arteries isolated from CHF rats (**$p<0.01$ vs. CHF).
These effects were abolished by the NOS inhibitor LNNA (10^{-4}M). In nonprecontracted CHF coronary arteries (in the presence of LNNA 10^{-4}M), Ach induced concentration-dependent, endothelium-dependent contractions that were not affected by IVA. In CHF mesenteric arteries, the cyclooxygenase inhibitor diclofenac (10^{-5}M) improved FMD to a similar extend in untreated and IVA-treated rats.



Thus, long term HRR with IVA protects coronary and peripheral endothelial function in CHF, mostly through an improved endothelial NO production, without affecting the EDCF pathway.

P469 Characterisation of first time admitted heart failure patients compared to patients treated in a specialised heart failure unit

M. Elhenicky, M. Resl, D. Stelzeneder, M. Clodi, A. Luger, M. Huelsmann, R. Pacher. *Medical University Vienna, Cardiology, Vienna, Austria*

Purpose: Many studies have proven the efficiency of specialised heart failure (HF) care. The purpose of this study is to characterise the population of HF patients continually cared for in a specialised HF outpatient unit compared to HF patients admitted for the first time in a clinical setting.
Methods: We compared 273 of our regular HF patients (group1) to 111 of newly admitted patients (group2). We therefore performed patient interviews to assess NYHA functional class, evaluate the medication therapy and determine patient's awareness of prescribed drugs. A blood sample was drawn to quantify NT-BNP. Quality of life was measured with the Minnesota Living with HF Questionnaire (MLHQ). Follow up was performed, for 4.5 months on average, to assign the rate of unplanned cardiovascular hospitalisation and mortality.
Results: Comparing the groups we found out that both groups did not differ in age, gender, history of hypertension and CAD. We detected significant differences in clinical markers such as NYHA functional class ($p<0,005$), quality of life ($p<0,005$), LVEF ($p<0,05$) and NT-BNP (2190 ± 4610 in group1 vs. 3839 ± 5593 in group2; $p<0,005$). Patients of group1 had significantly more ACE-Inhibitor, ARB, beta-blocker and Aldosteronagonist therapy ($p<0.002$ for all). We found that only 22% (vs. group1 73%, $p<0,0001$) of group2 had a combination of beta-blocker and RAAS in a dosage of at least 50% as recommended. Only 8% (vs. group1 40%, $p<0,0001$) had a combination therapy of ACE- inhibitors, beta-blockers and ARBs as recommended by the ESC-Guidelines. Moreover, we could reveal that patients of group1 have a significantly higher awareness of their medication ($p<0,0001$). Finally, we detected a significantly better outcome in group1: All cause re-hospitalisation rate was 22% compared 33% in group2 ($p<0.05$). Reason for re-admission was cardiovascular in 15% vs. 25% ($p<0.05$) and heart failure 10% vs. 19% ($p<0.05$ for group1 vs. group2,respectively). Combined endpoints of unplanned cardiovascular hospitalisation and death as well as unplanned HF hospitalisation and death were lower in this group (11% vs. 24% $p<0.01$ and 9% vs. 18%; $p< 0,05$, respectively). This also held true in Kaplan-Meier analysis ($p<0.005$, $p<0.05$ respectively).
Conclusions: Also in a clinical setting we can show that patients cared for in a specialised HF outpatient's department do have better drug therapy and compliance, which might explain their better clinical markers and short-term outcome.

P470 Valsartan attenuated myocardial fibrosis and diastolic dysfunction of hypertensive hearts in humans. Assessments using integrated backscatter analysis

Y. Mizuta, H. Kai, M. Mizoguchi, T. Imaizumi. *Kurume University, Cardio-vascular Medicine, Kurume, Japan*

Purpose: Myocardial fibrosis is the major determinant of diastolic property of the left ventricle (LV). Myocardial integrated backscatter peak-to-peak intensity (PPI) is a non-invasive indicator of myocardial fibrosis. Angiotensin receptor blockers (ARBs) have been shown to prevent myocardial fibrosis of hypertrophied hearts in several hypertension models. We examined the effects of long-term treatment with valsartan, an ARB, on myocardial fibrosis and diastolic dysfunction in hypertensive patients.
Methods and Results: This study included 43 consecutive hypertensives (63 ± 3 years) having diastolic dysfunction (E/A ratio of transmitral Doppler flow velocity50%). Myocardial PPI was measured before (baseline) and after 12-month valsartan treatment (40-160 mg/day). High PPI (less fibrotic) group consisted of 20 patients with PPI>5.09 dB (the average of 43 patients at baseline). Low PPI (more fibrotic) group included 23 patients with PPI<5.09. At baseline, systolic blood pressure (SBP), LV mass index (LVMI) and E/A ratio did not differ between the two groups. Although SBP and LVMI were decreased to the similar extent in both groups, valsartan significantly increased PPI and E/A ratio only in low PPI group (*$p<0.05$ vs. baseline. dp<0.05 vs. high PPI group).

Effects of 12-month valsartan treatment

	High PPI		Low PPI	
	Baseline	Post-treatment	Baseline	Post-treatment
SBP (mmHg)	161 ± 3	137 ± 3*	166 ± 4	134 ± 3*
LVMI (g/m^2)	121 ± 7	109 ± 7*	128 ± 7	114 ± 7*
PPI (dB)	5.51 ± 0.09	5.98 ± 0.19	4.78 ± 0.05d	5.36 ± 0.13*
E/A ratio	0.66 ± 0.03	0.76 ± 0.04	0.72 ± 0.03	0.87 ± 0.06*

Conclusion: Long-term valsartan treatment attenuated myocardial fibrosis and improved diastolic function in hypertensive patients, especially patients with greater myocardial fibrosis.

P471 Effect of PARP-inhibitors and ACE-inhibitors on the progression of isoproterenol-induced heart failure

E. Bartha[1], R. Halmosi[2], G.Y. Kulcsar[1], G.Y.N. Kiss[1], E. Kalman[1], B. Sumegi[1], T. Kalai[1], K. Hideg[1], K. Toth[1]. *[1]University of Pecs, 1St Department of Medicine, Pecs, Hungary; [2]University of Pecs, 1st Department of Medicine, Pecs, Hungary*

Purpose: Increased activation of poly(ADP-ribose) polymerase enzyme (PARP) is a crucial step in the development of oxidative stress-induced cell injury. Oxidative stress also plays a pathogenetic role in chronic heart failure. We have demonstrated previously the protective effect of PARP inhibitors against isoproterenol-induced heart failure. The aim of our recent work was to compare the efficacy of the PARP-inhibitor L-2286 and ACE-inhibitor enalapril in our heart failure model.
Methods: Adult male CFY rats received two subcutaneous injections (separated by a 24-hour interval) of 80 mg/kg isoproterenol. Twenty-four hours after the second injection the surviving animals were randomly assigned to receive either no medical treatment, or 5 mg/kg L-2286, or 10 mg/kg enalapril for 10 weeks. In the fourth group the control animals did not receive any drugs. At the end of the 10 week period, gravimetric and echocardiographic measurements were performed. Plasma BNP activity was determined. The degree of postinfarction myocardial remodeling was also determined. The phosphorylation state of Akt, GSK-3β, PKC and MAPK cascades were monitored by Western blotting.
Results: After the 10 week long treatment period the weight of left ventricles increased ($p<0,05$), the systolic left ventricular function decreased ($p<0,01$), while the plasma BNP level increased ($p<0,05$) compared to the control group. Histological analysis showed the signs of a significant myocardial remodeling (e.g. interstitial fibrosis). Treatment with either L-2286 or enalapril decreased markedly the raise of left ventricular weight ($p<0,05$), the plasma BNP concentration ($p<0,05$) and increased the activity of antihypertrophic signaling pathways. The left ventricular function determined by echocardiography was significantly better preserved in the PARP-inhibitor group ($p<0,05$) than in enalapril group. The other measured parameters were only moderately different in the two treatment group.
Conclusion: We could demonstrate, that PARP-inhibitors decrease markedly the

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

postinfarction myocardial remodeling, and this beneficial effect of PARP-inhibitors exceeds the protective effect of ACE-inhibitors in our heart failure model.

P472 The effect of renin-angiotensin system blockade on left ventricular global and regional function in diastolic heart failure (heart failure with a normal ejection fraction)

J.E. Sanderson[1], M. Wang[2], T. Wang[1], S. Chan[1], G.W.K. Yip[1], W.H. Fung[1], L. Yeung[1], T. Yip[1], C.P. Lau[3], C.M. Yu[1]. *[1]University of Birmingham, Cardiovascular Medicine, Birmingham, United Kingdom; [2]Chinese University of Hong Kong, Cardiology, Hong Kong, Hong Kong SAR, People's Republic of China; [3]University of Hong Kong, Cardiology, Hong Kong, Hong Kong SAR, People's Republic of China*

Background: Although heart failure with a preserved or normal ejection fraction (HFNEF or diastolic heart failure) is common there is sparse information on the effect of standard treatments such as diuretics and inhibitors of the renin-angiotensin system on myocardial structure and function in this condition.
Methods and Results: 150 patients admitted into hospital with a clinical history of heart failure and a chest X-ray demonstrating pulmonary congestion, and a LV ejection fraction $>$ 45% were randomly allocated to one of 3 treatments: (1) diuretics alone, (2) diuretics plus irbesartan, or (3) diuretic plus ramipril. Full 2D-echocardiography with tissue Doppler imaging was performed at baseline, 12, 24 and 52 weeks. At baseline LV longitudinal function - peak early diastolic lengthening (Em) and systolic mitral annular shortening (Sm) velocities- were significantly lower in HFNEF patients compared to age-matched normal subjects and left atrial dimension and E/Em (an index of LV filling pressure) were higher (all $p<0.001$). Both Em and Sm increased in all treatment groups after 1 year, which was statistically significant with both irbesartan and ramipril ($p<0.05$) but not diuretics alone. LV mass was also reduced significantly by irbesartan. There were no significant changes in LV dimensions or LVEF in any group.
Conclusions: Irbesartan and ramipril in combination with diuretics can improve LV longitudinal function, in both systole and diastole, in patients with HFNEF.

P473 Effect of angiotensin converting enzyme inhibitors or beta-blockers on outcomes in the African-American Heart Failure Trial

J.K. Ghali[1], A.L. Taylor[2], S.W. Tam[3], K.C. Ferdinand[4], M.L. Sabolinski[2], M. Worcel[2], J. Lindenfeld[5], J.N. Cohn[4] on behalf of A-HeFT investigators. *[1]Wayne State University, Medicine, Detroit, United States of America; [2]University of Minnesota, Medicine, Minneapolis, United States of America; [3]NitroMed, Inc., Clinical, Lexington, United States of America; [4]Association of Black Cardiologists, Atlanta, United States of America; [5]University of Colorado, Medicine, Denver, United States of America*

Purpose: In the African-American Heart Failure Trial (A-HeFT), fixed-dose combination of isosorbide dinitrate/hydralazine (FDC I/H) decreased mortality and morbidity compared to contemporary HF therapy alone (placebo group) in patients with heart failure (HF). We investigated the within group treatment effects of contemporary HF medications in the FDC I/H and placebo groups.
Methods: In 1,050 A-HeFT patients, Kaplan-Meier survival analyses were performed for between group and within group comparisons of the FDC I/H and placebo groups.
Results: Compared to placebo, FDC I/H decreased all-cause mortality by 43% (HR=0.57, 95% CI 0.37-089, P=0.012) and all-cause mortality or first HF hospitalization by 37% (HR=0.63 95%, CI 0.49-0.81, $P<0.001$) in patients with background therapy including ACE-I or ARB (93%) and beta blockers (87%). Within the placebo group the use of ACE-I was associated with significant decrease in mortality and a non-significant trend toward decreasing mortality or first HF hospitalization. In contrast, within the FDC I/H group the use of ACE-I was not associated with a decrease of either mortality or combined mortality or first HF hospitalization. On the other hand, the use of beta-blockers was associated with significant reduction of mortality as well as mortality or first HF hospitalization in both the placebo and the FDC I/H groups.

ACE-I or beta-blockers on outcomes

Outcome	Baseline Use	HR, Placebo Group	HR, FDC I/H Group
All-cause mortality	ACE-I	0.41 ($p<0.001$)	1.12 (p=0.791)
Mortality or 1st HF Hospitalization	ACE-I	0.75 (p=0.111)	1.07 (p=0.756)
All-cause mortality	Beta-blockers	0.33 ($p<0.001$)	0.44 (p=0.029)
Mortality or 1st HF Hospitalization	Beta-blockers	0.58 (p=0.002)	0.62 (p=0.034)

Conclusion: In A-HeFT, FDC I/H was superior to placebo with or without beta-blockers or ACE-I use in decreasing mortality and morbidity. Beta-blockers improved HF outcomes within both the placebo and FDC I/H groups. In contrast, ACE-I provided benefits only within the placebo group and showed no treatment effect within the FDC I/H group. These findings are hypotheses generating and would need to be investigated in prospective trials.

P474 Effect of levosimendan on left atrial functions in patients with ischemic heart failure

H. Duygu[1], F. Ozerkan[2], M. Zoghi[2], S. Nalbantgil[2], A. Akilli[2], M. Akin[2]. *[1]Ege University Medical Faculty, Cardiology, Kardiyoloji Anabilimdali, Izmir, Turkey; [2]Ege University Medical Faculty, Cardiology, Izmir, Turkey*

Purpose: Levosimendan is a novel positive inotropic calcium sensitizer agent used in acute heart failure. Although its favorable effects on left ventricular systolic and diastolic functions are well known, its effect on left atrial functions are not established. In this study, the effect of levosimendan on left atrial functions were evaluated by comparing with dobutamine in a prospective, randomized, patient-blind manner in patients with acute ischemic systolic left heart failure.
Methods: Patients having decompensated left heart failure with sinus rhythm and LVEF$<$40% were included to this study. Patients were randomized to levosimendan (6-12 μg/kg loading, 0.1 μg/kg/min 24-hours IV infusion, n=30, 63% male, mean age: 64$\pm$10 years) or to dobutamine (5-10 μg/kg/min 24-hours infusion, n=32, 54% male, mean age: 66$\pm$8 years). Left atrial functions were evaluated pre-treatment and after 24 hours in post-treatment periods. From the left atrial volumes, active emptying fraction (AEF), passive emptying fraction (PEF), reservoir fraction (RF) and stroke volume (SV) were calculated.
Results: Baseline left atrial functions, age, gender, concomitant medications were similar in both groups ($p>0.05$). All of the left atrial functions (AEF, PEF, RF and stroke volume) were improved significantly after levosimendan treatment whereas among the left atrial functions only AEF was improved significantly following dobutamine treatment (Table). In levosimendan group, the improvement of AEF was greater than the dobutamine group (p=0.001).

	Levosimendan(before/after, p value)	Dobutamine(before/after, p value)
LA diameter (mm)	52$\pm$11/48.7$\pm$11.5 p=0.001	51$\pm$8.5/50.1$\pm$9.8 p=NS
AEF	0.05$\pm$0.01/0.19$\pm$0.09 p=0.01	0.04$\pm$0.02/0.05$\pm$0.04 p=0.04
PEF	0.12$\pm$0.08/0.21$\pm$0.06 p=0.04	0.11$\pm$0.04/0.11$\pm$0.005 p=NS
Stroke volume (ml/m^2)	20.5$\pm$18.1/25.5$\pm$8.8 p=0.009	18.8$\pm$17.1/18.3$\pm$11.8 p=NS
RF	0.23$\pm$0.04/0.38$\pm$0.03 p=0.001	0.21$\pm$0.04/0.22$\pm$0.02 p=NS

Conclusions: In acute systolic left heart failure, levosimendan improves left atrial active and passive functions compared to dobutamine. Dobutamine provides an improvement only in AEF. However, this improvement was less than levosimendan.

P475 Fixed-dose combination of isosorbide dinitrate/hydralazine improves outcomes in elderly heart failure patients in the African-American Heart Failure Trial

A. Taylor[1], M. Sabolinski[2], S.W. Tam[1], M. Worcel[1], J. Cohn[2]. *[1]University of Minnesota Medical School, Medicine/Cardiology, Minneapolis, Mn, United States of America; [2]NitroMed, Inc., Lexington, Ma, United States of America*

Purpose: The fixed-dose combination of isosorbide dinitrate/hydralazine (FDC I/H) significantly improved mortality and morbidity in patients with advanced heart failure, treated with neurohormonal therapy in the African-American Heart failure Trial (A-HeFT). We investigated whether FDC I/H improved HF outcomes in patients ages $\geq$ 65 yr old.
Methods: Subgroup analysis was performed on the A-HeFT cohort $<$ 65 or $\geq$ 65 yr old. Time-to-event analyses were performed by the Kaplan Meier method.
Results: Baseline differences shown in the table showed that patients $\geq$ 65 yr old had significant lower risk factors such as higher systolic BP and better QOL score and increased risk factors such as higher plasma BNP and creatinine levels. Patients $\geq$ 65 yr old also had significantly lower use of contemporary HF medications. The hazard ratios for FDC I/H compared to placebo for the $\geq$ 65 yr old group compared to the $<$65 yr old group are: mortality (HR=0.33, p=0.005 vs. 0.70, p=0.18); first HF hospitalization (HR=0.71, p=0.16 vs. 0.56, $p<0.001$); and mortality or first HF hospitalization (HR=0.70, p=0.12 vs. 0.60, $p<0.001$).

A-HeFT Patient Baseline Characteristics

Characteristics (SD)	$<$65 yr (n=742)	$\geq$ 65 yr (n=308)	P Value
BMI	33.2 (8.7)	28.4 (5.5)	$<$0.0001
Systolic BP, mmHg	125.2 (17.8)	128.9 (17.4)	0.002
Diastolic BP, mmHg	77.4 (10.4)	74.7 (10.4)	0.0002
Baseline QOL score	53.6 (25.4)	44.4 (23.5)	$<$0.0001
Plasma BNP, pg/mL	262 (354)	412 (495)	$<$0.0001
Plasma creatinine, mg/dL	1.21 (0.49)	1.37 (0.52)	$<$0.0001
Ischemic HF Etiology, %	17.9	35.4	$<$0.0001
Hypertensive HF Etiology, %	39.2	28.3	0.0002
Beta Blocker use, %	86.4	74.7	$<$0.0001
ACE-I use, %	77.6	68.2	0.002
ACE-I or ARB use, %	93.9	89.6	0.019
Spironolactone use, %	41.6	32.5	0.006

Conclusion: In A-HeFT, despite significant baseline differences the fixed-dose combination of I/H improved outcomes in HF patients $<$ or $\geq$ 65 yr. Patients $\geq$ 65 yr, a group at the greatest risk for mortality compared to $<$ 65 yr, showed the most significant improvement in survival with FDC I/H treatment.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P476 Levosimendan versus dobutamine in patients with moderate to severe right ventricular dysfunction on top of severe left ventricular failure

M.B. Yilmaz, C. Yontar, A. Erdem, F. Karadas, K. Yalta, O.O. Turgut, A. Yilmaz, I. Tandogan. *Cumhuriyet University School of Medicine, Cardiology, Sivas, Turkey*

Poor right ventricular (RV) function was an independent prognostic marker in patients with HF. Levosimendan (L) is a unique inotrope, used in severe left ventricular (LV) failure. We compared Levosimendan versus Dobutamine (D) in patients with significant RV dysfunction on top of severe LV failure.

Methods: Forty consecutive patients, judged for inotropic therapy by their primary physicians, with acutely decompensated systolic HF and having moderate-to-severe RV dysfunction with RV fractional area change (RVFAC) of $\leq$24% were randomized to L and D in a 2:1 fashion. Mean age and sex were not different between groups. Two groups were comparable in terms of degree of RV dysfunction and other parameters. After the infusion, EF improved, SPAP decreased significantly almost to similar extent in both groups. TAPSE, known to have an independent prognostic role in HF, and RVFAC were improved significantly in patients with L compared to patients with D (L:TAPSE from 12.3$\pm$1.3 mm to 14.2$\pm$2.5 mm, $p<0.001$; D:TAPSE from 12.8$\pm$1.2 mm to 13.1$\pm$1.6 mm, p=0.197 and L:RVFAC from 18.7$\pm$3.7% to 23.8$\pm$4.6%, $p<0.001$; D:RVFAC from 19.7$\pm$3.2% to 20.4$\pm$2.8%, p=0.253). Furthermore, L improved both urine output and creatinine, whereas, D did small, but significant, improvement in urine output without in creatinine levels. Interestingly, L improved ALT levels after the infusion with near significance (p=0.082), adding further data up on improvement of reduced RV performance and hence decreased splanchnic load, whereas D did no change. However, there is a need for further work up for this issue. On the other hand, such improvements with L were reflected by the clinical results such that mean time period of hospitalization was significantly less in the L arm compared to D arm (9$\pm$1.8 days vs. 11.3$\pm$3.1 days, p=0.024) with less requirement for intravenous loop diuretic (total dose divided by number of days of hospitalization) during the hospitalization period (mean intravenous dose per day 44 mg vs. 72 mg, p=0.003). Furthermore, hospitalization period was negatively correlated with the percent change in 24-hour urine output in all group (r= -0.573, p=0.007).

Conclusion: We shown beneficial effects of Levosimendan in a specific group of patients with significant right ventricular dysfunction on top of severe left ventricular failure along with clinical positive results in terms of improved urine output, and creatinine, improved right ventricular systolic functions, decreased hospitalization period and decreased use of intravenous loop diuretics, compared to Dobutamine.

P477 Fondaparinux reduces symptomatic pulmonary embolism and death in patients hospitalized with congestive heart failure: a sub-analysis of the randomized ARTEMIS trial

J. Eikelboom[1], A.T. Cohen[2], A.G.G. Turpie[3] on behalf of ARTEMIS. *[1]HHS - General Hospital, Thrombosis Service - McMaster Clinic, Hamilton, Canada; [2]Guy's, King's, St Thomas' School of Medicine, Academic Department of Surgery, London, United Kingdom; [3]HHS - General Division, Department of Medicine, Hamilton, Canada*

Introduction: There are limited data to support the use of anticoagulant prophylaxis in patients with congestive heart failure (CHF). In the randomized, double-blind ARTEMIS trial, fondaparinux 2.5 mg sc once daily significantly reduced the risk of total venous thromboembolism in acutely ill medical patients compared with placebo (relative risk [RR]: 0.53; p=0.029). Data are presented here from a post hoc analysis in the subgroup of patients hospitalized for CHF.

Methods: ARTEMIS randomized 849 patients $\geq$60 years old hospitalized for congestive heart failure (NYHA class III/IV), or acute respiratory, infectious or inflammatory disease and expected to remain bedridden for $\geq$4 days. Treatment with fondaparinux or placebo was continued for 6-14 days.

Results: Among all randomized patients, 308 patients (36.3%) had CHF, 79 (25.6%) in NYHA class IV. Median age [range] was 77 [60-96] years. Fondaparinux was more effective than placebo on clinically relevant endpoints including death due to all causes (Table). Symptomatic pulmonary embolism (PE) occurred in 1 patient treated with fondaparinux group and in 5 patients receiving placebo. No major bleeding occurred in the fondaparinux group while there was 1 major bleed in the placebo group.

Conclusion: Fondaparinux significantly reduced death and symptomatic pulmonary embolism at Day 32 in patients hospitalized with CHF in this analysis from the ARTEMIS study.

P478 Unlike other beta2-adrenoceptor agonists, clenbuterol predominantly activates the Gi protein in isolated rat ventricular myocytes

U. Siedlecka[1], M. Arora[1], G.K. Soppa[1], J. Lee[1], M. Stagg[1], K. Karkasfalvi[1], M.H. Yacoub[1], C. Terracciano[2]. *[1]Imperial College London, Heart Science Centre, London, United Kingdom; [2]Imperial College, Heart Science Centre, Harefield, United Kingdom*

Clenbuterol, a β_2 -adrenoceptor (AR) agonist, has been employed in combination with other pharmacological agents and LVADs to treat patients with severe heart failure (HF). We have previously shown that in isolated cardiac myocytes chronic administration of clenbuterol (CLEN) increases expression of Ca regulatory proteins resulting in improved contractility. However, the acute effects of CLEN compared to other β_2 -AR agonists and the signaling pathway of CLEN remain undefined.

In our study CLEN was compared to two other clinically used β_2 -AR agonists, fenoterol (FEN) and salbutamol (SAL). Isolated rat ventricular myocytes were superfused with increasing concentrations of the β_2 AR agonists and sarcomere shortening was measured. CLEN produced a negative inotropic response (30 μM: 65.3$\pm$9.7% of control, n=9; $p<0.05$; 100 μM: 37.9$\pm$8.0%, n=9; $p<0.01$) whereas FEN showed a positive inotropic response (30 μM: 155.3$\pm$13.3% of control, n=5; $p<0.01$; 100 μM: 170.9$\pm$16.6%, n=5; $p<0.01$). SAL had no significant effect. Selective β_1 AR blockade with 300 nM CGP 20712A did not affect CLEN's action on sarcomere shortening but significantly reduced the contractile response to FEN and SAL ($p<0.05$). Additional blockade of β_2 AR-G_s with 50 nM ICI 118,551 unveiled a negative inotropic response to FEN (100 μM: 52.2$\pm$3.9% of control, n=4; $p<0.01$) and SAL (100 μM: 75.0$\pm$4.8% of control, n=3; $p<0.05$) and did not alter the response to CLEN. Incubation with 2 μg/ml pertussis toxin (PTX) almost abolished the negative inotropic effects of CLEN: 30 μM (PTX: 95.1$\pm$ 4.9%, n=6 vs control: 73.9$\pm$5.5%, n=7; $p<0.05$) and 100 μM (PTX: 96.2$\pm$9.6%, n=6 vs control: 21.7$\pm$5.5%, n=7; $p<0.001$), suggesting the involvement of the inhibitory guanine nucleotide binding protein (G_i).

In summary, CLEN significantly depresses contractility of normal isolated rat ventricular myocytes, an effect not seen with FEN or SAL. CLEN predominantly acts through G_i and the consequent downstream signaling pathways activation may explain the beneficial effects observed during chronic administration of CLEN in patients treated with LVADs.

P479 Carvedilol sensitizes beta1- and beta2-adrenergic receptors in human myocardium by inhibiting a phosphatidylinositol-3 kinase mediated pathway

P. Boehmer, I.-O. Lee, K.-I. Schmidt, B. Cremers, H.-J. Schaefers, M. Bohm, C. Maack. *Universitaetsklinikum des Saarlandes, Cardiology, Homburg/Saar, Germany*

In chronic heart failure (CHF), myocardial density of beta-adrenergic receptors (beta-ARs) is downregulated, blunting the response to catecholamines. Although both carvedilol (CARV) and metoprolol (METO) improve cardiac function and survival, only METO, but not CARV, upregulates beta-ARs in CHF. However, in patients treated with either beta-blocker, the beta1-AR agonist dobutamine increases cardiac output to similar extents. Thus, we hypothesized that CARV sensitizes beta-ARs independent of receptor density by improving downstream signaling events. Isometric force of contraction was determined on isolated atrial trabeculae of 54 patients undergoing cardiac surgery. Beta1/beta2-AR stimulation was obtained with isoproterenol (ISO), selective beta1-AR stimulation with norepinephrine (NE; after alpha-/beta2-AR blockade), and selective beta2-AR stimulation with epinephrine (EPI; after alpha-/beta1-AR blockade). The EC50 values for ISO-induced positive inotropic effects displayed a variability that could not be explained by patient characteristics (clinical status, treatment). The patients were divided along the median of the EC50-value for ISO into those with normal (EC50 lower than -6.8 logM) and desensitized beta-ARs (EC50$>$-6.8 logM). Both METO (1 μM) and CARV (10 nM) shifted the ISO EC50 to the right in tissue with normal beta-AR affinity. In contrast, in desensitized tissue, CARV led to a pronounced leftward shift of the ISO response (EC50: Control, -5.5$\pm$0.2 logM; CARV, -7.5$\pm$0.3 logM; n=11/9; $p<0.001$), while METO produced a rightward shift (-4.5$\pm$0.3 logM). Selective beta1-AR stimulation with NE led to an initial positive and a subsequent negative inotropic effect in 56% of patients. The secondary negative inotropic effect was completely eliminated by inhibiting phospatidylinositol-3 kinase (PI3K) with LY294002. In the remaining 44%, a monophasic positive inotropic effect was observed. A similar PI3K-mediated biphasic inotropic effect was observed after beta2-AR stimulation with EPI (67% of patients). CARV completely inhibited the PI3K-mediated negative inotropic effect after beta1- or beta2-AR stimulation, without affecting the positive inotropic effect. In contrast, METO competitively antagonized the positive inotropic effect without affecting the negative inotropic component. We conclude that in human myocardium, desensitization

Abstract P477 – Clinical events at Day 32

Day 32	Fondaparinux		Placebo		RR fondaparinux vs placebo [95% CI]	
	All patients (N=429)	Patients with CHF (N=153)	All patients (N=420)	Patients with CHF (N=155)	All patients	Patients with CHF (N=308)
Symptomatic PE	4 (0.9%)	1 (0.7%)	11 (2.6%)	5 (3.2%)	0.36 [0.11;1.11]	0.20 [0.02;1.71]
All deaths	14 (3.3%)	5 (3.3%)	25 (6.0%)	14 (9.0%)	0.55 [0.29;1.04]	0.36 [0.13;0.98]
Symptomatic PE + all deaths	15 (3.5%)	6 (3.9%)	29 (6.9%)	17 (11.0%)	0.51 [0.28;0.93]	0.36 [0.14;0.88]
Major bleed	1 (0.2%)	0	1 (0.2%)	1 (0.7%)	–	–

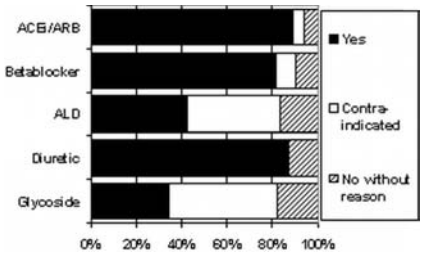
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

of beta-ARs is associated with coupling to PI3K. CARV sensitizes beta-ARs by blocking this PI3K-mediated pathway. This may explain the restored in vivo response to dobutamine in CHF patients treated with CARV despite the lack of upregulation of beta-AR density.

P480 Implementing the guidelines for pharmacological treatment in chronic heart failure - improvements and shortcomings

S. Stork[1], G. Gelbrich[2], G. Guder[3], C. Hoyer[2], G. Ertl[2], C.E. Angermann[2] on behalf of for the INH-Study Group of the German Heart Failure Network of Competence. *[1]University of Wurzburg, Department of Medicine I, Wurzburg, Germany; [2]University of Leipzig, Center of Controlled Clinical Trials, Leipzig, Germany; [3]University of Wurzburg, Medicine I, Wurzburg, Germany*

Purpose: We assessed quality of chronic systolic heart failure (CSHF) pharmacotherapy using the Guideline Adherence Indicator (GAI: number of CSHF drugs taken divided by number of drugs indicated).
Methods: Patients hospitalized for symptomatic CSHF in 9 (non)academic hospitals with LVEF <41% were eligible (n=687). GAI3 considers: betablockers, ACEi/ARB, aldosterone blocker (ALD); GAI5, in addition, considers diuretic and glycoside.
Result: Mean age was 68+12y, 30% female, frequency of NYHA class I/II/III/IV was 2/58/36/4%. The figure shows percentage of pharmacotherapy also including contraindications. The mean GAI3 (GAI5) was 0.91(0.87) in NYHA class I/II, and 0.82(0.80) in NYHA class III/IV. Differences in treatment quality between NYHA I/II and III/IV (both P<0.001) were mostly attributable to use of ALD. In multivariable logistic regression, the following variables predicted worse adherence (all P<0.05). For ACEi/ARB: depression, odds ratio (OR) 2.2 (95%CI 1.0-4.6); for betablockers: higher age, OR 1.3 per 10y (1.0-1.6); for ALD: NYHA class III/IV, OR 4.5 (2.6-7.7) and higher age, OR 1.4 per 10y (1.1-1.7); for diuretic: NYHA class I/II, OR 2.1 (1.2-3.6) and normal renal function, OR 3.9 (2.1-7.3); for glycoside: NYHA class III/IV, OR 3.5 (2.2-5.7). Only 20% received target doses of ACEi/ARB, and 7% did not tolerate higher doses (for betablockers: 13% and 9%, respectively). In all other patients, these drugs were underdosed without reason.



Pharmacotherapy in CSHF

Conclusions: Compared with previous surveys, implementation of treatment guidelines for CSHF seems to improve in patients hospitalized for CSHF, and is close to optimal regarding treatment initiation. However, target doses are reached only in a minority. Follow-up of these patients will clarify the possible impact of up-titration on outcome.

P481 Long-term effects of combined chelation therapy in thalassemia major patients with iron-induced cardiomyopathy

A. Pepe[1], R. Grady[2], S. Vacquer[3], P. Carta[3], F. Sau[3], P. Bina[4], P. Cianciulli[5], A. Maggio[6], M. Lombardi[3], M.E. Lai[6]. *[1]Institute of Clinical Physiology, CNR, Pisa, Pisa, Italy; [2]Cornell University Medical Collage, New York, United States of America; [3]University of Cagliari, Talassemici Adulti Unit, Cagliari, Italy; [4]Microcitemico Hospital, Cagliari, Italy; [5]S. Eugenio Hospital, Roma, Italy; [6]Cervello Hospital, Palermo, Italy*

Purpose: Various protocols of chelation treatments are being explored for more effective removal of cardiac iron in thalassemia major (TM). We designed a prospective trial to evaluate the long-term effects of combined DFO/DFP treatment in cardiopatic TM patients. The primary outcome was to assess the cardiac death and hospitalization for cardiac causes in a cohort of TM patients treated by DFO/DFP vs a matched cohort treated with DFO alone. The secondary outcome was to evaluate the improvement of the LVEF and the serum ferritin in these 2 cohorts.
Methods: Among 101 TM patients attending the Thalassemic Centre, we screened 28 with cardiac disease. The history supported a high pre-test likelihood of iron-induced cardiomyopathy, in absence of validated techniques for the identification of cardiac iron at that time. We proposed the combined DFO/DFP treatment to all patients (DFO 40 mg/kg/day + DFP 75 mg/kg/day). Ten patients refused and 3 patients withdrew from combined chelation because of adverse events during the roll in. These latter 13 patients continued DFO (40 mg/kg/day). Thus, we identified 2 matched groups: 15 patients treated with combined DFO/DFP and 13 treated with standard DFO. Patients were followed until 42±6 months. LVEF was calculated as [(EDV–ESV)/EDV] x 100 by echocardiography. We evaluated the myocardial and liver iron overload by the T2* MRI in our survival study population at the end of the study.
Results: 4 major cardiac events (3 cardiac deaths and 1 hospitalization for congestive heart failure) occurred in the DFO-treated patients vs none in the DFO/DFP-treated group (P=0.03). The DFO-treated patients did not exhibit a significant reduction of the serum ferritin concentrations and a significant improvement in the LVEF. DFO/DFP-treated patients showed a significant reduction of the serum ferritin (3006±2228 ng/ml at baseline, vs 1109±1169 ng/ml at the end; P = 0.001) and a significant improvement in the LVEF (53.5±5% at baseline, vs 63±4.3% at the end; P = 0.0009). At the end of the study in the surviving patients, we did not find significant differences in the T2* values in the mid-ventricular septum (22±10 ms vs 22±15 ms; P = 0.9) and in the liver T2* values (19±13 ms vs 16±12 ms; P = 0.6) between the 2 groups.
Conclusions: This is the first report in which a prospective study DFO/DFP combine treatment vs DFO alone was performed in TM patients with heart damage. We showed the efficacy of combination therapy preventing major cardiac events. Other proved prognostic indicators in TM population as the serum ferritin and the LVEF showed the benefits of combine chelation.

P482 Mortality and morbidity with beta-blockers in very elderly heart failure outpatients

G. Borelli, L. Rondinini, M. Coceani, A. Barison, I. Morelli, L. Conte, R. Mariotti. *University of Pisa, CardioThoracic Department, Cardio-Thoracic, Pisa, Italy*

Background: Randomised controlled trials, which typically enroll relatively young patients, have demonstrated that beta-blockers (BB) reduce mortality and morbidity in chronic heart failure (HF). Recently, the SENIORS and BRING-UP2 trials have extended the indications of treatment with BB to older patients with HF. However, data regarding the potential benefits of BB in very old patients with HF is limited. The purpose of the present study was to assess the effectiveness and safety profile of beta-blockers in octagenerian HF outpatients.
Methods: 201 elderly outpatients (median age 82 years, 56% male) affected by either systolic or diastolic HF (52% of ischaemic origin, 42% secondary to arterial hypertension), with a mean follow-up of 22±10 months, were divided into two groups according to therapy with (BB+, 66%) or without (BB-, 34%) BB. All patients were on standard therapy with ACE-inhibitors or angiotensin receptor blockers, as well as diuretics and digoxin as clinically indicated.
Results: The baseline characteristics of the two groups (demographic parameters, coronary risk profile, comorbidities, laboratory analyses and concomitant medical therapy) were similar. Compared to BB- patients, BB+ patients presented more severe left ventricular systolic (ejection fraction [LVEF]: 37% vs. 42%, p=0.002; prevalence LVEF <35%: 78% vs. 55%, p=0.001; end-systolic volume index: 47 vs. 34 ml/m^2, p=0.001) and diastolic dysfunction (1.24 vs. 1.01, p=0.02), but similar NYHA class (2.5 vs. 2.3, p=NS) and pro-BNP levels (1480 vs. 1176 pg/ml, p=NS). During follow-up, there were no significant differences between groups with regards to changes in echocardiographic parameters (left ventricular remodelling, systolic and diastolic function, systolic pulmonary artery pressure, severity of mitral regurgitation). A tendency towards reduced mortality was observed in BB+ compared to BB- (12.9% vs. 20.3%, p=NS), which became statistically significant in the subset of patients with LVEF <35% (18.3% vs. 45.0%, p=0.02). Similar results were observed with regards to HF rehospitalisation (BB+ 11.3% vs. BB- 17.4%, p=NS; BB+ and LVEF <35% 12.2% vs. BB- and LVEF <35% 25.6%, p=0.03). These findings were associated with a very low rate of therapy withdrawl (3.5%) in BB+.
Conclusions: BB improve prognosis and may be used safely in very elderly subjects with HF, especially in the presence of a severely depressed left ventricular ejection fraction.

P483 Addition of spironolactone to candesartan improves myocardial strain associated with regression of fibrosis and reverse remodeling in chronic heart failure

M. Wang, T. Wang, A. Chan, Y.Y. Lam, G. Yip, W. Lam, L. Yeung, C.M. Yu, J.E. Sanderson. *The Chinese University of Hong Kong, Medicine & Therapeutic, Division of Cardilogy, Hong Kong, Hong Kong SAR, People's Republic of China*

Background: It is not known if reversal of myocardial fibrosis by spironolactone leads to an improvement in myocardial deformation or strain in patients with chronic heart failure with reduced ejection fraction and ventricular remodeling.
Methods: 48 chronic heart failure patients with left ventricular ejection fraction (LVEF) <40% and ventricular dilatation on standard therapy including ACEI for more than six months were randomized to candesartan 8 mg daily plus spironolactone 25mg daily (C+S group, N=23) or candesartan 8mg daily alone (C group, N=25) for one year. Cardiac MRI and echocardiography with TDI were done at baseline, 6 and 12 months. Mean systolic and diastolic myocardial velocities of six-LV basal segments were measured by TDI (Sm, Em). Mean strain of six-basal segments, cyclic variation of integrated backscatter (CVIB, an indicator of myocardial fibrosis) and standard deviation of time to peak systolic myocardial systolic velocity of 12 segments (Ts-SD, am measure of dyssynchrony) were assessed.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: the 2 groups had comparable demographic data, LVEF by MRI and echo variables at baseline. LVEF by MRI significantly improved at one year in the C+S group compared to C group (D 54±19% vs D 9± 5% p=0.01); LV mass by MRI significantly reduced in the C+S group but increased in the C group (D -11±4% vs D 7±4%, p=0.002). Meanwhile, C+S group showed a significant increase in strain (13±1% vs 16±1%, p<0.05), Sm (3.4±0.2 vs 4.0±0.3 cm/s, p<0.05), CVIB (11 ±0.7 vs 13±1, p<0.05), and decreased in diastolic filling pressure (E/Em 33±5 vs 20±2, p<0.01) from baseline to one year. There was a trend for Ts-SD to decrease in C+S group (43±3 vs 37±4ms, p>0.05). However, there was no change in the C group for strain, Sm, CVIB, E/Em and Ts-SD from baseline to one year follow-up.
Conclusion: the addition of spironolactone to candesartan improves myocardial strain, and hence contractility, while reducing myocardial fibrosis and inducing reverse remodeling in chronic heart failure. Therefore, spironolactone can produce significant improvement in overall myocardial function.

P484 How early should eplerenone be initiated in acute myocardial infarction complicated by heart failure? An analysis of early vs. late initiation in the EPHESUS trial

F. Zannad[1], C. Adamopoulos[2], R. Fay[1], A. Ahmed[3], G. Filippatos[4], B. Pitt[5]. *[1]Hopital Jeanne D'arc, Centre D'investigation Clinique (Cic), Dommartin-Les-Toul Cedex, France; [2]Nancy, France; [3]Birmingham, United States of America; [4]Athens, Greece; [5]Ann Arbor, United States of America*

Background: In patients with acute myocardial infarction (AMI) high aldosterone levels on admission are associated with adverse outcomes and early aldosterone blockade prevents left ventricular remodeling. However, the effect of early aldosterone blockade on long-term mortality and morbidity in AMI patients complicated by heart failure is unknown. In this post hoc analysis of the EPHESUS trial, we investigated the relative efficacy of early vs. late initiation of eplerenone on mortality and cardiovascular (CV) outcomes.
Methods: In EPHESUS, 6631 patients were randomly assigned to eplerenone or placebo 3 to 14 days after AMI (median, 7 days). In this analysis (Cox regression), we compared two subgroups of patients based on their median randomization time: "early" (≤7 days; n=3596) vs. "late" (>7 days; n=3035).
Results: Baseline characteristics were comparable between eplerenone and placebo patients for both "early" and "late" subgroups. In the "early" group, 16.3% of placebo patients and 12.8% of eplerenone patients died from all causes during a mean follow up of 16 months (hazard ratio {HR}=0.77, 95% confidence interval {CI}=0.65-0.92, p=0.003). In placebo and eplerenone patients respectively, CV mortality/CV hospitalization occurred in 29.5% and 25.5% (HR=0.85, 95%CI=0.75-0.96, p=0.01) and sudden cardiac death (SCD) in 6.8% and 4.4% (HR=0.63, 95%CI=0.48-0.84, p=0.002). In contrast, in the "late" group, use of eplerenone was not significantly associated with reduction in all-cause mortality (HR=0.92, 95%CI=0.78-1.10, p=0.37), CV mortality/CV hospitalization (HR=0.89, 95%CI=0.78-1.01, p=0.08), or SCD (HR=1.03, 95%CI=0.76-1.40, p=0.86).
Conclusions: In patients with AMI, LV dysfunction and heart failure, early (3-7days) compared to delayed (8-14days) initiation of eplerenone was more effective on CV outcome, including SCD. Although in EPHESUS, patients were not randomized < 3 days from admission, the fact that aldosterone levels are elevated on admission and associated with CV outcome would suggest that earlier administration of eplerenone might be even more beneficial and should be prospectively evaluated.

P485 Pentoxifylline increases hemoglobin in anaemic patients with chronic heart failure

M. Lainscak[1], S.D. Anker[2], S. Von Haehling[1], P. Ponikowski[3], C. Libhaber[4], K. Sliwa[2]. *[1]General Hospital Murska Sobota, Department of Internal Medicine, Murska Sobota, Slovenia; [2]Berlin, Germany; [3]Wroclaw, Poland; [4]Johannesburg, South Africa*

Background: Anaemia is present in 8-15% of patients with chronic heart failure (CHF) and is associated with poor prognosis. Whilst treatment with erythropoietin and/or intravenous iron showed promising results, many patients with CHF still fail to respond to treatment. In anaemic chronic renal disease patients, treated with immunomodulating drug pentoxyfilline (PTX), an increase of haemoglobin was reported. We thus hypothesised that PTX could increase haemoglobin in anaemic patients with CHF.
Methods: Patients from three randomised placebo controlled double-blind trials with PTX were pooled for this analysis. Finally, we evaluated 102 patients (52±11 years, 67% men, 49% in NYHA class III/IV) with CHF due to coronary artery disease (N=33) or idiopathic CHF (N=69). Of those, 19 patients (11 receiving PTX and 8 receiving placebo) complied with WHO criteria for anaemia (haemoglobin <120 g/l for women and <130 g/l for men). Due to immunoimodulatory effects of PTX, we also specifically analysed 39 patients with C-reactive protein (CRP) above the upper normal limit of 9 mg/l. Blood samples were taken at baseline and after six months of treatment with PTX 400mg tid or matching placebo.
Results: In 9/11 anaemic patients PTX increased haemoglobin level (120±3 to 136±5 g/l, p=0.008). Simultaneously, it reduced TNF-alpha concentration (6.7±0.6 to 2.5±0.7 pg/ml, p=0.002) and increased left ventricular ejection fraction (25±2 to 38±4%, p=0.006). No such changes were observed for placebo group. In patients with chronic inflammation (CRP >9 mg/l), PTX (N=20) reduced the TNF-alpha concentration (5.4±1.2 to 2.6±0.4 mg/l, p=0.024) without any significant changes of haemoglobin.
Conclusions: Treatment with PTX increased haemoglobin levels in anaemic patients with CHF whilst no such changes were observed in patients with elevated CRP. The potential for adjunctive therapy in intervention trials with erythropoietin and/or intravenous iron needs to be addressed.

P486 Prospective study of an out-patient based intravenous diuretic programme for acute decompensated heart failure

M. Ryder, N. Murphy, D. Mccaffrey, C. Oloughlin, C. Conlon, M. Ledwidge, K. McDonald. *St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*

Background: 15% of patients with chronic heart failure (HF) require hospital admission annually, resulting in significant morbidity and health care costs. Incipient volume overload can be managed in many cases at out-patient level with an increase in oral diuretics and/or alterations in other HF therapies. In certain circumstances, out-patient intravenous (IV) diuretic therapy may be of further help in preventing hospitalisation (i.e., poor response to adjustment in oral therapy or the presence of right heart failure (RHF)). However the effectiveness of an out-patient IV diuretic treatment regime has not yet been thoroughly studied.
Methods: Approximately 1200 patients attend our out-patient HF unit. Between 2002-2006, 107 patients required IV diuretic therapy for acute decompensated heart failure (ADHF). These episodes occurred remotely from adjustments in HF therapies. This cohort was followed prospectively for 1 month post IV diuretic administration. The primary end-point was death or cardiac related hospitalisation. Patients were clinically reviewed and electrolytes were assessed within 24 hours of IV diuretic administration and sequential doses administered as required.
Results: The mean age of this cohort was 72±11 years, 75% male and mean LVEF=32%. 60% had initially received an increase in oral diuretic with unsatisfactory response. The majority of the remainder had RHF, for which IV therapy was the initial intervention. 80% of the cohort achieved clinical stability at out-patient level. There was an increase in urea (14±7 vs. 15±8mmol/L, p<.001) and creatinine (156±66vs.165±75umol/L, p=.001), a decrease in BNP (1060±1210vs.905±1191 pg/ml, p=.002) and no change in potassium (p=.79) from IV diuretic administration to stability post administration. There were 21 events during the follow-up period (2 deaths, 17 HF admissions and 2 other cardiac admissions). Adjusting for age, gender and urea, systemic hypotension (SBP<100mmHg:OR:4.8, p=.01) and those initially uptitrated on oral diuretics (OR:3.0, p=.05) were identified as independent predictors of the primary end point.
Conclusion: The majority of patients who present with ADHF to a specialised HF unit can be successfully and safely managed with out-patient IV diuretic administration. This intervention has the potential to reduce hospital admissions and health care costs. However, this study had identified a patient subgroup, in particular those with systemic hypotension, who may prove more difficult to manage in this manner. Further study is required to see whether alternative out-patient strategies may be of value in these settings.

P487 Dual effects of novel muscarinic bronchodilator, tiotropium, on COPD and heart failure: a randomized, double blind, cross-over, placebo-controlled clinical trial

M. Kato, K. Komamura, M. Kitakaze. *National Cardiovascular Center, Department of Cardiology, Suita, Japan*

Background: Unrecognized and latent chronic heart failure (CHF) is common in elderly patients with combination of chronic obstructive pulmonary disease (COPD). We sought to investigate if the treatment with tiotropium, a novel muscarinic bronchodilator for COPD may improve CHF.
Methods: Consecutive 40 patients with mild to moderate COPD and left-sided CHF mainly due to ischemic cardiomyopathy were randomly divided into two groups and were enrolled to the placebo-controlled cross-over trial using tiotropium. In Group A [n=20, 70±7 years, ejection fraction (EF) 36.3 ±2.4%, brain natriuretic peptide (BNP) 369±102 pg/ml], an inhalation of tiotropium (18μmg) once a day was continued for 28 days and an inhalation of placebo (lactose) was continued for another 28 days. In Group B [n=20, 70±7 years, EF 36.6±1.8%, BNP 369±119 pg/ml), the other patients were treated with tiotropium for 28 days following the inhalation of placebo for 28 days. We measured arterial

Symptoms score; by the St. George's Respiratory Questionaire

		Day 1	Day 29	Day 56
Group A	Symptoms score	44.7±7.4	37.8±9.3	43.2±5.9
	6 minutes walk distance [m]	405±57	424±46	405±63
	Norepinephrine [pg/ml]	821±251	448±203	501±191
	BNP [pg/ml]	369±102	258±97	288±85
	LVEF [%]	36.3±2.4	41.8±5.9	37.8±7.8
Group B	Symptoms score	45.1±7.4	47.9±9.7	36.8±8.3
	6 minutes walk distance [m]	404±70	399±74	422±58
	Norepinephrine [pg/ml]	826±248	747±241	446±197
	BNP [pg/ml]	369±119	358±110	246±101
	LVEF [%]	36.6±1.8	35.7±3.8	41.6±3.8

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

oxygen saturation (SpO2), distance of 6 minutes walk (6MW), laboratory markers including BNP levels and echocardiographic parameters at Day-1, Day-29 and Day-56 each.
Results: In both groups, 28 days inhalation of tiotropium substantially improved the symptoms score, 6MW and SpO2 compared with the untreated conditions. Furthermore, tiotropium improved both EF and BNP levels without right ventricular hemodynamics.
Conclusion: The treatment with tiotropium improved not only COPD, cardiorespiratory symptoms or exercise capacity, but also ameliorated the severity of CHF.

PULMONARY CIRCULATION: BASIC

P488 Modulation of gene expression by cardiomyocyte-specific NOS3 overexpression in the pressure-overloaded right heart

P. Pokreisz[1], G. Marsboom[1], P. Vermeersch[1], X. Liu[2], H. Gillijns[1], M. Pellens[1], F. Van De Werf[2], D. Collen[1], K. Bloch[3], S. Janssens[1]. *[1]Katholieke Universiteit Leuven and VIB, Division of Experimental Cardiology, Leuven, Belgium; [2]Katholieke Universiteit Leuven, Division of Cardiology, Leuven, Belgium; [3]MGH, CVRC and Harvard Medical School, Boston, United States of America*

Purpose: Right ventricular (RV) dysfunction contributes to the morbidity and mortality in a variety of cardiopulmonary diseases. The molecular mechanisms of RV hypertrophy, a hallmark of the remodeling in the pressure-overloaded heart during pulmonary hypertension, are incompletely understood. Nitric oxide (NO) is a signaling molecule with potential anti-hypertrophic effects. We investigated the role of NO on RV adaptation following chronic hypoxia-induced RV pressure overload in mice with cardiomyocyte-specific NO-synthase 3 overexpression (NOS3-TG) and in wild type littermates (WT).
Methods: Selective RV-pressure overload was induced by exposure of NOS3-TG and WT mice to 10% normobaric hypoxia for 6 weeks. RV and systemic hemodynamics were measured during closed chest catheterization in anesthetized, mechanically ventilated mice. After 6w hypoxia, RV remodeling was quantified by measuring fractional RV weight (RV/LV plus septal weight), cardiomyocyte width, cross-sectional area (CSA), and extent of fibrosis. Transcriptome analysis in RVs from NOS3-TG and WT (22k cDNA chip) was compared to pooled normoxic WT mice and differences confirmed using real time PCR. Protein expression and activation was analyzed using immunoblotting and immunohistochemistry.
Results: After 6w hypoxia, RV systolic pressure was higher in WT than in NOS3-TG (36±5 vs 28±3 mmHg, $P<0.05$), with comparable RV systolic function but better preserved RV relaxation (dP/dt-min -2459±501 vs -1852±424 mmHg/s, $P<0.05$). NOS3-TG developed less hypertrophy than WT mice as evidenced by reduced fractional heart weights (0.35±0.03 vs 0.42±0.04, $P<0.05$), cardiomyocyte width (8.5±0.1 vs 10.7±0.2 μm, $P<0.05$), and CSA (260±23 vs 383±28 μm^2, $P<0.05$). After 6w hypoxia, 146 genes were differentially expressed in NOS3-TG compared to WT mice. The most abundantly upregulated genes included ATP-binding cassette B3, cyclin-dependent kinase inhibitor, and cytosolic phospholipase A2, while glycogen phosphorylase, potassium voltage-gated channel 5 and mitogen activated protein 3 kinase were among the most significantly downregulated genes. Immunoblotting revealed that RV hypertrophy in WT mice was associated with significantly increased phosphorylation and nuclear translocation of extracellular signal-regulated kinases.
Conclusion: Cardiomyocyte-restricted NOS3 overexpression is associated with reduced hypertrophy in the murine pressure-overloaded RV. Differential expression of genes involved in cellular hypertrophy, matrix modulation, programmed cell death, fatty acid and glycogen metabolism suggests potential novel treatment strategies.

P489 Endotoxin causes pulmonary hypertension by changing the ETB receptor balance: loss of endothelial and concomitant gain of vascular smooth muscle receptors

T. Dschietzig[1], M. Bobzin[1], K. Stangl[1], F. Brunner[2]. *[1]University Medical Center Charite (Mitte), Cardiology and Angiology, Berlin, Germany; [2]K. Franzens University, Graz, Austria*

It is now generally accepted that the interplay between ET-1 and NO governs the hemodynamic response in endotoxemia. In the rat – which represents a widely used model animal in sepsis research – accumulating experimental evidence points to the relevance of increased ETB receptor expression as underlying mechanism for endotoxin-induced systemic hypotension and death. We investigated, in a rat isolated perfused lung model (IPL) and in cultured pulmonary endothelial (RPAEC) and vascular smooth muscle cells (RPVSMC), the regulation of endothelin receptor expression under septic conditions in pulmonary circulation, which usually responds to endotoxemic states with increased vascular tone. In response to a 6-hour endotoxin challenge, IPL developed significant pulmonary hypertension which could be completely abolished by mixed ET-1 antagonism (PD-145065) and partially reduced by selective ETA (A-127722) or ETB (A-192621) blockade. ET-3, an ETB agonist, evoked vasodilation in control IPL but vasoconstriction in endotoxemic IPL. In all models, endotoxin increased peptide levels of big ET-1 and ET-1 and gene expression of prepro-ET-1. In IPL and RPAEC, the significant rise of mature ET-1 seen in controls after ETB receptor blockade or mixed ET-1 antagonism completely disappeared in response to endotoxin. However, this effect was preserved after endotoxin exposure in RPVSMC. In RPAEC, endotoxin dramatically down-regulated maximum ETB binding sites as assessed by 125I-ET-1 binding assay and at mRNA level whereas in RPVSMC, it generated a substantial ETB up-regulation. The endotoxin-induced alterations of ETB receptor expression in RPAEC and RPVSMC were inhibited by the aldose reductase inhibitor sorbinil. In conclusion, our findings in rat models indicate that endotoxin exposure induces pulmonary hypertension which can be attributed to the loss of endothelial ETB receptor function and the concomitant gain of ETB receptor function on vascular smooth muscle cells. These dramatic changes are principally mediated via aldose reductase.

P490 Procoagulant microparticles of endothelial origin circulate in the jugular vein and pulmonary artery of patients with pulmonary arterial hypertension and correlate with the severity of the disease

B. Bakouboula[1], O. Morel[1], A. Faure[1], L. Jesel[1], A. Trinh[1], M. Zupan[1], L. Grunebaum[2], J.-M. Freyssinet[3], F. Toti[4], A. Chaouat[5]. *[1]Federation de cardiologie, Strasbourg, France; [2]Departement d'Hemostase, CHU, Bas rhin, Strasbourg, France; [3]INSERM U770, Bas rhin, Strasbourg, France; [4]INSERM U770, Paris XI, ULP, Bas rhin, Strasbourg, France; [5]Departement de pneumologie, Nancy, France*

Rationale: Vascular inflammation, cell damage and thrombotic propensity, seem to be involved in pulmonary arterial hypertension (PAH). Procoagulant microparticles (MP) constitute valuable hallmarks of cell damages known to occur in PAH. In the vessel, MP behave as cellular effectors promoting cell cross-talk. We hypothesized that the extent of the vascular cell damage measured by circulating MP could be related to the severity of PAH.
Methods: Circulating biomarkers of vascular damage and cell activation, including MP, were measured in blood samples from 20 patients with PAH. Samples were withdrawn from pulmonary artery (PA) and from the jugular vein (JV). Peripheral venous blood samples were obtained in 23 matched patients as a control subset.
Results: Circulating markers of endothelial damage (sVCAM-1, PAI-1), pro-inflammatory chemokines (RANTES, sMCP-1) and C-reactive protein were significantly higher in the plasma from PAH patients (2 times higher). Concentrations of sVCAM-1 measured in PA were correlated to the mean pulmonary artery pressure, as well as to the pulmonary vascular resistance, the cardiac output and to brain natriuretic peptid concentration. In PAH, plasma concentrations of MP followed a typical gradient pattern, values being higher in PA than in JV. Measurements of MP bearing active Tissue Factor (TF) revealed higher levels in PA and JV than in the peripheral blood of the control subset. MP bearing active TF values in PA and JV were correlated with the reduced performances recorded in a 6-min walk test ($r=-0.52$; $p=0.046$ and $r=-0.62$; $p=0.017$). Furthermore, the MP captured onto annexin V mean gradient values were correlated with mPAP and endothelial MP bearing CD105 mean gradient ($r=0.631$; $p<0.01$ and $r=0.749$; $p<0.01$, respectively).
Conclusion: Circulating markers of endothelium damage, neurohormonal activation and cell stimulation appear valuable tools in the ranking of the severity of PAH. The MP gradient observed between PA and peripheral JV suggests tissue trapping following pulmonary release. Whether procoagulant MP promote thrombus formation contributing to the raise of the arterial pulmonary pressure in PAH remains to be established.

P491 Functional autoantibodies against the a1-adrenergic receptor and endothelin1 ETA receptor in the sera of patients with primary pulmonary hypertension

G. Wallukat[1], M. Dandel[2], J. Mueller[1], S. Bartel[1], W. Schulze[1], R. Hetzer[1]. *[1]Max-Delbruck-Centrum F. Molek. Med., Berlin, Germany; [2]Berlin, Germany*

Background: Primary pulmonary hypertension (PH) is a progressive fatal disease of unknown cause. This disease is accompanied by an increase the tonus and a remodelling of pulmonary vessels. The tonus increase is associated with a right ventricular hypertension. It was shown that the synthesis of vasoconstrictors (endothelin 1, thromboxane A2, serotonine) is elevated in patients with PH.
Material and Methods: We analyzed sera of patients with PH with regards to functional autoantibodies (AABs) against G-protein coupled receptors using spontaneously beating rat cardiomyocytes as bioassay. Furthermore, we measured the influence of the AAB on the translocation of the transcription factors NFκB and AP-1 by means of both immunofluorescence and a commercial kit.
Results: The sera of patients with PH contain functional AABs against the α1-adrenergic (α1-AR) and the endothelin1 ETA receptor. In both cases the natural agonists against these receptors cause vasocontraction. We purified the AABs by affinity chromatography. The agonist-like effect of the AABs was dose-dependent and blocked by prazosine (α1-AR antagonist) and BQ610 (ETA antagonist). The AABs against the α1-AR recognize epitopes on the first (sequences FWAFGR and GRAFCDV) or second (sequence ITEEAGY and ERFCGI) extracellular loop.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

The AABs against the ETA-receptor recognize the epitope MLNATSK on the second extracellular loop. The α1-AR AABs as well as the ETA-receptor AABs induce a permanent stimulation without desensitization of the receptor mediated signal cascade. The α1-adrenergic agonist phenylephrine and endothelin1 as ET receptor agonist cause a translocation of the transcription factor NFκB and AP-1 from the cytosol into the nucleus. The same translocation was observed using the AABs against the α1-AR and ETA receptor.
Conclusion: The agonist-like AABs against the α1-AR and the ETA receptor influence in vitro the signalling of cultured cells. Moreover, the AABs prevent the desensitization of the receptor mediated signal cascade normally seen by ongoing receptor stimulation. Therefore, we assumed that the AABs against the α1-AR and the ETA receptor may be involved in the pathogenesis of PH.

P492 Polymorphisms of the angiotensin system and nitric oxide synthase genes in pulmonary hypertension

M.D. Martin Cid, M. Garcia Castro, J.J. Rodriguez Reguero, E. Coto, C. Garcia, C. Moris De La Tassa. *University Central Hospital of Asturias, Cardiology Service, Oviedo, Spain*

Introduction: Capillary blood vessels in the lung are one of the major sites of angiotensin converting enzyme (ACE) expression and angiotensin II production. Polymorphisms in the genes encoding angiotensinogen (AGT), ACE, and angiotensin II type 1 receptor (AT1) have been associated with the development of pulmonary hypertension (PH). Nitric oxide (NO) synthases could also involved in PH through the impaired NO and prostanoid production. We genotyped several polymorphisms in these genes in a patients with PH and healthy controls.
Methods: The cause of PH was thromboembolic (33%), Eisenmenger's Syndrome (24%), idiopatic (18%), portopulmonary (12,5%), and colagenosis and other causes (12,5%). DNA from the 66 patients and 200 healthy controls was genotyped for 4 polymorphisms in the ACE, AGT, AT1, and eNOS. We compared the genotypes frequencies between the two groups.
Results: We did not find significant differences between patients and healthy controls for the 4 polymorphisms. Patients with Eisenmenger's syndrome and PH had a higher frequency of homozygous for the eNOS deletion allele (4-repeats). Portopulmonary hypertension and PH associated to colagenosis was associated with the AT1-CC genotype.

Genotypes frequencies

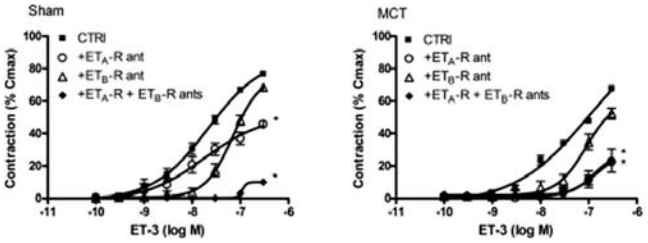
	Total n=66	TEP n=22	Eisenmenger n=16	Primary n=12	Portopulmonary n=8	Colagenosis and other n=8	Controls n=200
ECA							
II	9 (14%)	2 (9%)	2 (13%)	3 (25%)	1 (13%)	1 (12%)	17 (9%)
ID	38 (57%)	13 (59%)	10 (63%)	6 (50%)	4 (50%)	5 (64%)	103 (51%)
DD	19 (29%)	7 (32%)	4 (25%)	3 (25%)	3 (37%)	2 (24%)	80(40%)
AT1							
CC	4 (6%)	1 (5%)	0	3 (25%)	3 (37%)	0	15 (8%)
CA	29 (44%)	9 (41%)	8 (50%)	5 (42%)	5 (63%)	4(50%)	87 (43%)
AA	33 (50%)	12 (54%)	8 (50%)	4 (33%)	0	4 (50%)	98 (49%)
AGT							
MM	27 (41%)	9 (41%)	8 (50%)	4 (33%)	3 (37%)	3 (37%)	75 (37%)
MT	28 (42%)	10 (45%)	6 (37%)	5 (42%)	4 (50%)	3 (37%)	92 (46%)
TT	11 (17%)	3 (14%)	2(13%)	3 (25%)	1 (13%)	2 (26%)	33 (17%)
Nos vntr							
55	50 (76%)	15 (77%)	14 (87%)	8 (67%)	6 (75%)	5 (63%)	147(73%)
45	14 (21%)	7 (23%)	0	4 (33%)	2 (25%)	3 (37%)	51 (25%)
44	2 (3%)	0	2 (13%)	0	0	0	1 (1%)
46	0	0	0	0	0	0	1 (1%)

Conclusion: PH associated to Eisenmenger's syndrome was associated with the endothelial NOS variation, suggesting a role for these gene in the risk of developing this form of PH. This suggests that pharmacological intervention to modify NO production could be a valuable tool to treat PH, at least in a subgroup of patients.

P493 Endothelin-3 -dependent pulmonary vasoconstriction in monocrotaline-induced pulmonary arterial hypertension

S. Sauvageau, E. Thorin, J. Dupuis. *Montreal Heart Institute, Montreal, Canada*

Background: Activation of the endothelin (ET) system contributes to the development and maintenance of pulmonary arterial hypertension (PAH). There are three known isoforms of ET (ET-1, ET-2 and ET-3). The contribution of ET-3 and its interaction with the ET-Rs have not been characterized in pulmonary resistance vessels.
Methods and Results: Sham or monocrotaline (MCT)-injected rats were evaluated after 5 weeks. Reactivity of isolated pulmonary resistance arteries to ET-3 was measured in the presence of ET-R antagonists (A): ETA-RA (10 nM), ETB-RA (1 μM) and the combination of both. ET-3 plasma levels (0.96±0.09 pg/ml vs 0.81±0.39, p=0.0549) tended to increase in PAH. Using immunofluorescence microscopy analysis, we found that ET-3 was mainly localized in the smooth muscle layer of pulmonary resistance arteries. ET-3 induced similar pulmonary vasoconstrictions in both groups. In sham animals, the ETA-RA greatly reduced the maximal response to ET-3 while the ETB-RA shifted the EC50 without affecting Emax. However, the combination of both completely abolished ET-3 response (figure, * < 0.001 vs CTRL). In PAH, the ETA-RA also markedly reduced the maximal response and shifted the EC50 while the ETB-RA only shifted the EC50 without affecting the maximal response. The combination of both did not further reduce the constriction compared to the ETA-RA alone.



ET-3 constriction of pulmonary arteries

Conclusion: ET-3 causes important pulmonary vasoconstriction mediated by both the ETA-R and ET-B-R. ET-3 responses suggest interdependance (cross-talk) between ETA/ETB-Rs that is modified by PAH. ET-3 may therefore also contribute to the development of PAH.

PULMONARY CIRCULATION: EXPERIMENTAL

P494 Both bone marrow-derived endothelial progenitor cell implantation and cilostazol therapy attenuate monocrotaline-induced pulmonary arterial hypertension in rats

H.K. Yip. *Chang Gung Memorial Hospital, Cardiology Division, Kaohsiung, Taiwan*

Background: We investigated whether bone marrow-derived endothelial progenitor cell (BMDEPC) transfusion and cilostazol therapeutic ameliorates monocrotaline (MCT)-induced pulmonary arterial hypertension (PAH) in rat model.
Methods and Results: Male Spraque-Dawley rats were randomized to received MCT (75 mg/kg) only (group 1), MCT plus autologous BMDEPC (1.2 x 106 cells) transplantation (group 2), MCT plus cilostazol (group 3), and saline injection only (group 4). Mononuclear cells were obtained from femoral bone marrow of group 2 rats and then isolated by Ficoll gradient centrifugation. These cells were cultured for 21 days in endothelial culture medium. Pulmonary blood flow and pathologic and hemodynamic findings on day 28 following MCT treatment identified the development of significant PHA on MCT-treated groups. Cilostazol was given to group 2 (20 gm/kg/day orally) from day 28 and BMDEPCs were intravenously transplanted in group 3 on day 28 after MCT-induced PAH. Fluorescent image study demonstrated that fluorescently labeled BMDEPCs were attracted in pulmonary arterioles at 20 minutes following transplantation. On day 90 following MCT treatment, the right ventricular systolic pressure (RVSP) and RV weight were higher in group 1 than in groups 2-4 (all p values < 0.01). Additionally, the numbers of alveolar sacs and small arterioles of lung sections were lower in group 1 than in groups 2-4 (all p values < 0.01). Furthermore, Western blot analysis demonstrated that the phosphatase and tensin homologue deleted on chromosome 10 and signal transducer and activator of transcription 3 expressions of lung tissue were s increased and connexin43 expression of lung tissue and RV myocardium were lower in group 2 than in groups 2-4 (all p values < 0.01).
Conclusions: Both BMDEPC transplantation and cilostazol therapy are effective for amelioration of MCT-induced PAH.

P495 Effects of PDE5-inhibition by sildenafil in the pressure overloaded right heart

A. Andersen[1], J.E. Nielsen-Kudsk[1], J.M. Nielsen[1], U.K. Skov[2], C.D. Peters[2], E. Sloth[1]. *[1]Aarhus university hospital, Skejby Sygehus, Department of cardiology B, research unit, Aarhus, Denmark; [2]University of Aarhus, Health Sciences, The water and salt research centre faculty, Aarhus, Denmark*

Background: Several cardiovascular and pulmonary disorders expose the right heart to a sustained pressure overload causing hypertrophy and heart failure. In the pressure overloaded left ventricle (LV), cyclic GMP has been demonstrated to protect against development of pathological hypertrophy. Sildenafil elevates the intracellular levels of cyclic GMP by inhibition of PDE5.
Hypothesis/Aim: Sildenafil prevents and revert ventricular hypertrophy and dysfunction in the pressure overloaded right heart.
Materials and methods: Rats (male Wistar, n=31) were pulmonary trunk banded (PTB) in universal anaesthesia. One group of rats (n=14; prevention group) was immediately after operation randomized to receive sildenafil (100 mg/kg/day added to the drinking water) (n=6) or vehicle (n=8) in order to test whether sildenafil prevents development of right ventricular hypertrophy and dysfunction. Transthoracic echocardiography (TTE) was performed after a treatment period of

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

3 weeks. Tricuspid annular plane systolic excursion (TAPSE) was determined as a measure of RV contractile function. The rats were then sacrificed and the hearts removed. The right ventricle (RV) and LV including the septum were weighed separately. In another group of rats (n=17; reversion group), it was tested whether sildenafil reverts established RV hypertrophy and dysfunction. These rats were investigated by TTE 3 weeks after pulmonary trunk banding and then randomized to either sildenafil (100 mg/kg/day) (n=9) or vehicle (n=8). TTE and determination of RV and LV/septum weights were performed at week 6 after operation.
Results: In the prevention-group of rats, a significant increase of RV weight was observed in the sildenafil treated animals compared with controls (RV/BW: 0.099 vs. 0.081, $p<0.028$). There was no significant increase in TAPSE (0.208 vs. 0.177 cm p=0.061). In the reversal-group of rats, there was no difference in RV weight between sildenafil and vehicle treated animals, but there was a significant increase in TAPSE (0.185 vs. 0.139 cm, $p\leq0.001$).
Conclusion: PDE5-inhibition by sildenafil improved ventricular systolic function in the pressure overloaded right heart, but it failed to prevent or revert right ventricular hypertrophy.

P496 Hemodynamic effects of replacement of RBC with small-size liposomal hemoglobin on pulmonary hypertensive rat

S. Mohri, Y. Katanosaka, A. Yamada, K. Naruse. *Okayama University, Cardiovascular Physiology Dept., Okayama, Japan*

Purpose: Primary pulmonary hypertension (PPH) progressively increases pulmonary resistance and causes right ventricular failure. While many vasodilatory agents have been used for PPH treatment, their tolerances are major limitations and the development of the novel therapy is expected for a better outcome. Hypothesis: According to Poiseuille's law, lowering the blood viscosity can decrease vascular resistance. We therefore investigated whether the partial replacement of red blood cells with small-size (200 nm in diameter), polyethylene glycol-modified liposomal hemoglobin (LHb) decreased pulmonary resistance by its lower viscosity using rat model.
Methods: PH was induced by monocrotaline injection in SD rats (6 mg/100gBW sc). LHb suspension included approximately 6 g/dL Hb (LHb suspended in physiological saline; Terumo, Japan) and 6g/dl albumin. LHb suspension was intravenously infused with intra-arterial withdrawal of blood at a rate of 1 ml/min for 10 min, resulting in 50% blood-LHb exchange transfusion. Pulmonary arterial pressure (PAP), aortic pressure (AoP), left ventricular pressure (LVP), and cardiac output (CO) were measured to evaluate hemodynamics before and after exchange transfusion. Systemic and pulmonary resistances were calculated as mAoP/CO and (mPAP - LVEDP)/CO respectively.
Results: CO was increased from 16±2.0 to 22±2.1 ml/min. mAoP and mPAP were unchanged (from 58±2.6 to 60±2.9 and from 49±2.3 to 50±3.2 mmHg). Systemic and pulmonary resistances were significantly decreased (from 3.6±0.5 to 2.8±0.1 and from 2.9 ±0.4 to 2.0±0.2 mmHg•min/ml). Increased LV preload i.e. LVEDP (from 3.3±2.1 to 6.6±3.2 mmHg) preserved mAoP by an increase of CO despite a decrease of systemic resistance.
Conclusions: LHb effectively decreased pulmonary vascular resistance without a drop of AoP by an increase of CO. Because of different mechanisms from vasodilatory agents in a decrease of vascular resistance, LHb administration can be a novel treatment for PPH.

P497 Anti-remodeling and anti-inflammatory effects of elastase inhibition in a rat model of pulmonary hypertension and right heart failure

M. Klein[1], F. Kramer[2], S. Golz[2], F. Von Nussbaum[1], R. Kast[1], S. Schaefer[1]. *[1]Cardiovascular Research, Bayer HealthCare AG, Institute of Cardiovascular Research, Wuppertal, Germany; [2]Target Discovery, Bayer HealthCare AG, Institute of Cardiovascular Research, Wuppertal, Germany*

Pulmonary arterial hypertension results from increased vasomotor tone and extracellular matrix remodeling of pulmonary arteries. The extracellular matrix glycoprotein tenascin-C, the matrix metalloproteinase-2 (MMP-2) and the chemokine IL-8 are involved in extracellular matrix maintenance, cell-migration and cell proliferation, with a potential role in pathobiology of pulmonary hypertension. Furthermore, o veractivation of human neutrophil elastase (HNE), a serine protease that hydrolyses components of the extracellular matrix, has been implicated in the pathogenesis of pulmonary arterial hypertension. We therefore investigated the efficacy of the novel selective HNE inhibitor BR4946 in a rat model of pulmonary hypertension. Four weeks after a single subcutaneous injection of monocrotaline (MCT, 60mg/kg), male Sprague-Dawley rats displayed severely elevated right ventricular systolic pressure and marked right ventricular hypertrophy with a concomitant increase in plasma MMP-2 activity and B-type natriuretic peptide levels (proBNP). Furthermore there was a significant increase in pulmonary IL 8 (~2-fold) and right ventricular tenascin-C (~100-fold) expression. Treatment with BR4946 (50 mg/kg bid p.o., n = 12-14) from day 14-28 significantly reduced right ventricular pressure and right ventricular hypertrophy with preservation of systemic arterial pressure (Table). Furthermore, BR4946 normalized plasma MMP2-activity and pulmonary IL 8 expression and significantly reduced plasma proBNP levels and right ventricular tenascin-C expression.

	RVP, mmHg	RV/(LV+S)	Active MMP 2, ng/ml	proBNP, pg/100ml
Control	26.9±0.8*	0.26±0.01*	8.03±0.85*	13.95±0.79*
MCT + Vehicle	68.3±6.2	0.50±0.03	16.03±1.46	41.09±4.91
MCT + Elastase Inhibitor	48.1±3.1*	0.35±0.02*	9.86±1.55*	27.05±4.69*

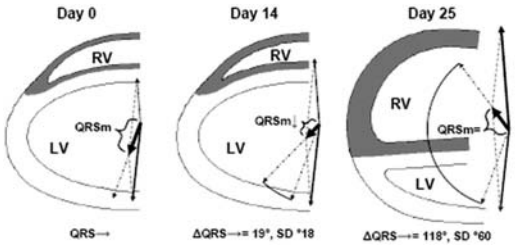
Mean ± SEM. N=12-14/group.*, $p<0.05$ vs. vehicle, RVP=right ventricular pressure.

Conclusion: Monocrotalin-induced p ulmonary arterial hypertension in rats is characterized by significantly elevated plasma concentrations of active MMP-2 and proBNP and increased expression of Tenascin C and IL-8. Selective inhibition of human neutrophil elastase significantly improves these biomarkers, indicating substantial anti-remodeling and anti-inflammatory effects.

P498 Sequential body surface ECG recordings detect early changes in rat hearts with developing pulmonary arterial hypertension

I.R. Henkens[1], K.T.B. Mouchaers[2], H.W. Vliegen[3], W.J. Van Der Laarse[4], C.A. Swenne[1], A.C. Maan[1], H.H.M. Draisma[1], E.E. Van Der Wall[1], M.J. Schalij[1], A. Vonk Noordegraaf[4]. *[1]Leiden University Medical Centre, Cardiology, Leiden, Netherlands; [2]VU Medical Center, Physiology and Pulmonology, Amsterdam, Netherlands; [3]Leiden University Medical Center, Cardiology, Leiden, Netherlands; [4]VU Medical Center, Physiology, Amsterdam, Netherlands*

Background: Recognizing early changes in the right ventricle (RV) as a result of developing pulmonary arterial hypertension (PAH) may allow for timely detection and treatment of this fatal disease.
Study aim: To assess 3-dimensional ECG changes with developing pulmonary arterial hypertension (PAH).
Methods: Fifteen male Wistar rats were injected with 40 mg/kg of monocrotaline (MCT) to induce PAH. Five healthy rats served as controls. Three orthogonal leads were recorded on day 0, 14 and 25, and analyzed with dedicated software. In addition, left ventricular (LV) and right ventricular (RV) fractional shortening ratio were determined using echocardiography. On day 25 rats were sacrificed.
Results: Mean RV systolic pressure on day 25 was 64 mmHg (SD 10) in MCT rats vs. 25 mmHg (SD 2) in controls ($p<0.001$). Baseline ECGs of controls and MCT rats were similar. ECGs of controls did not change over time. In MCT rats depolarization changes were already present on day 14 (Figure): increased RV electromotive forces decreased mean QRS vector magnitude (QRSm), and changed QRS-axis orientation (QRS→). On day 25 there were marked depolarization and repolarization abnormalities (QRS-T spatial angle had changed from 61° (SD 35) to 153° (SD 25), $p<0.001$). ECG changes reflect increasing RV electromotive forces as a consequence of developing PAH. Echocardiographic LV to RV fractional shortening ratios had not changed on day 14, but had increased on day 25.



ECG changes in rats with developing PAH

Conclusion: Developing pulmonary arterial hypertension is characterized by early depolarization changes, whereas severe pulmonary arterial hypertension is characterized by both marked depolarization abnormalities and abnormalities in repolarization related parameters. 3-Dimensional ECG analysis appears to be very sensitive to early changes in RV afterload.

PULMONARY CIRCULATION: VARIA

P499 Both tezosentan and vardenafil attenuate hypoxic pulmonary vasoconstriction

R. Geiger, A. Kleinsasser, A. Loeckinger, B. Treml. *Medical University, Pediatric Cardiology, Innsbruck, Austria*

Rationale: Excessive hypoxic pulmonary vasoconstriction may lead to pulmonary edema, right heart failure and death. Increased phosphodiesterase activity as well as increased levels of endothelin-1 have been discussed molecular mechanisms.
Objective: To investigate the hemodynamic and intrapulmonary effects of the intravenous dual endothelin A and B receptor blocker tezosentan, and of the phosphodiesterase-5 (PDE-5) antagonist vardenafil in a pig model of normobaric hypoxic pulmonary hypertension.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Methodes: Twenty-four 4 week-old ventilated white farm pigs were exposed to normobaric hypoxia (FiO_2 12%) and randomly assigned to four groups in order to receive either intravenous tezosentan or vardenafil or combined tezosentan and vardenafil or to serve as control.
Results: Hypoxia increased mean pulmonary artery pressure (Ppa) by mean 70% and pulmonary vascular resistance index (PVRI) by mean 112%. After 90 minutes of treatment, Ppa and PVRI were significantly lower in all treatment groups as compared to controls ($p < 0.001$). Cardiac index increased significantly with vardenafil alone ($2.8 \text{ l} \cdot \text{min}^{-1} \cdot \text{m}^2 \pm 0.7$ to $4.2 \text{ l} \cdot \text{min} \cdot \text{m}^2 \pm 0.7$, $p = 0.0003$). Ventilation-perfusion matching was not significantly altered during treatment. Combining tezosentan and vardenafil did not result in additive or supraadditive changes in hemodynamics and gas exchange.
Conclusions: Intravenous tezosentan, as well as vardenafil equipotently attenuate hypoxic pulmonary vasoconstriction without afflicting pulmonary gas exchange. However, cardiac index is increased by vardenafil only.

P500 Larger sympathetic response to high altitude in children may explain excessive increase in pulmonary artery pressure

C. Jansen[1], A.Z. Linka[2], A. Kessel[3], S. Kriemler[4], M. Kohler[3], M. Zehnder[3], H.P. Brunner[1]. *[1]University Hospital Basel, Cardiology, Basel, Switzerland; [2]Winterthur, Switzerland; [3]Basel, Switzerland; [4]Zuerich, Switzerland*

Background: It has become increasingly popular for families to spend vacation in high mountain areas while undertaking fairly heavy physical exercise. As shown preciously, prepubertal healthy children, when exposed to high altitude, develop higher pulmonary artery pressure than their parental counterparts. However, potential underlying mechanisms of this finding as well as the haemodynamic response to high altitude induced hypoxia in children remains unknown. Thus, we tested the haemodynamic response to high altitude 3 to 4 hours after arrival at Jungfraujoch (JFJ: 3450m) at rest, after physical exercise for several hours at high altitude on the afternoon of day 2, and the following morning at rest before descent in prepubertal children (age 10 to 12 years) in comparison to their fathers.
Methods: Twenty healthy children (4 girls and 16 boys; age 11±1 years) and their healthy fathers (age 44±4 years) were included in this study. Within 3 weeks prior to ascent, echocardiography (Toshiba Aplio) was performed at rest at low altitude (Zurich-Irchel 500m). Subjects travelled within 2 hours from low altitude to JFJ. Calculation of stroke volume and cardiac index based on time velocity integral measurements of the both right and left ventricular outflow-tract (identical results).
Results: On the first day at high altitude in comparison to low altitude, O2-saturation decreased similarly in both groups (children: 98±1% to 90±3%, adults 97±1% to 89±3%). Heart rate (19±17% vs. 12±15%, p=0.03) and cardiac index (16±35% vs. 7±9%, p=0.04) increased significantly more in children. Systolic blood pressure (BP) increased in children, whereas it fell in adults (6±14% vs. -2±7%, p=0.03). In parallel, pulmonary artery pressure increased significantly more in children (15±11 mmHg vs. 6±9 mmHg, p=0.03). On day 2 after recovery from exercise, heart rate increased further in both (7±12% vs. 9±16%, n.s.) and blood pressure significantly more in children (systolic 9±14% vs 2±7%, p=0.04; diastolic: 19±23% vs. 5±12%, p=0.03). Cardiac index remained unchanged in both children and adults.
Conclusion: In comparison to their parental counterparts, prepubertal healthy children exhibited a larger sympathetic response to high altitude related hypoxia. This may explain, in part, the larger increase in pulmonary artery pressure. Further studies are needed to investigate if additional mechanisms are of importance.

P501 Pulmonary arteriovenous malformations are associated with migraine with aura

M.C. Post[1], J.G.L.M. Luermans[1], R.J. Snijder[1], J.J. Mager[1], W. Jaarsma[1], W.J. Schonewille[1], V. Thijs[2], C.J.J. Westermann[1]. *[1]St Antonius Hospital, Cardiology, Nieuwegein, Netherlands; [2]University Hospital Gasthuisberg, Neurology, Leuven, Belgium*

Purpose: Recently, retrospective studies report a high prevalence of migraine in patients with PAVM. In this prospective study we evaluate the association between size and presence of PAVM, diagnosed by transthoracic contrast echocardiography (TTE), and migraine.
Methods: Two-hundred fifteen out of 228 persons (94%) who were referred to our hospital for HHT screening between 05-2004 and 11-2006 underwent a TTE for detecting PAVM. All patients received a structured headache questionnaire. Two neurologists diagnosed migraine according to International Headache Society criteria.
Results: One-hundred and ninety-nine subjects (63% female, mean age 44.7±14.2 years) completed the questionnaire. A PAVM was present in 36%. The overall prevalence of migraine was 23% (13% in male, 29% in female; p=0.01) and MA 10% (7% in male, 12% in female; p=0.25). In patients with a PAVM the prevalence of overall migraine was 21% compared to 24% in patients without PAVM (p=0.68), with no association between the size of the shunt and overall migraine. In the 44 patients with migraine (79.5% female, 44.1±12.7 years) there was no difference in frequency (p=0.64), severity (6.7 versus 6.0, p=0.19), and duration (13.9h versus 16.3h, p=0.71) between patients with and without PAVM. The prevalence of MA was 16% in patients with a PAVM compared to 8% in those without a PAVM (p=0.06). In the 20 patients (75% female, mean age 44.5±12.6 years) with MA there was no significant difference in frequency (p=0.1), severity (6.8 versus 5.6, p=0.19), and duration of headache (13.7h versus 8.3h, p=0.52) between patients with and without PAVM. MA occurred in 28% in patients with a large shunt (>100 bubbles), 21% in patients with a at least a moderate shunt (>20 bubbles), and 10% in the presence of a small shunt (<20 bubbles) (p for trend is 0.005). Kappa coefficient for interobserver reliability was 0.9 ($p < 0.001$).
Conclusion: Only MA seems to be associated with the presence of PAVM. However, there is no difference in migraine characteristics between patients with and without PAVM. Interestingly, the prevalence of MA increases with increasing size of the pulmonary shunt measured by TTE.

P502 Screening for pulmonary arteriovenous malformation using transthoracic echocardiography: a prospective study

M.C. Post, J.G.L.M. Luermans, R.J. Snijder, J.J. Mager, W. Jaarsma, T.T. Overtoom, C.J.J. Westermann. *St Antonius Hospital, Cardiology, Nieuwegein, Netherlands*

Purpose: A pulmonary arteriovenous malformation (PAVM) is often associated with HHT and constitutes a right-to-left shunt. These PAVM causes hypoxemia, and often serious complications such as stroke or cerebral abscesses, and might be prevented by embolization therapy. We prospectively evaluated the diagnostic value of non-invasive tests for screening PAVM, using the high-resolution CT (HRCT) of the chest as the "golden" standard.
Methods: All patients (> 6 years of age) who were screened for HHT between 05-2004 and 12-2006, and underwent a HRCT of the chest, were included. In almost all patients screening for PAVM was done by a chest radiograph (n=221), arterial oxygen pressure measurement (n=196) or RLS measurement by the 100% oxygen technique (only if the arterial oxygen pressure was less than 12 kPa (n=66)), and a transthoracic contrast echocardiography (TTE (n=208)), all on the same day. The sensitivity and negative predictive values (NPV) with their 95% confidence intervals (CI) were measured for each test using the HRCT as the golden standard.
Results: Two-hundred and twenty-five patients (65% female, mean age 44.5±14.7 years) underwent a HRCT of the chest and could be included in the study. A PAVM was present in 20% of the patients screened for HHT. Using the chest radiograph alone the sensitivity was 29.5% (95% CI 24.5-60.9) and the NPV was 85.1% (95% CI 79.5-89.6). An arterial oxygen pressure of less than 12 kPa had a sensitivity of 73.7% (95% CI 56.9-86.6) and a NPV of 90.0% (95% CI 82.4-95.1). An abnormal RLS measurement (> 5% shunt fraction) had a sensitivity of 82.6% (95% CI 61.2-95.1), and a NPV of 90.5% (95% CI 77.4-97.3). The combination of chest radiograph and RLS measurement gives a sensitivity of 48.9% (95% CI 33.7-64.2), and a NPV of 88.3% (95% CI 82.9-92.4). For TTE the sensitivity was 95.3% (95% CI 84.2-99.4), and the NPV was 98% (95% CI 94.6-99.8). In two patients the HRCT was positive were in both the TTE and chest radiograph were negative. In 37 patients (17% of total) a pulmonary shunt was suggested by TTE whereas the HRCT was negative for PAVM.
Conclusion: In our prospective study, contrast echocardiography is the best non-invasive diagnostic test for PAVM with the highest specificity and negative predictive value. Probably the test is even more sensitive in diagnosing a pulmonary shunt compared to the main "golden" standard a HRCT of the chest.

P503 Perioperative stent implantation for management of pulmonary artery stenoses in infants with single ventricle physiology

N. Sreeram, M. Emmel, K. Brockmeier, G. Bennink. *University hospital of Cologne, paediatric cardiology, Cologne, Germany*

Objectives: To evaluate the safety and efficacy of stent implantation to facilitate perioperative management of pulmonary arterial stenoses in infants with single ventricle physiology, undergoing staged surgical palliation.
Patients and Methods: Nine infants (weight range 4.7 - 9.6 kg; age 3 - 6.5 months) with complex single ventricle physiology were evaluated by cardiac catheterization immediately following (3-18 days post-surgery) a bidirectional superior cavopulmonary (bidirectional Glenn - BDG) shunt, due to persistent SVC syndrome, hypoxemia, and raised SVC pressure (mean 18 - 25 mm Hg). Single or multiple stenoses affecting the left pulmonary artery (either directly behind the Damus <aortopulmonary> anastomosis (n=7), or at the BDG anastomosis (n=2)), or the right pulmonary artery (n=3, at the BDG anastomosis) weer identified. The minimum diameter of the stenoses ranged from 1.5 mm to 3.2 mm. Via the internal jugular vein, premounted Palmaz-Genesis stents (on 6 mm, 8 mm or 10 mm diameter balloons) were delivered to the stenoses.
Results: All stents (n=13) were successfully implanted, with relief of all treated stenoses. The final diameter of the treated segments ranged from 5.8 to 9.6 mm. One infant developed a tear of the left pulmonary artery at a site remote from the surgical scar, and required immediate reoperation and repair of the vessel (the stent was removed). In the remaining patients the mean SVC pressure decreased to between 14 and 18 mm Hg within 72 hours of the procedure. Six infants have undergone successful Fontan completion; 2 are awaiting further evaluation and surgery. One infant (with LPA tear) died due to recurrent thrombotic obstruction of

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

the pulmonary arteries, caused by an as yet uncharacterised familial coagulation disorder.
Conclusions: Perioperative stent therapy may be life-saving. It produces effective relief of stenoses, without the need for surgical reintervention in the majority of patients, and improves the clinical outcome of thsi subgroup of patients. Stent implantation across fresh surgical suture lines in the immediate post-operative period appears to be safe.

P504 Exaggerated exercise-induced pulmonary vasoconstriction in re-entry pulmonary edema-prone subjects and in offspring of preeclampsia

T. Stuber[1], C. Sartori[2], M. Schwab[2], S. Thalmann[2], J. Bloch[2], P.Y. Jayet[2], H. Spielvogel[3], C. Salinas[2], U. Scherrer[3], Y. Allemann[1].
[1]Department of Cardiology, University Hospital, Cardiology, Bern, Switzerland; [2]Internal Medicine, University Hospital, Lausanne, Switzerland; [3]Instituto Boliviano de Biologia de Altura, La Paz, Bolivia

Offspring of mothers suffering from preeclampsia and subjects with a history of reentry high-altitude pulmonary edema (re-entry HAPE) display sustained hypoxic pulmonary hypertension when living at high altitude and a predisposition to pulmonary edema. The underlying mechanisms are unknown. We hypothesized that the predisposition to pulmonary edema could be caused by capillary stress failure related to exaggerated pulmonary hypertension. We, therefore, estimated the pulmonary artery pressure response (Doppler echocardiography) to mild exercise in 18 re-entry HAPE-prone subjects, 12 offspring of preeclampsia and 29 controls, all born and living in La Paz, Bolivia (3600 m). As expected, mean±SD systolic right ventricular to right atrial pressure gradient at rest was higher in re-entry HAPE prone subjects and offspring of preeclampsia than in controls (37±7 and 32±8 vs. 25±7 mm Hg, $P<0.001$). Most importantly, the exercise-induced increase in systolic right ventricular to right atrial pressure gradient was 30 percent larger in the two groups of subjects at risk than in controls (21±8 and 21±10 vs. 14±7 mm Hg, P=0.02). These data provide the first evidence for a markedly exaggerated pulmonary vasoconstrictor response to exercise in high altitude dwellers known to have an augmented susceptibility to develop pulmonary edema. We speculate that this exaggerated response may predispose them to pulmonary edema by causing capillary stress failure.

P505 Characterisation of the vasodilatory action of 17 beta oestradiol in the human pulmonary circulation

A.M. Smith[1], R.K. Sandher[2], R.T. Bennett[3], T.H. Jones[4], R.D. Jones[4], M.E. Cowen[2], K.S. Channer[3]. *[1]Royal Hallamshire Hospital, Cardiology, Sheffield, United Kingdom; [2]University of Sheffield, Hormone and Vascular Biology group, Sheffield, United Kingdom; [3]Castle Hill Hospital, Cardiothoracic surgery, Hull, United Kingdom; [4]Barnsley District Hospital, Diabetes and Endocrinology, Barnsley, United Kingdom*

Purpose: This study was carried out to assess for the first time, the vasodilatory effect of 17β oestradiol in the human pulmonary circulation. The influence of gender upon the response to 17β oestradiol was studied in isolated human pulmonary arteries and in isolated perfused whole lungs.
Methods: Isolated human pulmonary arteries were studied by wire myography. Vessels were obtained from male (n=6, age 70±4 years) and female (n=5, age 61±4 years) patients. Vessels were preconstricted with U46619 (1μM) and endothelial integrity was tested with acetylcholine (1μM). Vessels were then washed before the addition of U46619 (1μM) prior to exposing them to either 17β oestradiol (1nM-100μm) or ethanol vehicle and the maximum vasodilatory response was recorded. Isolated lungs were studied in a ventilated and perfused model (methodology described in [Bennett et al, 2004]). Lung samples (n=6) were obtained from male(n=3 age 65±7 years) and female patients(n=3 age 68±3 years). They were exposed to potassium chloride (KCl) (100mM), prior to the addition of either 17β oestradiol (1nM-100μM) or ethanol vehicle and the maximum vasodilatory response was recorded.
Results: In the isolated human pulmonary arteries, 17β oestradiol caused significant vasodilatation (Table 1). Results from the isolated perfused human lung model showed greater responses to 17β oestradiol than the pulmonary arteries (Table 1). There was however no significant difference in the magnitude of the response to 17β oestradiol between the sexes.

Table 1

Experiment details	17β oestradiol				
	1mM	3mM	10mM	30mM	100mM
Isolated pulmonary artery	-2(±1.0)*	-2(±2.2)*	-4.0(±1.2)*	-8.0(±2.3)*	-23.3(±2.8)*
Isolated and perfused lung	-1.5(±5.2)	-11.1(±4.3)	-24.3(±7.5)*	-30.0 (±6.1)*	-69.2 (±3.5)*

% relaxation mean (SEM), *significant dilation compared to ethanol, $P<0.05$ via Wilcoxon signed rank test.

Conclusion: This is the first study to show the vasodilatory properties of 17β oestradiol in the human pulmonary circulation, with no significant differences between male and female vessels. This finding may therefore have therapeutic implications for patients with pulmonary vascular disease, for example pulmonary hypertension.

P506 Pregnancy and cardiac disease

G.F. Lopez Soutric, V. Crosa, S. Robert, H. Ruda Vega, J. Lerman, M. Vazquez Blanco. *Hospital de Clinicas, Cardiology, Buenos Aires, Argentina*

Background: pregnancy in patients with cardiac disease has been viewed with concern, due to an increase in fetal and maternal morbidity and mortality.
Objectives: to analyze the course of pregnancy, delivery and post partum, in patients with cardiac disease, compared with normal pregnant women, assisted in our institution between 1990 and 2006.
Material and Methods: Group I (GI):123 patients (141 pregnancies) with cardiac disease, 89 acquired, 52 congenital. Group II (GII): 40 pregnant women without structural heart disease. We assessed the course of pregnancy, delivery and post partum from maternal records, and gestational age (GA), weight (W) and Apgar score (AS) from neonatal records.
Results: There were no differences in age. Twenty five patients (17.6%) in GI had maternal cardiac complications and one died due to a non cardiac disease. There were no differences in the evolution between congenital or acquired heart diseases. Rates of caesarean section were greater in GI. Mean AS in GI was 8.1±1.25 (95% CI 7.8-8.4) and 8.7 (95% CI 8.5-8.9) in GII (p=0.04). Mean W in GI was 2.874 grams (95% CI 2.737-3.012) vs 3.371 (95% CI 3.238-3.504) in GII (p= 0.0001) and mean GA in GI was 36.3 weeks (95% CI 35.1-37.6) vs 39.3 (95% CI 38.9-39.7) in GII (p= 0.0001). In unvaried analysis the age, the existence of acquired disease and pulmonary hypertension were associated with maternal cardiac complications, but in multivariate analysis only pulmonary hypertension remained significant OR 2.81 (95% CI 1.06-7.45). The only variable associated with low newborn weight was the existence of pulmonary hypertension OR 2.96 (95% CI 1.29-6.81).
Conclusion: Pregnancy in patients with cardiac disease can be carried out with a low incidence of maternal complications. The newborns of patients with cardiac diseases, had a lower Apgar score, gestational age and weight compared with normal. The existence of pulmonary hypertension predicts a higher maternal and fetal risk.

PRIMARY PERCUTANEOUS CORONARY INTERVENTION

P507 Effect of thrombectomy in STEMI pts during primary PCI: acute clinical and angiographic results

G. Sardella[1], M. Mancone[2], A. Di Roma[1], R. Colantonio[1], G. Conti[1], L. Lucisano[1], A. Bisciglia[1], F. Rotolo[1], F. Fedele[1]. *[1]Policlinico Umberto I - Dept.of Cardiology-, Rome, Italy; [2]Policlinico Umberto I - Dept.of Cardiology-, Rome, Italy*

Background: In STEMI pts impairment of microcirculatory function is a negative independent predictor of myocardial function recovery. Compared with conventional stenting pretreatment with thrombectomy during primary PCI improves the parameters of myocardial tissue perfusion reducing the incidence of left ventricular remodeling at 6 months.In the present single-center, prospective randomized study we sought to evaluate the safety and efficacy of manual thrombectomy device in STEMI patients undergoing to primary angioplasty.
Methods: We randomized 125 pts (mean age 64.3±10.2 85 male) referred to our Hospital with a STEMI in order to undergo primary PCI (<9 hours from symptoms onset) with an occlusive thrombus at basal angio, to thromboaspiration with a manual device ((n=63) (E)) and standard PCI (n=62)(C). The primary end points of the study were the comparison of TIMI ≥ II, thrombus score (TS) ≤ 1 post thrombectomy, MBG ≥ 2 and ST-segment resolution (STr)≥ 70% post-stenting.
Results: No differences on baseline,clinical and angiographic preprocedural findings were observed between the two groups. Presence of an intracoronary thrombus at basal angiography was observed in all pts. (Pre-thrombectomy TS 3.57±0.66 (E) vs. 3.60±0.72 (C) p=ns). At baseline TIMI 0 flow was found in 81.1%(E) vs 82.3%(C), and TIMI 1 in 18.9%(E) vs 17.7%(C) (p=ns). After trombectomy, we observed a TIMI II flow in 38.6%(C) vs 19.6% (E) (p=0.054) and TIMI III was 30.7 (C) vs 72.5% (E) ($p<0.0001$). Patients treated with E had a highly significant reduction in the culprit artery thrombus burden (1.27±0.82 (E) vs 2.15±0.75 (C)) ($p<0.0001$). The patients enrolled in E group had a significantly higher incidence of TS 1 post thrombectomy (69.01% (E) vs 12.5% (C) ($p<0.001$); postprocedural MBG 3 was 70,3% (E) vs 28,7% (C) ($p<.01$) and 90' ST-segment resolution ws 80% (E) vs 37.5% (C) ($p<.01$).
Conclusions: Compared with conventional stenting, a pretreatment with thrombectomy during primary PCI, improves epicardial flow and microvascular function probably due to a major reduction of TS post thrombectomy.The assess of a best ST-segment resolution in the pts. treated with thromboaspiration could be probably associated with a better clinical outcome in these patients.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P508 A comparison of thrombus aspiration devices for the treatment of thrombus laden lesions in Acute Coronary Syndrome

G. Minocha[1], M.I.T.U. Minocha[2]. [1]*Metro Heart Institute, N Delhi, India;* [2]*N.Delhi, India*

Purpose: Percutaneous Coronary Interventions (PCI) in lesions with large thrombus load increases the procedural complications. Adjunctive Thrombus aspiration devices to protect the microcirculation have been developed.We compared 2 devices, Export Catheter (medtronic) (EC)and Diver C.E (ev3) (DC) in reducing Thrombus burden and improving coronary flow in Acute Coronary Syndrome (ACS) patients.
Methods: In this single centre randomised trial, 97 patients with ACS and angiographic thrombus were randomised to EC (n=50) or DC (n=47). Adjunctive dilatation and stenting were done to achieve good angiographic result.TIMI flow and thrombus Grading (TG) were assessed in all patients.
Results: Baseline Clinical and Angiographic characteristics were similar between the 2 groups. Presentation with Acute myocardial infarction was 36% in the EC group Vs. 34% in DC group (p = 0.991). LAD was the dominant culprit artery (50% Vs. 48%; p = 1.00). 2b/3a inhibitor use was comparable between the 2 groups. (70% vs. 72.3%; p = 0.976) Thrombus load was completely removed in 54% patients in the EC group vs. 55.3% in DC group (p = 0.941) following Thrombosuction alone. TIMI flow improved following Thrombosuction in 96% vs. 93.6% patients. (p = 0.671). Postsuction,there was significant improvement in TIMI flow (0.7±1.1 to 2.5±0.8; $p < 0.05$) in EC Group and DC group (0.8±1.0 to 2.6±0.7; $p < 0.05$). Postsuction TIMI flow was similar between the 2 groups (p = 0.3). There was a significant reduction in TG postsuction in EC (3.2±0.9 to 0.94±0.12; $p < 0.05$) and DC group (3.0±0.8 vs. 0.94±0.1; $p < 0.05$). Post suction TG was similar between the 2 groups (p = 0.9). Final TIMI Flow (2.92± 0.12 vs. 2.9±0.12; p 0.58) and final TG (0.09±0.52 vs. 0.09± 0.48; p = 0.9) were similar between the 2 groups. In subset with STEMI, ST resolution > 50%, was comparable in the 2 groups (80% vs 76.5; p = 0.6). There was no difference in slow flow or distal embolisation (20% vs. 19%; p = 0.88). There was no major procedural or in-hospital complication in either group.
Conclusion: Export & Diver Catheters are safe and comparably effective in improving coronary flow and reducing Thrombus burden in ACS. Myocardial reperfusion rates are similar in primary PCI.

P509 Short and long-term outcomes in reperfusion with aspiration or pulse infusion thrombolysis prior to direct PCI for AMI: RAPID trial

S. Oshima[1], T. Saito[2], H. Shimomura[3], Y. Shibata[4], N. Nakamura[5], K. Hirata[6], K. Ooshiro[7], O. Arasaki[8], H. Nakashima[9], I. Oomura[10]. [1]*Kumamoto Central Hospital, Cardiology Department, Kumamoto City, Japan;* [2]*Fukuoka City, Japan;* [3]*Kasuga City, Japan;* [4]*Miyazaki City, Japan;* [5]*Beppu City, Japan;* [6]*Okinawa City, Japan;* [7]*Urasoe City, Japan;* [8]*Tomishiro City, Japan;* [9]*Kagoshima City, Japan;* [10]*Touno City, Japan*

We have reported that pulse infusion thrombolysis(PIT) prior to percutaneous coronary intervention (PCI) may be an effective strategy for preventing no-reflow during reperfusion therapy for acute myocardial infarction (AMI), especially with large coronary thrombus. The RAPID trial was a prospective randomized trial at 10 institutions enrolling 105 patients with ST-segment elevation myocardial infarction. Patients were randomized to receive PCI after PIT with t-PA (PIT Group, n=56) or PCI after aspiration/distal protection (Suction Group, n=49). Clinical and angiographic outcomes of both groups were compared. Baseline clinical characteristics and infarct locations were balanced. TIMI 3 flow and Blush score 3, after PIT or aspiration, were obtained significantly earlier in the PIT Group than in the Suction Group (TIMI 3 flow: 60% vs 35%, $p<0.05$; Blush score 3: 46% vs 10%, p=0.003). The number of final TIMI 3 flow after PCI was not significantly different between the two groups (89.0% in PIT vs 92% in Suction); however, the percentage of patients having final blush score 3 was significantly higher in the PIT Group than in the Suction Group (80% vs 47%, $p<0.05$). The incidence of major adverse cardiac events (MACE:death, re-MI, re-PCI, CABG), bleeding complications and/or maximum CPK levels during admission were not different between the two groups. The incidence rates of MACE within 6months after PCI were significantly lower in the PIT Group than in the Suction Group (10.7% in PIT vs 26.6% in Suction, p=0.03), however, mean left ventricle ejection fractions(%) were not different between the two groups (59.1 in PIT vs 56.1 in Suction).
Conclusions: PIT or aspiration may both be effective strategies to restore the final epicardial coronary flow; however, PIT may be more effective to restore myocardial microperfusion and may improve long-term outcomes in AMI patients.

P510 Bleeding risk related to the use of gp IIb/IIIa blockers in early pci post fibrinolysis. secondary analysis of the optimal study

L. Belle[1], C. Loubeyre[2], D. Savary[1], M. Elbaz[3], S. Charpentier[3], Y. Cottin[4], L. Soulat[5], V. Bongard[5], P.G. Steg[6], J. Puel[6] on behalf of OPTIMAL Study Group. [1]*Annecy Hospital, Annecy, France;* [2]*Saint Laurent Polyclinic, Rennes, France;* [3]*University Hospital, Toulouse, France;* [4]*University Hospital, Dijon, France;* [5]*Chateauroux Hospital, Chateauroux, France;* [6]*Bichat Hospital, Paris, France*

Background: Rescue or urgent coronary angioplasty is becoming standard immediately after fibrinolysis in myocardial infarction with ST-segment elevation (STEMI). In this context, GP IIb/IIIa blockers could be associated with an increased risk of hemorrhage.
Method: The study is a prospective cohort conducted between Nov 2004 and Nov 2005. Patients with STEMI, treated by pre-hospital fibrinolysis (PHF) and systematic coronary angiography performed within 6 hours were included. Immediate angioplasty and use of GP IIb/IIIa blockers were left to the discretion of the physicians. The use of platelet inhibitors and anticoagulants were recommended as suggested by international guidelines. The main criterion for this analysis was the onset of a major bleeding event (requiring surgery and/or transfusion) and cerebral complication (including ischemic stroke and intracranial haemmorrhage), in the first 7 days of the hospital stay for the patient treated with or without GP IIb/IIIa blockers.
Results: A total of 930 patients (mean age: 60.4 years; male sex: 81.9%), were included. Eightynine patients (9.5%) received a GP IIb/IIIa blockers. The fibrinolytic used was TNK-tPA in 96.6% of patients. 58% had a TIMI 3 flow on the initial coronarography and immediate PCI was performed in 86.2%. The median delay between PHF and angiography was 120 mn. The patients treated with GP IIbIIIa blockers were more often male (17.1% vs 7.9%, p=0.003), treated more by radial approach (48.2% vs 38.7%, p=0.038), and underwent coronary angioplasty more frequently (92.8% v 85.3%, p=0.015). The frequency of major bleeding complications (2% vs 2.19%, p=0.90) and cerebral complication (0.9% v 2.7%, p=0.48) did not differ significantly between patients treated with or without GP IIb/IIIa blockers, respectively.
Conclusion: A selected use of GPIIb/IIIa blockers in early PCI immediately after pre-hospital fibrinolysis with TNK-tPA was not associated with an excess of major bleeding events. This favorable preliminary experience in early PCI has to be confirmed with a larger cohort.

P511 No-reflow phenomenon after acute myocardial infarction is associated with reduced clot permeability and susceptibility to lysis

J. Zalewski[1], A. Undas[2], J. Goldewski[2], E. Stepien[2], K. Zmudka[1]. [1]*John Paul II Hospital, Dept. of Hemodynamics And Angiocardiography, Krakow, Poland;* [2]*Jagiellonian University, Krakow, Poland*

Purpose: Since it is not known whether fibrin clot features are related to the occurrence of the no-reflow phenomenon, we have assessed fibrin clot properties in patients with impaired epicardial and microvascular reperfusion after primary coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI).
Methods: Epicardial blood flow was assessed by TIMI scale and corrected TIMI frame count (cTFC) and perfusion by TIMI Myocardial Perfusion Grade (TMPG) after PCI. After 6-14 (mean 10,2±2,5) months from PCI ex vivo clot permeability (Ks, [10^{-9} cm^2]) and susceptibility to lysis in assays using exogenous thrombin (t-50%, [min]) and without thrombin (t-TF, [min]) were evaluated in 30 no-reflow phenomenon patients (TIMI<3 after PCI in STEMI) and in 31 control patients with TIMI-3, matched for age, sex, risk factors and concomitant treatment. Myocardial injury was expressed as a maximal level of CK-MB release (CK-MBmax, [U/l]) during reperfusion.
Results: Patients with TIMI<3 had lower Ks by 18% (8,36±0,67 vs. 9,9±0,66; p<0,0001) and prolonged fibrinolysis by 33% for t-50% (10,28±1,00 vs. 7,74±1,09; p<0,0001) and by 45% for t-TF (88,3±13,7 vs. 60,1±14,9; p<0,0001) compared with those with TIMI-3. Ks was negatively correlated with fibrinogen level, cTFC and CK-MBmax (r=-0,6; r=-0,56; r=-0,54 respectively, p<0,001 for all). t-50% and t-TF were correlated with cTFC (r=0,49 and r=0,54 respectively, p<0,001 for both) and CK-MBmax (r=0,51 and r=0,53 respectively, p<0,001 for both). Ks increased in a stepwise fashion with TIMI flow (p<0,0001) and TMPG (p<0,0001). Both fibrinolysis times decreased in a stepwise fashion with TIMI flow (p<0,0001 for both) and TMPG (p<0,01 for both). Multiple regression models showed that Ks and fibrinogen level were independent predictors of cTFC value (coefficient for Ks -11,9; 95% CI -21,9 to -2,0; p<0,05, coefficient for fibrinogen -5,9; 95% CI -11,0 to -0,6; p<0,05), TIMI<3 flow (OR for Ks 13,2; 95% CI 1,3-88,1; p<0,05, OR for fibrinogen 4,3; 95% CI 1,3-17,4; p<0,05) and TMPG-0/1 (OR for Ks 4,9; 95% CI 0,9-16,2; p<0,05, OR for fibrinogen 1,9; 95% CI 0,8-4,0; p<0,05).
Conclusions: Fibrin clots in patients with impaired epicardial and tissue perfusion are composed more compact fibrin network, relatively resistant to lysis. This suggests that unfavourably altered clot properties may characterise patients with the no-reflow phenomenon.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

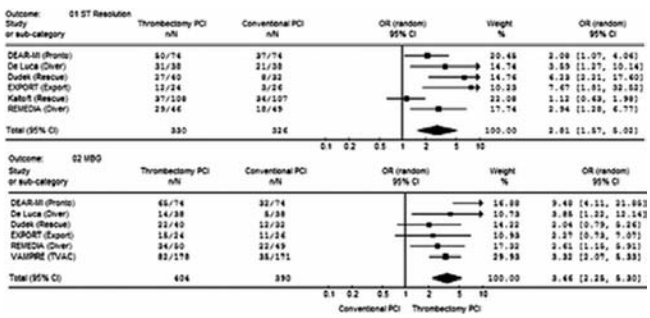
P512 Impact of simple manual aspiration thrombectomy on myocardial perfusion in patients with ST elevation myocardial infarction: a meta-analysis of seven randomized trials

A. Sanchez Recalde, R. Moreno, F. Rivero, R. Martin Reyes, M.A. Navas, C. Martinez Peredo, G. Galeote, L. Calvo, J.L. Lopez Sendon. *Hospital Universitario La Paz, Hemodinamica y Cardiologia Intervencionista, Madrid, Spain*

Controversy still remains about whether thrombectomy devices might improve myocardial reperfusion by reducing coronary thrombus burden and distal embolization in patients underwent primary percutaneous coronary intervention (PCI). Manual aspiration thrombectomy devices are simple catheters with a central lumen connected to a syringe for manual aspiration. Nowadays, the use of these devices has increased mainly due to their simplicity, but the results in primary PCI are controversial.

Methods: We performed a meta-analysis from 7 randomized trials that evaluated the efficacy of manual thrombus aspiration devices (Pronto, Export, Rescue, Diver and Vacuum Aspiration catheters) in primary PCI: REMEDIA (n=99), DEAR-MI (n=148), EXPORT (n=50), De Luca et al (n=76), Dudek et al (n=72), Kaltoft et al (n=215) and VAMPIRE (n=355). The overall number of patients included was 1,016 (514 thrombectomy and 501 conventional PCI). Odds Ratio was used as the measure of effect for each dichotomous outcome: ST-segment resolution (> 70%) from data of 6 studies and myocardial blush grade (MBG) 3 (except in REMEDIA, MBG ≥ 2) from 6 studies. Random effect model was used accordingly to the Q-test for heterogeneity: Chi2: 13.5; df=5 [p=0.02] for ST resolution; and Chi2:7.8; df=5 [0.15] for MBG.

Results: There were benefits in favour of thrombectomy during PCI in terms of postprocedural myocardial perfusion: ST-segment resolution (>70%): 56.4% vs 37.1%, OR 2.81 [95% CI 1.57-5.02], p= 0.0005; and optimal MBG: 57.4% vs 30%, OR 3.46 [95% CI 2.25-5.30], p<0.00001.



Conclusion: Simple manual aspiration thrombectomy significantly improves myocardial perfusion during PCI in acute myocardial infarction.

P513 Adverse outcomes in fibrinolytic-based facilitated PCI: insights from the ASSENT-4 PCI electrocardiographic substudy

M.A. McDonald[1], Y. Fu[1], U. Zeymer[2], G.S. Wagner[3], S.G. Goodman[4], A.M. Ross[5], C.B. Granger[1], F. Van De Werf[6], P.W. Armstrong[5] on behalf of ASSENT-4 PCI Investigators. *[1]University of Alberta, Department of Medicine, Edmonton, Canada; [2]Medizinische Klinik II, Kassel, Germany; [3]Duke Clinical Research Institute, Durham, United States of America; [4]University of Toronto, Cardiology, Toronto, Canada; [5]George Washington University Medical Center, Washington, United States of America; [6]University Hospital Gasthuisberg, Leuven, Belgium*

Purpose: In ASSENT-4 PCI, patients undergoing tenecteplase (TNK)-facilitated PCI unexpectedly had more frequent adverse events than primary PCI patients. We undertook a prospective ECG analysis which may provide further insight into this outcome.

Methods: 537 patients in the facilitated PCI and 527 patients in the primary PCI group comprised the study. The association between time from symptom onset to treatment, baseline Q waves (Qs), and subsequent ST resolution was examined as well as their impact on clinical events.

Results: Among TNK/PCI-treated pts who presented > 3 hrs, a significantly higher percent of complete ST resolution (≥70% ST resolution) was seen at 60 and 180 minutes amongst those without a baseline Q, in addition to a lower rate of 90-day mortality (2.5% vs. 10.4%, p=0.047 adjusted). For those TNK/PCI patients presenting ≤3 hours without baseline Qs, there was also more frequent complete 180 min ST resolution as compared to those with Q waves. In TNK/PCI patients with baseline Qs presenting ≤3 hrs, there was a higher percent of complete ST resolution at 60 and 180 min as compared to those presenting >3 hours (25.6% vs. 15.6%, p=0.035; 49.4% vs. 37%, p= 0.037, respectively). In contrast, these temporal and ECG patterns were not evident in the PCI group.

Conclusion: Outcomes in TNK-facilitated PCI depend on the ability to achieve complete ST resolution at 60 and 180 minutes. Risks of TNK-facilitated PCI appear to outweigh potential benefits in patients presenting >3 hours from symptom onset with Q waves on the baseline ECG thereby providing novel opportunities for treatment of such patients.

	TNK-Facilitated PCI			Primary PCI		
	Q Waves	No Q waves	P	Q Waves	No Q waves	P
≥3hrs n =	135	79		122	73	
≥70% ST resl. 60min	15.6	34.2	0.002	14.8	15.1	1.00
≥70% ST resl. 180min	37.0	51.9	0.045	40.2	52.1	0.136
90-day death %	10.4	2.5	0.056	3.3	0.0	0.299
<3hrs n =	172	151		167	165	
≥70% ST resl. 60min	25.6	24.5	0.898	13.2	18.2	0.229
≥70% ST resl. 180min	49.4	62.9	0.018	50.9	57.6	0.228
90-day death %	4.7	2.0	0.228	3.0	2.4	0.750

PRIMARY AND FACILITATED PERCUTANEOUS CORONARY INTERVENTION – VARIOUS ASPECTS

P514 A new model for predicting mortality in acute ST elevation myocardial infarction treated with primary PCI: results from the APEX AMI trial

A.L. Stebbins[1], K. Lee[1], P.W. Armstrong[2], C. Hamm[3], F. Van De Werf[4], S. James[5], T. Toftegaard Nielsen[6], R. Seabra-Gomes[7], H.D. White[8], C.B. Granger[2] on behalf of APEX AMI Investigators. *[1]Duke Clinical Research Institute, Durham, United States of America; [2]University of Alberta, Edmonton, Canada; [3]Kerckhoff Heart Centre, Bad Nauheim, Germany; [4]University Hospital Gathuisberg, Leuven, Belgium; [5]Uppsala University Hospital, Uppsala, Sweden; [6]Skejby University Hospital, Aarhus, Denmark; [7]Santa Cruz Hospital, Carnaxide, Portugal; [8]Auckland City Hospital, Auckland, New Zealand*

Background: Acute ST elevation myocardial infarction (STEMI) is a major cause of death, despite improvements with contemporary treatment afforded by primary percutaneous coronary intervention (PCI) and other therapies.

Methods: We evaluated data from the 5,745 patients in the APEX-AMI trial with acute STEMI (including anterior and high-risk inferior locations) treated with primary PCI, comprising the largest clinical trial ever conducted in this population. A multivariable Cox model was developed using baseline variables. These potential covariates were evaluated for the prediction of all-cause 90-day mortality (n=5,606).

Results: The final model included 7 variables, 6 of which were previously found to be predictors of mortality in other acute MI populations. The variables with greatest predictive value for higher risk were older age, lower systolic blood pressure, higher heart rate, Killip Class 3 or 4, higher total ST deviation at baseline, history of diabetes and anterior MI location. The overall 90-day mortality rate was 4.72%.

Predictor	Hazard Ratio	95% CI	Adjusted chi-square
Age in 10 years	2.14	(1.90, 2.41)	157.8
Systolic BP <135 mmHg	0.77	(0.72, 0.82)	58.3
Heart rate >70, <110 bpm	1.42	(1.29, 1.57)	49.5
Heart rate ≤ 70 bpm	1.04	(0.83, 1.30)	0.09
Killip Class 3 or 4	3.63	(2.50, 5.27)	46.0
Total ST deviation at baseline	1.29	(1.15, 1.45)	18.8
Diabetes	1.60	(1.20, 2.12)	10.4
Anterior MI	1.47	(1.12, 1.94)	7.5

The c-index was robust at 0.814, and internal validation with bootstrapping confirmed minimal over-optimism (c-index 0.809).

Conclusions: In a large contemporary population of acute ST elevation MI treated with primary PCI, simple variables at the time of presentation accurately stratify risk. These variables are remarkably similar to those previously known to be predictive in STEMI treated with fibrinolytic therapy. Hence this new model should be helpful for both clinical and quality improvement/research purposes.

P515 Prevalence, predictors, time course and long-term clinical implications of left ventricular functional recovery after mechanical reperfusion for acute myocardial infarction

G. Parodi, G. Memisha, N. Carrabba, U. Signorini, R. Valenti, D. Antoniucci. *Careggi Hospital, Department of Cardiology, Florence, Italy*

Objectives: We prospectively evaluated the prevalence, predictors, time course and prognostic impact of LV functional recovery after acute myocardial infarction (AMI) successfully treated with primary percutaneous coronary intervention (PCI).

Background: The prevalence, predictors, time course and long-term clinical implications of LV functional recovery after primary PCI are still to be fully elucidated.

Methods: In 228 consecutive patients with AMI and LV dysfunction treated with primary PCI, serial echocardiographic exams within 24 hours (T1), at 1 (T2) and 6 months (T3) after AMI were performed. Long-term (60±15 months) clinical follow-up data were collected.

Results: Overall, 133 (58%) patients showed significant LV functional recovery (>10% ejection fraction [EF] increase as compared to T1 or EF > or = than 50%) at T3. Early (from T1 to T2) and late (from T2 to T3) significant functional recovery

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

patterns were detected in 102 (44%) and 31 (14%) patients, respectively. Independent predictors of LV functional recovery were small enzymatic infarct size (p=0.0001), short time of ischemia (p=0.022), limited baseline wall motion abnormalities (0.007), and female gender (0.019). Six-month LV remodeling (>20% end-diastolic volume increase as compared to T1) rates were 36% and 64% in patients with and without LV functional recovery (p=0.001). Cardiac death rate was significantly lower among patients with than those without LV functional recovery (8% versus 18%, respectively; p=0.024). Time course of LV functional recovery during 6 months did not significantly affect long-term survival.
Conclusions: After successful mechanical reperfusion of AMI nearly half of patients show poor LV functional recovery. The presence of significant LV functional recovery 6 months following reperfused AMI, but not the specific time course of recovery, is clearly associated with a better long-term clinical outcome. Simple baseline variables are able to predict the improvement of cardiac function after reperfused AMI.

P516 Major determinants of non invasive coronary flow reserve impairment after acute myocardial infarction treated with primary coronary angioplasty

R. Montisci[1], M. Ruscazio[1], F. Tona[2], C. Sarais[2], S. Pontarollo[2], F. Corbetti[2], L. Cacciavillani[2], A. Ramondo[2], L. Meloni[1], S. Iliceto[2].
[1]University of Cagliari, Clinical Cardiology, Cagliari, Italy; [2]University of Padua, Clinical Cardiology, Padua, Italy

Purpose: Previous experimental data have demonstrated that prolonged ischemia impaires myocardial perfusion as a function of the interval after reperfusion and subsequent extent of myocardial necrosis, with a reduction of coronary flow reserve (CFR). Aim of this study was to evaluate determinants of CFR in patients with reperfused anterior myocardial infarction.
Methods: Forty consecutive patients (mean age 60±12) with anterior acute myocardial infarction underwent non invasive CFR assessment in the left anterior descending coronary artery with adenosine transthoracic echocardiography and GE-MRI 8.5±3.6 days after primary coronary angioplasty. A 17-segment model of the left ventricle was used to analyze both wall motion abnormalities and trasmural extent of necrosis at GE-MRI as assessed by hyperenhancement (HE) extent. At GE-MRI we evaluated also hypoenhancement, inside of HE zone, to detect microvascular obstruction. A necrosis score was derived for each segment in the predicted risk area (myocardial segments supplied by left anterior descending coronary artery) considering HE thickness extent (1:no HE;2:HE less than 25%;3: HE more than 25% and less than 50%;4: HE more than 50% and less than 75%;5: HE more than 75%). In each patient a wall motion score index (WMSI), a necrosis score index (NSI) and a trasmurality score index (TSI) were calculated in the risk area.
Results: At univariate analysis CFR was related to NSI (p=0.003), TSI (p=0.001), CPK peak value (p=0.002), Troponin I peak (r=-0.330,P=003) and heart rate (r=-0.248,P=0.03) At stepwise logistic regression analysis TSI (β -0.33, p=0.0002) was the only independent predictor of reduced CFR. We found no correlation between CFR and precoronary time, diabetes or hypercholesterolemia.
Conclusions: The presence of trasmural necrosis, and its severity independently contribute to reduce non invasive CFR in patients after reperfused AMI.

P517 Relation of admission hematological indices with microvascular reperfusion abnormalities after primary angioplasty in patients with STEMI

O. Maden, F. Kacmaz, M.T. Selcuk, H. Selcuk, T. Aksu, O. Alyan, F. Metin, O. Tufekcioglu, Y. Balbay, E. Ilkay. *Turkiye Yuksek Ihtisas Hospital, cardiology, Ankara, Turkey*

Background: Mean platelet volume(MPV) is related to platelet activity and shown to be predictive of unfavourable outcome among survivors of STEMI patients. Reports regarding relation of MPV with reperfusıon abnormalities is few.
Objectives: we aimed to evaluate the value of MPV and white blood cell count(WBC-C) for prediction of impaired microvascular reperfusion in patients with acute STEMI treated with primary angıoplasty.
Methods: Blood samples for MPV and WBC measurement were obtained on admission in 325 consecutive patients presenting with STEMI who underwent succesfull primary angioplasty. 12 lead ECG on admission and 90th minute after angioplasty were recorded for ST resolution(STR) measurement. According to STR ratio patients were divided into impaired reperfusion and normal perfusion groups and statistical analysis were performed between the two.
Results: When we compared reperfusion and impaired reperfusion groups the patients in impaired reperfusion group were older, had more often anterior MI, longer pain to balloon time. The patients in impaired reperfusion group were more likely to have LAD as infarct related artery and multivessel disease. They were less likely to have a patent IRA on admission. According to STR threshold of 70%, 39.6% of patients found to have impaired reperfusion despite achievement of TIMI 3 flow in infarct related artery(IRA). In impaired reperfusion group admission MPV and WBC-C were higher compared to reperfusion group. Best cut off value of MPVs for predicting impaired reperfusion was determined to be 9.05 Fl with a sensitivity of 73.3% and specifity of 78.3%.
Conclusions: Elevated MPV and WBC-C on admission is strong, independent predictor of impaired microvascular reperfusion in STEMI patients treated with primary PCI. Admission MPV and WBC may be used in estimation of reperfusion abnormality and need for adjunctive therapy to improve outcome in patients with STEMI undergoing primary angioplasty.

Table 1

	Reperfusion group	impaired reperfusion group	P value
Leucocyte count(/mm^3)	12.35±3.87	15.09±5.47	0.0001
Platelet count	282.4±74.8	277.97±99.1	0.656
MPV(fl)	8.62±0.94	9.79±1.3	0.0001
fibrinogen	3.09±1.15	3.24±1.14	0.0001

Comparison of admission hematological parameters between reperfusion and impaired reperfusion groups.

P518 Late percutaneous coronary intervention following Acute Myocardial Infarction: a meta-analysis of the effects on cardiac function and remodeling

A. Abbate[1], G.G.L. Biondi-Zoccai[2], D.L. Appleton[1], M.J. Lipinski[3], V. Ramachandran[2], A. Varma[2], P. Agostoni[4], G.W. Vetrovec[3].
[1]Richmond, United States of America; [2]Turin, Italy; [3]Charlottesville, United States of America; [4]Anterp, Belgium

Background: We sought to perform a systematic review and meta-analysis of randomized controlled trials comparing percutaneous coronary intervention (PCI) with optimal medical therapy in patients with infarct-related artery (IRA) occlusion more than 12 hours after onset of acute myocardial infarction (AMI), focusing on on left ventricular function and remodeling.
Methods and Results: PubMed CENTRAL, and mRCT were searched for eligible studies. Studies were included in the analysis if they were randomized controlled trials comparing conservative medical management with PCI performed at least 12 hours after the onset of symptoms of AMI, and data on left ventricular ejection fraction (LVEF) at baseline and follow-up were available. Studies were excluded if randomization occurred less than 12 hours after symptom onset, or if patients were hemodynamically unstable. Changes in LVEF was the primary outcome of interest, with changes in left ventricular end-diastolic volume index (LVEDVI) and end-systolic volume index (LVESVI) analyzed as secondary endpoints. We retrieved 5 studies in which baseline and follow up LVEF data were available enrolling a total of 648 patients: 342 patients randomized to PCI and 306 to medical treatment. There was a statistically significant difference in LVEF changes over time favoring PCI (+3.1%, 95% CI +1.0 to +5.2, P = 0.0004). In addition, there were statistically significant differences in changes in both LVEDVI (-5.1 ml in favor of PCI, 95% CI of -9.4 to -0.8, P = 0.02) and LVESVI (-5.3 ml in favor in PCI, 95% CI of -8.3 to -2.4, P=0.0005).
Conclusions: This meta-analysis suggests that late revascularization of an occluded IRA may improve left ventricular systolic function and remodeling, supporting the "open artery hypothesis". The reason why these changes have not resulted in clinical benefits in large clinical trials is object of debate.

P519 Percutaneous coronary intervention after early prehospital thrombolysis: reasonable, useless or dangerous?

H.R. Arntz[1], D. Mueller[1], H. Genzwuerker[2], L. Nibbe[3], B. Dirks[4], K. Ellinger[5], U. Zeymer[6]. *[1]Charite, Campus Benjamin Franklin, Cardiology Department, Berlin, Germany; [2]Klinikum Mannheim, Anaesthesiology, Mannheim, Germany; [3]Charite, Campus Rudolph Virchow, Nephrology, Berlin, Germany; [4]Universitaetsklinikum Ulm, Anaesthesiology, Ulm, Germany; [5]Klinikum Ravensburg, Anaesthesiology, Ravensburg, Germany; [6]Klinikum Ludwigshafen, Cardiology, Ludwigshafen, Germany*

Background: According to recent reports, PCI alone is superior to the combination of PCI following shortly after thrombolysis (TL). It is unclear whether these results are also true for pts with very early initiation of TL.
Methods: We analysed data from the prospective nationwide PREMIR registry on prehospital treatment of STEMI pts in the physician manned EMS in Germany.
Results: A total of 2187 pts were included into the study of whom 984 were treated with primary PCI (PPCI), 502 received prehospital thrombolysis (PHL) and 434 had no reperfusion Tx. Of the PHL pts 216 (43%) were treated with PHL alone (PHL-), 286 (57%) had additional PCI (PHL+) performed in 64% within 2 hrs,in 15% within 2 to 6 hrs and in 21% >6 hrs after hospital admission. No differences between the PHL+ and PHL- groups existed regarding sex (77% males), history of STEMI (16%), PCI (8%), CABG (3%), hypertension (57%), and diabetes (18%). PHL+ pts had a shorter mean symptom duration to start of PHL (91 Min) and were younger (mean 62 years) compared to PHL- pts (106 Min and 64 years respectively, p<0.01). Frequency of anterior infarction was slightly higher in PHL+ (45%) compared to PHL- pts (42%, p=ns). Total mortality to discharge was 6.9% for all pts, 4.3% for pts treated by PPCI and 5.8% for pts treated by PHL (difference between PHL and PPCI=ns) but was 14.5% for pts without reperfusion Tx (p<0.001 compared to the active treatment groups). Outcome for the PHL+ and the PHL- groups was similar with respect to mortality, cardiogenic shock, heart failure, and stroke (5.6%, 11.7%, 8.5%, and 0.7% for PHL+ pts vs 6.1%, 7.5%, 11.7%, and 2.8% for PHL- pts, p=ns). Re-infarction, however, was more frequent in PCI+ pts (7.1%) vs 2.8% in PCI- pts, p<0.04). With respect to time delay to PCI there were less major adverse cardiac events in pts with a delay <2 hrs compared

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

to those with a longer delay (MACE rate 28% vs 46%, p=0.02), which may in part caused by selection bias.
Conclusion: As shown in randomised trials, TL initiated early (within 2-3hrs after symptom onset) may be an adaequate stand-alone reperfusion strategy for STEMI and - in contrast recent study results- may be also safely combined with early PCI. It must, however, be defined in future studies which pts may profit from the combination of early TL rapidly followed by PCI.

P520 Can rescue angioplasty following failed fibrinolysis achieve the same clinical benefit as primary angioplasty? A matched control comparison

R. Kiamco, M. Masotti, V. Delgado, S. Romani, R. Ruiz-Salmeron, C. Fernandez-Gomez, H. Salazar, R. Mora, A. Betriu. *Thorax Institute - Hospital Clinic, Cardiology, Barcelona, Spain*

Background: Primary percutaneous intervention (PCI) has been shown to be superior to fibrinolysis (lysis), as it further decreases mortality and non-fatal reinfarction (re-MI). Comparatively, the role of rescue PCI following failed lysis remains to be fully clarified.
Aims: To assess whether a policy of routine stand-by rescue PCI yields clinical outcomes comparable to those achieved with primary PCI. The primary end-point of the analysis was the 6-month rate of cardiac death and reMI. Secondary endpoints were left ventricular function and ischemic driven revascularization at 6 months.
Methods: The study population consisted of 132 Killip class I-III patients that underwent early (within 12 hours of MI) rescue PCI between January 2002 and June 2005. Matched controls were 200 out of 311 fibrinolytic eligible patients managed with primary PCI within the same time frame. Matching included age, admission Killip class, blood pressure and heart rate, previous MI, and anterior MI location.
Results: Time from symptom onset to balloon inflation was longer in rescue PCI than in primary PCI patients (7.7 versus 5.8 hours; $p<0.001$). Successful reperfusion (TIMI 3 grade flow) was achieved in 82% of patients treated with rescue PCI and 90% of those undergoing primary PCI (p=0.047). Outcomes at 6 months were as follows: cardiac mortality 2.3% versus 2.5% and reMI 5.3% versus 4.0% (rescue versus primary PCI, respectively). The rates of stroke (0.8% versus 1.0%), heart failure (0.8% versus 0%), and repeat revascularization (5.3% versus 4.0%), were also similar in the two treatment groups.
Conclusions: Timely rescue PCI might achieve clinical outcomes comparable to those of primary PCI. Whether the results of this study might apply to patients treated later in the course of MI requires further investigation.

P521 Direct stenting and final TIMI-3 flow are independent predictors of survival after primary PCI

P. Garot[1], T. Lefevre[2], Y. Louvard[3], C. Pouges[4], J.Y. Le Tarnec[5], A. Margenet[6], T. Unterseeh[3], J.C. Robart[5], K. Tazarourte[4], P. Dumas[2]. *[1]ICPS, Quincy, France; [2]Icps, Cardiologie Interventionnelle,Angio/Icps, Massy, France; [3]ICPS, Massy, France; [4]SAMU 91, Corbeil-Essonnes, France; [5]SAMU 77, Melun, France; [6]SAMU 94, Creteil, France*

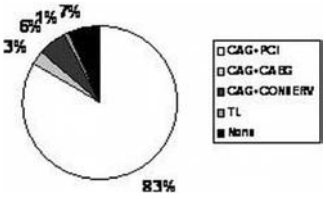
Background: In acute ST elevation myocardial infarction (STEMI), direct stenting (DS) has been shown to improve myocardial tissue reperfusion by reducing the incidence and magnitude of post-ischemic myocardial injury.
Objectives: Between 1995 and 2006, all patients with STEMI $<$ 12 hours were directly admitted to the cath-lab of our institution to undergo immediate PCI and were included in a prospective registry. In 1998, we provided data from a randomised trial in this setting showing the benefit of DS compared to predilatation and stent in improving ST-segment resolution on ECG. Since 1998, DS has become a routine approach in STEMI. The objective of this study was to determine the predictors of in-hospital death in STEMI patients and to assess the role of direct stenting.
Methods: Univariate an multivariate analysis including all clinical, angiographic and procedural data were performed in the first 2600 STEMI patients included in the registry.
Results: The mean age was 62$\pm$14 and 78% were males. Infarct location was anterior in 45% and shock was present on admission in 11% of the pts. The mean time elapsed between chest pain onset and admission was 295$\pm$251 minutes and 25% of the pts were treated by prehospital lysis. Direct stenting wa used in 42% of cases. The results of univariate and multivariate analysis (all with p value $<$ 0.0001), are summarized in the table.
Conclusion: In unselected STEMI patients treated with primary PCI, older age, resuscitated cardiac arrest and Killip class 4 are independant predictor of death, while direct stenting and final TIMI-3 flow are the only independent predictors of in-hospital survival.

Survival	Death	P value	Variable	OR [95%CI]
61%	68%	$<$0.0001	Age	1.03 [1.01-1.05]
2%	18%	$<$0.0001	Resuscitated CA	2.09 [1.11-3.94]
6%	63%	$<$0.0001	Killip 4	18.2 [11.3-29.3]
44%	53%	$<$0.05	Anterior MI	–
23%	11%	$<$0.0005	Prehospital lysis	–
24%	13%	$<$0.005	Pre-PCI TIMI-3	–
48%	30%	$<$0.0005	Direct stenting	0.58 [0.37-0.91]
91%	69%	$<$0.0001	Post-PCI TIMI-3	0.48 [0.27-0.85]

P522 Incidence, treatment strategies and outcomes of acute myocardial infarction in a central European country, fully covered by primary angioplasty services

P. Widimsky[1], M. Zelizko[2], P. Jansky[3], F. Tousek[4], F. Holm[5], M. Aschermann[6] on behalf of Czech Society of Cardiology. *[1]3rd Faculty of Medicine, Charles University, Cardiocenter, Prague, Czech Republic; [2]IKEM, Prague, Czech Republic; [3]2nd Faculty of Medicine, Charles University, Prague, Czech Republic; [4]Regional Hospital, Cardiocenter, Ceske Budejovice, Czech Republic; [5]Regional Hospital, Cardiocenter, Liberec, Czech Republic; [6]1st Faculty of Medicine, Charles University, Cardiology, Prague, Czech Republic*

Background: PCI is the most effective treatment of acute myocardial infarction (AMI) and is recommended by guidelines for AMI with ST elevations (STEMI) and with ST depressions (STDMI). The aim of this registry was to analyze the incidence, treatment strategies and outcomes of AMI and assess guidelines implementation in practice.
Methods: All non-PCI hospitals (n = 15) in two Czech rural counties (population 1,053 million) and all PCI-hospitals (n = 21) in the whole country (population 10,3 million) participated. Admissions (n = 1921) to internal or cardiology departments during November 2005 were screened and 922 AMI confirmed. Admission diagnosis was STEMI (n=467), non-STEMI (n=302) and other (n=153). Discharge diagnosis was Q-wave AMI in 423 and non-Q-wave AMI in 499 patients.
Results: The calculated annual AMI incidence in the Czech population was 1960 cases per million inhabitants, for STEMI the annual incidence was 661 per million. The overall in-hospital mortality of all confirmed AMI was 6,9%. Among AMI subgroups mortality was 8,6% with ST elevations, 5,9% with ST depressions, 10,0% with Q-wave development and 4.4% without Q wave development. Reperfusion strategy was used in 93% of all STEMI patients. (For comparison: a Czech survey held in 1996 revealed 44% use of reperfusion therapy in this setting.) Among 430 pts, who underwent emergent CAG for STEMI, primary PCI was performed in 90,2%, CABG in 3,3%, and conservative therapy (due either too diffuse or too mild coronary disease) in 6,5%.



Reperfusion strategies for STEMI

Conclusions: The incidence of hospital admissions for confirmed AMI is nearly 2000 cases per million per year. Nationwide application of primary PCI strategy for STEMI in a network of PCI and non-PCI hospitals is feasible and increases the overall use of reperfusion therapy to 93% of STEMI patients.

P523 Impact of TIMI 3 patency before percutaneous coronary intervention for ST elevation myocardial infarction on mortality. Results from the ASSENT-4 PCI trial

U. Zeymer[1], K. Huber[2], A. Ross[3], P. Armstrong[4], C. Granger[5], P. Goldstein[6], F. Van De Werf[7] on behalf of the ASSENT- PCI Investigators. *[1]Herzzentrum Klinikum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany; [2]Vienna, Austria; [3]Washington, United States of America; [4]Edmonton, Canada; [5]Durham, United States of America; [6]Lille, France; [7]Leuven, Belgium*

Background: Early restoration of coronary flow in the infarct related artery is associated with an improved outcome in patients with STEMI. Previous studies demonstrate lower mortality in patients with TIMI 3 flow before primary PCI. Most likely these patients had spontaneous recanalization of the infarct vessel and might constitute a low risk subgroup. Purpose of the present analysis was to investigate whether TIMI 3 flow achieved by fibrinolysis before PCI is associated with comparable clinical outcomes to that occurring spontaneously.
Methods: Patients with STEMI $<$ 6 h enrolled in the ASSENT-4 PCI study were randomized to facilitated PCI with Tenecteplase or primary PCI. In the current analysis patients were classified according to TIMI flow of the infarct vessel before PCI into three groups: TIMI 0/1, TIMI 2, and TIMI 3, respectively. The TIMI flow after PCI as well as 90 day clinical events are given in the table.

Table 1. 90-day clinical events

	TIMI 0/1	TIMI 2	TIMI 3
TIMI 3 after PCI	84.5%	89.7%	95.1%
Death	6.1%	4.7%	4.0%
Cardiogenic shock	6.2%	5.5%	3.6%
Heart failure	11.2%	10.2%	9.7%

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

The rate of TIMI 3 flow before PCI was higher in the facilatewd PCI group than in the primary PCI group (43.5% versus 15.0%). The 90 day mortality in patients with TIMI 3 flow before PCI was identical in both groups (14/349, 4.0% versus 5/124, 4.0%).
Conclusion: In this post hoc analysis of the ASSENT-4 PCI trial TIMI 3 flow of the infarct related artery before PCI, occurring either spontaneously or achieved by fibrinolysis is associated with a similar favourable clinical outcome at 90 days.

P524 Safety and feasibility of immediately returning patients transferred for primary percutaneous coronary intervention in ST-elevation myocardial infarction

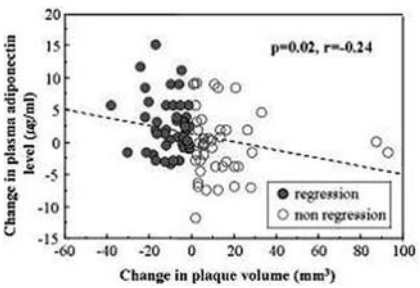
A. Matteau, S. Rinfret, M. Dorais, J. Lelorier, F. Reeves. *Centre Hospitalier Universite de Montreal, Montreal, Canada*

Purpose: Primary percutaneous coronary intervention (PPCI) has become the reperfusion strategy of choice for ST-elevation myocardial infarction (STEMI). However, bed shortages in most Canadian tertiary hospitals limit access to PPCI for patients presenting to community hospitals who need to be transferred for the procedure. Strategies to expand the availability of this effective treatment are required.
Methods: We describe our experience in a high-volume tertiary academic center, which offers PPCI 24 hours a day, 7 days a week. In a cohort of 246 patients who underwent PPCI after transfer from a community hospital, 166 (67%) were transferred back to their original hospitals immediately after PPCI. Criterias for immediate re-transfer were: 1)hemodynamically stable patient and 2)absence of immediate post-PCI complication. We reviewed the charts from all patients in their referring hospital to evaluate in-hospital outcomes.
Results: Patients were 59±12 years old and most (75%) were male. Risk factors included hypertension (35%) and diabetes (17%). Location of the STEMI was anterior in 39%, and 91% were Killip class 1. In this selected cohort, 75% of patients underwent a PPCI strategy and 25% received rescue intervention after failed fibrinolysis. The majority of patients (93%) underwent stent implantation. Radial access was used in 74% of patients. Femoral closure devices were used in 77% of the others. Adjunctive antiplatelet therapies included clopidogrel in 96% and glycoprotein IIbIIIa inhibitors in 58%. During transportation by ambulance to the referral hospital after PPCI, no death, significant arrhythmia or bleeding occurred. In-hospital outcomes were favourable, with a low incidence of death (2.4%), re-infarction (3.6%) and stroke (1.2%). TIMI major bleeding occurred in 1.8% (catheter-related in 0.6%). Median length of stay was 5 days.
Conclusion: In this carefully selected population of stable STEMI patients, immediate re-transfer after PPCI to the referring hospital is feasible and associated with a low risk of major clinical adverse events. In case of bed shortages, this strategy can be safely used to increase PPCI availability to patients presenting with STEMI in community hospitals.

P526 Coronary plaque regression is closely related to the decrease of necrotic-core with increase of plasma adiponectin level: 6-month binary studies with virtual histology intravascular ultrasound

D. Ogasawara, J. Shite, T. Shinke, H. Otake, Y. Tanino, T. Sawada, P. Oscar, M. Yokoyama. *Kobe University Graduate School of Medicine, Cardiology Department, Kobe, Japan*

Background: Coronary plaque volume decreases with intensive medical therapy. However there are few reports referred to what coronary plaque components and cytokine play an important role in plaque regression.
Methods: We enrolled 92 lesions of 56 patients with coronary artery disease. At coronary intervention, non-culprit, mild-obstructive de novo lesions (<75%) were examined by virtual histology intravascular ultrasound (VH-IVUS) and obtained the plaque volume and each plaque component volume [fibrous (FI), fibro-fatty (FF), dense-calcium (DC) and necrotic-core (NC)]. After 6-month of intensive medical treatments, same lesions were evaluated with VH-IVUS again. In addition, the changes of plasma adiponectin levels were evaluated.
Results: Decrease in plaque volume was observed in 47 lesions (regression group) and other 45 lesions showed no change or plaque progression (non-regression group). The mean change in plaque volume was -10.6±8.3% in regression group and 13.3±18.7% in non-regression group. In regression group, all four plaque component volume decreased significantly and ratio of NC volume decreased and FI increased, while non-regression group showed inverse changes. (regression vs non-regression groups; ΔNC: -2.1±8.1% vs 1.6±9.0%, p<0.05, ΔFI: 3.4±3.6% vs -1.5± 11.7%, p<0.05). Plasma adiponectin level increased significantly in regression group (regression vs non-regression group; 2.6±4.3 μg/ml vs -0.2 ±5.1 μg/ml p<0.01). Furthermore, there was a significant inverse correlation between the changes in plaque volume and the changes in plasma adiponectin level (p=0.02, r=-0.24, Figure).
Conclusion: Coronary plaque regression was closely related to decrease in necrotic-core component and increase of fibrous component with increase of plasma adiponectin level.



STEMI AND THROMBOSIS

P527 The smokers paradox continues: reduced risk of reocclusion, but no improved long-term outcome after successful fibrinolysis

P.C. Kievit[1], M.A. Brouwer[1], G. Veen[2], W.R.M. Aengevaeren[2], P.J.P.C. Van Den Bergh[2], A.J. Van Boven[1], D.P. Hertzberger[1], F.W.A. Verheugt[2]. *[1]Radboud University Medical Center Nijmegen, 670 Cardiology, Nijmegen, Netherlands; [2]Interuniversity Cardiology Institute, Utrecht, Netherlands*

Background: In smokers treated with fibrinolysis for acute myocardial infarction (MI) a paradoxical beneficial short-term outcome has been reported. This was attributed to favorable baseline variables as younger age, less severe coronary disease and a better response to fibrinolysis. We studied the effects of smoking on angiographic and long-term clinical outcome in patients after successful fibrinolysis.
Methods: In the Antithrombotics in the Prevention of Reocclusion In COronary Thrombolysis trials (APRICOT-1 and -2) 499 patients with ST-elevation MI who had an open infarct related artery 24-48 hours after fibrinolysis received randomized antithrombotic treatment until follow-up angiography scheduled at 3 months. Five-year clinical follow-up was collected.
Results: At baseline 64% (317/499) of patients were current smokers. As compared to non-smokers, smokers were younger (54±9 versus 60± 9 years, p<0.01) and had less often a history of previous MI (6% versus 14%, p<0.01), diabetes (4% vs 8%, p=0.02), hypertension (22% vs 31%, p=0.02) or a positive family history (34% vs 47%, p<0.02). At baseline angiography smokers more often had single vessel disease (61% vs 49%, p=0.02), smooth infarct lesions (64% vs 52%, p<0.01) and had less severe residual stenosis of the infarct artery (58.9% vs 62.0%, p=0.01). Median peak Ck-levels were higher in smokers: 1116 (IQR 563-2146) U/L vs 862 (IQR 401-1825) U/L (p<0.01). Baseline ejection fraction did not differ: 52.4% vs 53.5%.
At follow-up angiography reocclusion rates were 21% (67/317) in smokers versus 32% (59/182) in non-smokers (p<0.01). Rates of reocclusion occurring without reinfarction were 17% and 27%, respectively (p<0.01). Three-month reinfarction rates were 6.3% in smokers and 6.6% in non-smokers (p=ns). Five-year infarct-free survival did not differ either: 80% versus 82%. At multivariable analysis smoking status independently predicted sustained patency of the infarct artery (RR 0.63, 95%CI 0.33-0.99, p<0.05), but not infarct-free survival (HR 1.19, 95%CI 0.73-1.94, p=ns).
Conclusions: After successful fibrinolysis smokers have more favorable baseline clinical and angiographic characteristics than non-smokers. Although smoking status is independently associated with a reduced risk of reocclusion, this does not translate in better long-term clinical outcome. As smokers are much younger at the time of the infarction both primary and secondary prevention remain of pivotal importance in this setting.

P528 Serial snapshot electrocardiograms and continuous ST monitoring for the prediction of intravenous thrombolysis outcome in patients with STEMI

M. Zairis, S. Makrygiannis, O. Ampartzidou, N. Patsourakos, D. Xenos, P. Smilakos, J. Hatzissavas, E. Adamopoulou, S. Argyrakis, S. Foussas. *Tzanio Hospital, Cardiology, Piraeus, Greece*

Purpose: To compare the effectiveness of serial snapshot ECGs and continuous 12-lead ECG ST-segment monitoring for the prediction of intravenous thrombolysis outcome in pts with STEMI.
Methods: A total of 786 consecutive patients with STEMI, who received intravenous thrombolysis in the first 6 hours from index pain were studied. The incidence of successful thrombolysis with both methods and 1-year cardiac death, were the prespecified study endpoints. Successful thrombolysis was defined as the presence of sustained ≥50% ST-segment recovery in the lead with the higher ST elevation during the first 90 min after intravenous thrombolysis starting.
Results: There was a clear 7.1% difference in the estimation of thrombolysis success between the 2 methods. In particular the incidence of successful intravenous thrombolysis was 49.7% and 42.6% using serial snapshot ECGs and continuous 12-lead ECG ST-segment monitoring respectively. By 1-year the incidence of cardiac death was 16.8%. The 7.1% of pts who were diagnosed as having successful thrombolysis by serial snapshot ECGs but not by continuous 12-lead ECG ST-segment monitoring (Group A) were at significantly higher risk of 1-year cardiac

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

death than those who were classified as having successful thrombolysis by both methods (Group B) (25% vs 7.2%; RR=3.1, p<0.001). Moreover the former were at similar risk of 1-year cardiac death than those who were classified as having failed thrombolysis by both methods (Group C) (25% vs 23.8%; RR=1.1, p=0.9) (Figure 1).

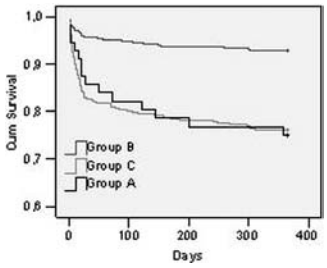


Figure 1

Conclusions: Continuous 12-lead ECG ST-segment monitoring is superior to serial snapshot ECGs for the prediction of intravenous thrombolysis outcome in pts with STEMI.

P529 Predictors of angiographic patency and ST-segment resolution following pre-hospital thrombolysis in patients with ST-segment Elevation Myocardial Infarction

V. Bongard[1], L. Belle[2], D. Savary[1], S. Charpentier[3], L. Soulat[4], P.H.G. Steg[5], C. Loubeyre[6], Y. Cottin[7], D. Miljkovic[8], J. Puel[9] on behalf of OPTIMAL Study group. *[1]CHU de Toulouse - INSERM U558, Epidemiology, Toulouse, France; [2]Centre Hospitalier d'Annecy, Cardiology, Annecy, France; [3]Centre Hospitalier Universitaire de Toulouse, Emergency, Toulouse, France; [4]Centre Hospitalier de Chateauroux, Emergency, Chateauroux, France; [5]Hopital Bichat, Cardiology, Paris, France; [6]Polyclinique Saint Laurent, Cardiology, Rennes, France; [7]Centre Hospitalier Universitaire de Dijon, Cardiology, Dijon, France; [8]Boehringer-Ingelheim, Paris, France; [9]Hopital Rangueil - CHU de Toulouse, Cardiology B, Toulouse, France*

Purpose: In ST-segment elevation myocardial infarction (STEMI), thrombolysis aims to promptly restore coronary flow and tissue perfusion, but is not always successful. TIMI flow grade and electrocardiogram (ECG) ST-segment resolution (STR) after thrombolysis are commonly used as indicators of coronary patency and myocardial reperfusion, respectively. The aim of this study was to assess independent predictors of infarct artery patency (TIMI flow) and STR after pre-hospital thrombolysis. The prognostic value of TIMI flow and STR in in-hospital mortality were also studied.
Methods: Consecutive French patients presenting with STEMI were enrolled in 2004-05 and received pre-hospital thrombolysis within 6 hours of symptom onset by mobile emergency care units and coronary angiography was done within 6 hours of thrombolysis. Patency was defined as TIMI grade 3 flow in the infarct artery, before PCI. Two ECGs were collected (before thrombolysis and immediately before coronary angiography). STR was defined as at least 70% ST resolution in the single lead with the greatest baseline ST elevation. Coronary angiography and ECG data were assessed in blinded core laboratories.
Results: The sample comprised 800 patients (82% of men, median age 59). The median delay between symptom onset and thrombolysis was 110 minutes. The proportions of patients with TIMI 3 flow and STR $\geq$ 70% were 51% and 42%, respectively. In-hospital mortality was significantly associated with STR (1.8% for STR $\geq$ 70% versus 4.4% otherwise, p=0.046) but not with TIMI flow (2.5% vs 4.2% for TIMI 3 flow vs 0-2, p=0.186). In multivariate logistic regression adjusted for acute phase treatments other than thrombolysis, independent predictors of TIMI 3 flow were smoking (current or past vs non, odds ratio (OR) 1.41, p=0.022), lack of hypertension (OR=1.40, p=0.019) and extent of ST elevation ($\leq$5 leads vs >5, OR=1.60, p<0.01). More variables were independently associated with STR: delay between symptom onset and thrombolysis ($\leq$1 hour vs >1, OR=1.98, p<0.01), body mass index (BMI) < 30 kg/m^2 (OR=1.96, p<0.01), current or past smoking (OR=1.65, p<0.01), non-anterior STEMI (OR=1.63, p<0.01) and maximum ST-segment elevation ($\leq$2 mm vs >2, OR=2.18, p<0.0001).
Conclusion: In this "real life" study, STR had a stronger association with in-hospital mortality than TIMI flow. Independent predictors of STR included delay of thrombolysis, BMI, smoking, STEMI location and magnitude of maximum ST elevation. This information may help the triage for emergency angiography in patients receiving pre-hospital thrombolysis.

NON-ST ELEVATION – ACUTE CORONARY SYNDROME

P530 Prevalence and predictive factors of heart failure after non ST segment elevation myocardial infarction

O. Barthez, J.-C. Eicher, Y. Cottin, M. Zeller, P. Morelon, P. Buffet, A. Goguey, P. Auplat, J.E. Wolf. *Centre Hospitalo-Universitaire, Centre de Cardiologie, Dijon, France*

Background: Coronary artery disease is the most frequent etiology of heart failure (HF). The prevalence of HF after ST segment elevation myocardial infarction (STEMI) is estimated between 18 and 37%, and is closely related to the amount of necrosed myocardium. Little is known about the prevalence and the predictive factors of HF complicating Non ST Segment Elevation Myocardial Infarction (NSTEMI).
Purpose: The aim of the present study was 1) to establish the prevalence of HF two years after a NSTEMI and 2) to determine the risk factors associated with this complication.
Methods: Patients were selected from the RICO survey database. The patients who had been admitted for NSTEMI in the ICU of Dijon hospital between November 2003 and July 2004, who were living in the city of Dijon and its suburbs, and whose LVEF at discharge was >45% were included. Clinical examination, echocardiography and Nt-proBNP level evaluation were performed on average 27 months after the acute coronary syndrome.
Results: 105 patients were included: mean age was 64±1,2 years, 75% were men. At follow up, 14 patients (13%) presented with symptoms of HF. They had a lower LVEF (38±2 vs 60±1%, p<0,001) and higher Nt-proBNP levels (1631±706 pg/ml vs 304±87 pg/ml, p < 0,05) than the others. In univariate analysis, factors associated with HF were age (70±4 vs 62±1 yrs, p = 0,045), prior coronary artery bypass (36 vs 9%, p = 0,016), LVEF on admission (52±2 vs 62±1%, p < 0,001), lesion of the left anterior descending coronary artery (100 vs 73%, p = 0,035), glomerular filtration rate (54±6 vs 71± 3 ml/min, p = 0,035) and plasma level of Nt-proBNP on admission (356± 93 vs 144±44 pg/ml, p <.0,001). Plasma concentrations of biological markers of myocardial infarction, door to balloon delay, proportion of complete revascularization and pharmacological treatment did not differ statistically between HF patients and others. In multivariate analysis, Nt-proBNP level on admission was the only predictive factor of HF after a NSTEMI, independently of age, LVEF, renal function and number of coronary artery lesions.
Conclusion: HF is a frequent complication of NSTEMI. Unlike STEMI, where the risk of developping HF is linked to the extent of myocyte necrosis, usual initial risk factors such as Killip class, TIMI score, enzyme release or anterior location do no predict HF occurence after NSTEMI. Despite normal discharge LVEF, some patients will develop late remodelling and HF: Nt-proBNP level could help to identify high risk patients for this complication.

P531 Influence of heightened platelet reactivity after clopidogrel treatment on long-term adverse outcomes in non-ST elevation myocardial infarction

B. Samaniego, A. Diego, A. De Miguel, D. Alonso, F. Fernandez-Vazquez, C. Cuellas, R. Carbonell, C. Pascual, N. Alonso-Orcajo, A. Perez De Prado on behalf of RASCA Investigators. *Hospital De Leon, Servicio De Cardiologia, Leon, Spain*

Purpose: To determine whether platelet reactivity following clopidogrel treatment relates to the incidence of major adverse cardiovascular events (MACE) at 1-year follow-up in patients with non-ST elevation myocardial infarction (NSTEMI).
Methods: This prospective, observational study included 120 patients with NSTEMI (troponin T level $\geq$0.10 ng/mL) and an early coronary angiography. Of the patients included in the study 65 (55%) underwent percutaneous coronary intervention (PCI) and 18 (15%) coronary artery bypass grafts (CABG). All were treated with a 300 mg-loading dose of clopidogrel on admission plus 75 mg daily. Platelet reactivity was measured with a point-of-care P2Y12 specific device. Post-treatment platelet reactivity (PPR) is expressed in platelet reactivity units (PRU). A 1-year follow up was performed to evaluate MACE.
Results: 108 patients (90%) completed a 392±229-day follow-up. Incidence of MACE was 13%: 8 deaths, 3 new NSTEMI, 2 strokes and 3 new revascularizations. A heightened PPR was associated with the occurrence of MACE (158±69 vs. 203±61 PRU; p=0.026). Patients who suffered MACE showed significant differences in the following variables: older age (74±8 vs. 68± 11 years; p=0.014), hypertension (100% vs. 53%; p=0.001), diabetes receiving treatment (57% vs. 20%; p=0.006), previous CABG (21% vs. 4%; p=0.045), previous antiplatelet treatment (71% vs. 30%; p=0.005), lower haemoglobin level (12.1±1.4 vs. 13.6±1.6 mg/dL; p=0.001), more diseased vessels (2.4±0.8 vs. 1.7±1.1 vessels; p=0.008) and a greater use of unfractionated heparin (86% vs. 32%; p=0.001). Multivariate stepwise regression analysis indicated that PPR was an independent predictor of 1-year MACE (p=0.012) as were hypertension (p=0.023), previous CABG (p=0.025), haemoglobin level (p=0.013), and use of unfractionated heparin (p=0.001).
Conclusions: Heightened platelet reactivity following clopidogrel treatment in NSTEMI is an independent predictor of poorer prognosis at long-term follow up.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P532 Prediction of 1-year cardiovascular events in patients with chest pain admitted in Emergency Department by a multi-marker approach

R. Della Bona[1], L.M. Biasucci[1], I. Dato[1], V. Loria[1], D. D'amario[1], N. Gentiloni[1], A. Ciervo[2], M. Piro[1], G. Niccoli[1], F. Crea[1]. [1]*Catholic University, Department of Cardiovascular Medicine, Rome, Italy;* [2]*Istituto Superiore di Sanita, Department of Infectious, Parasitic, and Immu, Rome, Italy*

Purpose: long term risk stratification of patients with chest pain suggestive for Acute Coronary Syndrome (ACS) admitted to Emergency Department (ED) is often challenging and new biochemical tools are needed to this aim. We assessed the one year predictive power of NT-proBNP, C Reactive Protein, IgG anti-CpHSP60 and Cystatin C in a multimarker approach in a chest pain population recruited in ED within 24 hours from the onset of symptoms.
Methods: we measured serum levels of NT-proBNP, hs-CRP, Cystatin C, IgG anti-CpHSP60, and TnT in 224 patients admitted to the ED with chest pain. Thirty-eight were discharged with a definite diagnosis of ACS and 186 of no-ACS. As events we considered the occurrence of the composite end-point of Death (8) + new ACS (36) at 1 year-follow up. Biochemical variables were analysed as quartiles; univariate and multivariate logistic analysis were performed.
Results: at univariate analysis NT-proBNP (p=0.0001), TnT (p=0.045), diabetes (p=0.044), hypertension (p=0.025), EKG changes (p=0.021) were predictive of the composite end-point, but only NT-proBNP (p=0.002) and family history (p=0.045) were independent predictors. Death alone was predicted independently only by TnT and NT pro-BNP (respectively p=0.001 and p=0.014). Intriguingly IgG anti-CpHSP60 were independently but inversely associated with adverse composite end-point (p=0.025). In the EKG and TnT negative population at univariate analysis NT-proBNP (p=0.006), diabetes (p=0.015), family history (0.015) and previous cardiovascular events (p=0.0001) were predictive. At multivariate analysis, however, only NT-proBNP and family history were independent predictors of the composite events at one year (all p=0.021). In the 186 no-ACS pts 29 cardiovascular events were observed after 1 year, in this population history of previous cardiovascular disease and NT- proBNP were the only parameters associated with the events ($p<0.01$).
Conclusions: our study demonstrates that NT-proBNP and TnT are powerful and independent markers of future cardiovascular events in the heterogeneous population of chest pain patients admitted to ED. More importantly NT-proBNP predicts the occurrence of new events at one year in pts with chest pain but without elevated entry levels of TnT and EKG ischemic changes and also in those without a diagnosis of ACS at hospital discharge. Of note we also found a significant and independent inverse association of ab anti Cp-HSP60 and events, at variance from previous studies, possibly related to the long term protective role of these unfolding proteins.

P533 Pathophysiologic mechanisms and prognostic value of persisting cardiac troponin I elevation in stabilized patients after an episode of acute coronary syndrome

K.M. Eggers, B. Lagerqvist, P. Venge, L. Wallentin, B. Lindahl. *Uppsala University Hospital, Dept. of Medical Sciences, Cardiology, Uppsala, Sweden*

Background: Minor cardiac troponin I (cTnI) elevation can frequently be detected in the stable phase after an acute coronary syndrome (ACS). We studied the pathophysiologic mechanisms and the prognostic importance of persisting cTnI elevation in relation to LV-function, angiographic findings and treatment strategy in 898 stabilized patients from the FRISC II trial in which patients with nonSTE-ACS were randomized to an invasive vs. a non-invasive strategy and to 3-month treatment with dalteparin vs. placebo.
Methods: cTnI was measured at 6 weeks, 3 and 6 months after randomization in patients without a myocardial infarction (AMI) or coronary procedure within the last 14 days using the recently refined Access AccuTnI assay. A cut-off of 0.01 μg/L close to the 10% CV level was chosen. All patients were followed up for at least 5 years. The prevalence and prognostic importance of persisting cTnI elevation $>$ 0.01 μg/L at all three measurement instances was evaluated by different multivariate models adjusted for age, gender, previous AMI, creatinine-clearance (n=898), LV-EF $<$ 0.45 during hospitalization, treatment strategy, NT-pro BNP $\geq$ 232 ng/L (median) at 6 months (n=683), and for findings on coronary angiography (n=335; invasive arm only).
Results: Persisting cTnI elevation was detected in 233 patients (26%), having a mortality of 13% and a rate of AMI of 19% during 5-year follow-up. NT-pro BNP (OR 2.2; 95% CI 1.9-2.7), male gender (OR 2.5; 95% CI 1.6-4.1) and randomization to the invasive arm (OR 1.8; 95% CI 1.2-2.7) but not angiographic findings independently predicted persisting cTnI elevation. Persisting cTnI elevation independently predicted mortality (OR 2.2; 95% CI 1.3-3.8) but lost its prognostic value after adjustment for NT-pro BNP. In that model, NT-pro BNP was the only independent predictor for mortality (OR 2.5; 95% CI 1.9-3.3) and, apart from a previous AMI, for AMI (OR 1.8; 95% CI 1.4-2.2) during 5-year follow-up.
Conclusion: Persisting cTnI elevation $>$ 0.01 μg/L in stabilized patients after an episode of ACS is strongly correlated to NT-pro BNP levels at 6 months, indicating that impaired LV-function is the major cause for cTnI elevation in this setting. NT-pro BNP was the most important predictor for adverse events during 5 year follow-up and offered prognostic value beyond that obtained from cTnI results. Even randomization to the invasive arm independently predicted persisting cTnI elevation but not adverse outcome. This indicates that other pathophysiologic mechanisms than depressed LV-function cause cTnI elevation in this cohort.

P534 Acute coronary syndromes without angiographic significant coronary artery disease - a comparative analysis in hospitalized patients

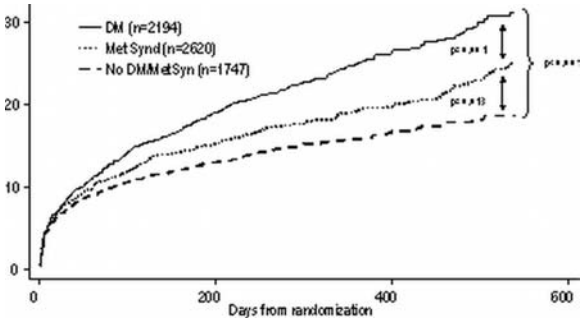
A. Goncalves, M. Patacho, A. Azevedo, R. Lopes, V. Araujo, P. Dias, J. Mota Garcia, M.ªJ. Maciel. *Hospital Sao Joao, Cardiology, Porto, Portugal*

Background and Objectives: The prevalence, predictors, and outcomes of patients with acute coronary syndromes (ACS), without significant angiographic coronary artery disease remain poorly characterized. The purpose of this study is to evaluate the real prevalence of non-significant coronary artery disease, to describe these patients' characteristics and to identify alternative substrates of myocardial ischemia.
Methods: We analyzed 567 patients admitted in our Department with the diagnosis of ACS from January to December 2006, who underwent cardiac catheterization, in order to determine the prevalence and factors associated with insignificant CAD (coronary stenosis $<$30%) and inhospital outcomes.
Results: A total of 59 (8.8%) among the 567 had non-significant angiographic CAD. Forty-six patients had "normal" coronary arteries at the angiography and 17 had insignificant CAD. Of these, 36 (61.0%) were women and 23 (39.0%) were men, with a mean age of 60,1$\pm$13 yrs. Alternative substrates of acute myocardial ischemia included supraventricular arrhythmias (4 patients, 6.7%), aortic stenosis (4 patients, 6.7%), aortic insufficiency (2 patients, 3.3%), stress-induced (Takotsubo) cardiomyopathy (4 patients, 6.7%), coronary spasm (2 patients, 3.3%), embolism (2 patients, 3.3%), hypertrophic myocardiopathy (2 patients, 3.3%), myocarditis (2 patients, 3.3%), cardiac syndrome X (1 patient, 1.7%) and congenital coagulation disorders (1 patient, 1.7%). No alternative substrates were found in 35 (59.3%) patients. Patients with ACS and non-significant angiographic CAD were more frequently women (61.0% vs. 25.2% $p<0.0001$), had more commonly preserved left ventricle systolic function (75.9% vs. 62.3% p=0.037), and had less frequently diabetes mellitus (16.9% vs. 31.9% p=0.018) and smoking habits (27.1% vs. 47.4% p=0.003). We found no significant differences regarding age, arterial hypertension, obesity, dyslipidemia, family history of CAD and inhospital complications. In a multivariate logistic regression model, only female sex and absence of diabetes mellitus were significantly and independently associated with non-significant angiographic CAD among patients with ACS.
Conclusion: Among patients with admission diagnosis of ACS there is a substantial group with non-significant angiographic CAD, for whom no alternative substrates for ischemia were found. Alternative aetiological factors could be detected in 40.7% of patients. These findings highlight the need for additional diagnostic procedures and research to understand the pathophysiology of myocardial ischemia in this population.

P535 Clinical outcomes in patients with diabetes or the metabolic syndrome with non-ST-elevation acute coronary syndrome in the MERLIN-TIMI 36 Trial

B.M. Scirica[1], D.A. Morrow[1], H. Hod[2], P. Theroux[3], P. Molhoek[4], E. Karwatowska-Prokopczuk[5], J. Qin[5], S. Murhpy[5], C.H. Mccabe[5], E. Braunwald[5] on behalf of MERLIN-TIMI 36 Investigators. [1]*TIMI Study Group/Brigham and Women's Hospital, Cardiovascular Division, Dept of Medicine, Boston, United States of America;* [2]*Tel Hashomer, Israel;* [3]*Montreal, Canada;* [4]*Enschede, Netherlands;* [5]*CV Therapeutics, Palo Alto, United States of America*

Purpose: To evaluate the prevalence and outcome of patients with diabetes and metabolic syndrome admitted with NSTEACS (UA/NSTEMI) and determine if ranolazine affects this relationship.
Methods: MERLIN-TIMI 36 randomized 6560 patients at presentation with NSTEACS to placebo or the anti-ischemic agent ranolazine, which may improve glycemic parameters. Median clinical follow-up was 12 months. Metabolic syndrome was defined as having any 3 of the following: 1) waist circumference $>$102cm (men) and $>$88cm (women), 2) TG $>$150 mg/dL or drug treatment for



CV Death/MI/Severe Recurrent Ischemia

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

elevated TG, 3) HDL 130 mmHg or DBP >85 mmHg or drug treatment for hypertension, and 5) fasting glucose >100 mg/dL.
Results: Preliminary results show that at randomization, 2194 (33.4%) of all patient carried a diagnosis of DM and 2620 (39.9%) patients had metabolic syndrome. Patients with DM and metabolic syndrome were more likely to be female, have known CAD and had higher TIMI Risk scores at presentation. The rate of revascularization was similar among all groups (40.4% v. 39.7% v. 37.3%, p=0.10). There was a stepwise increase in the risk of severe recurrent ischemia, myocardial infarction, and cardiovascular death in patients with DM at highest risk followed by those with metabolic syndrome and then patients with neither at lowest risk. (Figure) Final results, including the effect of ranolazine in patients with DM, will be available at the time of presentation.
Conclusions: Metabolic syndrome and diabetes are common among patients presenting with NSTEACS and confer increased cardiovascular risk.

P536 Do treatment delays influence outcomes following presentation with non-ST elevation acute coronary syndrome? The GRACE registry

G. Devlin[1], N. Swanson[1], A. Silverstone[1], G. Montalescot[2], K.A. Eagle[3], S.G. Goodman[4], W. Huang[5], D. Brieger[6] on behalf of the GRACE Investigators. *[1]Waikato Hospital, Cardiology Dept., Hamilton, New Zealand; [2]Hospital Pitie-Salpetriere, Paris, France; [3]University of Michigan Health System, Ann Arbor, United States of America; [4]University of Toronto, Toronto, Canada; [5]UMASS Medical School, Worcester, United States of America; [6]Concord Hospital, Sydney, Australia*

Purpose: Guidelines currently recommend early angiography (i.e. within 72 hours) and subsequent revascularization, if appropriate, in high-risk patients with acute coronary syndromes (ACS). In many healthcare systems this is not achievable. GRACE is a multinational prospective registry of ACS, spanning several healthcare models, which presents an opportunity to investigate whether these time delays influence patient outcome.
Methods: We report on in-hospital and 6-month outcomes in patients undergoing angiography after presentation with high-risk non-ST elevation (NSTE) ACS (ST changes or positive troponin). Patients were stratified according to time of angiography. The primary study endpoint was stroke, death or myocardial infarction within 6 months of admission.
Results: Of 23,595 patients with high-risk NSTE ACS, full admission and 6-month follow-up data were available in 10,882 (82%) and 8732 (80%), respectively; 13,307 (57%) patients had angiography done during the index admission. Median delay to angiography was 46 h, with 3680 (33%) waiting ≥72 hours. Groups were well matched on presentation. Renal failure was, however, more common in the late angiography group (5% vs 3% P<0.001). Recurrent in-hospital ischaemia (33% vs 22%, P<0.001), reinfarction (8% vs 5%, P<0.001) and heart failure (14% vs 9%, P<0.001) were more frequently noted in the late angiography group. The primary study endpoint (death/MI/CVA) at 6 months was significantly higher in the group waiting longest for catheterization (16% vs 12%, P<0.001; Table). Multivariable analysis, adjusting for potential confounders, showed increased 6-month mortality in the delayed angiography group (OR 1.5, 95%CI 1.1-2.0, P<0.01).

Outcomes from admission to 6-months

Outcome	Delay to catheterization		P value
	<72 h n/N %	≥72 h n/N %	
Death	346/7196 4.8%	224/3679 6.1%	<0.01
Myocardial infarction	500/7181 7.0%	369/3664 10%	<0.001
Stroke	85/7187 1.2%	66/3674 1.8%	<0.01
MACE (death/MI or CVA)	853/7201 12%	583/3680 16%	<0.001

CVA, cardiovascular accident; MACE, major adverse cardiac event.

Conclusions: One in three high-risk NSTE ACS patients undergoing angiography does not have it performed within 72 h of presentation. These delays, whilst likely to be multifactorial, may adversely affect patient outcomes at 6 months.

HYPERGLYCEMIA/RENAL FAILURE AND ACUTE CORONARY SYNDROME

P537 The impact of renal function on bleeding complications in real world acute coronary syndromes patients treated with anticoagulants European perspective

A. Porter[1], Z. Iakobishvilli[2], S. Behar[3], V. Boyko[3], A. Battler[4], D. Hasdai[2]. *[1]Rabin Medical Center, Dept. of Cardiology, Petah Tikva, Israel; [2]Rabin Medical Center, Petah Tiqva, Israel; [3]Tel Hashomer, The Neufeld Cardiac Research Center, Ramat Gan, Israel; [4]Rabin medical center, Petah Tiqva, Israel*

Background: The anticoagulant effect of low molecular weigh heparin (LMWH) but not unfractionated heparin (UFH) is affected by renal function. Thus, their use in ACS pts may be differentially effective by renal function. Aim - To assess the impact of renal dysfunction on bleeding complications in "real world" ACS patients treated with UFH or LMWH.
Methods: Analysis of pts enrolled in the second European ACS Survey and who were treated by UFH or LMWH. Glomerular filtration rate (GFR) <60 ml/min was considered renal dysfunction.
Results: Of the 6385 ACS pts, 4612 (72.2%) received anticoagulants and had a calculated GFR. Median GFR was 73.8 ml/min (25.0-75.1). Renal dysfunction was detected in 1283 pts (27.8%). LMWH was used in 2836 pts (61.5%) of whom 763 (27%) had renal dysfunction. UFH was used in 1776 pts (38.5%) of whom 520 (29.3%) had renal dysfunction. Renal dysfunction did not impact on bleeding rates among UFH treated pts (2.1% vs. 1.3% for pts with and without renal dysfunction, p=0.24), but did impact on bleeding rates among LMWH treated pts (3.1% vs. 0.6% for pts with and without renal dysfunction, p< 0.0001). LMWH in renal dysfunction pts compared to normal renal function pts was independently associated with major bleeding (OR 3.3, CI: 1.7-6.7).
Conclusion: Nearly 1/3 of "real-world" ACS pts have renal dysfunction. The use of LMWH among these pts is associated with higher bleeding rates, indicating that the choice of anticoagulant should be tailored based on renal function.

P538 Time course of glucometabolic abnormalities during the acute phase of myocardial infarction

G. Sideris[1], W. Smida[1], A. Ouadhour[1], V. Stratiev[1], F. Tarragano[1], M. Sirol[1], D. Logeard[1], P. Henry[2]. *[1]AP-HP Lariboisiere, Cardiology, Paris, France; [2]Hopital Lariboisiere, Service De Cardiologie, Paris Cedex 10, France*

Background: hyperglycemia and insulin resistance are common in non-diabetic patients presenting with acute myocardial infarction (AMI). These abnormalities are partly due to the stress of AMI. The aim of this study was to characterize the time course of glucometabolic abnormalities in non-diabetic patients during AMI.
Methods: 25 patients (mean age 58 yrs, 70% male) hospitalized for primary angioplasty during AMI (<6h) were studied. Patients with previously known diabetes mellitus, a fasting blood glucose at admission >11.0 mmol/L or a Killip class > 1 were excluded. Fasting (≥6 hours) blood glucose and insulinemia were measured just before primary angioplasty, at the end of primary angioplasty, and then 6, 12, 24, 48 and 72 h after admission. Beta-cell function (normal value = 100%) and the insulin resistance index (normal value = 1) were calculated through the homeostasis model assesment (HOMA 2) modelling.
Results: the table shows the mean glucose and insulin levels for each measurement, the calculated beta-cell function and the insulin resistance index. Insulin resistance was pronounced during the first 24 hours post-AMI associated with a decrease in beta-cell function lasting the first 72 hours. Glucometabolic abnormalities had disappeared by 72 hours post-AMI. There was no clear relationship between glucometabolic abnormalities and peak CPK level or troponine.

Glucometablic profile during AMI

	Fasting glucose (mmol/L)	Fasting insulin (pmol/L)	Beta cell function (Normal = 100%)	Insulin resistance index (Normal = 1)
Before angioplasty	8.4	165.9	78	3.21
After angioplasty	7.9	130.3	73	2.55
6 hours	6.8	61.3	56	1.17
12 hours	6.7	94.8	53	1.87
24 hours	6.3	49.4	57	1.00
48 hours	5.6	51.4	69	0.94
72 hours	4.8	45.8	92	0.90

Conclusion: glucometabolic status demonstrates marked variations during first 3 days after primary angioplasty for AMI. These findings indicate that the assesment of basal glucometabolic state should not be performed before day 3 post-AMI.

P539 Association of creatinine clearance and in-hospital mortality in patients with acute coronary syndromes; the GREECS study

D.B. Panagiotakos[1], C. Pitsavos[1], P. Stravopodis[2], S. Arapi[1], T. Gialernios[1], Y. Koyias[3], Y. Mantas[4], S. Zobolos[5], E. Tsiamis[1], C. Stefanadis[1]. *[1]Athens, Greece; [2]Zakynthos, Greece; [3]Karditsa, Greece; [4]Halkida, Greece; [5]Kalamata, Greece*

Background: The relationship between renal dysfunction and mortality in patients with myocardial infarction (MI) has been extensively investigated. In this work, we sought to investigate whether renal insufficiency is an independent predictor for in-hospital mortality among pateints presented with all the spectrum of acute coronary syndromes (ACS).
Methods: We enrolled 2172 patients presented with ACS in 6 Greek hospitals. Creatinine clearance rates were estimated by the Cockcroft-Gault formula.
Results: Five percent of patients presented at the hospital with severe renal dysfunction, 27% with moderate and the other 68% with normal. Patients with moderate or severe renal dysfunction were older, more likely to be women and more likely to have history of hypertension and diabetes mellitus compared to those with normal renal function. In comparison with patients with normal renal function, those with moderate and severe renal dysfunction were 3 and 12 times more likely to die, respectively. Moreover, moderate and severe renal insufficiency continues to be prognostic factor for mortality, even after controlling for potential confounders.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Abstract P539 – Table 1. Unadjusted and adjusted odds ratios for in-hospital mortality in all patients by diagnosis stratified by creatinine clearance

	Odds Ratio (95% CI)*	Odds Ratio (95% CI)**	Odds Ratio (95% CI)***
Patients presented with all clinical presentations of ACS			
Estimated creatinine clearance rate:			
Normal/minimally impaired renal function (≥60 ml/min)	1.00	1.00	1.00
Moderate renal dysfunction (60-30 ml/min)	4.05 (2.31–7.09)	2.70 (1.40–5.15)	3.03 (1.02–9.47)
Severe renal dysfunction (<30 ml/min)	10.94 (5.52–21.69)	6.95 (3.18–15.19)	11.7 (3.36–40.92)
ST-segment elevation AMI			
Estimated creatinine clearance rate:			
Normal/minimally impaired renal function (≥60 ml/min)	1.00	1.00	1.00
Moderate renal dysfunction (60-30 ml/min)	5.13 (2.40–10.88)	2.67 (1.09–6.55)	4.67 (1.02–22.22)
Severe renal dysfunction (<30 ml/min)	20.96 (8.05–54.55)	11.49 (3.85–34.3)	24.17 (3.1–185.8)
Non-ST-segment elevation AMI/Unstable angina			
Estimated creatinine clearance rate:			
Normal/minimally impaired renal function (≥60 ml/min)	1.00	1.00	1.00
Moderate renal dysfunction (60-30 ml/min)	3.67 (1.57–8.57)	2.92 (1.09–7.77)	1.83 (0.29–11.22)
Severe renal dysfunction (<30 ml/min)	7.70 (2.67–22.25)	5.99 (1.79–20.06)	6.31 (1.06 – 37.48)

*Without controlling for potential confounders; **After controlling for age, sex; ***After controlling for age, sex, smoking habits, Body Mass Index, history of coronary heart disease, history of hypertension, history of diabetes, CPK-MB, blood pressure levels at the admission, ECG changes (only among all patients), thrombolysis (only among all patients and among patients with ST-segment elevation AMI) and time between the onset of symptoms and admission.

Conclusions: Creatinine clearance rate is an important independent predictor of in-hospital mortality. Therefore, patients with ACS complicated by renal dysfunction should receive more aggressive medical care.

P540 Effect of statins on renal function and serum uric acid and their relation to recurrent vascular events in coronary heart disease patients with or without metabolic syndrome

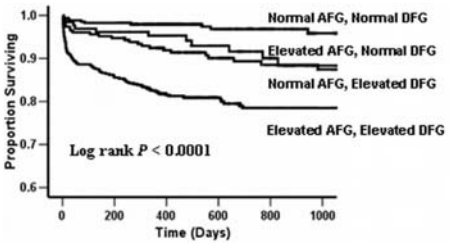
V. Athyros[1], D.P. Mikhailidis[2], E.N. Liberopoulos[3], A.I. Kakafika[1], A. Karagiannis[1], A. Papageorgiou[1], K. Tziomalos[1], E. Ganotakis[4], M. Elisaf[4] on behalf of The GREACE Collaborative Group. *[1]Aristotelean University, Dept. of Internal Medicine, Thessaloniki, Greece; [2]Royal Free University, London, United Kingdom; [3]University of Ioannina, Ioannina, Greece; [4]University of Creete, Dept. of Internal Medicine, Heraclion, Greece*

Background: Metabolic syndrome (MetS) is associated with increased risk for both vascular and chronic kidney disease. Whether statins ameliorate these risks is not established.
Methods: This post hoc analysis of the GREek-Atorvastatin-and-Coronary heart disease (CHD)-Evaluation (GREACE) examines the effect of statins on estimated glomerular filtration rate (e-GFR) and serum uric acid (SUA) levels and their relation to recurrent vascular events (fatal and non-fatal MI, fatal and non-fatal stroke) in CHD patients with MetS. MetS patients were divided into 2 groups: Group A (n=365, most followed by our clinic) received lifestyle advice, target-driven treatment with statins (mainly atorvastatin), and treatment for hypertension and elevated glucose. Group B (n=347, all followed by their physicians) received the above except for statins. Patients without MetS were divided into those who received similar treatment with Group A and Group B [Groups C (n=504, most followed by our clinic) and D (n=384, all followed by their physicians), respectively].
Results: During a mean 3-year follow-up period 12.1% of patients in Group A experienced a recurrent vascular event vs 28% in Group B; risk ratio (RR) 0.43, 95% confidence interval (CI) 0.20-0.64, p<0.0001, while in those without MetS (Group C vs D) the respective RR was 0.59, 95% CI 0.41-0.79, p<0.0001. In Group A, e-GFR increased by 13.7% and SUA levels fell by 8.9%, while in Group B e-GFR was reduced by 5.8% and SUA increased by 4.3% (p<0.005). Stepwise regression analysis showed that e-GFR and SUA changes were independently related to vascular events.
Conclusion: Among CHD patients, those with MetS benefited more (had fewer recurrent vascular events) from statin treatment than those without MetS. This benefit could be partially attributed to favourable changes in e-GFR and SUA levels probably induced by statin treatment.

P541 Changes in fasting glucose during hospitalization and long-term mortality in patients with acute myocardial infarction

D. Aronson[1], H. Hammerman[2], A. Suleiman[1], R. Beyar[1], M. Suleiman[1], W. Markiewicz[1]. *[1]Rambam Medical Center, Cardiology Dept., Haifa, Israel; [2]Haifa, Israel*

Introduction: Elevated fasting glucose (FG) on admission is associated with increased mortality in patients with acute myocardial infarction (AMI). However, the clinical significance of changes in FG during hospital stay is not known.
Methods: We prospectively studied 1154 nondiabetic patients (pts) presenting with AMI. FG was obtained at admission (AFG) and prior to discharge (DFG). The pts were categorized into 4 groups: 1) normal AFG (<100 mg/dL) and normal DFG, n = 129; 2) elevated AFG and normal DFG, n = 340; 3) normal AFG and elevated DFG, n = 228; and 4) elevated AFG and DFG (n = 457). Cox proportional hazards analyses were performed to determine the relation between categories of FG and mortality adjusting for the Global Registry of Acute Coronary Events (GRACE) risk score and for ejection fraction.
Results: The median follow-up after hospital discharge was 20 months (range 6-48). Kaplan-Meier survival curves according to AFG and DFG categories are shown in the Figure. Compared with pts with normal AFG and DFG, pts with elevated AFG had an increased mortality even if their DFG returned to normal level (HR 3.0; 95% CI 1.3-7.0, P = 0.01). Mortality was also increased in pts with normal AFG who developed elevated DFG (HR 3.2 95% CI 1.8-5.3, P = 0.002). Pts with persistent elevation of FG incurred the highest mortality (HR 5.4; 95% CI 2.9-10.2, P < 0.0001).



Survival According to FG Changes

Conclusion: Fluctuations in FG during hospitalization are frequent among pts with AMI. Persistent elevation of FG is associated with poor long-term outcome. However, mortality is increased even in pts with transient FG elevation at admission. Increasing FG during hospitalization also portends higher long-term mortality.

P542 Impact of fasting glycemia on short-term prognosis after acute myocardial infarction

B. Verges[1], M. Zeller[2], G. Dentan[3], J.C. Beer[1], Y. Laurent[4], L. Janin-Manificat[5], P. Sicard[5], H. Makki[6], J.E. Wolf[4], Y. Cottin[4]. *[1]CHU, Endrocrinology service, Dijon, France; [2]LPPCE IFR sante STIC, RICO, Dijon, France; [3]Clinique, Cardiology service, Fontaine Les Dijon, France; [4]CH, Cardiology service, Semur En Auxois, France; [5]CH, Cardiology service, Beaune, France; [6]CH, Cardiology service, Chatillon Sur Seine, France*

Objective: The prognosis of patients with acute Myocardial Infarction (MI), according to the new criteria for Impaired Fasting Glucose (IFG) (FG: 100 to 126 mg/dl) has not been evaluated.
Research Design and Methods. 2353 patients with acute MI and surviving at day 5 after admission were analysed for short-term morbidity and mortality. FG was obtained at day 4 and 5. Patients were classified as diabetics (DM) (known diabetes or FG≥126 mg/dl), high IFG (110 ≤ FG <126 mg/dl), low IFG (100 ≤ FG<110 mg/dl) and normal fasting glucose (NFG) (FG< 100 mg/dl).
Results: Among the 2353 patients, 968 (41%) had DM, 262 (11%) had high IFG, 332 (14%) had low IFG and 791 (34%) had NFG. Compared to NFG patients, 30-day CV mortality was increased in high but not in low IFG subjects. In-hospital heart failure was increased in high IFG subjects (42% vs. 20% for NFG, p<0.0001), but not in low IFG subjects (21% vs. 20%). High IFG, but not low IFG, was an independent factor associated with 30-day CV mortality (OR: 2.33 [1.55-3.47]) and in-hospital heart failure (OR: 1.70 [1.36-2.07]). The optimal threshold levels of FG on the ROC curves to predict mortality and in-hospital heart failure were 114 mg/dl and 112 mg/dl, respectively.
Conclusion: The present study, based on a non-selected cohort of MI patients, underscores the high prevalence of IFG (25%) and highlights the clinical relevance of 110 mg/dl, but not of 100 mg/dl, as a cut-off value to define the risk for a worse outcome.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P543 The role of renal dysfunction and hyperglycemia in the long-term outcome after acute myocardial infarction

J.C. Nicolau, E.P. Gomes, R. Truffa, M.V.B. Gaz, R. Karbstein, L.M. Baracioli, C.V. Serrano Jr, R.R. Giraldez, R. Kalil Filho, J.A.F. Ramires. *Heart Institute (InCor) - HCFMUSP, Acute Coronary Disease Unit, Sao Paulo, Brazil*

Background: it is very well demonstrated the prognostic value of creatinine clearance (CRCL), creatinine (CR) and glucose levels (GLU) in the short-term post-acute myocardial infarction (AMI). However, little is known about the prognostic value of these variables in the long-term outcome after AMI.
Methods: 1198 pts with AMI (median age 64 y.o., 72.5% men), included prospectively in a databank and followed for up to 8.56 years (median 3.6 years), were analyzed. The studied variables were divided in quartiles; Kaplan-Meier curves were constructed for each one of the variables, and Log-Rank (univariate analysis) and Cox Stepwise Regression (multivariable analysis), were utilized in the statistical calculations. The adjusted models included 24 baseline and in-hospital variables.
Results: (a) Non-adjusted models: taking into account quartiles 1, 2, 3 and 4, the mean survival times for CRCL were, respectively 2166.85± 85.59, 2435.17±68.18, 2699.26±54.69 and 2823.55±47.70 days ($P<0.001$). The Hazard-ratios (HR) for quartiles 1, 2 and 3 relatively to quartile 4 were, respectively, 4.36 (95% CI 2.8 to 6.8; $P<0.001$), 2.66 (95% CI 1.68 to 4.2; $P<0.001$), and 1.46 (0.88 to 2.4; P=0.0.14); for CR, the survival times were 2725.00±69.24, 2769.68±46.99, 2556.03 ±62.30 and 2195.58±74.37 days ($P<0.001$); the HR were 0.29 (95% CI 0.17 to 0.51; $P<0.001$), 0.31 (95% CI 0.22 to 0.46; $P<0.001$) and 0.58 (95% CI 0.42 to 0.80; P=0.001), respectively; for GLU, the survival times were 2555.34±63.22, 2596.92±60.34, 2474.11±71.17 and 2546.56 ±67.77 days (P=0.29); the HR were 0.9 (95% CI 0.60 to 1.34; P=0.6), 0.84 (95% CI 0.84 to 1.26; P=0.4) and 1.19 (0.82 to 1.74; P=0.36). Excluding in-hospital deaths, similar patterns were obtained. (b) Adjusted models: from the 3 analyzed variables, only CR correlated significantly and independently with long-term mortality (HR=1.55 for the whole population, $P<0.001$, and HR=1.58 excluding in-hospital deaths, $P<0.001$). In conclusion, baseline creatinine was a better predictor of long-term mortality after acute myocardial infarction, relatively to creatinine clearance or glucose levels.

P544 Impact of admission blood glucose on outcome of non-diabetic patients with acute ST-elevation myocardial infarction: results from 5866 patients from the ACOS Registry

C. Naber[1], R.H. Metha[2], C. Juenger[3], R. Erbel[4], U. Zeymer[3], A. Gitt[3], J. Senges[3] on behalf of ACOS-Study Group. *[1]University of Essen, Cardiology Dept, Essen, Germany; [2]Durham, United States of America; [3]Ludwigshafen, Germany; [4]Essen, Germany*

Background: High glucose levels in patients with acute coronary syndromes (ACS) have been suggested to cause an adverse short-term outcome in diabetics and non-diabetics. However, the relationship of admission glucose to long-term outcomes has not been examined. Accordingly, we aimed to investigate if admission blood glucose levels impacted long-term outcomes of non-diabetic patients with ST-elevation myocardial infarction (STEMI).
Methods: Consecutive STEMI patients without diabetes were enrolled at 155 sites in the German Acute Coronary Syndromes (ACOS) Registry. Clinical endpoints of interest were long term mortality and composite of death, reinfarction, stroke or rehospitalization (MACCE). Patients were categorized into tertiles based on their admission blood glucose level.
Results: Of 5866 patients with STEMI, 36.9% had a blood glucose <120 mg/dl, 33.1% between 120 and 150 mg/dl, and 30.0% >150 mg/dl. Admission blood glucose was significantly related to increased risk of not only in-hospital events (death, adjusted OR >150 vs. <120 mg/dl: 2.86; 95%CI 2.13-3.82, $p<0.0001$ and MACCE (OR >150 vs. <120 mg/dl: 1.88; 95%CI 1.52-2.33; $p<0.0001$), but this increased risk persisted beyond the acute phase during long term follow up of at mean 380 days (death, adjusted OR >150 vs. <120 mg/dl: 1.11; 95%CI 0.79-1.56, p=0.08 and MACCE (OR >150 vs. <120 mg/dl: 1.46; 95%CI 1.04-2.03; $p<0.0001$) (Figure 1).

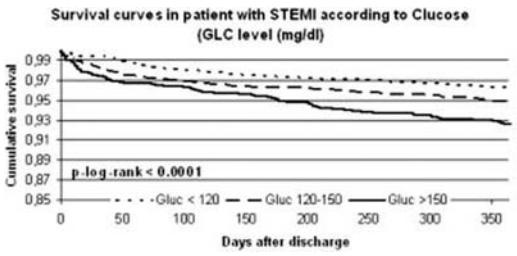


Figure 1

Conclusions: High blood glucose at admission to hospital is an independent predictor of not only short- but also long-term mortality in STEMI patients. Thus, admission glucose levels must be incorporated into the risk stratification of STEMI patients with STEMI and may potentially important target for therapy and risk modulation of these patients.

ACUTE CORONARY SYNDROME AND ARRHYTHMIAS

P545 Prediction of fatal or near-fatal ventricular tachyarrhythmias in patients with depressed left ventricular function after acute myocardial infarction: the CARISMA study

H.V. Huikuri[1], M.J.P. Raatikainen[1], R. Moerch Joergensen[2], J. Hartikainen[3], V. Virtanen[4], J. Boland[5], O. Anttonen[6], J. Rokkedal[7], M. Messier[8], P.E. Bloch Thomsen[4] on behalf of Carisma Investigators. *[1]University of Oulu, Cardiology, Oulu, Finland; [2]KAS Gentofte, Kardiologisk Afdeling, Hellerup, Denmark; [3]University Hospital Kuopio, Oulu, Kuopio, Finland; [4]University Hospital Tampere, Cardiology, Tampere, Finland; [5]CHR La Citadelle Liege, Cardiologie, Liege, Belgium; [6]Paijat-Hame Central Hospital - Lahti, Cardiology, Lahti, Finland; [7]Amtssygehuset i Glostrup, Medicinsk afdeling CF, Glostrup, Denmark; [8]Bakken Research Center-Medtronic, Clin.Outcomes Research and Biometry, Maastricht, Netherlands*

Background: Several risk markers have been proposed to identify patients at increased risk of cardiac death after an acute myocardial infarction (AMI). The CARISMA study investigated the ability of invasive and non-invasive tests, performed 6 weeks post-AMI, to predict a primary end-point defined as documented ventricular fibrillation (VF) or poorly tolerated sustained ventricular tachycardia (VT) adjudicated to be treatable with an implantable cardioverter-defibrillator (ICD).
Methods: 1393 of 5869 patients screened in the acute phase (3-21 days) of MI had an EF≤40%. Of these, 312 patients (mean age 65 years, EF 31±6%) consented to participate. A loop-recorder was implanted to document arrhythmic events over a 2-year follow-up. The following tests were performed at 6 weeks: 24-hour Holter, signal-averaged ECG (SAEG), T-wave Alternans (TWA) (exercise or pacing) and invasive EP testing.
Results: Over the average follow-up of 1.8 years there were 25 patients with a primary end-point (8%). Significant predictors of treatable VT/VF events were QRS-width by SAEG, several heart rate variability parameters, and inducible VT/VF at EP testing. Neither TWA nor nsVT on Holter were predictors. Combining heart rate variability and QRS-width in a linear model produces a risk criterion with a high hazard ratio and a high negative predictive value for treatable VT/VF events.

	Hazard ratio HR (95% range)	ROC AUC p-value	Sens %	Spec %	PPV %	NPV %
SDNN ≤ (1.53 x QRSwidth - 56) ms*	23.1 (3 to 175) p=0.002	0.80 p=0.0001	94	61	17	99
QRS width by SAEG >120 ms	4.5 (1.8 to 11.3) p=0.0015	0.70 p=0.005	44	85	20	95
SDNN <70 ms	4.3 (1.6 to 1.7) p=0.0037	0.68 p=0.01	35	90	21	95
Electrophysiology (EP): VT/VF inducible	3.9 (1.5 to 10.1) p=0.005		53	78	14	96
T-Wave Alternans: TWA (+/- paced): not negative	1.2 (0.4 to 3.3) p=0.71		60	51	8	95
Non Sustained VT (nsVT) by Holter	0.93 (0.6 to 1.4) p=0.72		25	85	11	94

AUC: Area Under the Receiving Operating Characteristics (ROC) Curve, *Parameters optimized and tested in the same patient population. Sens: Sensitivity. Spec: Specificity. PPV: Pos.Predictive Value. NPV: Neg.Predictive Value.

Conclusions: QRS width (by SAEG), heart rate variability and electrophysiological testing, at 6 weeks after an MI, are significant predictors of treatable VT/VF in patients with impaired EF. Combination of the non-invasive test results allows identification of a low risk group unlikely to benefit from ICD therapy during the 2 years after MI.

P546 Effect of 17beta-estradiol on ventricular susceptibility in post-infarcted rats

T.-M. Lee[1], M.S. Lin[2], N.C. Chang[3]. *[1]Chi-Mei Medical Center, Dept. of Int. Med., Cardiology Section, Tainan, Taiwan; [2]National Taiwan University and Hospital, Department of Pharmacy, Taipei, Taiwan; [3]Taipei Medical University and Hospital, Department of Medicine, Taipei, Taiwan*

17beta-estradiol (E2) has been shown to exert antiarrhythmic effect after myocardial infarction; however, the mechanisms remain unclear. This study was performed to determine whether E2 exerts beneficial effects through attenuated sympathetic hyperreinnervation after infarction. Two weeks after ovariectomy, age-matched female Wistar rats underwent one of three treatments: 1) subcutaneous vehicle treatment, 2) subcutaneous low E2 treatment (0.5 mg 17beta-estradiol pellet, similar physiological E2 levels) or 3) subcutaneous high E2 treatment (50 mg 17beta-estradiol pellet, supraphysiological levels). Two weeks later, rats were randomly assigned to coronary artery ligation or sham-operation and followed for 4 weeks. E2 status did not affect left ventricular function in sham rats. At 4 weeks after infarction, the impairment of left ventricular function was similar across in-

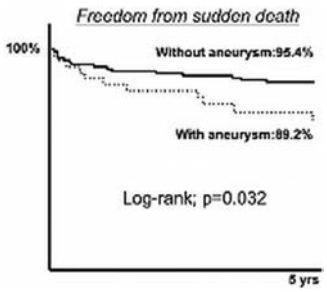
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

farcted groups, as measured by echocardiography and direct ventricular catheterization. Myocardial endothelin-1 levels in the remote zone revealed a significant elevation in vehicle-treated rats compared with sham-operated rats, which is consistent with increased activity of endothelin-1 after infarction. Sympathetic reinnervation was parallel to endothelin-1 levels. Sympathetic hyperinnervation was blunted after giving the rats E2 in a dose-dependent manner, assessed by immunohistochemical analysis of tyrosine hydroxylase, growth associated protein 43 and neurofilament, and Western blotting and real-time quantitative RT-PCR of nerve growth factor. Arrhythmic scores during programmed stimulation in E2-treated rats were significantly lower in a dose-dependent manner than in vehicle-treated rats. Our data indicated that E2 has an important role for the sympathetic reinnervation after infarction probably through an endothelin-1-depedent pathway.

P547 Long term freedom from sudden death in patients with left ventricular aneurysm after myocardial infarction

T. Yamada, M. Iwabuchi, H. Yokoi, H. Yasumoto, H. Nosaka, M. Nobuyoshi. *Kokura Memorial Hospital, Department of Cardiology, Kitakyushu, Japan*

Background: Left ventricular aneurysm after myocardial infarction indicate less or no viability of myocardium and might have electorical substrate that cause ventricular tachy-arrythmia.
Method and result: Percutaneous coronary revascularization were performed in 557 pts with low ejection fraction(below 40%) and they were divided into two groups: patients with left ventricular aneurysm (group A: n=102) and without aneurysm (group NA: n=455). Age (A/NA: 62.4/64.4 p=0.0954), male gender (A/NA: 74%/80% p=0.1483) were similar in two groups. Diabetes (A/NA: 32%/33% p=0.8714), renal insufficiency (A/NA: 14%/10% p=0.153), multi-vessel disease (A/NA: 73%/76% p=0.4588) and complete revascularization rate (A/NA: 35%/41% p=0.1483) were also similar, but ejection fraction were lower in A group (23%/29% p<0.0001). Five year freedom from all-cause death in Kaplan-Meier method were similar between two groups (A/NA: 78%/81% p=0.5565) but lower ejection fraction (below 30%) significantly correlated with long-term mortality (below/above: 79%/86% p=0.0327). However five years freedom from sudden death were significantly lower in A group (A/NA: 89%/95% p=0.032), but lower ejection fraction were independent of sudden death (below/above: 96%/93% p=0.8007).



Kaplan Meier

Conclusion: 1) Left ventricular aneurysm related myocardial infarction might predict higher frequency of sudden death in patients with reduced cardiac function for long-term follow-up. 2) Though lower ejection fraction were independent of sudden death, correlated with long-term all-cause death rate.

P548 Prognostic impact of discharge heart rate after acute myocardial infarction according to use of beta-blockers: data from the French FAST-MI registry

R. Geha[1], P. Gueret[2], N. Meneveau[3], H. Eltchaninoff[4], P. Asseman[5], D. Vilarem[6], G. Mulak[7], T. Simon[1], J.P. Cambou[1], N. Danchin[1] on behalf of FAST-MI investigators. *[1]HEGP, Cardiology, Paris, France; [2]CHU Mondor, Cardiology, Creteil, France; [3]CHU Besancon, Cardiology, Besancon, France; [4]CHU Rouen, Cardiology, Rouen, France; [5]CHU Lille, Cardiology, Lille, France; [6]Valenciennes, France; [7]Paris, France*

Background: Admission heart rate (HR) is a recognised prognostic indicator at the acute stage of MI. Little information is available as regards the prognostic role of discharge HR.
Aim: to assess the impact of discharge HR on 6-month mortality in hospital survivors of AMI, according to use of beta-blockers.
Methods: The FAST-MI registry included consecutive patients admitted for ST-elevation (STEMI) or non-ST elevation myocardial infarction <48 hours of symptom onset, in 223 French intensive care units over 1 month from October 2005. In all, 3059 patients were recruited, of whom 2557 were discharged alive and had discharge HR recorded. Six-month follow-up of mortality was 99% complete.
Results: Using multivariate regression analysis, factors increasing the risk of being in the upper quartile of discharge HR (Q4) were: lack of beta-blocker at discharge (p<0.001), increased admission HR (p<0.001), female sex (p<0.001), prescription of diuretics at discharge (p<0.001), use of transfusion during hospital stay (p=0.001), ST-elevation MI (p<0.01), history of angina before MI (p<0.05) and history of COPD (p<0.05). 6-month mortality was 3.6%, 5.6% and 7.6% respectively for the first, second and third, and fourth (Q4) quartiles of discharge HR (p=0.007). There was no interaction between the prognostic impact of HR and prescription of beta-blockers at discharge: increased discharge HR was associated with poorer survival in both patients with or without beta-blockers (6-month mortality: 6.4, 10.0 and 14.3% respectively in patients without beta-blockers, and 2.7, 4.0 and 5.1% respectively in patients with beta-blockers). Using Cox multivariate analysis, increasing HR at discharge was an independent predictor of 6-month mortality (for each 1bpm increment of HR, OR 1.01; 95% CI: 1.00-1.03, p<0.04), along with age, diabetes mellitus, history of MI, renal failure, previous use of digoxin, higher Killip class, anterior STEMI, lower systolic BP on admission, lack of use of angioplasty during hospital stay, lack of use of antiplatelet agents and use of diuretics at discharge. Prescription of beta-blockers at discharge was associated with a strong trend for improved 6-month survival (OR 0.79; 95% CI: 0.50-1.03, p=0.07). When discharge HR was removed from the model, prescription of beta-blockers at discharge became highly significant (OR: 0.61, p=0.004).
Conclusion: higher HR at discharge in patients with AMI is an independent predictor of 6-month mortality. The favourable effect of beta-blockers appears largely mediated by their impact on HR.

P549 Pre-discharge heart rate measured by 24H Holter monitoring and long term survival after acute myocardial infarction. Data from the RICO survey

D. Moreau[1], D. Potard[1], L. Mock[2], I. L'huillier[1], M. Vincent Martin[3], P. Sicard[4], Y. Laurent[5], H. Makki[6], M. Zeller[6], Y. Cottin[4] on behalf of RICO Survey Working Group. *[1]CHU, Cardiology service, Dijon, France; [2]Clinique, Cardiology service, Fontaine Les Dijon, France; [3]CH, Cardiology service, Beaune, France; [4]LPPCE IFR sante STIC, RI, Dijon, France; [5]CH, Cardiology service, Semur En Auxois, France; [6]CH, Cardiology service, Chatillon Sur Seine, France*

Objective: Recent findings demonstrated the strong association between resting heart rate (HR) and sudden cardiac death in middle-aged men at long term follow-up, reflecting the relationship of autonomic tone with CV events. From a current myocardial infarction (MI) registry, we aimed to evaluate the predictive value of HR assessed from 24H Holter monitoring for future mortality in survivors of MI.
Patients: Data from consecutive MI patients survivors of acute MI and who benefited from 24H Holter monitoring obtained at hospital discharge were analysed. Baseline characteristics, treatments and Left ventricular ejection fraction (LVEF) were determined by echocardiography at 3±1 day. Patients were followed up at one year for all-cause deaths.
Results: Among the 703 patients included in the analysis, 28% were female, age 64(52-76) y, with mean (IR) HR values at 65(59-72) bpm. 80% were under beta blocker therapy at hospital discharge. At 1 year follow-up, 53(8%) patients died. Age, LVEF and HR were univariate predictors of survival. Calculation of ROC curves for the best dichotomy value of HR revealed a cut-off value of 68, resulting in a relative risk of 2.46(95%CI:1.40-4.34, p=0.002). Backward logistic regression analysis revealed LVEF (chi-square: 8.58, p=0.003), age (chi-square: 17.55, p<0.0001), and HR (chi-square: 12.67, p=0.0004) as independent prognostic factors associated with survival.
Conclusion: The present study reveals that in survivors of an acute MI, increased HR on pre-discharge 24H holter monitoring above 68 bpm yields predictive power for subsequent long-term mortality. This simple and feasible parameter provides useful risk stratification at hospital discharge, beyond other traditional prognostic factors and suggest the interest for optimising bradychardic therapies.

ACUTE MYOCARDIAL INFARCTION

P550 Prognostic value of the intensity of cellular inflammation and coronary microcirculation by myocardial contrast echocardiography post acute coronary syndrome

J. Azevedo, J. Abecasis, L.C. Bronze Carvalho, J. Monge, J. Galvao, J. Coucello, H. Custodio, I. Arroja, A. Aleixo, J. Silva. *Hospital Francisco Xavier, Cardiology, Lisbon, Portugal*

Background: Myocardial contrast echocardiography (MCE) has the capacity to assess the reduction of coronary microcirculation blood flow and the area at risk pos acute coronary syndrome (ACS), and its left ventricular (LV) segmental and spatial distribution can be related with the degree of the cellular inflammatory process. Aim: to evaluate the relationship between the intensity of the cell inflammatory process, LV segmental MCE and global LV function post ACS, in a long term follow-up.
Material and methods: We studied 34 ACS pts, 56% male gender, by MCE between day 1 (D1) and 3 (D3) post ACS. In each case, we evaluated the serum levels of high sensitivity C-reactive protein (hs-CRP-mg/ml) and monocyte cell membrane receptors CD4 and CD40 (n/mm^3), and to establish the absolute and % variation (Δ) of these values between D3/D1 as an index of the time changes intensity of the myocardial cell and capillary inflammation post ACS. The intensity of the cellular inflammatory process was established in 3 grades, according to Δ<25%, 25-50% and >50%. MCE study was performed at D3 post ACS using

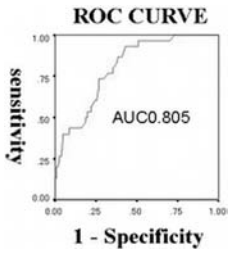
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

a 2nd generation ultrasound contrast agent (SonoVue®, Bracco, Italy) during a 3 min iv continuous infusion. The LV % ejection fraction (LV%EF-%) and its variation (Δ) was estimated at D3 and 6th month post ACS, the MCE patterns were classified as normal flow (P0), late filling (P1), heterogeneous (P2) and and no flow (P4), its mean value/pt and LV segmental perfusion index (SPI) were also calculated.
Results: Direct correlations were obtained between individual SPI and hs-CRP (r=0.40; p=0.01), ΔCD40 (r=0.47; p=0.01), LV %EF at D3 (r=0.36; p=0.03) and 6th months (r=0.48; p=0.01) post ACS. Direct correlations were also obtained between hs-CRP and certain MCE patterns, such as P1 (r=0.37; p=0.01) and P2 (r=0.53; p<0.01) and between ΔLV%EF and P1 (r=0.34; p=0.04) and P2 (r=0.41; p=0.02).
Conclusions: We obtained a direct relationship between the intensity of the cell inflammatory process post ACS based on certain serum markers, and the MCE perfusion patterns, factors that were related with some prognostic indicators such as the LV global funtion at 6 months post ACS.

P551 Efficacy of myocardial contrast echocardiography in predicting adverse cardiac event after reperfused myocardial infarction

S. Hosokawa, Y. Hiasa, S. Miyazaki, R. Ogura, N. Suzuki, T. Takahashi, K. Kishi. *Tokushima Red Cross Hospital, Cardiology Division, Komatsushima, Japan*

Background: In patients with acute myocardial infarction (AMI), myocardial contrast echocardiography (MCE) provide incremental prognostic information by qualitative analysis.
Objective: To determine whether MCE predicts adverse cardiac event by quantitative analysis.
Method: 284 patients with reperfused anterior AMI were included. Intravenous MCE was performed with a Sonos5500 instrument using levovist at two weeks after PCI. Contrast defect was calculated as contrast defect area/myocardial area. All patients were followed for 3.55±0.7 years, and major adverse cardiac events (MACE: death, re-hospitalization caused by heart failure) were found in 28 patients(10%). All patients were divided three groups by size of contrast defect: group1 (0-10%), group2 (11-20%), group3 (>21%).
Results: The mean age was 64 years and 74% were men. MACE were occurred 2.1% (2/96) in group1, 9.7% (12/124) in group2 and 21.9% (14/64) in group3 (p<0.001, respectively). Multivariate logistic analysis demonstrated that contrast defect area (p<0.001) is an independent predictor of MACE. ROC curve analysis demonstrated that contrast defect area>15% predicted MACE with sensitivity and specificity of 78% and 72% (AUC=0.805).

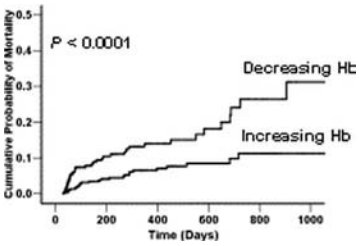


Conclusion: Quantitative analysis of MCE is useful for the objective estimation of clinical outcome.

P552 Prevalence and prognostic significance of persistent anemia after acute myocardial infarction

T. Hasin, A. Sorkin, Y. Agmon, A. Suleiman, M. Blich, M. Kapeliovich, M. Beyar, W. Markiewicz, H. Hammerman, D. Aronson. *Rambam Medical Center, Haifa, Israel*

Background: Recent studies have shown that anemia occurring during an acute myocardial infarction (AMI) is an independent indicator of mortality. Anemia may be viewed as a transient phenomenon, secondary to antithrombotic agents and invasive procedures. However, anaemia might worsen or fail to improve after hospital discharge.
Methods: We studied 828 pts with AMI who survived the acute event. Hemoglobin (Hb) levels were obtained at hospital discharge and >1 month post discharge (median 7 month). The relationship between post-discharge Hb and the primary endpoints of all-cause mortality were evaluated using Cox models, adjusting for age, gender, creatinine, previous infarction, diabetes, hypertension, smoking, anterior infarction, coronary revascularization, Killip class at admission, pre-discharge Hb and pre-discharge ejection fraction.
Results: Using the WHO definition (Hb < 13 g/dL in men and < 12 g/dL in women), anemia was present in 295 pts at hospital discharge (36.8%). At follow up, anemia was present in 141 (47.8%) and 88 (17.0%) pts with and without anemia at hospital discharge, respectively. During a median follow up of 12 months (range 2 to 26) after the post-discharge Hb measurements, 67 patients died (8.1%). In a multivariable Cox regression model, the adjusted HR was 1.5 for each 1 gr/dL decrease in post discharge Hb (95% CI 1.3-1.8, P < 0.0001). In a similar model, the HR for mortality in pts with decreasing Hb after hospital discharge was 2.5 (95% CI 1.4-4.4, P = 0.001) compared with pts with increasing Hb level (Figure).



Survival According to Hb Change

Conclusion: Pts after AMI who are discharged with anemia frequently fail to increase their Hb levels. Persistent or worsening anemia after AMI is associated with markedly increased risk for mortality.

P553 Prognosis after acute myocardial infarction in patients with prior coronary artery bypass surgery; 19-year experience

P.M. Mitrovic, B. Stefanovic, V. Vukcevic, N. Radovanovic, M. Radovanovic, D. Rajic, G. Matic, Z. Vasiljevic. *Institute for CVD, Clinical Center of Serbia, Clinical Center of Serbia, Beograd, Serbia*

The prognosis of patients (pts) after coronary artery bypass surgery (CABS) has been noted in many studies, but only few studies analyzed prognosis of pts with acute myocardial infarction (AMI) after prior CABS. The aim of this study was to present early and late prognosis of pts with AMI and prior CABS. The study population consisted of 748 pts with AMI after prior CABS (post bypass group) and control group of 1080 pts with AMI and without prior CABS, who were followed from April 1988 to January 2007. At baseline post bypass group was slightly younger (p=0.0316), with more men (p=0.0001) and with more pts with previous angina (p=0.0336) and previous AMI (p=0.0001). Control group of pts had more hypertensives (p=0.0182), smokers (p=0.0002) and heredians (p=0.0001). Post bypass group had in prior therapy more beta-blockers (p=0.0001) and anticoagulants (p=0.0001). Other baselines characteristics were similar in both groups of patients. Indexes of infarct size were lower in post bypass group (p=0.0001). There were more VF (p=0.0106) in post bypass group and AV block rhythm disturbances (p=0.0039) in control group of pts. In-hospital mortality was similar (p=0.3675). Approximately 9 years after discharge, post bypass pts had more new coronary events (p=0.0001), heart failure (p=0.0159), recurrent CABS (p=0.0001), reinfarction (p=0.0001) and unstable angina (p=0.0014) than did control pts. Cumulative mortality was better in control group than in post bypass group (p=0.0403). Multivariate proportional hazards analysis showed that previous angina (p=0.0005), diabetes (p=0.0058) and age (p=0.0102) were undependable prediction factors for survival. Use of digitalis and diuretics, together with previous angina influenced on survival too (p=0.0092) as well as male gender, older pts and diabetes together (p=0.0420).
Conclusions: Patients with AMI after prior CABS had smaller infarct, but more reinfarction, reoperation, heart failure and angina. Previous angina, diabetes and age undependable as well as use of digitalis, diuretic and angina together and male gender, older pts and diabetes together, influenced worse survival in post bypass group of pts.

P554 Improvement of long-term outcome of survivors after a first myocardial infarction documented by an epidemiological survey (MONICA-BELLUX)

E.S. Schroeder[1], J.F. Fils[2], S. Swales[2], B. Masuy[2], M. Mouchard[2], M. Jeanjean[2]. *[1]Cliniques Universitaires De Mont-Godinne, Service De Cardiologie, Yvoir, Belgium; [2]UCL, Institute of Statistics, Louvain-La-Neuve, Belgium*

Aim: To assess the predictive factors of long-term outcome of survival after a first myocardial infarction (MI), we followed 3.120 victims of a first MI (surviving at 28 days) within the WHO-MONICA registry of the Belgian province of Luxembourg (target population: age: 25-74 yrs; n=142.344 in 2003).
Methods: Patients were enrolled between 1.1.1985 and 31.12.2002. The baseline characteristics were: mean age was 60±4; female gender: 24.2%; diabetes: 7.5%, typical myocardial infarction (NF1 according to the MONICA criteria): 78.3%, thrombolysis at hospital admission: 38%; subsequent coronary angiography: 69%; subsequent myocardial revascularization: PTCA in 25% and CABG in 10.2%; late inclusion period (1991-2002): 60.8%. The survival status was assessed in all patients on Dec. 31st, 2003. During the follow-up, cardiac death (F1, F2, F9 according to the WHO-MONICA criteria) occurred in 9.5%, non cardiac death in 6%.
Results: Multivariate analysis on the following items was performed: date of occurrence of the index myocardial infarction, age, gender, site of hospital admis-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

sion, type of therapeutic/diagnostic approach (thrombolysis, coronary angiography, PTCA, CABG, ...), type of myocardial infarction (NF2 vs NF1: possible versus typical) and diabetes.
Four variables predicted outcome: diabetes (HR 2.48), age (per year: HR 1.02), possible MI (NF2 vs NF: HR 0.62) and late inclusion (1991-2002 vs 1985-1990: HR 0.58).
Adjusted cardiac survival at 5 years was 93.8% for the patients victims of MI between 1981-2002, in comparison to 90.2% for the patients included between 1985-1990 ($p < 0.001$).
Conclusions: Gender and treatment approach did not affect the long-term prognosis in our study population. According to the literature, the negative impact of older age, diabetes and the extend of myocardial infarction was confirmed.
We report – for the first time to our knowledge – an improvement of long-term outcome (survival) over a time period (1985-2002) in routine clinical practice, confirming the efficacy of secondary preventive interventions in a non-selected population.

P555 Chronic exposure to second hand smoke and 30-day prognosis of hospitalised patients with acute coronary syndromes: the GREECS study

D. Panagiotakos[1], C. Pitsavos[1], E. Tsiamis[1], Y. Mantas[2], P. Stravopodis[3], G. Giannopoulos[1], S. Zombolos[4], Y. Koyias[5], N. Daskalopoulos[2], C. Stefanadis[2]. *[1]Athens, Greece; [2]Halkida, Greece; [3]Zakynthos, Greece; [4]Kalamata, Greece; [5]Karditsa, Greece*

Objective: In this work we sought to investigate the association between chronic exposure to second hand smoke (SHS) and the short-term prognosis of hospitalized patients with acute coronary syndromes.
Methods: Between October 1, 2003 and September 30, 2004 we enrolled 2172 consecutive patients with acute coronary syndromes that entered in the cardiology clinics or the emergency units of six major hospitals, in Greece. Exposure to SHS was measured through a questionnaire administrated during a specific interview, after the second day of the hospitalisation. The main outcome of interest was the 30-day status of these patients (death, or re-hospitalization due to coronary heart disease).
Results: 1003 (46%) of the patients were exposed to SHS. Patients reporting exposure to SHS had 61% (95% confidence interval, 14% to 118%) higher risk of having an event during the first 30-day following hospitalization as compared to patients who were not exposed to SHS, after taking into account the effect of several potential confounders. A dose-response linear relationship was observed between the risk of having re-current events and the years of exposure to SHS ($rho = 0.17$, $p < 0.001$).
Conclusions: Exposure to SHS increases significantly the risk of re-current events in patients who had survived a cardiac event.

COMBINED STROKE/PERIPHERAL CIRCULATION

P556 Intraarterial and intramuscular autologous stem cell transplantation in patients with severe chronic limb ischemia

T. Bartsch, T. Zeus, M. Brehm, B.E. Strauer. *University of Duesseldorf, Department of Internal Medicine, Duesseldorf, Germany*

Background: Therapeutical benefit of intramuscular as well as intraarterial transplantation of autologous bone marrow stem cells (BMCs) in patients with chronic limb ischemia had been shown in the past. This study analyzed the effects of a combined intraarterial and intramuscular transplantation with a follow up time of up to 13 months.
Methods: In transplantation group we recruted 12 patients (age 69 ±7 years) with chronic ischemic limbs because of peripheral arterial disease, Fontaine stage II or less. Bone marrow was harvested from the hip and mononuclear cells were separated. The cell suspension was transplanted intramuscular (5 ml into the thigh and 5 ml into the lower leg) and intraarterial (10 ml into the femoral artery) into in the ischemic limb. First follow-up examination was performed after 2 months, second after 13 months.
The control group consists of patients, who were exclusive conservatively treated. The follow up time of the this group was 4 months.
Findings
After 2 months patients of the transplantation group had a significantly increased pain free walking distance (from136±85 meters to 496± 641 meters, p=0,002). Furthermore the ankle brachial index was significantly improved at rest (before 0,7±0,2 and after transplantation 0,8± 0,2, p=0,005) and after stress (from 0,6±0,2 to 0,8±0,2, p=0,008). Similar improvements documented the capillary-venous oxygen-saturation (thigh: from 59% ±9% to 67% ±4%, p=0,006, lower leg: from 56% ± 14% to 64% ±6%, p=0,028) and the venous occlusion plethysmography at rest (from 2,1±0,7 to 2,6±0,7ml/100ml tissue/min, p=0,011), reactive hyperemia (from 6,7±2,9 to 9,8±2,2 ml/100ml tissue/min, p=0,003) and peak flow (from 7,1±3,2 to 10,7±2,9 ml/100ml tissue/min, p=0,003). All these parameters stayed alike after the follow-up time of 13 months, no significant decrease could be seen. No side effects or complications were monitored. In contrast, in the control group all perfusion parameters and maximal walking distance decreased slightly during time of monitoring.
Conclusion: These results demonstrate, that combined intraarterial and intramuscular transplantation of autologous, mononuclear bone marrow stem cells is a clinical feasible and minimal invasive therapeutic option for patients with severe chronic limb ischemia. It leads to a significant improvement of perfusion indices. Positive effects could already be detected 2 months after transplantation and persisted during follow up time of 1 year.

P557 Assessment of renal artery stenosis: side-by-side comparison of angiography, duplex ultrasound and MRI with pressure gradient measurements

G. Sarno[1], B. Drieghe[1], P. Vanhoenacker[2], I. Decramer[2], T. Cuisset[1], J. Bartunek[1], G. Heyndrickx[1], B. De Bruyne[1]. *[1]Cardiovascular Center Aalst, Belgium; [2]Radiology Department Olv-Z, Aalst, Belgium*

Purpose: A ratio of distal renal pressure to aortic pressure (P_d/P_a) < 0.90 is associated with an increased renin production and, therefore, this value could be considered a threshold for defining a significant renal artery stenosis (RAS). The aim of this study was to compare side by side quantitative renal angiography (QRA), colour duplex ultrasound (CDUS) and quantitative renal MRI to transstenotic pressure measurements (P_d/P_a) in RAS assessment.
Methods: Fifty-six RAS in 47 patients were evaluated by angiography and CDUS. Angiography-derived percent diameter stenosis (DS_{angio}%) minimal luminal diameter (MLD, mm), Doppler-derived peak systolic velocity (PSV, cm.s-1), end-diastolic velocity (EDV, cm.s-1) and renal-to-aortic ratio (RAR) were obtained. Among these patients 20 RAS were evaluated also by MRI and a quantitative MRI-derived percent diameter stenosis (DS_{mri}%) was obtained. These parameters were compared to transstenotic pressure measurements obtained with a guiding catheter (aortic pressure, P_a) and pressure wire (distal renal pressure, P_d) prior to renal angioplasty. A P_d/P_a value <0.90 defined a hemodynamically significant RAS.
Results: P_d/P_a correlated with both angiography- and CDUS-derived parameters. The best correlation was observed with RAR ($r=-0.69$, $p<0.001$). There was no correlation with the DS_{mri} % ($r=-0.17$, p=0,5).To identify stenosis associated with a P_d/P_a < 0.90, the diagnostic accuracy of DS_{angio} >50%, MLD<2 mm, PSV>180 cm.s-1, EDV>90 cm.s-1, RAR>3.5 and DS_{mri} >50% were respectively 64%, 79%, 46%, 79%, 80% and 60%. Yet, for all parameters there was a high proportion of false positives (34%, 13%, 54%, 9%, 14% and 15%, respectively).
Conclusions: Conventional renal angiography, CDUS and the renal MRI overestimate the actual severity of RAS. This "overdiagnosis" is likely the main cause of the disappointing results of renal angioplasty for renovascular hypertension.

P559 Irbesartan improves erectile dysfunction in ApoE-KO-mice and cardiovascular high-risk patients

M. Baumhaekel[1], N. Schlimmer[1], F. Muenzel[2], M. Boehm[2]. *[1]University Hospital of the Saarland, Cardiology, Homburg, Germany; [2]Bristol-Myers Squibb, Munich, Germany*

Background: Erectile dysfunction (ED) is associated with cardiovascular risk factors and the related endothelial dysfunction. The AT-1-antagonist irbesartan was demonstrated to improve endothelial function in cardiovascular high-risk patients. Therefore, improvemnt of ED by treatment with irbesartan is likely.
Methods: Patients with metabolic syndrome from the DO-IT-trial (n=1069) were treated either with irbesartan (150/300mg) or the combination with a hydrochlorothiazide (HTC, 12.5mg) for six months. Evaluation of ED was performed with two validated questionnaires at baseline and after three/six months (KEED; IIEF). The ApoE-KO-mouse, was used as a model of generalized atherosclerosis. Mice were treated with cholesterol-rich-diet for 7 weeks. Animals were additionaly fed with irbesartan (50mg/kg), hydralazine (250mg/l) or placebo. WT mice served as a control. Endothelial function was measured in aortic rings, erectile function in corpora cavernosa in an organ bath chamber under physiological conditions.
Results: Treatment with irbesartan decreased prevalence of erectile dysfunction significantly (58.3% to 38.5%, p<0.0001) and improved erectile function (p<0.0001) independent on additional treatment with a diuretic. In multivariable analysis, body mass index, HbA1c-concentration, diastolic blood pressure, heart rate, waist circumference and present heart failure could be detected as independent predictors of change in erectile function in patients with a metabolic syndrome. In ApoE-KO mice, irbesartan and hydralazine decreased systolic blood pressure significantly compared to WT- or placebo-mice (p<0.01). Erectile function as well as endothelial function increased significantly in animals treated with irbesartan (n=20) compared to hydralazine- (n=19, p<0.05) or placebo-treated mice (n=20, p<0.01) and was raised to the WT-mice level.
Conclusion: Treatment with irbesartan or irbesartan/HTC improved erectile function in cardiovascular high-risk patients. The independent predictors for these beneficial effects as well as the evidence for endothelial related effects indicate the outstanding role of AT-1-antagonists in the treatment of cardiovascular high-risk patients, even in terms of erectile function.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P560 Functional improvement associated with inflammatory response down-regulation in PAD patients treated with trimetazidine

A. Buzin[1], N. Sharkova[2], A. Obukhov[3], A. Baranov[3], M. Bocharova[3], D. Obukhov[4]. *[1]Russian State Medical University, Propedeutics of internal diseases, Moscow, Russian Federation; [2]Moscow State Medical and Dentistry University, Propedeutics of internal diseases, Moscow, Russian Federation; [3]Moscow State University, Therapy, Moscow, Russian Federation; [4]Moscow, Russian Federation*

Background and objectives: Peripheral artery disease (PAD) is one of the cardinal manifestation of systemic atherosclerosis and remains one of the most actual problems in the modern angiology due to high prevalence and being underestimated. The purpose of the study was to evaluate antioxidant serum state, anti-inflammatory effect and clinical outcomes in patients with peripheral artery disease (PAD) treated with standard dose of trimetazidine MR for 6 months.
Patients and methods: 68 male patients mean age 64.3±3.5 years with PAD (mean baseline ankle-brachial index (ABI) 0.75±0.06) were enrolled into open-label parallel-group randomized study. Baseline procedures included treadmill test (according to graded Gardner-Skinner protocol) with pain-free walking distance (PFWD) and maximum walking distance (MWD) recording. Inflammatory serum activity was evaluated by high sensitive C-reactive protein levels (hs-CRP). Endothelial function assessed by serum concentration of soluble vascular call adhesion molecule (sVCAM-1). Antioxidant serum state was estimated by parameters of induced serum flow chemiluminescence measured with certified photocolorimeter. 38 patients randomized into the active treatment group received standard dose of modified release trimetazidine (MR trimetazidine) 35 mg twice a day for 6 months. Another group of 30 patients did not received active treatment and served as control group. On completion of treatment period the examination and tests were repeated.
Results: Clinical response was found to be beneficial in group treated by MR trimetazidine, showing the significant improvement of treadmill test results (increase of PFWD up to 193.0±21.3 m vs. baseline 82.5±22.0 m and MWD up to 372.8±20.5 m vs. baseline 120±19.7 m, $p<0.01$), and control group walking performance did not change significantly. However, ABI was found unchanged in both groups. sVCAM-1 level in MR trimetazidine group decreased by 34.2% ($p<0.01$), and in control group – insignificantly by 2.3%. Significantly elevated baseline hs-CRP levels in active treatment group returned within reference range while minimal trend in control group was not significant. Serum antioxidant status improvement was found in MR trimetazidine group during the study.
Conclusion: Study results show that treatment with MR trimetazidine lead to significant improvement in functional condition of patients with PAD. This can also be described with shown positive changes in antioxidant, anti-inflammatory serum status and endothelial function in PAD patients.

P561 Incidence of renal artery stenosis in diabetic patients undergoing coronary angiography

H. Joshi, S. Dani, J. Prajapati, S. Jain, S. Thanvi, K. Sharma, S. Ghosh, J. Shah, H. Shah, T. Madan on behalf of CVHF. *U.N.Mehta Institute of Cardiology, Cardiology, Ahmedabad, India*

Objective: India is the country which has maximum number of diabetic patients and diabetes is a risk factor for both coronary artery disease & renal artery stenosis (RAS). So this study is to find out incidence of RAS in Diabetic Patients.
Methodology: At our centre we routinely perform renal angio with coronary angiography. We had selected diabetic patients which were having indications for coronary angiography (CAG) according to ACC/AHA guidelines. CAG along with screening renal angiography was done in all these patients.
Results: Total 156 diabetic patients had undergone CAG & Renal Angio. Out of these, 108 patients (69.2%) were having well controlled Diabetes Mellitus (DM) with mean HbA1c level 6.8 (±3) & patients (30.7%) were with uncontrolled DM with mean HbA1c level 8.4 (±4). 120 (76.9%) patients were hypertensive out of which 58 (48.3%) patients were with controlled hypertension & 62 (51.6%) with poorly controlled hypertension. Out of 156 patients 37 patients (23.7%) had renal artery involvement, 21 patients (13.4%) was detected to have significant RAS (> 50% lumen compromised). Out of 21 patients 2 (9%) patients were having bilateral RAS, 15 patients (71.4%) have uncontrolled DM & 6 patients (28.5%) have well controlled DM. 14 (66.6%) patients out of 21 were with uncontrolled hypertension and 7 (33.3%) patients with controlled hypertension. Another 16 patients out of 156 (10.2%) had insignificant RAS (< 50% lumen compromised) of which 11 patients (68.7%) have uncontrolled DM and 5 patients (31.2%) have well controlled DM. 9 (56.2%) out of 16 were have been poorly controlled hypertension and 7 (43.7%) patients were having well controlled hypertension.
Conclusion: Renal artery stenosis is more common in diabetic patients with uncontrolled DM than well controlled DM & overall incidence of RAS in Diabetic Patients is 23.7%. It reflects that early effective detection & management of this problem might prevent deterioration of renal function for which diabetic patients are already prone.

P562 Beta-receptor-blocker improve erectile function in atherosclerotic ApoE-Knockout mice

M. Baumhaekel, N. Schlimmer, D. Arifi, M. Boehm. *University Hospital of the Saarland, Cardiology, Homburg, Germany*

Background: Erectile dysfunction (ED) is a major problem in elderly men. Especially patients with cardiovascular diseases suffer from erectile dysfunction due to the association of cardiovascular risk factors and ED. Hence, drugs used in treatment of cardiovascular diseases, especially β-blockers, are likely to have negative influence on erectile function in men. Therefore, the effect of treatment with different β-blockers were evaluated in atherosclerotic ApoE-KO-mice.
Methods: ApoE-Knockout mice were fed with cholesterol-rich diet (21% fat, 19.5% casein and 1.25% cholesterol) for 7 weeks to induce atherosclerosis. Mice were additionaly treated with nebivolol (10mg/kg), metoprolol (90mg/kg) or carvedilol (30mg/kg). WT mice treated with cholesterol-rich diet were used as control. Endothelial function was measured in aortic rings, erectile function in corpora cavernosa (CCS) in an organ bath chamber under physiological conditions (pH 7.4, 37°C). Tissues were precontracted with phenylephrine. Relaxation was measured after addition of carbachol (endothelial dependent) and nitroglycerin (endothelial independent).
Results: Serum cholesterol concentrations were significantly increased in all ApoE-KO mice ($p<0.001$). Heart rate was significantly decreased ($p<0.01$) in mice treated with nebivolol (549+9 bpm) and carvedilol (560+10 bpm) compared to ApoE-placebo (612+10 bpm) or WT (626+18 bpm). Treatment with metoprolol-succinate did not lead to a significant reduction in heart rate (600+14 bpm). Systolic blood pressure was not different in all groups (n.s.). Endothelium dependent relaxation of CCS to carbachol was significantly decreased in ApoE-KO-mice compared to WT mice ($p<0.01$). Treatment with β-blockers increased relaxation to carbachol ($p<0.05$) with a trend to nebivolol for best improvement. In contrast, endothelial function of aortic rings was improved in nebivolol treated mice only ($p<0.05$). Treatment with metoprolol or carvedilol did not affect endothelial dependent relaxation to carbachol (n.s. vs. ApoE). Endothelium independent relaxation was not significantly different between all groups in CCS and aortic rings (n.s.).
Conclusion: Treatment with β-blockers does not decrease erectile function in atherosclerotic ApoE-KO-mice. In contrast, nebivolol, metoprolol and carvedilol improve erectile function significantly. Endothelial function in aortic rings was demonstrated to be increased in nebivolol treated mice only. Thus, especially nebivolol seems to restore endothelial function with a possible impact on erectile function in the model of atherosclerotic mice.

P563 Intensive risk factor control reduces cardiovascular events in patients with peripheral vascular disease

M. Lafitte[1], X. Pillois[2], V. Richeboeuf[1], C. Boulon[1], J. Bonnet[1], T. Couffinhal[1]. *[1]CHU Haut Leveque, Service De Cardiologie, Pessac, France; [2]Inserm U828, Pessac, France*

Background: Peripheral vascular disease (PVD) is associated with a high risk of events after an acute coronary syndrome (ACS). The effect of optimal control of atherosclerosis risk factors has not been established in these patients. Aim: To compare the prognosis of post-ACS patients with and without associated peripheral vascular disease. We hypothesized that optimal secondary prevention treatment and risk factor reduction would improve the prognosis of PVD patients as well as non PVD after ACS.
Patients and methods: 787 consecutive patients benefited from a 2 days hospitalization 3 months after an ACS focused on evaluating risk factors and atherosclerosis lesions, and on optimizing treatment and education. We compared the impact of our intensive management on long-term risk factors, drug observance and clinical outcomes in three groups (1) group 1 with Coronary Artery Disease (CAD) alone (n=598, 76%), (2) group 2 with CAD and one-bed PVD (peripheral arterial disease (PAD) defined by abnormal Ankle Brachial Index (ABI) 1.4 or Carotid Stenosis (CS) detected by ultrasound examination (n=171; 21.7%)), (3) group 3 with CAD and 2-beds PVD (PAD and CS) (n=18; 2.3%).
Results: At a median follow-up of 18 months, all groups reached recommended secondary prevention goals in term of lipids, blood pressure, glycemia and showed no significant difference in drug prescription and risk profile. However, group 3 remained at higher risk of total cardiovascular events than group 1 despite optimal management of risk factors, but a single-bed PVD (group 2) was not significantly associated with CV events at 18 months. Diabetes mellitus (DM), metabolic syndrome, creatinin and hypertension were greater in PVD patients (group 2 and 3) with an event than without. Patients with PVD and associated DM remained at higher risk for CV events (HR 4.64; 95%CI 1.63-13.24) than PVD patients without DM (HR 1.17; 95%CI 0.60-2.29), or diabetics without PVD (HR 0.56; 95%CI 0.22-1.46).
Conclusion: Optimization of secondary prevention treatment after an ACS improves prognosis of PVD patients without DM, but a poorer outcome remains in patients with PVD and DM.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P564 Effects of L-arginine (the substrate of eNOS) administration improves endothelial function and arterial stiffness in healthy smokers

G. Siasos, D. Tousoulis, C. Vlachopoulos, N. Ioakimidis, K. Zisimos, C. Antoniades, A. Papavasiliou, C. Stefanadis. *Athens, Greece*

Evidence suggest that endothelial dysfunction is accompanied by increased arterial stiffness and L-arginine is the substrate for endothelial nitric oxide synthase. The effect of short term L-arginine administration on vascular function in chronic healthly smokers is unknown. Aim: We investigated the effects of a short-term daily L-arginine administration on endothelial function inflammatory process and arterial stifness in healthy smokers.

Methods: We administered 3-day oral administration of L-arginine in 12 healthy smokers (aged 24±3yrs) on 3 occasions (day0: baseline measurements, day1 and day3). The study was carried out on two separate arms, one with L-arginine (7gr tid) and one with placebo according to a randomized, placebo-controlled, double-blind, cross-over design. All measurements were performed one hour after L-arginine or placebo intake. Endothelial function was evaluated with flow-mediated dilatation (FMD) of the brachial artery. Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (AIx) as a measure of arterial wave reflections. Plasma levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and soluble intercellular adhesion molecule (sICAM-1) were measured with ELISA.

Results: Compared to placebo, L-arginine led to a progressive increase of FMD (by 1.74%, p=NS at day 1 and by 1.96%, $p<0.05$ at day 3), indicating a favorable effect on endothelial function. Moreover, L-arginine intake led to a progressive decrease of PWV (by 0.32 m/s at day1 and by 0.36 m/s at day 3, both $p<0.01$) and of AIx (by 5.1%, $p<0.01$ at day 1 and by 9.3%, $p<0.001$ at day3), indicating a decrease in aortic stiffness and wave reflections. Finally, 3-day oral administration of L-arginine decreased the level of sICAM ($p<0.05$), whereas, there was no effect on the expression of pro-inflammatory cytokines, IL-6 and TNF-α.

Conclusion: Short-term daily administration of L-arginine, a precursor of nitric oxide synthesis in vascular endothelium, improves endothelial function, arterial performance and decreases soluble intercellular adhesion molecule in healthy smokers. These findings may indicate that L-arginine exerts its beneficial effects on arterial stifness through the improvement of endothelial function.

P565 Low fibrin clot permeability and susceptibility to fibrinolysis in patients with advanced peripheral artery occlusive disease

T. Nowakowski, A. Undas, A. Szczeklik. *Jagiellonian University Collegium Medicum, II Department of Internal Medicine, Krakow, Poland*

Purpose: The aim of the study was to evaluate fibrin clot properties, such as permeability and susceptibility to fibrinolysis, and identify factors which influence these variables in patients with peripheral atherosclerotic occlusive disease (PAOD) and Buerger disease (thrombangiitis obliterans –TAO).

Materials and Methods: Fifty-five consecutive patients with PAOD and 16 patients with TAO were enrolled to the study. Control groups consisted of 30 and 17 healthy age-matched volunteers, respectively.The lower extremity ischaemia was assessed using non-invasive tests and angiography. Blood samples were drawn for measurement of lipids, fibrinogen, C-reactive protein, interleukin-6, intercellular adhesion molecule-1 (ICAM-1), plasma and cellular fibronectin, fibinopeptide A, tissue plasminogen activator antigen (tPA), plasminogen activator inhibitor-1 antigen (PAI-1) and D-dimers. Fibrin clots obtained from citrate plasma samples were used for the measurement of clot permeation, expressed by the permeability coefficient, Ks. Clot susceptibility to fibrinolysis was assessed by serial measurements of D-dimers in the buffer percolating through fibrin gels after addition of recombinant tPA.

Results: Fibrin clot permeability was above twofold lower in patients with TAO than in PAOD patients. In PAOD patients with more advanced disease in angiography the Ks coefficient was significantly lower (by 14.3%, p=0.001) in comparison to those with milder disease. In the TAO group, the clot permeability significantly correlated with the maximum velocity of the increase in D-dimer levels (r=0.59; p=0.01), claudication distance (r=0.9; p=0.002) and inversely correlated with plasma fibronectin concentrations (r=-0.77; p=0.0004). The clot permeability in patients with PAOD was associated with the max.velocity of the increase in D-dimer levels (r=0.42; p=0.001), fibrinogen concentration (r=-0.35; p=0.008) and PAI-1 (r=-0.55; p=0.00001). In the TAO group, cellular fibronectin levels were more than three-fold higher than in the control group and twofold higher than in the PAOD group (4.47 vs 1.17 vs 1.71 μg/ml respectively, $p<0.0001$). Susceptibility to fibrinolysis was also impaired in patients with TAO compared to those with PAOD and controls ($p<0.001$).

Conclusions: Decreased fibrin clot permeability and fibrinolysis characterize patients with advanced peripheral artery occlusive disease. It is particularly pronounced in patients with Buerger disease. This novel observation might be involved in the pathogenesis of TAO. Increased cellular fibronectin level could be useful in the differentiation of TAO from PAOD.

P566 Value of duplex scanning in differentiating embolic from thrombotic arterial occlusion in acute limb ischemia

M. Elmahdy, H. Kassem, K. Said, E. Baligh, H. Hussien, S. Ghareeb. *Kasr ElAini-hospital, Cardiology, Cairo, Egypt*

Background: The management of acute limb ischemia is largely based on the etiology of arterial occlusion (embolic vs. thrombotic). To our knowledge, the ability of duplex scanning to differentiate embolic from thrombotic occlusion has not been previously reported.

Purpose: To determine the ability of duplex scanning to differentiate embolic from thrombotic acute arterial occlusion.

Methods: We prospectively recruited 97 patients (50.3 + 19.7 years; 55% males) with 107 non-traumatic acute arterial occlusion in the native arteries of upper and lower limbs. All patients underwent surgical revascularization. Pre-operative Duplex scan detected arterial occlusion in the following arteries: iliac (11), femoral (38), popliteal (38), infrapopliteal (3), subclavian (3), axillary (1), brachial (9) and forearm arteries (4). We measured the arterial diameters at the site of occlusion (d_{occl}) and at the corresponding contralateral healthy side (d_{contra}). The difference (Δ) between the two diameters was calculated as (d_{occl} - d_{contra}). Duplex scan was also used to assess the state of the arterial wall whether healthy or atherosclerotic and the presence of calcification or collaterals. According to surgical findings, limbs were classified into embolic (E-group= 55 limbs) and thrombotic (T-group= 52 limbs) groups.

Results: Both groups were comparable regarding age, gender, diabetes, hypertension, smoking, atrial fibrillation and time of presentation. The status of arterial wall at the site of occlusion and presence of calcification or collaterals were all similar in both groups. Δ in E group was 0.95 ±0.92 mm vs. -0.13±1.02 mm in T group ($p<0.001$). A value of ≥ 0.5 mm for Δ had 85% sensitivity and 76% specificity for the diagnosis of embolic occlusion (CI 0.72 to 0.90, $p<0.001$), whereas a value of ≤ -0.5 mm for Δ had 85% sensitivity and 76% specificity for thrombotic occlusion (CI 0.72 to 0.90, $p<0.001$).

Conclusion: In acute arterial occlusion, ≥ 0.5 mm dilatation or diminution in the occluded artery diameter is a useful duplex sign for diagnosing embolic or thrombotic occlusion respectively.

P567 Evaluation of ankle-brachial index by automatic measurement of Blood Pressure in inpatients with Acute Coronary Sindrome

A.M. Garcia-Lopez, P. Mazon Ramos, C. Penha Gil, M. Pedreira, F. Soto Loureiro, E. Abu Assi, R.C. Vidal Perez, J.R. Glez Juanatey, A. Amaro Cendon. *Complejo Hospitalario Universitario, Santiago De Compostela, Spain*

Objective: Peripheral arteriopathy disease (PAD) is highly prevalent in patients suffering from Acute Coronary Sindrome (ACS), nevertheless, its evaluation in inpatients is limited by the need of specialized equipment and also for being time consuming. Our aim was to validate the automated measurement and comparing with the results obtained by continuous wave Doppler ultrasound, chosen as the gold-standard method.

Methods: We carried out evaluation of Blood Pressure (BP) in 25 consecutive patients hospitalized in a tertiary Hospital by an ACS. In every patient we performed systolic BP measurements in both brachial and pedal pulses by using automated and continuous wave Doppler. We calculated ankle-brachial index (ABI) by both methods. BP measures were compared by intraclass correlation coefficient and we classified patients as affected or not by PAD if ABI were ≤ 0.9. Concordance in classifying patients were evaluated by kappa coefficient.

Results: 23 out of 25 patients (92%) were classified in the same way by both methods. Kappa coefficient was κ = 0,802 $p<0,0001$. 7 patients were classified of suffering from PAD by Doppler method. 6 out of these 7 (85.71%) patients were also classified as PAD by automated method. In only 2 patients we found discrepancies while cataloguing patients: 1 patient showed only PAD by Doppler measure and 1 only by automated method.

The intraclass correlation coefficients are shown in the next figure:

Intraclass correlation coefficients

Right arm	0,834 IC 95% (0,658-0,923) $p<0,0001$
Left arm	0,721 IC 95% (0,462-0,867) $p<0,0001$
Right leg	0,753 IC 95% (0,516-0,883) $p<0,0001$
Left leg	0,850 IC 95% (0,688-0,931) $p<0,0001$

Conclusion: Measurement of BP in pedal pulses, and consequent realization of ABI with an automated method is simple and reliable and shows a good correlation with data acquired by continuous wave Doppler. It is a straightforward way of making diagnosis of PAD and facilitates the appropriate therapy. For this reason, we believe that it should be performed in every patient with ACS.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P568 Percutaneous transluminal angioplasty and stenting of extracranial vertebral artery stenoses

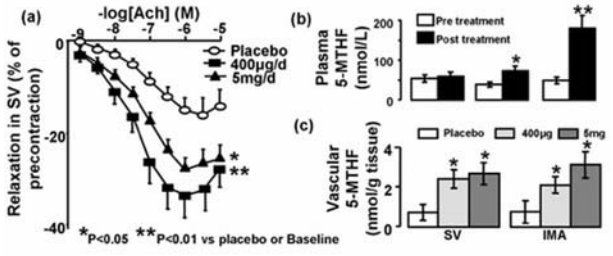
M. Henry[1], A. Polydorou[2], I. Henry[3], A.D. Polydorou[2], M. Hugel[4]. *[1]Cabinet De Cardiologie, Nancy, France; [2]Nikaia Hospital, Nikaea Piraeus, Greece; [3]Polyclinique Bois Bernard, Bois Bernard, France; [4]Cabinet de Cardiologie, Nancy, France*

Purpose: To evaluate the safety and efficiency of angioplasty and stenting of symptomatic vertebral artery (VA) stenosis.
Material and methods: 71 angioplasties attempted in 65 patients (M:48, F:17) mean age 68,4±6,9 years (22-84) right 33 left 38. All patients had multivascular diseases (carotid stenoses: 45, subclavian stenoses:13, renal stenoses:11, peripheral vascular diseases:17, coronary diseases: 45). 69 lesions were atheromatous, 2 inflammatory diseases. Mean lesion length: 9,5±2,5 mm (5-14), mean arterial diameter: 4,6±0,6 mm (4-6). 63 lesions at VO segment (ostium) 5 at V1 segment and 2 at V2 segments. Indications for angioplasty included: dizziness (65), bilateral weakness (9), visual changes (9), diplopia (8), drop attacks (8), TIA (5), ataxia (4). A protection device (filter) was used in 3 patients. 13 subclavian artery angioplasties performed at the same time of VA angioplasty, 4 carotid angioplasties.
Results: Technical success 69/71. Clinical success 63/65. 2 failures in elderly patients with very tortuous calcified arteries. 6 lesions were treated by angioplasty alone (3 VO lesions, first 3 patients, 2 V1, 1 V2 lesion). 1 patient with inflammatory disease was treated by cutting balloon alone. 59 lesions stented with balloon expandable stents (peripheral stents: 18, coronary stents: 41). 3 V1 and 1 V2 lesions were treated with self-expandable stents. No per or post-procedure neurological complications. Angiographic success, (≤ 20%) residual stenosis without in hospital emergency surgery, stroke and death: 69/71 lesions (97%). Post-procedure arterial diameter: 4,55±0,8 mm (4-6). Mean residual stenosis 2,2±3,5%. 4 patients (8%) developed symptomatic restenosis during the follow-up (mean follow-up: 28.5±27.4 months). 3 after PTA alone, 1 after PTA and stent (1 occlusion treated medically, 3 stenoses successfully treated with balloon angioplasty).
Conclusion: Endovascular treatment of VAS can be performed safely and effectively with a high technical success rate, a low complication rate, a low restenosis rate and a durable clinical success in patients with symptomatic VAS Stents seem to improve immediate and long-term results.

P569 Folic acid induces maximal vascular effects at dosage equivalent to the recommended daily allowance (RDA): Implications for folic acid treatment in fortified populations

C. Antoniades[1], C. Shirodaria[2], C. Ratnatunga[1], R. Pillai[1], H. Refsum[1], S. Neubauer[1], K.M. Channon[1]. *[1]University of Oxford, Cardiovascular Medicine Dept, Lab 3, Oxford, United Kingdom; [2]Oxford, United Kingdom*

Homocysteine is an independent risk factor for atherosclerosis, but homocysteine lowering with folic acid (FA) failed to improve clinical outcome in populations receiving folate-fortified diets.
Aim: We compared the effects of low-dose (equivalent to the RDA) and high dose FA (equivalent to the dosage administered in clinical trials) on vascular nitric oxide bioavailability and superoxide (O2-) production in patients with coronary artery disease.
Methods: In a double-blind placebo controlled study, 56 patients with CAD received FA 5mg/d (n=22) or 400μg/d (n=20) or placebo (n=14) for 6 weeks before CABG. Vasomotor responses to acetylcholine (ACh) were evaluated in saphenous vein (SV) segments harvested during CABG. Vascular O2- was determined by lucigenin chemiluminescence in SV and internal mammary arteries (IMA), and vascular/plasma 5-methyl-tetrahydrofolate (5MTHF) was measured.
Results: Vasomotor responses to ACh were similarly improved in 5mg/d and 400 μg/d groups, compared with placebo (Fig. a). Vascular O2- was also similarly decreased in SV and IMA of both 400μg/d (1.6±0.2 and 1.6±0.3 RLU/sec/mg) and 5mg/d (1.5±0.2 and 1.7±0.2 RLU/sec/mg) compared to placebo (2.5±0.3 and 3.4±0.9 RLU/sec/mg, p<0.05 vs both treated groups). Despite the higher circulating 5MTHF levels in the 5mg/d group (Fig. b), a similar elevation of vascular 5MTHF was achieved in both FA-treated groups (Fig. c).



Conclusions: Low-dose FA improves vascular NO bioavailability and O2- production in patients with atherosclerosis. Higher dosage of FA fails to induce further improvements, since vascular endothelium reaches its maximum capacity for 5-MTHF after low-dose FA treatment, explaining the failure of high-dose FA to improve clinical outcome, in folate-fortified populations.

P570 Gender differences of left ventricular mass index in function of retinal vessel score

D. Duprez[1], N. Florea[2], J. Xu[1], G. Grandits[1], L. Hoke[1], J.N. Cohn[1]. *[1]University of Minnesota, Cardiovascular Division -Vcrc Room 270, Minneapolis, United States of America; [2]University of Minnesota, Cardiovascular Division, Minneapolis, United States of America*

Purpose: The retinal microvasculature offers an easily accessible site for non-invasive evaluation of the condition of the microcirculation. The clinical and prognostic significance of initial retinal alterations remains controversial. Therefore, we assessed the relationship of retinal abnormalities with a prognostically validated marker of target organ damage, left ventricular mass index (LVMI) in function of gender in a primary prevention population.
Methods: A total number of 1124 subjects (651 male and 470 female) with no symptomatic cardiovascular disease underwent an optic fundus imaging with a digital camera. Fundus photos were analyzed for the A/V (arteriovenous) ratio and the prresence of A/V crossing changes. Arterial blood pressure was measured in sitting positio. An echocardiographic exam was performed and LVMI was calculated. The different parameters were then categorized in function of retinal score: 0 for normal grade, 1 for borderline (grade 1 and 2) and 2 for abnormal (grade 3 and 4). Table 1 summarizes the results following gender.

Table 1

Measure	Retinal Score			P-value	adj P-value
	0	1	2		
Male					
Age (years)	47.9±10.8	53.9±10.2	54.6±11.3	<0.001	
SBP (mmHg)	124.9±13.8	129.2±15.9	135.4±17.9	<0.001	<0.001
DBP (mmHg)	80.5±9.8	81.7±11.0	85.1±11.0	<0.001	<0.001
LVMI (g/m^2)	78.5±18.6	80.9±21.9	81.2±18.6	0.30	0.99
Female					
Age	49.5±11.4	54.7±10.4	56.5±10.1	<0.001	
SBP (mmHg)	118.4±16.2	129.7±18.1	134.9±19.4	<0.001	<0.001
DBP (mmHg)	74.5±9.2	78.2±10.2	81.9±8.3	<0.001	<0.001
LVMI (g/m^2)	65.1±14.0	69.7±17.5	72.0±19.5	0.004	0.033

adj P-value: age-adjusted.

Conclusion: An increase in retinal vessel abnormalities is associated with increase in left ventricular mass in women, but not in men. These data suggest a gender difference in LVMI as a marker for cardiovascular disease.

P571 Impact of antiretroviral therapy and lipodystrophy syndrome on aortic stiffness in HIV-infected patients

F. Boccara[1], C. Meuleman[2], S. Ederhy[2], M. Feron[2], S. Lang[2], S. Janower[2], G. Dufaitre[2], F. Raoux[2], P.M. Girard[2], A. Cohen[2]. *[1]Assisrtance Publique-Hopitaux de Paris, Cardiology Department, Paris, France; [2]Assistance Publique-Hopitaux de Paris, Cardiology, Paris, France*

Purpose: HIV-infected patients are at higher risk of cardiovascular disease because of metabolic complications including lipodystrophy syndrome (LS), insulin resistance and dyslipidemia due to antiretroviral therapy (ART). The impact of LS and ART particularly protease inhibitors on aortic stiffness, a surrogate marker of cardiovascular events, remains controversial.
Methods: In 152 HIV-infected patients (mean age: 48±8.9 years, 90% men), we evaluated non-invasively aortic pulse wave velocity (aPWV) using SphygmoCor technology.
Results: Sixty nine (45%) patients had a LS (LS+) and 83 (55%) were controls (LS-). LS+ were thinner (23±3 versus 24.7±3.3 kg/m^2, p=0.002) and had longer duration of HIV infection compared with LS- patients (14.4±5.7 versus 11±6.5 years, p=0.001). Cardiovascular disease risk factors were well balanced in the 2 groups. HDLc was lower in LS+ compared with LS- (43±14 versus 51±24 mg/dL, p=0.03). The prevalence of metabolic syndrome (NCEP/ATPIII definition) was similar in both groups (17.4% versus 21.7%, p =0.5). Aortic stiffness was also not different in both groups (9.51±1.73 versus 9.78±2.65 m x s (-1), p =0.46). In univariate analysis, aortic stiffness was associated with age (< 0.001), waist to hip ratio (0.02), hypertension (< 0.001), and systolic, diastolic, mean arterial pressures (< 0.001). LS and ART were not associated with aortic stiffness in HIV-infected patients.
Conclusions: We did not found any association between lipodystrophy syndrome or antiretroviral therapy and aortic stiffness in HIV-infected patients.

P572 Increased cholesterol levels decrease large and small artery elasticity

D. Duprez, N. Florea, L. Hoke, K. Jones, G. Grandits, J. Neaton, J.N. Cohn. *University of Minnesota, Cardiovascular Division, Minneapolis, United States of America*

Purpose: Increased cholesterol is associated with atherosclerotic risk. Increased arterial stiffness is an independent risk marker for cardiovascular disease. This

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

study aimed to examine the influence of serum cholesterol on large and small artery elasticity in a group of subjects with no overt cardiovascular disease (CVD) undergoing a cardiovascular screening.
Methods: 920 subjects free of overt CVD participated in the study. A fasting venous blood sample was taken for total serum cholesterol. Large and small artery elasticity were determined by pulse wave registration at the radial artery using pulse contour analysis. The study group was divided in quartiles anoung the distribution of serum cholesterol.
Results: Table 1 summarizes the results. There was no difference in age, resting sytolic (SBP) and diastolic (DBP) blood pressure among the 4 quartiles.

Table 1

	Quartiles of Total Cholesterol (mg/dl)				P-value
	<180	180-202	203-226	>226	
Number of Patients	233	232	225	230	
Mean Age (years)	50.9±13.1	50.6±11.2	51.9±10.3	52.1±9.9	0.14
SBP (mmHg)	127.3±17.2	125.0±17.1	125.0±15.0	127.9±18.6	0.75
DBP (mmHg)	80.2±10.2	79.9±10.6	84.0±10.2	81.4±11.7	0.37
Large Artery Elasticity (ml/mmHgx10)	17.7±5.8	17.5±6.2	17.1±5.7	15.9±5.3	0.0008
Small Artery Elasticity (ml/mmHgx100)	7.0±3.4	6.8±3.2	6.5±3.1	5.8±3.0	0.0001

Conclusions: Higher cholesterol levels were accompanied with a progressive decrease in small artery elasticity, while a decrease in large artery elasticity was only found in the highest quartile of serum cholesterol. These results suggest that a progressive higher cholesterol contributes to impaired endothelial function, which affects the small arteries. Only a higher cholesterol affects not only the small but also the larger arteries in their elastic behaviour.
These observations support the hypothesis of sequential changes of functional vascular abnormalities from small to large arteries in function of the cholesterol level.

P573 Variation in patient outcome between hospitals after vascular surgery is predominantly determined by differences in patient characteristics

S. Hoeks[1], W.J.M. Scholte Op Reimer[1], H.F. Lingsma[2], H. Van Urk[1], P.J.G. Jorning[3], E. Boersma[2], M.L. Simoons[2], D. Poldermans[2].
[1]Erasmus MC, Thoraxcenter/Klep Group/Ba559, Rotterdam, Netherlands; [2]Erasmus Mc, Rotterdam, Netherlands; [3]Isala Klinieken, Zwolle, Netherlands

Background: Mortality has been proposed and used as an indicator of quality of care across health care providers. The aim of this study was to investigate whether mortality can be used to assess quality of care after vascular surgery among a large number of hospitals.
Methods: In 11 hospitals in the Netherlands, 711 consecutive peripheral artery disease patients undergoing vascular surgery were enrolled. Stepwise multiple regression models were used to relate patient characteristics and quality of care indicators to all-cause mortality at 1 year. In the first model we included age, sex and the Lee-Index and we added remaining risk factors in the second model. Thirdly, selected quality of hospital care indicators (e.g. non-invasive cardiac testing, beta-blocker therapy and antiplatelet therapy) were added to the model. These quality indicators were chosen because they are recommended in the ACC/AHA guidelines for patients undergoing vascualr surgery. The contribution of each step was expressed by the Akaike Information Criterion (AIC) and by the area under the ROC curve.
Results: Total 1-year mortality was 11%, ranging from 6% to 26% between hospitals. Large differences in patient characteristics and quality indicators were observed between hospitals(e.g. age > 70 years: 28% to 58%; open vascular surgery: 20% to 100%; beta-blocker therapy: 39% to 87%). The adjusted analyses showed that the major part of variation in outcome was explained by patient characteristics. Quality of care parameters explained a smaller but significant part of the variation in outcome.

Determinants of outcome

	AIC (χ^2 -2*df)	Model AIC	P-value	Area under ROC curve
Step 1: age, sex, lee-index	44.65	44.65	<.001	.74
Step 2: risk factors	1.48	46.13	.036	.77
Step 3: quality of care	12.43	69.26	<.001	.80

Conclusions: Large variations in mortality between hospitals are predominantly explained by differences in patient characteristics. Unadjusted mortality rates after vascular surgery are therefore not useful as indicators of quality of care.

P574 Late clinical success and complications in endovascular aortic stent graft repair: 13 years' long-term follow-up experience

C.M. Ahn[1], W.H. Shim[1], S.H. Park[1], P.K. Min[1], B.K. Kim[2], Y.G. Ko[2], D.H. Choi[2], Y.S. Jang[2], D.Y. Lee[2], B.C. Chang[2]. *[1]Yonsei University College of Medicine, Seoul, Korea, Republic of; [2]National health insurance Ilsan hosp, Seoul, Korea, Republic of*

Background: Mid-term favorable outcomes and safety were frequently reported for endovascular aortic stent-graft placement with less procedure-related mortality and morbidity, but its long-term outcomes have not been clearly understood. The object of study is to assess its long-term outcomes of over 48 months after procedure and late complications and clinical pitfalls in managing various aortoiliac pathology based on our 13 years' experience.
Methods: A retrospective analysis was conducted on the data of 90 patients (age 62.9±11.4) who underwent stent-graft repair at our center from September, 1994 to February, 2003. The indications included progression of aortic pathology irresponsive to medical therapy, aggravation of pain, or other medically uncontrollable complications.
Results: Median follow-up duration was 7.6 years (90.8±28 months). Follow-up lost patients were seven after initial procedure and discharge. Clinical diagnoses were thoracic and abdominal aneurysm with or without iliac involvement (52 pts, 57.8%), type B aortic dissection (36pts, 40.0%), and ruptured aorta due to either dissection or aneurysm (2 pts, 2.2%). Angiographic and immediate clinical success, defined as immediate obliteration of target lesion without major endoleak and absence of readmission in 3 months follow-up, was obtained in 78/90 patients(86.7%). Late clinical success, defined as durability and safety over 48 months of follow-up periods after stent-graft implantation without additional surgical or interventional manipulations, was achieved in 61/90(67.8%). Additional procedures were operative revision such as ipsilateral fem-to-fem bypass or graft interposition, another stent-graft insertion or coiling embolization due to iliac segment thrombosis (6 pts), malapposition or migration of stent-graft due to remodeling of aortic wall, (6 pts), persistent endoleak (4 pts), late aortic rupture (2 pts). The most important prognostic factor for determining survival was co-morbidities including coronary artery disease (33 pts), renal failure (11 pts), and peripheral artery disease (8 pts).
Conclusions: Endoluminal stent-graft repair should be accepted as a safe and effective alternative treatment option for aortic pathology particularly in patients with a high risk of surgical mortality. However, late clinical success might be achieved not only by early procedural techniques but also by control of cormobidities and case-pertinent medical therapy for preventing thrombosis or aortic wall remodeling.

P576 Renal Angioplasty and Stenting under embolic protection devices. A must?

M. Henry[1], I. Henry[2], A. Polydorou[3], A.D. Polydorou[2], M. Hugel[4]. *[1]Cabinet De Cardiologie, Nancy, France; [2]Polyclinique Bois Bernard, Bois Bernard, France; [3]Nikaia Hospital, Nikaea Piraeus, Greece; [4]Cabinet de Cardiologie, Nancy, France*

Purpose: Despite good immediate and long-term results, post procedural deterioration of the renal function may occur after Renal Artery Angioplasty and Stenting (RAAS) in 20-40% of the patients, which limits the immediate benefits of the technique. Atheroembolism seems to play an important role. We evaluate the feasibility and safety of RAAS utilizing a distal protection device (DPD) to reduce the risk of intra-procedural atheroembolism and avoid deteriorations of the RF.
Methods: 124 RAAS were performed under protection in 105 hypertensive patients (M: 72). Mean age: 64.5±11.7 yrs (22-87) with atherosclerotic renal artery stenosis (18 bilateral). 9 patients had solitary kidneys, 38 renal insufficiency. We used occlusion balloon (n=46) or filters (n=78), which allow a continuous flow. We recently experimented a new filter (FiberNetTM), which can capture particles of 30-40 microns without compromising the flow. Generated debris were removed and analyzed. Blood pressure and serum creatinine levels followed.
Results: Immediate technical success: 100%. 96/124 lesions stented directly. Visible debris were aspirated with Percusurge from all patients and removed with filters in 80% of the cases (100% with FiberNet). Mean particle number: 98.1±60.00. Mean diameter: 201.2±76μ (38-6206). Mean occlusion time: 6.55±2.46 min (Percusurge). Mean time in situ (filters): 4.2±1.1 min. With the FiberNet 5 times more particles were removed. We observed one acute RF deterioration. Mean follow-up: 18.2±8 months. Mean creatinine level remains constant during follow-up. At 6 months (91 patients) 69 patients stabilized, 21 with baseline renal insufficiency improved and we had only one RF deterioration (1.1%) in a patient with moderate renal insufficiency. At 2 years 54 patients stabilized, 19 improved and we had only 2 RF deterioration (3%).
Conclusion: The preliminary results suggest the feasibility and safety of distal protection during renal interventions to protect against atheroembolism and to avoid RF deterioration after the procedure and in the long-term. The beneficial effects of this technique should be evaluated by randomized studies.

P577 Evaluation of L-citrulline for the treatment of Peripheral Obstructive Artery Disease (PAOD) patients

A. Leizorovicz[1], A. Pokrovsky[2], F. Becker[3], E. Presles[4], S. Varshavsky[5], W. Spickler[6], R.H. Boeger[7]. *[1]Faculte Rth Laennec, Service De Pharmacologie Clinique, Lyon Cedex 08, France; [2]A.V.Vishnevsky Institute of Surgery, Moscow, Russian Federation; [3]University, Besancon, France; [4]Hopital Bellevue, Saint Etienne, France; [5]Evidence, Los Altos, United States of America; [6]Angiogenix, Inc., Burlingame, United States of America; [7]Institute of Experimental and Clinical Pharma, Hamburg, Germany*

Purpose: Patients with PAOD have elevated asymmetric dimethylarginine (ADMA), the competitive inhibitor of L-arginine, resulting in reduced nitric oxide

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(NO) biosynthesis. Administration of L-arginine overcomes the inhibition of ADMA and increases limb blood flow and indices of NO biosynthesis. We hypothesized that L-citrulline, a precursor to L-arginine, combined with simvastatin will increase NO production and thereby improve limb blood flow and reduce the progression of the disease.
Methods: In a randomized, double-blind, placebo-controlled, two-parallel–group multicentre study
the efficacy of a 12 weeks treatment with oral formulation of L-citrulline (L-cit) 6 grams per day was compared to placebo (Pl) in PAOD patients on background of simvastatin. The primary outcome was the absolute claudication walking distance(ACWD) and secondary outcomes included pain-free walking distance (PFWD) and safety.
The main eligibility criteria were an intermittent claudication of at least 6 months in duration, a rest ankle-brachial index (ABI) $\leq$ 0.90 and ACWD on a standardized exercise treadmill test (ETT) $\geq$ 50 m but $\leq$ 300 m at screening (Fontaine stage II). After randomisation, ETTs were performed at weeks 6 and 12. Analyses were performed on an Intention to treat basis with last observation carried forward.
Results: A total of 186 patients were randomised: L- cit 95 and Pl 91. Baseline characteristics were well balanced between the two groups. The mean age was 60.9(7.3), 86.6% of patients were males. Mean ACWD in meters at baseline were respectively 192.0(65.0) and 185.3 (71.0) in the L- cit and the Pl groups; mean PFWD were 96.8 (41.5) and 102.7(50.6). The compliance with the study treatment was excellent in both groups. At 12 weeks 93 L-cit and 86 Pl patients performed the ETT. In both groups the walking distances improved. The mean absolute changes in ACWD from baseline were respectively 72.9(93.0) and 72.9(88.2) p=0.50, the corresponding changes in PFWD were 48.3(64.5) an 40.4(52.3) p=0.10. The 6 weeks results were consistent with the 12weeks results. There were no deaths, one possibly treatment related Serious Adverse Event and no major biological abnormalities observed in both groups over the 12 week period.
Conclusions: Despite a non significant trend in favour of L-cit on the improvement of PFWD, the study could not confirm that L-citrulline on top of simvastatin may be clinically helpful for the treatment of PAOD. These findings do not necessarily invalidate the hypothesis that increase in NO production might benefit to PAOD patients.

P578 Ultrasound guided percutaneous thrombin injection as a treatment of choice in 140 iatrogenic femoral artery pseudoaneurysms after heart catheterization

J. Madaric[1], I. Vulev[1], A. Mistrik[1], M. Vozar[1], P. Lederer[1], M. Gocar[1], I. Riecansky[1], B. De Bruyne[2], J. Bartunek[1]. *[1]National Cardiovascular Institute, Dept. of Cardiology, Bratislava, Slovak Republic; [2]Cardiovascular Center, Aalst, Belgium*

Background: Ultrasound guided percutaneous thrombin injection is frequently used for the treatment of iatrogenic femoral artery pseudoaneurysm. Aim: To evaluate efficacy of technique and to assess the risk factors associated with recurrence of femoral pseudoaneurysm after occlusion by thrombin injection.
Methods: From February 2002 to September 2006, 140 patients (pts, male/female: 39/101) aged 76 years (range 62-83) presented with femoral artery pseudoaneurysm after cardiac catheterization were treated by percutaneous ultrasound guided thrombin injection (500 IU/ml solution of activated human thrombin). The mean pseudoaneurysm diameter was 2.1x1.4cm. Very small cavities (less then 1.5x1.5cm) suitable for local compressive therapy, and very big cavities (5x5cm) scheduled for surgery, were excluded from the study. The factors associated with recurrence of pseudoaneurysm were retrospectively analyzed.
Results: Immediate success rate of thrombin occlusion was 85% (119/140). One hundred nineteen pts were successfully treated by one injection of activated thrombin (average amount 0.4$\pm$0.2ml). In 22 pts (16%), immediate short local compression (2 min) following injection was needed for complete occlusion. In one case, progression of pseudoaneurysm required conversion to surgical repair (0.8%). The procedure was well tolerated and no thrombotic complications occurred. During the 30-days follow-up recurrence of pseudoaneurysm occurred in 10 pts (7%), exclusively the second and the third day after the first injection. All of them were successfully treated by the second thrombin application. The recurrence of pseudoaneurysm was associated with obesity (BMI>30, r=0.42, 95% CI 0.26-0.56, p<0.0001), and with extensive combination of antiagregation and anticoagulation therapy (ASA, thienopyridins, LMWH), (r=0.64, 95% CI 0.53-0.73, p<0.0001).
Conclusion: Ultrasound-guided thrombin injection is a safe and effective treatment of iatrogenic femoral artery pseudoaneurysm. It should be considered as a method of choice in suitable pts. Low rates of recurrence are associated with obesity and extensive use of combined antiagregation and anticoagulation therapy.

P579 Predictors of patients with Peripheral Arterial Disease undergoing Peripheral Intervention

Y. Soga, K. Ando, T. Yamada, S. Shirai, K. Sakai, M. Goya, M. Iwabuchi, H. Yokoi, H. Yasumoto, M. Nobuyoshi. *Kokura Memorial Hospital, Department of Cardiology, Kitakyushu, Japan*

Background: A little is known about long-term outcomes of patients with PAD undergoing peripheral intervention (PI). In this study, we tried to evaluate its impact on survival.
Methods: This is the study of 679 consecutive patients (pts) with PAD that were treated by PI. We examined long-term clinical outcomes of pts received PI in our hospital from Jan.1990 to Dec.2003.
Results: This study population comprised of 679 pts with a mean age of 69$\pm$7 years, 82% of male gender, 51% with coronary artery disease (CAD), 33% with diabetes mellitus (DM), 14% with renal insufficiency (RI; Cre>1.5mg/dl), 39% with smoking, 19% with cerebrovascular accident (CVA) 62% with any vascular reconstruction including bypass surgery and vascular intervention and 38% with history of myocardial infarction (MI). A total of 918 endovascular procedures were performed and their 98% (stent 53%) were considered to be technically and clinically successful.
All patients were discharged alive and constituted the study population for long-term outcomes. Clinical follow-up information was obtained in 627 (93%) patients at a mean follow-up time of 7.2$\pm$3.1 years. During the follow-up period, 255 (38%) pts died (sudden death 9%, cardiac death 41%, malignancy 16%, cerebrovascular disease 9% and others 25%). Death occurred by any vascular event was 64%. Kaplan-Meyer curve showed that freedom from death was 72% (5 years), 61% (8 years), and 55% (10 years) and vascular-event free survival rate from death/MI/any vascular reconstruction/CVA/major and minor amputation was 36% (5 years), 24% (8 years), and 19% (10 years). Using multivariate Cox regression, age (Hazard ratio (HR) 1.04, 95% confidence interval (CI) 1.01 to 1.07, p=0.003), CAD (HR 4.4, 95% CI 3.5 to 6.8, p=0.002), DM (HR 2.4, 95% CI 1.5 to 3.8, p=0.002) and RI (HR 3.7, 95% CI 2.1 to 5.7, p=0.01) were identified as predictors in overall survival.
Conclusions: Regardless of successful PI, the survival of pts with PAD was poor. Age, CAD, DM, and RI were identified as independent predictors of late mortality.

COMBINED STROKE/PERIPHERAL CIRCULATION

P580 Exercise workload, risk evaluation and the risk of stroke in middle-aged men

S. Kurl[1], J. Sivenius[2], R. Rauramaa[3], J. Salonen[4], J. Laukkanen[4]. *[1]Kuopio, Finland; [2]Department of Neurology, University Hospital of Kuopio, Kuopio, Finland; [3]Kuopio Research Insitute of Exercise Medicine, Kuopio, Finland; [4]Research Insitute of Public Health, School of Public Health and Clinical nutritio, Kuopio, Finland*

Objective: We investigated the prognostic significance of risk score and exercise capacity with respect to stroke. Since there are no data concerning the value of exercise workload combined with European Systematic Coronary Risk Evaluation (SCORE) with respect to stroke.
Methods: Exercise workload was measured by exercise test with an electrically braked cycle ergometer. The study is based on a random population-based sample of 1639 men (42-60 years) without history of type II diabetes or atherosclerotic cardiovascular disease including coronary heart disease, stroke or claudication.
Results: During an average follow-up of 16 years, a total of 97 all strokes and 71 ischemic strokes occurred. Independent predictors for all strokes were European SCORE (for 1% increment, RR 1.12, 95% CI 1.02 to 1.22, p=0.017), maximal workload (for 20 watts increment, RR 0.87, 95% CI 0.80 to 0.95, p=0.003), and body mass index (for 5 kg/m^2 increment, RR 1.08, 95% CI 1.03 to 1.14, p=0.004), when adjusted for serum high-density lipoprotein, alcohol consumption, C-reactive protein, family history of coronary heart disease, exercise-induced ST changes and the use of medications for hypertension, dyslipidemia or aspirin. The risk was 2.54-fold (95% CI 1.27-5.09, p=0.008) for all strokes and 4.43-fold (95% CI 1.69-11.78, p=0.003) for ischemic stroke among men with exercise capacity less than 162 watts as compared to those with high exercise capacity over 230 watts, after adjustment for risk factors.
Conclusion: Low exercise workload predicts an especially high risk for stroke when combined with high risk SCORE.

P581 Time course of platelet activation and von Willebrand factor in patients with nonvalvular atrial fibrillation after ischemic stroke: evaluation of prognostic determinants

H.K. Yip, S.L. Lai, W.N. Chang, J.S. Liu, Y.F. Kao, Y.Y. Chang, C.H. Lu, W.H. Chen, H.H. Lin, C.W. Liou. *Chang Gung Memorial Hospital, Cardiology Division, Kaohsiung, Taiwan*

Background: This study investigated serial changes in platelet activation (expressed by CD62p) and von Willebrand factor (VWF), and the correlation between increased CD62p expression, VWF, and brain infarct volume (BIV: measured by MRI), and prognostic determinants in nonvalvular atrial fibrillation (NVAF) patients after acute ischemic stroke (IS).
Methods and Results: CD62p expression and plasma VWF levels were serially measured (< 48 h, on days 7, 21, and 90) using flow cytometry and ELISA respectively after acute IS in 61 NVAF patients. CD62p expression and VWF levels were also examined in 50 NVAF-risk control and 30 healthy subjects. VWF level had no significant changes at four intervals among the patients and did not differ among three groups at acute stroke phase. CD62p expression was significantly higher in the acute phase after IS than in both control groups (both p<0.0001).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

However, CD62p expression declined to a significantly lower level on day 7 and to a substantially lower level thereafter ($p<0.0001$). CD62p expression did not differ on day 90 among the three groups (both $p>0.5$). Linear regression analysis demonstrated that BIV and modified Rankin scale score (>3) were independently associated with increased CD62p expression (<48 h) (both $p<0.01$). Furthermore, the Cox proportional hazards model demonstrated that BIV was the only independent predictor of intermediate-term (8.8±4.4 months) combined recurrent stroke and death.

Conclusion: TheCD62p expression, which reflected increased BIV, was significantly increased in NVAF patients in acute-phase IS and substantially declined thereafter. The BIV was predictive of unfavorable intermediate-term clinical outcomes.

P582 Predictors of cerebral reperfusion injury after carotid stenting: the role of transcranial color-coded doppler ultrasonography

A. Kablak-Ziembicka, T. Przewlocki, P. Pieniazek, P. Musialek, A. Kozanecki, L. Tekieli, R. Drwila, K. Zmudka, W. Tracz. *Krakow, Poland*

Cerebral reperfusion injury (RI) is rare but life threatening complication following carotid endarterectomy and carotid stenting (CS). Study aimed to evaluate the possible role of Transcranial Color-Coded Doppler ultrasonography (TCCD) in RI prediction in patients undergoing CS for internal carotid artery stenosis (ICAS).

Material and methods: We included 111 (78M) out of 124 patients, aged 63.6±8.3 (range: 44-82)y. with a diagnostic TCCD referred to CS. The mean grade of ICAS subjected to CS was 85.9±9.1%. Contralateral ICA occlusion or near-occlusion (stenosis >90%) was noted in 26(23.4%) patients, history of stroke/TIA in 72 (64.9%), myocardial infarction in 39 (35.1%). 97 (87.4%) patients were hypertensive, 77 (69.4%) were present or former smokers, 96 (86.5%) had hyperlipidemia, 34 (30.6%) diabetes. TCCD was performed prior and during 24 hours after CS with assessment of peak-systolic velocity (PSV) in ipsilateral to CS site – middle cerebral artery (iMCA), as well as contralateral middle cerebral artery (cMCA).

Results: CS was uncomplicated in 106 (95.5%) patients. In these patients CS resulted in significant iMCA PSV increase from 67.5±21cm/s before to 102.1±27 cm/s after CS ($p<0.001$) as well as in cMCA from 84.9±31.6 cm/s to 100.7±29 cm/s ($p<0.001$). During CS, 2(1.8%) ischemic events (1 minor stroke, 1 TIA) occurred, which were related to iMCA PSV decrease after CS. RI occurred in 3(2.7%) patients, including 2 intracranial and 1 subarachnoid hemmorrhage during 2-12 hours following CS. All patients with RI were hypertensive with history of prior TIA or stroke, and they had a contralateral ICA occlusion. In patients with RI, significant PSV increase was noted bilaterally ranging 2.4-2.8-fold in iMCA and 2.5-7.4-fold cMCA, as compared to values before CS (both $p<0.001$). The mean iMCA and cMCA PSV increase after CS was 2.66±0,19 and 4.16±2.77 in RI patients, as compared to 1.59±0.56 and 1.26±0.47 in patients who did not develop RI ($p=0.001$ and $p<0.001$, respectively). From 19 analysed clinical, angiographic and TCCD variables, the following independent RI risk factors were identified by multiple regression analysis: low initial PSV in iMCA ($p=0.025$) and cMCA ($p=0.031$), high cMCA PSV increase after CS ($p<0.001$), non-functional posterior communicating artery ($p=0.037$) and bilateral ICAS ($p=0.052$).

Conclusions: The independent RI risk factors are low initial PSV in MCA bilaterally, a high cMCA PSV increase after CS, lack of posterior communicating artery and contralateral ICA oclussion.

P583 Anatomical and functional features of the patent foramen ovale related to cerebrovascular events

V. Yotova, T. Katova, V. Kostova. *National Heart Hospital, Department of Non-Invasive Cardiology, Sofia, Bulgaria*

The aim of the study was to describe the morphological and functional features of the patent foramen ovale (PFO) and to evaluate those characteristics of PFO which were related to cerebrovascular events (CVE).

Methods: TEE was performed in 578 consecutive patients, referred to our laboratory for different clinical reasons. As a part of TEE, in 97 patients contrast study was done to seek for PFO. TEE did not confirm PFO in 47 patients. During the TEE we measured: The separation between septum primum (SP) and septum secundum (SS); The whole length of the fossa ovalis membrane; The diameter of the shunt with Color Doppler. Contrast injections were repeated 3 times during normal respiration and during Valsalva manoeuver.

Results: From the unselected cohort PFO and/or ASA was found in 63: in 44(7.6%)-PFO; in 25(4.3%)- ASA; in 6(1.03%) -the both. 13 patients had moderate to intense contrast in LA at rest. In this group the percentage of CVE was high (61.5%). 49 patients had not contrast bubbles in LA at resting condition. New contrast was observed after the Valsalva manoeuvre in 37 patients. This group presented with 4 CVE (10.8%). The diameter of the tunnel between SS-SP (TEE SS-SP) and the diameter of the shunt (TEE Sh) did not correlate with the results of the contrast test at rest. They showed proportional correlation with the positive test during the Valsalva manoeuvre (Table 1).

Conclusions: The size of PFO and the diameter of the shunt determined by Color Doppler are the anatomic and the dynamic parameter which predict appearance and increase of the contrast flow in the LA during the Valsalva manoeuvre.The PFO has a high embologenic potential (OR 12.58; CI 7.57- 47. 27; $p<0.001$). The frequency of the CVE depends on the anatomical and functional characteristic of PFO.

Table 1. Correlation between the shunt diameter and the SS-SP distance with positive contrast test at rest and during Valsalva

	Correlation	+ contrast at rest	+ contrast during Valsalva
TEE SS-SP	r	-0.031	0.409
	p	0.908	0.004
	N	13	37
TEE Shunt	r	-0.016	0.700
	p	0.954	<0.000
	N	13	37

P584 Complementary value of contrast-enhanced transcranial Doppler used with transoesophageal echocardiography in the investigation and risk stratification of patients with cryptogenic stroke

L. O'toole, S. Kumar, M.S. Randall, C. Blank, G.S. Venables, J.N. West. *Sheffield Teaching Hospitals NHS Trust, Cardiology, Sheffield, United Kingdom*

Purpose: Young patients with stroke and patent foramen ovale (PFO) associated with inter-atrial septal aneurysm (IASA)) are at higher risk of recurrent cerebral ischaemic events and may benefit from PFO closure or anticoagulation rather than anti-platelet drugs. Transoesophageal Echo (TOE) is the standard investigation for the detection of right to left shunting (RLS), as well as other cardiac abnormalities. Contrast-enhanced Trans Cranial Doppler (TCD) is a simple non-invasive technique that allows validation of adequacy of the Valsalva manoeuvre for detection of RLS (defined as >25% fall in peak systolic velocity in middle cerebral artery) which TOE does not. This study describes the utility of the 2 techniques in a multi-disciplinary clinical setting.

Method: TCD & TOE were performed independently in 100 consecutive patients (<55 yrs old) with stroke/TIA. During both tests, agitated saline was given from the arm with Valsalva manoeuvre. On TCD, a major shunt was > 25 bubbles detected in the middle cerebral artery. Risk stratification took place in a multi-disciplinary case conference assessing neurological investigations, presence and degree of RLS on TCD, and TOE findings.

Results: RLS was detected in 55 pts (55%), in 51 by TCD and only 37 by TOE. A major shunt on TCD was found in 27 pts of whom TOE identified a shunt in only 18 (67%). A minor shunt was identified in 24 pts of whom TOE identified only 15 (62%). Four pts had RLS during TOE but not TCD. The negative predictive value of TCD for RLS was 94%, while that of TOE was only 69% ($p<0.01$). A morphological atrial septal abnormality was identified in 24 pts by TOE (septal defect in 3, aneurysm in 21). IASA with RLS was seen in 21 pts. 15 pts had other structural abnormalities at TOE (aortic atheroma 7, aortic valve abnormality 1, LVH 2, atrial thrombus 2, dilated right heart 1, mitral valve anomalies 3). Using both TCD and TOE, 67 of the 100 pts had a potentially significant abnormality for the genesis of stroke, 51 by TCD and 53 by TOE. Twenty pts (20%) were thought to be at high risk for recurrent stroke and offered the choice of anticoagulants or PFO closure.

Conclusion: This study reveals the added value of TCD used with TOE for the investigation of young people with cryptogenic stroke. Using both techniques, two-thirds of patients had a potentially significant finding for the genesis of stroke and one-fifth were thought to be at high risk for recurrent stroke and so suitable for anti-coagulation or PFO closure.

P585 Influence of factor VII -323 Del/Ins polymorphism in the prothrombotic state in atrial fibrillation. Implications in ischaemic stroke risk

V. Roldan[1], F. Marin[2], R. Gonzalez-Conejero[2], J. Corral[2], A. Garcia-Honrubia[1], G.Y. Lip[3], V. Vicente[3]. *[1]Universidad de Murcia, Centro Regional de Hemodonacion, Murcia, Spain; [2]Hospital General, Cardiology, Alicante, Spain; [3]City Hospital, Haemostasis, Thrombosis and Vascular Biology, Birmingham, United Kingdom*

Atrial fibrillation (AF) is associated with an increased risk of stroke, but this risk is not homogeneous. It was previously reported that elevated prothrombin fragment 1+2 (F1+2) levels were independently associated with the presence of AF, however, it remains unclear if hypercoagulable state has added value in predicting stroke. There are limited data on the influence of genetic polymorphisms on thromboembolic risk of AF. We firstly hypothesized that a functional haemostatic polymorphism, factor VII (FVII) -323 Del/Ins (that confers reduced FVII levels), could influence the prothrombotic state associated with AF (assessed by F1+2 levels), and secondly, to ischaemic stroke risk.

Methods: To test our first hypothesis, we recruited 119 consecutive patients with non-rheumatic AF lasting ≥4weeks, referred for the initiation of anticoagulation for primary prevention. None of the patients had previously been under anticoagulant therapy, although 56 were taking aspirin. Clinical risk factors for thromboembolism were recorded. To test our second hypothesis, we compared the previous 119 patients above with 96 additional patients with cardioembolic stroke secondary to AF admitted to a Neurology Unit from the same health area. None of them were

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

taking anticoagulation therapy, as AF was discovered on admission. F1+2 levels were assayed by ELISA and FVII coagulant levels were assayed in an automatic coagulometer. Genotyping of the –323 Del/Ins polymorphism of the FVII, were performed by PCR.
Results: AF patients carrying the –323 Ins allele had lower plasma F1+2 and FVII coagulant levels than patients carrying the Del/Del genotype (p=0.015 and p<0.001, respectively). Moreover, F1+2 and FVII coagulant leveles correlated significantly (r: 0.47; p<0.001). On multivariate analysis, advanced age was associated with a higher risk of cardioembolic stroke (OR 2.03; p=0.024), whilst the presence of FVII–323Ins allele was associated with a lower stroke risk (OR 0.50; p= 0.046).
Conclusions: We found that FVII –323 Del/Ins polymorphism reduced the risk of suffering a cardioembolic stroke by two-fold, even after adjusting for thromboembolic risk factors, and this was linked to low F1+2 levels.

P586 Enoxaparin versus unfractionated heparin in acute ischemic stroke in evolution-differential effects of enoxaparin on von willebrand factor release and a possible relation to improved clinical outcomes

A. Saleh, A. El Fiky, H. Awadalla. *Ain Shams University, Cardiovascular Medicine, Cairo, Egypt*

Background: The significance of low-molecular-weight heparins (LMWHs) in the management of acute stroke remains controversial.
Patients and Methods: 100 patients with acute ischemic stroke in evolution were enrolled (with symptoms of stroke within eight hours of randomization). Patients were randomized to receive Unfractionated Heparin (UFH) at a dose of 5000 IU by IV bolus, followed by a continuous IV infusion; or to Enoxaparin (ENOX) at a dose of 0.5 mg per kg body weight. Therapy was continued for 10 days. The plasma concentrations of von Willebrand factor (vWF) antigen were measured with a sandwich ELISA technique, on admission and 48 hours after initiation of theerapy. National Institutes of Health Stroke Scale (NIHSS) and a computed tomography (CT) scan of the brain were performed on all patients at the time of admission, and after forty eight hours of randomization. A composite clinical endpoint of (death, stroke, hemorrhagic complications, and deterioration in the NIHSS) was used for the purpose of assessing response to either UFH or Enoxaparin.
Results: The mean baseline NIHSS was 9.14±0.62 among patients randomized to UFH, vs. 7.86±0.54 among patients randomized to ENOX (p= 0.2). At discharge, the mean NIHSS showed a statistically significant difference in favor of the ENOX group (7.9±0.82 for the UFH arm vs. 4.96±0.54 for the ENOX arm; p=0.002). 60% of patients in the UFH arm demonstrated NIHSS improvement, as opposed to 80% of patients in the Enoxaparin arm (p=0.012). The mean NIHSS after therapy in patients who demonstrated neurological improvement was 5.6±0.46 in the UFH arm, as opposed to 3.65±0.39 in the ENOX arm (p=0.001). The incidence of composite clinical endpoint was 34% in the UFH group vs. 14% in the ENOX group (p=0.003). No statistically significant differences were observed for recurrent strokes, or death. The mean baseline percentage value for von Willebrand factor antigen in the UFH group was 119±3.9, as opposed to 124±3.54 in the ENOX group (p=0.32). The mean percentage value for vWF antigen after 48 hours of initiation of the study drug was 273±1 in the UFH group, as opposed to 184±0.7 in the ENOX group (p=0.0001).
Conclusion: Enoxaparin [+ aspirin] was superior to UFH [+ aspirin] in reducing neurological disability after acute ischemic stroke in evolution. This superiority was not associated with reductions in mortality, and could be explained by blunting of von Willebrand factor release by Enoxaparin.

P587 Ventricular arrhythmias in acute ischemic stroke

G. Polak[1], Z. Orzalkiewicz[2], R. Przybyl[1]. *[1]Municipal Hospital, Cardiology Department, Bydgoszcz, Poland; [2]Fado, Bydgoszcz, Poland*

Background: The neurogenic heart syndrome refers to the microstructural damage to the heart resulting from lesions of the central nervous system, leading to electrocardiographic changes, cardiac arrhythmias and unexpected sudden death.
Purpose: To determine the frequency and severity of ventricular arrhythmias in patients with acute ischemic hemispheric stroke.
Methods: We studied 42 right-handed patients (24 women, 18 men, aged 68±15) with the acute ischemic hemispheric stroke confirmed by computerized tomography. 24-hour electrocardiographic Holter recordings were performed on the 1st day and on the 7th day of stroke. The control group comprised 28 age- and sex-matched subjects. Differences between groups were evaluated by chi-squared test. Differences were considered statistically significant at p<0.05.

Cardiac arrhythmias in ischemic stroke

Ventricular arrhythmias	Controls n=28	1st day of stroke n=42	7th day of stroke n=42
single PVCs	19 (67%)	34 (81%)	31 (74%)
multiform PVCs	2 (7%)	19 (45%) ***	10 (24%)
couplets of PVCs	1 (3,5%)	15 (35%) **	15 (36%) **
nonsustained VT	0	7 (17%) *	4 (9,5%)

PVCs- premature ventricular complexes; VT- ventricular tachycardia;*p < 0.05, **p < 0.01, ***p < 0.001 - in comparison with controls.

Results: Results are presented in the table.
Conclusions: The ventricular arrhythmias are significantly more frequent in acute ischemic hemispheric stroke in comparison with controls.

P588 Mild and severe dyslipidaemia alter mouse cerebral artery elasticity and endothelium-dependent reactivity

A. Drouin, E. Thorin. *Montreal Heart Institute, Research Center, Montreal, Canada*

Purpose: Dyslipidaemia (DL) is a risk factor for peripheral vascular disease leading to endothelial dysfunction before the appearance of atherosclerotic lesion. Despite its established role in cardiovascular disease, there is a paucity of data on the impact of DL on the cerebral vasculature. The aim of this study was to investigate the impact of mild and severe DL on cerebral endothelial function and wall compliance.
Method: We used 3 month-old male C57Bl/6 (WT), DL (expressing the human apoB-100; apoB+/+) and severely DL (LDLr-/-; apoB+/+) mice. Posterior cerebral arteries were pressurized at 60 mm Hg in an arteriograph. Endothelium-dependent dilations to acetylcholine (ACh, 0.1nM to 30μM) were obtained after pre-constriction with phenylephrine (30 μM). Arterial wall compliance was assessed by measuring the changes in pressure for each 2μl-increase in intraluminal volume (up to 12 μl). Data are mean±SEM of n=6 mice.
Results: Total cholesterol and triglycerides (mg/dl) were significantly elevated in DL (159±14 and 204±38, respectively) and severely DL (745±77 and 732±70, respectively) compared to WT (107±8 and 147±24, respectively). ACh-induced maximal dilations from WT (45±6% of maximal diameter) were reduced (P<0.05) in DL (32±4%) and more in severely DL (26±2%) mice (Fig 1A). N-nitro-L-arginine (10 μM) reduced (P<0.05) ACh-induced dilation to 24±2% in WT and 13±4% in severely DL mice, while it had no significant effect in DL mice (23±3%). Compliance (mmHg/μl; WT: 0.07±0.004; Fig 1B) was increased in vessels from DL (0.10±0.001; P<0.05 vs WT) and even further in vessels from severely DL (0.13±0.0001; P<0.05 vs DL and WT) mice.

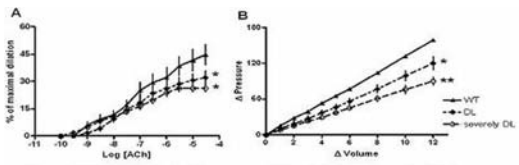


Figure 1. Effect of cholesterol increase on (A) endothelium-dependent dilation and (B) compliance of cerebral artery. (* p< 0.05 vs WT; ** p< 0.05 vs WT and DL)

Conclusion: Our results demonstrate that the endothelial dysfunction and the change in compliance of the cerebral artery are proportional to the level of DL.

P589 Role of high blood pressure in development of liquorodynamics dysfunctions in hypertensive diabetic patients

A. Falkovskaya[1], V.F. Mordovin[2], N.V. Belokopytova[1], P.I. Lukyanenok[1], R.S. Karpov[1], G.V. Semke[1]. *[1]Tomsk Research Institute of Cardiology, Hypertension Department, Tomsk, Russian Federation; [2]Tomsk Research Institute of Cardiology, Hypertension, Tomsk, Russian Federation*

Background: It is known that liquorodynamics dysfunctions are often associated with ischemic white matter lesion and may by caused by chronic arterial hypertension, however those changes at patients (pts) with essential hypertension (EH) and diabetes mellitus (DM) are insufficiently investigated.
Objective: to determine the role of highblood pressure (BP) and hyperglicemia in development of liquorodynamics dysfunctions.
Methods: We studied 51 pts with the mild/moderate EH and DM (11 men, aged 40 to 61 y.o) and 152 hypertensive patients without DM (EH group) matched for age and sex. There were estimated: 24-h ambulatory blood pressure monitoring (ABPM), plasma lipids, HbA1, fasting and postprandial insulin and glucose, liquorodynamics parameters by MRI.
Results: Brain MRI detected liquorodynamics dysfunctions in hypertensive diabetic pts more frequently than in hypertensive pts without DM (increased subarachnoidal spaces (SAS) -92% vs 50%, p<0.001, resp., enlarged lateral ventricles (LV) - 98% vs 38%, p<0.001, resp.) despite of lower levels of SBP/DBP and lower duration of EH in the EH+DM group than in the EH group (161/94 vs 178/111 mmHg, p<0.01 and 9±7 vs 12±7 y., p <0.05, resp.). Significant positive correlations between elevated of ABPM parameters and increase in linear size of LV (for SBP-24h R= 0.43, p<0.01, for DBP-24h, R= 0.50, p<0.01) and in SAS (for SBP-24h R=0.44, p<0.01, for DBP-24h R=0.37, p<0.01) but no with HbA1, fasting and postprandial plasma insulin and glucose were found in patients with EH and DM.
Conclusions: Increased blood pressure and gyperglicemic status per se independently of efficacy of glycemic control plays key role indevelopment of liquorodynamics dysfunctions in hypertensive diabetic patients.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P590 Carotid arteries with inflammatory atherosclerotic plaques are protected from restenosis due to expansive remodeling after carotid endarterectomy

W.E. Hellings[1], F.L. Moll[1], R.G.A. Ackerstaff[2], J.P.P. De Vries[1], D.P.V. De Kleijn[2], G. Pasterkamp[2]. [1]*University Medical Center, Experimental Cardiology, Utrecht, Netherlands;* [2]*St. Antonius Hospital, Clinical Neurophysiology, Nieuwegein, Netherlands*

Purpose: The relation between atherosclerotic plaque composition and the occurrence of restenosis following intervention is unknown. We studied the association between carotid plaque histology and future restenosis in patients undergoing carotid endarterectomy (CEA). In addition, we examined the association between plaque phenotype and the mode of remodeling after CEA (constrictive vs. expansive) which is a major determinant of restenosis following vascular injury.
Methods: Endarterectomy specimen (n=341) from patients undergoing CEA were stained and semi-quantitatively analyzed for fat, macrophages, smooth muscle cells, collagen, calcifications, intra-plaque bleeding and luminal thrombus. All patients underwent duplex follow-up for restenosis (peak systolic velocity > 125 cm/sec) 1 year after CEA. To assess the temporal course of vascular remodeling, the caliber of the carotid artery was measured by B-mode ultrasound in a subset of patients (n=50) pre-CEA, 6 weeks and after 1 year after CEA.
Results: Surprisingly, marked infiltration of the plaque with macrophages was associated with a lower incidence of restenosis compared to low macrophage infiltration (10.7 vs. 22.4%; p=0.008). Vessels housing plaques with intra-plaque bleeding were more prone to develop restenosis (20% vs. 8.5%; p=0.05). Clinical parameters predictive of restenosis were primary closure of the arteriotomy vs. patch closure (27% vs. 14%; p=0.008), female vs. male (24% vs. 15%; p=0.04) and asymptomatic vs. symptomatic clinical presentation (25% vs. 15%; p=0.03). In multivariate logistic regression analysis, primary closure (OR=5.21; p<0.001), low macrophage infiltration (OR=2.48; p=0.02) and intra-plaque bleeding (OR=3.47; p=0.01) were independent predictors of restenosis, but gender and symptom status were not. High macrophage infiltration was associated with expansive remodeling 6 weeks (+0.88mm) and 1 year (+0.97mm) after CEA (p=0.005), while other plaque characteristics were not associated with the mode and extent of carotid geometrical remodeling.
Conclusion: Histological appearance of the atherosclerotic carotid plaque is predictive of future restenosis after carotid endarterectomy. Vessels housing plaques with high macrophage infiltration are protected from restenosis due to expansive remodeling after the intervention.

P591 Sequential diffusion-weighted magnetic resonance imaging to time cerebral ischemia after emboli-protected carotid artery stenting

T. Tuebler[1], M. Arendt[1], J. Sandstede[2], M. Schlueter[1], J. Schofer[1]. [1]*Hamburg University Cardiovascular Center, Prof. Mathey, Prof. Schofer & Partners, Hamburg, Germany;* [2]*Roentgenzentrum Schaeferkampsallee, Hamburg, Germany*

Diffusion-weighted magnetic resonance imaging (DWMRI) has been shown to be highly efficacious in the detection of recent ischemic lesions of the brain. The timing of new cerebral ischemia after emboli-protected carotid-artery stenting (CAS) has not been elucidated.
Methods: We studied 347 patients (231 men [67%, 69±9 years]) who had undergone a total of 380 emboli-protected CAS procedures at our institution, each preceded and succeeded by DWMRI. In a subgroup of 28 patients (30 procedures) post-interventional DWMRI was performed twice: within 6 hours (T1) and at 18-24 hours (T2).
Results: New ischemic cerebral lesions were detected on DMWRI after 91 procedures (24%). In 10/91 cases (11%), neurological complications were observed predominantly during or immediately after the intervention (3 major strokes, 4 minor strokes, 1 retinal infarction, 2 transient ischaemic attacks). The ischaemic lesions on DWMRI were located in 78% (71 procedures) in the ipsilateral hemisphere, in 12% (11 procedures) in the contralateral hemisphere, and in 10% (9 procedures) in both hemispheres. In the subgroup of patients undergoing sequential post-interventional DWMRI, ischaemic lesions (10 ipsilateral, 2 contralateral, 1 bilateral) were detected in 13/30 cases (43%). In 8 of these 13 cases (54%), ischaemic lesions were only detected at T2. In 4 of 5 patients with ischaemic lesions present at T1, additional lesions were observed at T2, ipsilaterally in 3 patients and contralaterally in 1 patient.
Conclusions: Despite the use of embolic protection systems, new ischaemic cerebral lesions are observed in about one-quarter of procedures. In 90% of cases they remain clinically silent. Ischaemic lesions were located in about 20% in the contralateral hemisphere, presumably caused by catheter manipulation during carotid access. Sequential DWMRI revealed that ischaemic lesions occur in a high percentage of cases (12/13) only between 18 and 24 hours after the intervention. This finding suggests late embolism originating from the stented carotid-artery lesion. Therefore, improvements in carotid-access techniques and modified stent designs with improved carotid-lesion coverage may reduce the incidence of cerebral ischaemia after carotid-artery stenting.

P592 Anemia and renal insufficiency independently predict adverse events after carotid stenting: a long-term cohort study

A. Niessner[1], R. Hofmann[2], A. Kypta[1], C. Steinwender[1], K. Kerschner[1], M. Grund[1], J. Kammler[1], F. Leisch[1], K. Huber[3]. [1]*Medical University of Vienna, Dept. Int. Med. Ii, Cardiology, Vienna, Austria;* [2]*City Hospital Linz, Cardiovascular Division, Linz, Austria;* [3]*Wilhelminenhospital, Vienna, Austria*

Purpose: Anemia and renal insufficiency are associated with cardiovascular disease. Prior studies have shown that they are also related to increased risk after coronary interventions. We evaluated whether anemia and renal insufficiency predict the long-term outcome after carotid stenting.
Methods: We collected clinical and outcome data of 532 patients undergoing carotid stenting (median age: 71.0 yrs, IQR: 63.5-76.5 yrs, 67% male). Anemia was defined on the basis of preprocedural hemoglobin (Hb) levels (g/l) as absent (> 12), mild (10-12) and severe (< 10). Renal insufficiency was defined by a preprocedural glomerular filtration rate of < 30 ml/min calculated with the Crockroft-Gault formula. The primary combined endpoint (n = 100) including stroke, myocardial infarction and all-cause mortality was observed during a median follow-up of 28 months (IQR: 14-49 months).
Results: The 3-year event-free survival in patients with mild and severe anemia was 64% and 22%, respectively, compared to 87% in patients without anemia. After controlling for baseline characteristics, cardiovascular risk factors and lesion-related variables event rates remained significantly higher in patients with mild (adjusted hazard ratio: 2.4, 95% CI: 1.4-4.1) and severe anemia (adjusted hazard ratio: 3.2, 95% CI: 1.4-8.2) compared to non-anemic patients (P = 0.009). The 3-year event-free survival in patients with renal insufficiency was 79% compared to 87% in those without renal insufficiency. The adjusted hazard ratio in patients with renal insufficiency was 1.7 (95% CI: 1.0-2.8, P = 0.03). No interaction was found between the effects of anemia and renal insufficiency on event-free survival.
Conclusion: Anemia and renal insufficiency are independently associated with an increased long-term risk of adverse events after carotid stenting with the highest risk in patients with severe anemia.

P593 The CASES-PMS carotid artery stenting with emboli protection surveillance study: effect of age > 80 years on outcomes out to 1 year

M. Wholey[1], A. Echeneque[2], R. Matthews[3], K. White[4], D. Burkart[5], C. Zacharias[6], R. Chawla[7], S. Myla[8], D. Donohoe[9], L. Mauri[10] on behalf of the CASES-PMS Investigators. [1]*Pittsburg Vascular Institute, Pittsburg, Pa, United States of America;* [2]*South Florida Medical Imaging, Boca Raton, Fl, United States of America;* [3]*Good Samaritan Hospital, Los Angeles, Ca, United States of America;* [4]*Christus St. Patrick, Lake Charles, La, United States of America;* [5]*St. Joseph Heatlh Center, Lee Summitt, Mo, United States of America;* [6]*St. Mary's Hospital, Richmond, Va, United States of America;* [7]*Methodist Hospital, Arcadia, Ca, United States of America;* [8]*Hoag Hospital, Newport Beach, Ca, United States of America;* [9]*Cordis Corporation, Warren, Nj, United States of America;* [10]*Brigham and Women's Hospital and HCRI, Boston, Ma, United States of America*

Purpose: Treatment of vascular disease in octogenarians is associated with a higher risk for adverse outcomes. In the CASES-PMS carotid artery stenting (CAS) with emboli protection surveillance study, rates of adverse events were evaluated in patients < 80 years of age and in patients > 80 years of age.
Methods: High surgical-risk patients with de novo atherosclerotic or post-endarterectomy restenotic lesions in native carotid arteries were enrolled. Inclusion/exclusion criteria matched those of the SAPPHIRE trial. Primary endpoint was composite 30-day major adverse events (MAE) including death, any stroke, and/or myocardial infarction.
Results: Of the 1,493 patients enrolled, 1,107 ((74%) were < 80 years old and 386 (26%) were > 80 years of age. 30-day events are reported below. Age was both a univariate and multivariate predictor of MAE and stroke at 30 days. MAE and stroke rates at 30 days in symptomatic patients were significantly lower in patients < 80 years than in patients > 80 years, however, in asymptomatic patients MAE and stroke rates were not statistically significant between both age groups. Preliminary 1-year results show higher MAE rates with patients > 80 years (16.3%) as compared with patients < 80 years (10.2%) of age.

30-Day In-and-Out-of Hospital Events	All Patients (n=1493)	Under 80 (n=1107)	Over 80 (n=386)
MAE (Death, Any Stroke, MI)	5.0%	4.2%	7.3%
Death or Stroke	4.5%	3.5%	7.3%
Death	1.0%	0.8%	1.6%
Myocardial Infarction (Q Wave & Non-Q Wave)	0.8%	0.9%	0.5%
Stroke	3.8%	2.9%	6.2%
Major Ipsilateral	1.2%	0.7%	2.6%
Minor Ipsilateral	1.9%	1.4%	3.6%
TIA	3.2%	2.7%	4.7%

Conclusion: Consistent with outcomes in other studies involving vascular interventions, 30-day event rates are higher in patients > 80 years of age than in younger patients undergoing CAS with emboli protection. Octogenarians have

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

been excluded from most major carotid endarterectomy studies. Better patient selection criteria for CAS, based on patient and lesion characteristics, may help reduce the MAE rate to an acceptable level.

P594 Influence of diabetes mellitus on clinical results during carotid artery stenting (CAS) in clinical practice. Results from the ALKK CAS Registry

R. Zahn[1], T. Ischinger[2], E. Roth[3], M. Hochadel[4], U. Zeymer[1], K.E. Hauptmann[5], A. Schramm[6], I. Janicke[7], H. Mudra[3], J. Senges[2] on behalf of the ALKK study group. *[1]Nuernberg, Germany; [2]Muenchen, Germany; [3]Worms, Germany; [4]Ludwigshafen, Germany; [5]Trier, Germany; [6]Osnabrueck, Germany; [7]Duisburg, Germany*

Background: For many invasive procedures the presence of a diabetes mellitus has shown to be an independent predictor of adverse clinical events. However, there are few data on the prevalence of diabetes mellitus in patients undergoing carotis artery stenting (CAS) as well as on the influence of diabetes on complication rates of CAS.
Methods: We analysed the data from the prospective ALKK CAS Registry.
Results: Between 12/2000 and 9/2006 2116 CAS procedures at 31 hospitals were performed. Diabetes mellitus was present in 668 (32%) of patients. The proportion of diabetic patients remained unchanged over the last years (p for trend = 0.25). Patient - and interventional characteristics as well as in-hospital events are shown in the table. The presence of diabetes was not an independent predictor of in-hospital death or stroke: OR = 1.24, 95%CI: 0.69–2.30 p=0.463).

	Diabeticsn = 678 (100%)	Non-diabeticsn = 1438 (100%)	p-value
Age (years)	70.6	71.7	0.071
Male gender	69.5%	73.4%	0.057
Symptomatic stenosis	43.5%	40.9%	0.262
Coronary artery disease	73.1%	64.1%	<0.001
Prior myocardial infarction	33.3%	25.2%	<0.001
pAVD	30.4%	23.6%	<0.001
Calcified stenosis	31.8%	22.1%	<0.001
Ipsilateral TIA	2.8%	2.8%	0.980
Ipsilateral stroke	2.1%	1.8%	0.687
Myocardial infarction	0.1%	0.1%	1
Death	0.6%	0.6%	1
Death or stroke	3.1%	2.6%	0.492

Conclusions: In current clinical practice of CAS diabetes mellitus is present in 32% of patients. Diabetics do have more often a history of other cardiovascular diseases. In-hospital death or stroke rate however is not significantly elevated in diabetics undergoing CAS.

P595 Proximal endovascular clamping for carotid artery stenting: results from a prospective registry of 500 consecutive unselected patients

E. Stabile, G. Sorropago, L. Salemme, T. Tesorio, A. Cioppa, G. Popusoi, V. Ambrosini, W. Nammas, M. Miranda, P. Rubino. *Clinica Montevergine, Deptment of Invasive Cardiology, Mercogliano, Italy*

Background: In a single center study, the use ofproximal endovascular clamping (PEC) led to a significant reduction of cerebral microembolization, during carotid artery stenting (CAS). In recently published mltlcenter registry, the use of PEC was demonstrated to be safe and efficient in patient population, selected according to specific anatomic characteristics, undergoing CAS. In our registry we present the results of the use of PEC in an unselected patient population.
Methods: From September 2004 to December 2006, 500 consecutive patients underwent CAS using PEC. All patients had a > 70%, if asymptomatic, and >50%, if symptomatic, diameter stenosis of the internal carotid artery, measured according to the NASCET criteria using the distal, non tapering portion of the internal carotid artery as the reference segment. Patients mean [± SD] age, 69±8 years, male were 73%. The only exclusion criteria were the presence of critical stenosis of the ipsilateral common carotid artery and/or the occlusion of the ipsilateral external carotid artery. Patients received a detailed clinical assessment one hour, twenty four hours and 30 year after the procedure.
Results: Procedural success, defined as the ability to establish protection and deploy the stent, was achieved in 100%. The mean duration of flow blockage was 165±34 sec. Clamping intolerance, defined as a transient neurological deficits observed in this period of time, was observed in 37 patients (4,6%). In hospital MACCE included one death, three mayor strokes, two minor strokes and no AMI. The presence of complex anatomic conditions (type of lesion, type of aortic arch, occlusion of the controlateral carotid artery, presence of a critical stenosis of the ipsilateral external carotid artery) or of specific clinical conditions (age > 80 years, diabetes, chronic renal failure) did not precluded procedural success and were not associated with an increased incidence of MACCE over the follow up.
Conclusions: The use of proximal endovascular clamping is a safe and efficient neuroprotection system during CAS in an unselected patient population. Even the presence of anatomical and/or clinical complexity in not associated with an increased incidence of post procedural MACCE. The clinical relevance of these data could be important to design a multicenter randomized study investigating the role of PEC for carotid stenting.

P596 Coronary angiography to detect CAD in patients undergoing Carotid Artery Stenting: results from a single center experience

E. Stabile, L. Salemme, V. Ambrosini, T. Tesorio, G. Sorropago, G. Popusoi, A. Cioppa, W. Nammas, M. Miranda, P. Rubino. *Clinica Montevergine, Deptment of Invasive Cardiology, Mercogliano, Italy*

Background: Coronary events are mayor determinants of outcome after carotid artery stenting (CAS) or endoarterectomy (CEA). Patients with coronary artery disease (CAD) have worse outcome after CAS. In case of the simultaneous presence of coronary and carotid artery disease, the decision of which territory has priority of revascularization is debated. Here we reported the results of a therapeutic strategy based on a coronary angiography routinely performed at the time of CAS.
Methods: Six hundred and fifty patients underwent coronary angiography at the time of elective CAS from January 2003 to June 2006. Revascularization strategy (timing and territory) was decided on the basis of patient symptoms, non invasive tests and angiographic patterns. Patients were followed for at 30 days and 6 months after procedure with a detailed clinical exam.
Results: Patients mean age was 69±7,4 years (73% males, 36% diabetic). Thirty five percent of patients had an history of CAD or AMI. In hospital complications included 0,4% of death, 0,8% of strokes, 0,6% of minor strokes, 0,4% of TIAs, and no patients experience any AMI. In 74% of the patients the presence of at least one severe coronary stenosis was detected and were, were subjected to coronary revascularization within 3 wks after CAS, after having demonstrating evidence of inducible ischemia. In 8% patient, due to severe coronary angiographic findings, CAS was deferred after coronary revascularization. At 6 months follow-up, we observed a total of 2 AMI (0,3%) and no difference of outcomes were observed among patients with or without CAD at the time of CAS.
Conclusions: CAD in highly frequent in patient undergoing CAS. The decision to base the timing of revascularization on clinical, non invasive tests and angiographic findings seems appropriate to achieve a minimal incidence of adverse events even in the presence of severe CAD. This data could be of clinical relevance in reducing coronary events after carotid setting or endoarterectomy.

P597 Carotid artery stenting (CAS) versus carotid endarterectomy (CEA): meta-analysis of current randomised clinical trials

R. Zahn[1], M. Hochadel[2], U. Zeymer[1], B. Mark[1], H. Mudra[3], J. Senges[1]. *[1]Nuernberg, Germany; [2]Ludwigshafen, Germany; [3]Muenchen, Germany*

Background: Carotid artery stenting (CAS) is an alternative to carotid endarterectomy (CEA) for the treatment of carotid stenoses. Until now, the available randomised clinical trials (RCTs) comparing the two methods included only small numbers of patients, resulting in a limited power of each study to demonstrate significant differences.
Mehods: We performed a meta-analysis using available data from RCTs comparing CAS with CEA in symptomatic or asymptomatic patients with significant carotid stenoses.
Results: Out of the available 8 RCTs 4 (Naylor, Alberts, Brooks I + II) were excluded from further analysis due to methodological shortcomings. 2414 patients were recruited in the remaining 4 RCTs: 1267 treated with CAS and 1247 treated with CEA. 30-day results (death or stroke) are given in the table.
There was no heterogeneity concerning the endpoint of death or stroke between the studies (Breslow-Day Test: p = 0.11).

	CAS (n=1267)	CEA (n=1247)	OR	(95% CI)
CAVATAS	25/251 (10.0%)	25/253 (9.9%)	1.01	0.56-1.81
SAPPHIRE	7/156 (4.5%)	10/151 (6.6%)	0.67	0.25-1.77
SPACE	46/599 (7.7%)	38/584 (6.5%)	1.19	0.77-1.86
EVA-3S	25/261 (9.6%)	10/159 (3.9%)	2.48	1.25-4.92
Total	103/1267 (8.1%)	83/1247 (6.7%)	1.24	0.92-1.68

Conclusions: This actual meta-analysis of the RCTs comparing CAS with CEA for the treatment of carotid stenoses shows comparable 30 day results for the two methods (30-day death or stroke rate: 8.1 versus 6.7%; p=0.26).

P598 Carotid artery stenting in asymptomatic patients scheduled for cardiac surgery

U. Zeymer[1], R. Zahn[2], M. Hochadel[3], B. Mark[2], J. Senges[2] on behalf of ALKK-Study Group. *[1]Herzzentrum Klinikum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany; [2]Klinikum Nueremberg, Medizinische Klinik 8, Nueremberg, Germany; [3]Herzzentrum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany*

Background: There is still debate about the optimal strategy of patients scheduled for coronary artery bypass grafting or cardiac valve replacement procedures and concomitant high grade stenosis of the A. carotis. Therefore we analysed data from a large registry to evaluate outcome and complications of carotid artery stenting (CAS) in asymptomatic patients scheduled for cardiac surgery.
Methods: In a retrospective analysis of the prospective CAS registry of the ALKK

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

a total of 1096 asymptomatic patients were included. Concomitant diseases, procedural data and hospital complications were prospectively recorded and analyzed centrally.
Results: A total of 1096 patients fulfilled our inclusion criteria for this analysis. Mean age was 71 years, 74% were men, 31% diabetics 5% had had previuos CAS and 6% prevoius caroitis endarterectomy. The median stenosis was 90%, CAS of the A.carotis interna was performed in 95% and of the A. carotis communis in 5% of the patients. The inhospital events are shown in the table.

	Planned surgery (n=250)	Others (n=846)	p-value
Death	0.4%	0.4%	1.0
Stroke	1.7%	0.7%	0.2
TIA	4.5%	3.5%	0.4
Myocardial infarction	0%	0.1%	0.4

Conclusions: In clinical practice in unselected high risk patients with high grade carotid stenosis and planned cardiac surgery CAS is safe and effective. Therefore this approach is an alternative to combined cardiac and carotid surgery. A randomized clinical trial seems warranted to determine the optimal strategy in these patients.

P599 Determinants of death after -"tailored" carotid artery stenting: 5 year results from a registry of 450 consecutive cases

P. Pieniazek, P. Musialek, L. Tekieli, A. Kablak-Ziembicka, T. Przewlocki, A. Lesniak-Sobelga, K. Zmudka, W. Tracz. *Institute of Cardiology, Dept. of Cardiac and Vascular Disease, Krakow, Poland*

Background: Majority of carotid artery stenting (CAS) studies have used only one type of neuroprotection system (NP) and reported an average 30d complication rate of 5.5%. Determinants of long term mortality after CAS have not been identified.
Material: Over last 6y we performed 450 CAS procedures in 425 patients (pts, 44-86, mean 64±8.3 years, 64% symptomatic). Before CAS, all pts underwent CT angiography and extra/intracranial duplex Doppler to evaluate plaque content/morphology and the anatomy/function of intracranial circulation to select the most appropriate NP.
Results: Distal NP was used in 330 (73%) whereas proximal NP (PAES, Mo.Ma) in 120 (27%) procedures. Stenosis by QCA was 84.7±8.3% before and 11.0±8.8% after CAS (p<0,001). The minimal lumen diameter increased from 1.4±0.61 to 3.8±0.64mm (p<0,001). In the 30d period, 2 pt (0.4%) died due to intracranial bleeding, 5 (1.1%) pts had hyperperfusion syndrome, 4 (0,9%) had a minor ishaemic stroke, 14 (3.1%) TIA. Long-term follow up to 5 years, mean 24,6 months,15 pts (3.3%) lost to follow-up) revealed 25(5,5%) deaths. There were 14 (3.1%) deaths due to cardiovascular events. Statistical search for determinants of post-CAS mortality indicated that the risk of death after CAS is not related to the presence of neurological symptoms prior to CAS (p=NS, Fig 1) but it is strong related to coexisting coronary artery disease (p<0.008, Fig 1).

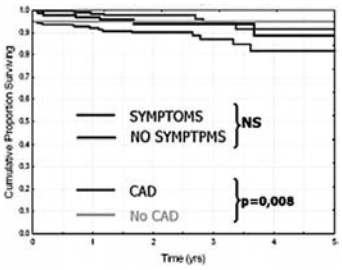


Figure 1. Cumulative proportion surviving (Kaplan-Meier).

Conclusions: CAS with NP tailored by a thorough non-invasive work-up is safe, it has a high procedural success rate and a low complication rate. Total mortality in up to 5 years after CAS is low. The use of tailored NP leads to a similar short- and long-term CAS efficacy in the symptomatic and asymptomatic patients. Long term mortality after CAS is strongly related to coexisting CAD.

P600 Carotid artery stenting in patients with diabetes

R. Hein, F. Beier, M. Hug, H. Strohm, C. Spes, M.C. Haufe, H. Mudra. *Klinikum Neuperlach, Cardiology Department, Munich, Germany*

Background: Diabetes is an independent risk factor for accelerated atherogenesis and increased intima-media thickness resulting in carotid artery stenosis. Both, type I and II diabetes, are suspected to have a significant impact on peri- and post-interventional vascular event rates of carotid patients.
Methods: From November 1999 to January 2007, a total of 444 consecutive patients (153 diabetics and 291 non-diabetics) underwent transcatheter carotid artery stenting at our center within a prospective controlled registry. The incidence of neurological events within 180 days before carotid intervention in the diabetic population was 34% (vs. 28.5% in the non-diabetic population, p=n.s.). Pre- and post-interventional neurological assessment was complete in 98%. Thirty days and overall follow-up data were analyzed (0-2237days, mean follow-up time 675.6±558 days).
Results: Peri-interventional major adverse cardiac and cerebrovascular events were documented in 0.7% % of the non-diabetic and 2% of the diabetic patients (p=n.s.). Statistical evaluation of the neurological event rate in diabetics during the first 30 days after intervention substantiated significantly higher incidences of any form of stroke (5.6% vs. 1%, p≤0.01), any ipsilateral stroke (4.9% vs. 1%, p≤0.025) and any minor stroke (2.8% vs. 0.4%, p≤0.05). The incidence for any major stroke (2.8% vs. 0.7%, p=n.s.), major ipsilateral stroke (2.8% vs. 0.7%, p=n.s.) and minor ipsilateral stroke (2.1% vs. 0.4%, p=n.s.) were higher in the diabetic group, but did not achieve statistical significance. Neither the incidence of death from any cause nor cardiac death differed between both groups at 30 days. Overall follow-up supported the short term results in some extent with a significantly higher rate for any ipsilateral stroke (5.3% vs. 1.8%, p≤0.05) and any minor stroke (3.3% vs. 0.7%, p≤0.05) in diabetics. In contrast to the 30 days results, diabetic patients had an increased incidence of death (16.1% vs. 9%, p≤0.05) and cardiac death (3.2% vs. 1%, p≤0.01) during long term follow-up.
Conclusion: Our data support low neurological peri- and post-interventional event rates from previous carotid stenting trials. The subgroup of diabetic patients presented an increased rate of peri-procedural complications as well as a higher incidence of neurological events after carotid stenting (though not proven statistically significant in all event qualities). We also observed a substantial increase of cardiovascular death in diabetics during long term follow-up representing the well known high-risk status of diabetic patients.

P601 Proximal neuroprotection [NP] as the system of choice in high risk carotid artery stenting: result from a single-center registry of 120 proximal-NP and 330 dystal-NP CAS

P. Pieniazek[1], P. Musialek[1], A. Kablak-Ziembicka[1], M. Pasowicz[2], L. Tekieli[1], T. Przewlocki[1], K. Zmudka[1], W. Tracz[1]. *[1]Institute of Cardiology, Dept. of Cardiac and Vascular Disease, Krakow, Poland; [2]The John Paul II Hospital, Krakow, Poland*

Background: Recent evidence indicates that the use of embolic protection devices (EPD) increases the safety of carotid artery stenting (CAS). Presently, most CAS procedures are performed with distal EPDs (filters or a distal occlusion balloon) that require unprotected lesion crossing before neuroprotection is implemented (and thus are associated with an additional embolization risk). Other disadvantages of distal EPD include potential incomplete filter apposition, provocation of internal carotid artery spasm or inability to catch and remove the debris completely. Aim: To evaluate safety and efficacy of the use of proximal protection systems for high-risk CAS.
Material and Methods: From Jan 2001 to Jan 2007 we have performed 450 CAS procedures in 425 patients (age 44–86 years, 64% symptomatic; all CAS procedures with EPD). For high-risk lesions [near-occlusion and/or thrombus-containing and/or soft long lesion in a highly tortuous vessel], proximal EPD was the system of choice. Thus 120/450(27%) CAS procedures were performed with cerebral flow reversal by Parodi Anti-Emboli System (PAES, n=86) or proximal flow blockade by Mo.Ma (n=34).
Results: Stenosis severity by QCA was significantly higher in the proximal EPD-treated lesions (90.4±8.5% vs. 82.5±10.0%, p< 0.001). Procedural success of proximal-protected CAS was similar to that of distal-protected CAS (97% vs. 98%, p=0.59). Not unexpectedly, direct stenting was possible in only 60,2% lesions treated under proximal EPD vs. 75,1% lesions treated under distal EPD (p=0.004). The rate of access-site complications was no different between the proximal and distal EPD group (1.6% vs. 1.8%, p=NS) despite the higher profile of proximal EPDs. In the proximal EPD group, during the peri-procedural period and up to 30 days there were 4(3,3% TIAs and 2 (1,6%) hemorrhagic stroke causing death; there were no minor strokes. In the distal EPD group there were 9 (2,5%) TIAs and 4 (1,2%) minor strokes. Statistical data evaluation for any difference in complication rate between the distal and proximal EPD group showed no significant difference (p=0.64 for TIA and p=0.74 for death and stroke) despite the significantly higher lesion severity in the proximal EPD group. In conclusion, the use of a proximal embolic protection system for CAS in patients with high risk lesions can lead to the peri-procedural and 30-day complication rate that is very low and is similar to that seen with mild-moderate risk lesions stented under distal neuroprotection. Thus every operator performing CAS should have a working knowledge of at least one proximal EPD.

P602 Antithrombotic effects of intensive cholesterol lowering therapy in elderly patients with atrial fibrillation

J.T. Van Kuilenburg[1], W. Van Heerde[2], I. Plesiewicz[2], G.P. Pop[2], F.W.A. Verheugt[2]. *[1]Nijmegen Heart Centre UMC St. Radboud, Cardiology, Nijmegen, Netherlands; [2]Laboratory of Hematology UMC St. Radboud, Hematology, Nijmegen, Netherlands*

Purpose: In elderly patients with atrial fibrillation (AF) silent ischemic brain infarctions occur despite adequate oral anticoagulation therapy. Thrombosis is closely

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

related to inflammation. Anti-inflammatory treatment with statins and Ezetimibe reduce atherothrombotic events. Our purpose is to investigate the hypothesis that anti-inflammatory treatment by intensive lowering of the plasma cholesterol in elderly patients with AF treated with oral anticoagulation will give additional antithrombotic profylaxis.
Methods: 33 elderly (69-85 years old) were randomized in a double blind fashion to the combination of Atorvastatin 40 mg and Ezetimibe 10 mg or placebo on top of oral anticagulation for the period of one year. Cholesterol profile and hsCRP were monitored every three months. The Nijmegen Hemostatic Assay was used for evaluation of the hemostatic and fibrinolytic activity. We used the measurements of Endogenous Thrombin Potential (ETP) and Plasmin Peak Height (PPH) respectively for evaluation of the thrombus forming activity and the fibrinolytic activity. Prothrombin Activation Fragment (Enzygnost F1+F2) analysis was performed to determine in vivo clotting actvity.
Results: Despite adequate oral anticoagulation (Internationalized Normal Ratio [INR] 2.0-3.0) a certain amount of thrombin is still present and active. In the treatment group (N=16) the ETP decreased significantly (p=0.002) compared to the placebo group (N=17). The PPH increased more than one and a half times in the treatment group (p=0.001), while no significant changes occured in the placebo group. There were no significant differences in F1 and F2 levels. The dose of Acenocoumarol was equal before and during our the study period. There were no hemorrhagic complications.
Conclusion: This pilot study demonstrates that despite adequate oral anticoagulation thrombin activity may still be present and active. Intensive cholesterol lowering by Atorvastatin and Ezetimibe reduce this thrombus forming activity on top op adequate oral anticoagulation. Higher INR levels have shown dramatic increase of hemorrhagic strokes in the elderly. Large clinical trials should determine whether the additive anti-thrombotic effects of Atorvastatin and Ezetimibe will be translated in less cerebrovascular atherothrombotic events in elderly AF patients treated with oral anticoagulation.

P603 Elevated soluble intercellular adhesion molecule-1 levels are associated with poor short-term prognosis in patients with acute ischaemic stroke

L. Rallidis[1], M. Zolindaki[2], M. Vikelis[3], G. Liakos[2], G. Pavlakis[1], D. Kremastinos[3]. *[1]University General Hospital Attikon, Second Department of Cardiology, Athens, Greece; [2]General Hospital of Nikea, Biochemistry Department, Piraeus, Greece; [3]Athens Naval Hospital, Neurology Department, Athens, Greece*

Purpose: There is increasing evidence that cellular adhesion molecules (CAMs) play an important role in the pathophysiology of acute ischaemic stroke. We examined the prognostic value of soluble intercellular adhesion molecule-1 (s ICAM-1) and soluble vascular cell adhesion molecule-1 (s VCAM-1) on in-hospital mortality in patients with ischaemic stroke.
Methods: We recruited 241 consecutive patients <66 years of age who were admitted with acute ischaemic stroke. Serum levels of sICAM-1 and sVCAM-1 were determined within 12 hours from admission. Seventy-six subjects without evidence of cardiovascular disease, matched for age and sex, served as controls.
Results: Patients with acute ischaemic stroke had higher sICAM levels compared to controls [267 (220-325) versus 200 (179-225) ng/ml, p<0.001]. Sixteen (6.6%) patients died during hospitalization. sICAM-1 and sVCAM-1 levels were significantly higher in patients who died compared to those who survived [370 (324-453) versus 260 (219-313) ng/ml, p<0.001 and 790 (495-985) versus 576 (494-671) ng/ml, p= 0.01, respectively] but only sICAM-1 levels were independently associated with early death, after adjusting for various confounding factors. For 10 ng/ml increase in sICAM-1 levels there was a 9% higher risk of dying. Cut-off point analysis revealed that sICAM-1 levels >322 ng/ml were the optimal points that discriminated those who died from the rest of the patients.
Conclusions: sICAM-1 levels can independently predict the risk of early death in ischaemic stroke patients emphasizing the role of inflammation in the evolution of ischaemic stroke.

ISSUES FOR PATIENTS AND NURSES

P604 Both primary and secondary prevention patients receiving their first implantable defibrillator are uncertain but optimistic: results from a pilot investigation

S. Carroll, H.M. Arthur. *McMaster University, Health Sciences (Nursing), Hamilton, Canada*

Purpose: Increasingly, patients are receiving implantable defibrillators (ICD) for primary prevention of sudden cardiac death. Primary prevention patients (PP) may be different from secondary prevention patients (SP), who have experienced a life threatening cardiac event. No studies have prospectively examined the emotional issues associated with ICDs in these two groups of patients. Objectives: 1) to determine if PP patients receiving ICD versus SP differ in uncertainty, optimism, and anxiety 2) to explore relationships among the variables. It was hypothesized that the groups would differ among the variables.
Methods: This was a prospective, descriptive, pilot study of 30 patients receiving their first ICD for PP or SP. Measurements included the Mishel Uncertainty in Illness Scale (MUIS-C), State-Trait Anxiety Inventory (STAI) and Life Orientation Test (LOT-R). Measurements were obtained pre-implant (baseline), at their first post-implant visit, and at one month.
Results: 15 PP and 15 SP patients consented to participate. Both groups were predominantly male (66.7%). The mean (SD) age in the PP group was 65.7(11.3) versus 67.9(7.7) in the SP group. Prior to ICD implant, patients in both groups had moderately high uncertainty scores (mean PP = 67.67(13.36), SP = 70.27(6.80); p = 0.507). Both groups had significant decreases in uncertainty between baseline and one-month follow-up ($F_{2,56}$ = 3.26; p < 0.05). At one month the PP group had significantly lower uncertainty scores than the SP group (mean 62.33(4.17) vs. 67.87(4.61); p = 0.002). Baseline LOT-R scores were 15.67(3.8) for PP and 16.47(3.6) for SP; p = 0.557. Between group state anxiety scores were not different at baseline (mean PP= 37.40(10.0), SP=37.73(13.6); p = 0.940). STAI scores decreased in both groups over time ($F_{2,56}$ = 3.61, p <0.05). No significant correlations were found among optimism, uncertainty, or state anxiety.
Conclusions: This pilot study reveals moderately high levels of uncertainty, an optimistic disposition but no significant anxiety in patients receiving ICDs for either PP or SP. The findings have important implications for nursing management of patients receiving ICDs. Further research is required regarding interventions to ameliorate uncertainty.

P605 Do Not Resuscitate (DNR) - orders in intensive coronary care units. Should the patient be informed? - a survey of attitudes and experiences of nurses in Norway

M. Naess. *Oslo, Norway*

Purpose: In some cases it is ethically right to abstain from resuscitation. When such a decision is made, a "Do Not Resuscitate" (DNR) -order is set to tell physicians and nurses that the patient shall not be resuscitated if cardiac arrest occurs. One of the questions that arise is whether a critically ill coronary patient should be informed about the DNR-decision? The aim of the present study was to investigate DNR attitudes and experiences of nurses working in intensive coronary care units (ICCUs).
Methods: A questionnaire was constructed in a web-based program. Invitations were generated anonymously and sent automatically by e-mail to 295 nurses working at ICCUs in eight different hospitals in Norway.
Results: The response rate was 60% (176/295). The majority of the nurses (158/176, 90%) had participated in discussions leading to a DNR – order, and 69% (121/176) had initiated the process that led to one. A total of 74% (130/176) of the nurses thought the patient should be informed about a DNR – order. Given a mentally adequate and conscious patient, 50% (88/176) answered that they "to a relatively high" or "a very high degree" had experienced non-informed patients with a DNR – order. Nurses who had experienced non-informed patients were less positive to inform about a DNR-order than other nurses without such experience (53/88 (60%) vs. 77/88 (88%), p<0,001).
Conclusions: In general, nurses seem to take active part in the DNR decision-making process. The study revealed a positive attitude among nurses concerning to inform patients about a DNR-order. Further, half of the nurses had experienced that such information was not given. There may be several explanations for this discrepancy. Patients are treated individually and the right to know does not mean that every patient wants to know or needs to know. The timing of the information and the opportunity to provide it can also be a problem for such critically ill patients in the ICCU.

P606 Is there a place for coronary calcification scoring in a nurse-led Rapid Access Chest Pain Clinic?

A. Pottle[1], J. Breen[2]. *[1]Royal Brompton & Harefield Nhs Trust, Dept. of Cardiology, Harefield, United Kingdom; [2]Royal Brompton & Harefield NHS Trust, Cardiology, Harefield, United Kingdom*

Purpose: The Rapid Access Chest Pain Clinic (RACPC) was set up to allow rapid assessment of patients suspected by their GP, of having new-onset angina. All patients attending the clinic have an ECG and chest x ray. 70% of patients also undergo an exercise test. CT coronary calcium scoring (CCS) was introduced into the clinic to investigate its use as an additional risk stratification tool.
Method: Between April 2004 and April 2006, 377 patients attended the nurse-led clinic. In addition to standard tests, CCS was carried out in all men over the age of 40 years and all women over the age of 50 years using an ECG-gated Multislice CT scanner. Scans are scored using the Agatston scoring system. Patients with a CCS >75th centile are considered to have a high risk of obstructive coronary artery disease (CAD) and those with a score <25th centile are felt to have a low risk. Results from the CCS were correlated with the patient symptoms and results from the exercise test, if performed. Patients with CCS <25th centile were sent a questionnaire 3 months after attendance at the clinic to establish if they had suffered any cardiac events in this time.
Results: A total of 313 CCS scans were performed. 74 patients had scores >75th centile (23.6%) and 156 patients had scores <25th centile (49.8%). Of the 74 patients with a high score, 15 had a positive exercise test, 16 had negative tests, 17 were unable to exercise, 13 had borderline or inconclusive tests and the test was not felt necessary in 13 patients. A total of 46 patients from this group underwent

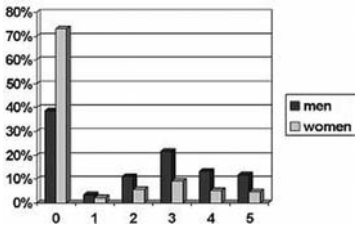
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

coronary angiography (62%) of whom only 8 (10.8%) were found to have normal coronary arteries.
In the group with CCS <25th centile, 7 had a positive exercise test, 81 had negative tests, 41 had inconclusive tests, 20 were unable to exercise and the test was not felt necessary in 7 patients. 14 patients in this group underwent coronary angiography (8.9%) of whom only one patient required any intervention, an angioplasty and insertion of a stent. 95 patients returned the questionnaire (60.8%) and none had suffered a cardiac event in the 3 months following the visit to the clinic.
Conclusion: A CCS of <25th centile is a useful tool in excluding significant CAD in patients with atypical pain and negative exercise tests. It is also useful in patients unable to exercise or with borderline tests as this study suggests that their chance of having significant CAD is low. Provision of this test in a nurse-led RACPC may help in reaching a diagnosis and may prevent the need for angiography or perfusion scans in this patient group.

P607 Perception of sexual dysfunction in patients with heart failure

B. Gonzalez, D. Mas, M. Arenas, J. Lupon, A. Urrutia, M. Domingo, C. Diez, S. Altimir, T. Pascual, V. Valle. *Hospital Universitari Germans Trias i Pujol, Badalona, Spain*

Background: sexuality is often considered not relevant and some times even not considered when patients (P) with heart failure (HF) are evaluated. Nevertheless, satisfaction with sexual functioning might be an important component of quality of life. Although it is probable that perception of sexual limitation does not correlate with actual sexual capacity, due to age or sexual needs, this perception is what we can really explore. Objective: to analyse how many P perceive a reduced sexual function as a result of HF and explore possible relationships of this perception with demographic and clinical variables.
Patients and Method: we analyse the question that addresses the influence of HF on sexual activity (MLWHFQ) in 604 P (71% men; median age 69 years; 73% living with partner). Scores asking about sexual activity limitation due to HF can range from 0 (no) to 5 (very much).
Results: Fifty-one percent of P reported some degree of sexual difficulty, and about 40% of them indicated that HF influenced their sexual function much or very much (scores 4-5). We found a significant ($p<0.001$) difference in the proportion of male (61%) and female (27%) that reported some degree of sexual difficulty (figure), and also in the proportion of P with (64%) and without partner (21%). Older P reported less problems compared to younger P (r= -0.20, $p<0.001$). No relationship with NYHA class, time of HF symptoms, and presence of diabetes, hypertension or depressive symptoms were observed. We found a week but statistically significant relationship with LVEF (r= -13, p=0.002) and with Barthel index (r= 0.15, $p<0.001$).



Sexual limitation perception scores

Conclusion: half or our P with HF reported some degree of sexual difficulty, and 40% of them considered it important. These P were mainly men, younger, and those living with partner.

P608 The process of changes in the recognition of disease by adults with congenital heart disease in Japan: a qualitative study

R. Ochiai[1], T. Kusakabe[1], M. Miyashita[1], H. Sato[2], A. Murakami[2], M. Kayama[3], K. Kazuma[3]. *[1]The University of Tokyo, Department of Adult Nursing, Tokyo, Japan; [2]Ibaraki Prefectural Univ. of Health Sciences, Center for Medical Sciences, Ibaraki, Japan; [3]St. Luke's College of Nursing, Psychiatric & Mental Health Nursing, Tokyo, Japan*

Purpose: To investigate the process of changes in the recognition of disease by adults with congenital heart disease, in order to enhance the quality of care provided by health care professionals.
Methods: A semi-structured interview was conducted with 17 adults (age range: 22 – 35 years) with congenital heart disease. Data from the interviews were analyzed in accordance with the grounded theory approach.
Results: Primary diseases and operative procedures performed on the subjects were varied, such as radical surgery for tetralogy of Fallot, surgical closure of ventricular septal defects, etc. The analysis revealed three stages of change in recognition of the disease during the course of transition to adulthood: (1) recognizing to have the disease as a normalcy for one's self (2) confronting the disease, and (3) finding meaning in one's life with the disease. During the first stage, subjects were aware that, no matter how severe their disease was, it was an inevitable physical characteristic of theirs, and that having the disease was to be their ordinary state. During the second stage, subjects faced the disease in several ways, such as by a conversion of a death-oriented consciousness to a survival-oriented awareness (triggered by a deterioration in their condition, or the death of another patient with the same disease), understanding the limits imposed on their social activities (triggered by problems related to employment, work, marriage, etc.) and attempting to become independent from their parents (triggered by beginning to visit outpatient clinics on their own, etc.) Recognition of the disease varied among individuals, depending on whether or not they had confronted the disease and what prompted them to confront it. With reference to the third stage, subjects who had confronted the disease were able to find positive meaning in life, saying for example: "I have gotten to know lots of people as a result of my disease." During this process, subjects needed (1) provision of information about the disease from childhood, (2) provision of psychological support, and (3) facilitation of close linkages between multiple specialties including pediatrics, cardiology and others.
Conclusions: Confronting the disease served as a turning point during the process of changes in recognition of the disease by adults with congenital heart disease. Though patients suffered while confronting the disease, those who had confronted the disease found positive meaning in their own life with the disease.

P609 Improvement of prognosis of acute coronary syndromes by modification of lifestyle

J. Ferrieres[1], P. Hericotte[2], C. Daugareil[2], M. Baudet[2]. *[1]Toulouse, France; [2]Centre Hospitalier General, Service de Cardiologie, Dax, France*

Purpose: Health education by a nurse might be an interesting approach to decrease relapses after an acute coronary syndrome (ACS).
Methods: 886 consecutive patients hospitalized for an ACS were educated by a nurse. The objective was to decrease the prevalence of the 6 major risk factors and to modify the food practices (evaluated by 15 items). Initial examinations allowed the collection of the items. Each answer was transformed into a numerical, positive score from 1 to 3 (in the direction of the aggravation of atherosclerosis), negative from -1 to -3 (in the direction of a protection), and 0 (without influence). The patients were re-examined every 6 months. Progress was observed for the control of risk factors (the score changed from 6.3 to 4.5, $p<0.001$) and the food patterns (1.5 to -7.1, $p<0.001$). The evolution was compared according to whether the patients were voluntary (Group 1, n=285) or not (Group 2, n=593) for a health education program.
Results: The two groups were similar according to sex, the scores of risk factors and of the food practices, the distribution of the coronary artery lesions, the ejection fraction and the treatment prescribed at discharge. On the other hand, patients were older in Group 2 (63.5 ± 12 versus 61 ± 12, $p<0.001$). 8 patients, lost to follow up, were eliminated from the analysis. With a 30 ± 14 month of follow up, Group 1 had less cardiovascular events (43 patients with events (15%) versus 172 (29%), $p<0.001$, even after adjustment for age), less myocardial infarction (4 (1%) versus 29 (5%), $p<0.02$), less heart failure (2 (1%) versus 48 (8%), $p<0.001$), or less other events related to atherosclerosis (34 (12%) versus 121 (20%), $p<0.01$). Group 1 was less often hospitalized for a cardiovascular disease (41 (14%) versus 161 (27%), $p<0.001$) and has undergone less revascularisation by by-pass surgery or angioplasty (17 (6%) versus 65 (11%), $p<0.02$). Total deaths were less frequent in Group 1 (4 (1%) versus 61 (10%); Kaplan-Meier analysis with Log-rank test ($p<0.001$); Relative Risk: 0.14; CI: 0.06-0.32) as well as cancers (5 (2%) versus 29 (5%), $p<0.05$).
Conclusions: Unfavourable lifestyle can be partially corrected. Improvement of lifestyle influenced prognosis in this sample of ACS.

P610 Do patients with congestive heart failure want the opportunity to have sexual counselling from the staff in an out-patient clinic?

J. Milton[1], C. Anker[1], K. Koertz[1], T. Poulsen[2], L. Videbaek[1], H. Mickley[1]. *[1]Odense University Hospital, Department of Cardiology, Odense, Denmark; [2]Odense University Hospital, Department of Cardiology B, Odense C, Denmark*

Purpose: One important element of cardiac rehabilitation is counselling about sexual activity. However, in patients with congestive heart failure (CHF), data addressing the importance of this issue are scarce. Consequently, we set out to assess the attitude of CHF patients with regard to sexual counselling in the setting of an out-patient clinic.
Methods: The investigation consisted of two sub-studies (study 1 and study 2). In study 1 the staff in our out-patient CHF clinic consecutively registered how often the patients spontaneously addressed the topic of sexuality and sexual functioning during their visits. In study 2, a semi- structured questionnaire was mailed to all patients one week before their scheduled visit. In the questionnaire the patients were asked to consider, whether sexual counselling would be of interest for CHF patients entering an out-patient clinic. Study 2 also included a registration of how often the patients actually addressed the issue of sexuality and sexual functioning during their subsequent visit.
Results: In study 1 a total of 264 CHF patients (196 men, 68 women) were included. Eight (3%) of these - all men - spontaneously talked about sexuality during

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

the following consultation. In study 2, the questionnaire was mailed to 145 consecutive patients (92 men, 53 women) of which 18 (12%) (15 men, 3 women) by themselves addressed the topic of sexuality during the subsequent visit. Fifty-seven of the 145 patients answered and returned the questionnaire, indicating a 40% response rate. Thirty-two of the 57 (56%) responders considered it of importance to have the opportunity to receive sexual counselling, and the large majority of these were males (5 women vs. 27 men). Contrary, patients who found it not relevant to receive sexual counselling from the staff in the CHF clinic more frequently were of female gender (11 women vs.13 men).
Conclusions: The results of our study indicate that the majority of CHF patients welcome the chance to talk more openly about sexuality and sexual functioning with the staff in an out-patient clinic. Women with CHF appear to be less likely to seek counselling about sexuality than their male counterparts.

P611 Nicotine dependence, smoking cessation and quality of life in Hellenic coronary heart disease patients

D. Tziallas[1], E. Papathanassoglou[2], C. Kastanioti[1], H. Milionis[1], P. Skapinakis[3], M. Gouva[4]. *[1]University Hospital of Ioannina, Critical care nursing, Ioannina, Greece; [2]University of Athens, Nursing School, Athens, Greece; [3]University of Ioannina, Medical School, Ioannina, Greece; [4]Technical University of Ioannina, Nursing, Ioannina, Greece*

Purpose: Cigarette smoking remains a significant risk factor for coronary heart disease, and smoking cessation rates in Hellas are low. Evidence regarding smoking cessation in Hellenic patients is very scarce. We conducted a pilot prospective correlation study to explore associations between nicotine dependence and a) smoking cessation, b) coronary heart disease, c) quality of life, and d) demographic characteristics in Hellenic patients undergoing coronary arteriography.
Methods: We studied 156 consecutive patients with a referral for coronary arteriography, for 6 months. Data were collected at the time of hospital admission and at 3 and 6 months post-discharge. Of the participants 86 were smokers, and 70 non-smokers. Nicotine dependence was evaluated by means of the Fangerstrom test, and quality of life was assessed by the SF-36 scale. Coronary heart disease severity was quantified through the NYHA classification.
Results: Of the smokers' group, 58% had ceased smoking within 6 months. The degree of nicotine dependence associated to neither smoking cessation nor the presence or severity of coronary lesions. No significant differences between smokers and non-smokers were observed in regard with total or subscale quality of life ratings, at baseline. Various associations between nicotine dependence scores and demographic characteristics were noted, including a moderate inverse association to educational level (Pearson's r (r)=0.29, p=0.02), a positive association to monthly income (p=0.033) and an association with type of occupation (p=0.021). In the smokers' group, the degree of nicotine dependence correlated inversely with the perception of general health status (r=-0.297, p=0.007), and positively with emotional well-being (r=0.302, $p<0.001$), at baseline. At 6 months, 25.6% of smokers exhibited increased nicotine dependence compared to the 3 month follow-up, while, 46.5% reported the same degree of dependence and 3.5% lower degree of dependence. The change in nicotine dependence scores associated with the perception of general health at 3 months (r=0.339, p=0.003) and at 6 months (r=0.339, p=0.007) of follow up.
Conclusions: These pilot results suggest that nicotine dependence may be a factor in the quality of life of Hellenic coronary disease patients. Specific groups in risk for nicotine dependence have been identified. These results may inform targeted interventions to enhance smoking cessation in Hellenic coronary care patients.

P612 Quality of life and depressive symptoms in HF patients compared with a population of community dwelling elderly: is it that bad?

I. Lesman-Leegte, T. Jaarsma, H.L. Hillege, D.J. Van Veldhuisen, R. Sanderman. *University Medical Center Groningen, Dept. Cardiology, Groningen, Netherlands*

Background: Heart Failure (HF) patients report lower quality of life (QoL) and more depressive symptoms compared to a healthy population. Knowledge about QoL in HF patients is mainly derived from clinical trials in which older patients, women and patients with co-morbidities are underrepresented.
Aim: To determine the unique impact of HF on QoL and depressive symptoms in HF patients and compare the latter with an age and gender matched elderly population according to gender and co-morbidities.
Methods: Data were collected in 781 HF patients (36% female; age 72±9; NYHA II-IV) and 781 elderly. Participants completed the RAND-36, the Ladder of life and the Centre for Epidemiologic Studies-Depression scale (CES-D).
Results: QoL on all domains and depressive symptoms (CES-D $\geq$ 16) were significant worse in HF patients but were most impaired in the domains reflecting physical health. In both men and women with HF, QoL (F= 38.53, $p<0.05$) and depressive symptoms (chi2=141.1, $p<0.001$) were more impaired compared with their elderly counterparts. In HF women physical, mental QoL (including depressive symptoms) and well being were significant worse compared with HF men. HF patients without chronic conditions had decreased QoL and more depressive symptoms even when compared with elderly with chronic conditions (table 1).

Table 1. QoL in both populations

RAND 36 (0-100)	Without co-morbidties		With co-morbidities	
	HF patients (n=208)	Elderly (n=392)	HF patients (n=573)	Elderly (n=389)
Physical functioning	42±28	73±25	32±25	61±28
Role limitations physical	26±38	72±38	17±32	60±42
Vitality	45±24	68±18	38±23	60±19
Mental health	69±23	77±16	65±23	73±18
Social functioning	58±30	83±22	53±32	74±25
Well being (0-10)	6.2±1.9	7.3±1.3	6.4±1.8	7.0±1.4
Depressive symptoms	32%	16%	42%	27%

Conclusions: HF has a dramatic impact on QoL and depressive symptoms of elderly women and patients with co-morbidities, and is much lower than a comparable elderly population. Adequate screening tools and (non)pharmacological interventions to improve QoL and depressive symptoms are necessary for these vulnerable groups.

P613 Heterogeneity in service delivery and inequity in access are common characteristics of chronic heart failure management programs

A. Driscoll[1], L. Worrall-Carter[1], D.L. Hare[2], P.M. Davidson[3], B. Riegel[4], A. Tonkin[5], S. Stewart[6]. *[1]Deakin University, School of Nursing, Melbourne, Australia; [2]University of Melbourne, Melbourne, Australia; [3]University of Western Sydney, Sydney, Australia; [4]University of Pennsylvania, Pennsylvania, United States of America; [5]Monash University, Melbourne, Australia; [6]Baker Institute, Melbourne, Australia*

Background: The prevalence of heart failure in Australia is similar to that of Europe. In Australia, chronic heart failure management programs (CHF-MPs) have become part of standard care for patients with Chronic Heart Failure (CHF). However, heterogeneity among programs is common which can result in variable patient outcomes.
Method: A national survey was undertaken of 59 post-discharge CHF-MPs identified from within the Australian health care system. Two had ceased operating and one centre declined to participate in the study. A 33-item investigator-developed questionnaire, examining the characteristics and interventions used within each CHF-MP, was sent to the remaining 56 CHF-MPs. A response rate of 100% was achieved.
Results: Our survey revealed a disproportional distribution of CHF-MPs across the Australian continent: the State of Victoria had 3.6 CHF-MPs/million population, New South Wales had 3.7 CHF-MPs/million population, Queensland had 1 program/million population, South Australia had 0.3 CHF-MPs/million population and Western Australia had 1 program/million population.Overall, 8000 post-discharge CHF pts (median: 126; IQR: 26-260) were managed via CHF-MPs. Approximately 40,000 CHF pts are discharged from metropolitan institutions nationally, this represents only 22% of the potential caseload for these cost-effective CHF-MPs. Only 8% of these programs were located within rural regions. The majority of CHF-MPs were located within an acute metropolitan hospital (52%) and 36% were community based (all associated with a hospital). Heterogeneity of CHF-MPs in applied models of care was evident with 75% of CHF-MPs offering CHF outpatient clinics and 77% conducting home visits. Of the programs offering home visits 78% were funded by regional government ($p<0.048$). There were no nurse-led CHF outpatient clinics. A hybrid approach to CHF-MPs was common with many CHF-MPs comprising an outpatient clinic, home visits and inpatient visits. Various medications were titrated by nurses in 43% of CHF-MPs. In the programs that allowed nurses to titrate medications 79% were located in an acute hospital ($p<0.011$).
Conclusion: Variability of service availability is of concern within the context of universal coverage. In addition, heterogeneity between programs and the diversity in models of care delivery highlights the inconsistency and questions the quality of health related outcomes. We are currently analysing health outcome data from the 1015 patients managed in these CHF-MPs to describe the relationship between quality of care and health outcomes.

P614 Factors associated with self-care behavior among patients with heart failure

N. Kato, N. Ito, K. Kinugawa, A. Yao, K. Kazuma. *The University of Tokyo, Department of Adult Nursing/Palliative Care, Tokyo, Japan*

Purpose: The frequency of readmissions among patients with heart failure (HF) is very high in Japan. It emphasizes the need for improvement in self-care behavior. Little is understood about the factors associated with self-care behavior among HF patients. The present study aimed to identify factors associated with self-care behavior among HF patients in Japan.
Methods: We applied a cross-sectional survey of outpatients diagnosed with HF (aged at least 20 years old) using a self-administered questionnaire and medical records. Self-care behavior was assessed using The European Heart Failure Self-Care Behavior Scale - Japanese version (EHFScBS-J) developed by our team. We investigated the followings: physical condition (e.g. brain natriuretic peptide: BNP, left ventricular ejection fraction: LVEF, experience of HF symptoms: shortness of breath, edema, fatigue, co-morbidity: hypertension, diabetes melli-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

tus, anemia etc.), perception and psychological states (e.g. knowledge and understanding of HF, depression), social issues (e.g. feeling free to question their doctor or nurse about anything they do not understand), and demographic attributes (e.g. age, job). Data were analyzed using multiple regression analysis to explore associated factors.
Results: A total of 125 patients provided written informed consent to participate in the survey and responses were obtained from 116 of them (94.3%). The mean age was 64.6±15.3 years, males accounted for 70.7% of the respondents and most of the etiology comprised ischemic heart disease and cardiomyopathy. Of the 116 patients, 56.0% had BNP <100 pg/ml, 6.0% had LVEF<30.0%, 43.1% had a full time job, 56.9% had edema, and 34.5% had diabetes mellitus. The mean EHFScBS-J score was 32.6±9.1. Multiple regression analysis indicated that a higher EHFScBS-J score meaning less HF self-care behavior, is associated with the occurrence of edema (standard partial regression coefficients: sb= -0.27, p <0.01), a lower BNP level (sb = -0.22, p = 0.02), less understanding of HF (sb = -0.21, p = 0.02), feeling free to question their doctor or nurse (sb = 0.19, p = 0.03), having a full time job (sb=0.19, p = 0.04) and diabetes mellitus (sb = 0.18, p = 0.04).
Conclusion: The results suggested that the experience of edema, BNP, comorbidity of diabetes mellitus and employment should be considered, and patients should be educated about pathophysiology and self-care behavior concerning HF to positively impact self-care behavior.

P615 Paroxysmal supraventricular tachyarrhythmia in a Swedish population: consequences on health-related quality of life

U. Walfridsson[1], A. Stromberg[2], M. Janzon[2], H. Walfridson[2]. *[1]University Hospital, Cardiology, Linkoping, Sweden; [2]Faculty of Health Sciences Linkopings Univers, Dept.of Medicine and Care Nursing Science, Linkoping, Sweden*

Patients with paroxysmal supraventricular tachyarrhythmia (PSVT) have both recurrent and often frequent symptoms. Living with the risk of experiencing an attack of PSVT not only affects the patient during an attack, it also influences the life situation between attacks. Health Related Quality of Life (HRQOL) has been studied in different contexts of patients with supraventricular arrhythmias, however at the time for this study as well as today, data from Scandinavia were lacking concerning HRQOL in PSVT patients.
The aim of this study was to describe the Health Related Quality of Life in patients with atrioventricular nodal reentry tachycardia (AVNRT) or Wolff-Parkinson-White (WPW) syndrome referred for RF-ablation and compare these patients to and an age and gender matched Swedish norm population.
Method: Health Related Quality of Life was assessed with two generic instrument: Short Form-36 (SF-36) and EuroQol (EQ-5D). The population consisted of 176 patients (n=97 AVNRT, n=79 WPW). Mean age was 53.1±16.2 years in patients with AVNRT and 42.4±14.5 years in WPW patients. In the AVNRT group 33% were men and in the WPW group 67%.
Results: The patients with PSVT scored their HRQOL lower in all dimensions of SF-36 except the dimension bodily pain compared with the norm population. Patients with PSVT with fewer arrhythmia attacks (<once a month) had better HRQOL in all eight of SF-36 dimensions and EQ-5D index score. However, the duration of the attacks did only affect the SF-36 dimension; general health. Patients suffering from symptoms like shortness of breath and anxiety at rest, during arrhytmia attack, percieved significantly lower general health and social functioning. Women with PSVT scored lower in mental health, physical function and vitality dimension and had a significantly lower index score in EQ-5D. Patients with AVNRT had lower HRQOL in the dimensions general health, physical function and bodily pain compared to patients with WPW.
Conclusion: PSVT is not classified as a life-threatening condition but these patients had a significantly lower HRQOL compared to an age and gender matched Swedish norm population. A lower HRQOL in some dimensions was found in women with PSVT compared to men, and in patients with AVNRT compared to WPW patients.

P616 Acute heart failure events in a cohort of elderly patients with chronic heart failure

S.C. Inglis[1], J.D. Horowitz[2], S. Stewart[3]. *[1]University of Queensland, Faculty of Health Sciences, Brisbane, Australia; [2]University of Adelaide, Woodville, Australia; [3]Baker Heart Research Institute, Melbourne, Australia*

Purpose: Acute heart failure (AHF) is not uncommon in patients with chronic heart failure (CHF); it may be recurrent and lead to a pattern of costly hospitalisations. Limited studies report the natural history of AHF in patients with CHF.
Methods: A detailed analysis of the pattern of non-fatal and fatal episodes of AHF in a cohort of elderly patients with a confirmed diagnosis of CHF (n=58) and subject to standard care was performed. Data were collected over a minimum period of 7.5 years.
Results: Of the 58 patients studied (59% male, mean age 76±10 years and mean LVEF 39±12% at the time of study recruitment), 44 patients (76%) had at least one admission to hospital for AHF and accumulated 79 AHF admissions in total (admission diagnoses: 66% APO, 33% left ventricular failure and 1% cardiogenic shock). Care delivered during these 79 admissions (mean 1.8±1.2 admissions/patient) included a total of 606 hours in ICU/HDU (mean 13.8±61.4 hours/patient) and 1182 hours in CCU (mean 26.9±63.3 hours/patient) for a total length of stay of 615 days (mean 14.0±10.1 days). Patients were managed with a range of vasoactive infusions and respiratory support relevant to the time period of these admissions (1997-2003). Patients with an admission for AHF had greater comorbidity as evidenced by a higher mean Charlson index (3.2 vs. 2.3, p=0.045). Of the 44 patients with an admission for, 34% experienced an unplanned readmission to hospital within 28 days of discharge (19 readmissions in total, 58% with an admission diagnosis of AHF), two patients (4.5%) died during an admission, with 4.5%, 13.6% and 11.4% dying within 3, 6 and 12 months respectively following an admission for AHF (p>0.05). The mean survival time from discharge for AHF to death was 21.1 months (95% CI 12.1, 30.1 months). Patients without an admission for AHF (n=14) survived 5.9 months longer on average than those with an admission (p=0.56). There were 4 occasions of presentation at an emergency services department for AHF without an admission. Seasonality also impacted on admissions for AHF with more admissions occurring in colder months (67%) compared to warmer months (37%) (p=0.03).
Conclusion: These data provide key insight into the long-term mortality in patients with CHF admitted with AHF. They also contrast other studies reporting higher short-term mortality in those admitted with AHF.

P617 Factors influencing the effectiveness of smoking cessation programs in patients with heart disease: a systematic review

D. Tziallas, C. Kastanioti, M. Fatoutou, D. Kaskanis, V. Tziallas, P. Skapinakis. *University Hospital of Ioannina, Ioannina, Greece*

Purpose: Smoking, is the single most important avoidable cause of mortality. While smoking cessation interventions have been shown to work, questions remain about how to increase their efficacy. The aim of this review was from a nursing percpective to describe the influencing factors of a smoking cessation program in heart disease patients.
Methods: Databases searched included MEDLINE, EMBASE, and COCHRANE, from the start of the database up to March 2004. The search strategy used both key words and MeSH term searches and took the form of: (Myocardial ischemia or coronary disease) and (smoking cessation) and (nicotine-bupropion - antidiprease) and (randomized controlled trial or synonyms). Any randomized controlled trial evaluating the efficacy of smoking cessation program by any method, e.g. brief counseling, nicotine replacement therapies, or combination of methods, in cigarette smokers with a diagnosis of coronary heart disease was included. Smoking status must be measured on at least two occasions to ascertain which smokers have quit. The "control group" therefore comprised those who continued to smoke and these are compared with those who ceased smoking. Two reviewers assessed studies that appeared to meet the inclusion criteria to determine acceptance in the review. The information collected from each trial included study design, time and setting of study, patient characteristics, length of follow-up, method of smoking cessation program and the efficacy of program (outcomes, effectiveness, p value)
Results: A total of 17 papers included in the review. Research findings consistent with previous reviewsshow that self-help strategies alone are ineffective, but counsellingand pharmacotherapy used either alone or in combination canimprove rates of success with quit attempts. Four studies provided ineffective results for brief counsellingintervention when it was only hospital-based.Four studies provided sufficient evidence of the efficacy of single pharmacotherapy, combined pharmacotherapy, and psychologic alinterventions. Finally, three studies showed strong evidence that all interventions included nurse counselling, self-help materials,either with or without pharmacotherapy and follow-up contact either in person or by telephone; affected the likelihood of quitting.
Conclusions: Clinicians can effectively treat tobacco use and dependence in the general population using counselling and first-line pharmacotherapies, especially in combination; self-help approaches alone are unlikely to suffice. Thus, all patients should be screened for tobacco use and offered effective treatment.

P619 Monitoring and follow-up of defibrillator devices able to detect fluid accumulation in the lungs

C. Segura[1], C. Rodriguez[2], M.D. Miranda[1], J.M. Arizon[2], J.C. Castillo[2], L. Pastor[1], J. Leal[1], A. Lopez[2]. *[1]Hospital Reina Sofia, Cordoba, Spain; [2]Hospital Nuestra Senora de Valme, Sevilla, Spain*

Introduction:- Heart failure is a complex syndrome that affects the capability of left ventricle for filling and expulsion, being a frequent cause of hospital admissions.There is an implantable device able to predict heart failure decompensations by monitoring the fluid accumulation through transthorathic impedance. When this parameter reaches a predefined programmable threshold the device triggers an acoustic or visual alert.
Materials and methods: Multicentre pilot study including 21 patients implanted with an automatic defibrillator provided with the algorithm that detects the level of in the chest. All these patients were included in an educational program guiding them in fluid accumulation control focusing on diet, weight, medication, acoustic alerts according to scheduled times and contacting directly with our clinics if

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

necessary. An external device was delivered to one patient allowing him to have access to visual alerts that could reflect fluid accumulation.
Results: We received 49 telephone calls from 12 out 21 patients (57%). All telephone calls appeared to be positive, being confirmed later with the device programmer that each of the patient were entering in heart failure decompensation since they showed fluid accumulation increase. In no case, patient admission was required, and only by means of home treatment modification, symptoms were eliminated, being later on confirmed by telephone.
Conclusions: This fluid accumulation monitoring algorithm is an effective feature for patients with heart failure. The educational program given in clinic office has been effective in our patients. The good training with the external device avoided unnecessary admissions and reduced the number of telephone consultations.

P620 Intensifying the care for heart failure patients with HF-nurses using new ICT-developments

C.M.H.B. Lucas, G.V.J. Cleuren. *Rijnland Hospital, Leiderdorp, Netherlands*

Purpose: The care for heart failure patients requests immediate and direct information exchange between many caregivers both in primary and secondary care, particularly heart failure nurses. It is known that minor changes in the physical condition of these patients can have major consequences resulting in (re) admission to the hospital or demice. Fast communication between the individual caregivers using ICT therefore is mandatory to provide optimal care.
Methods: At the Rijnland Hospital, Leiderdorp, during 2006 a program has started involving a computersystem (Medconnect) which enables cardiologists, heart failure nurses, home care, pharmacists and GP's to exchange information about their CHF-patients, at the moment the patients has contacted one of the mentioned caregivers. Therefore a regular internetsystem is used. In addition the netwerk itself includes a database providing every caregiver with recent knowledge and developments in CHF-care.
Results: Starting in 2006 sofar 2 heart failure nurses, 2 cardiologists, 8 GP's, 6 pharmacists, 15 elderly homes and 2 home care nurses are involved in the system supplying care to about 400 CHF-patients. The program itself is used on a regular base by all participants particularly the heart failure nurses as first persons being called upon by the CHF-patients in case of problems and questions. Several misunderstandings about care of patients have been prevented by having immediate knowledge about changes taking place or having been made by one of the caregivers. Extensive data will be present in the near future.
Conclusion: Using a regular ICT-network containing both a database with scientific information about heart failure and information about CHF-patients seems to be an efficient way to improve communication between caregivers and therefore quality of care given to a large cohort of heart failure patients. The system itself seems to be so succesfull that nowadays its application is being expanded to other categories of chronic patients demanding intensive care by more than 1 caregiver (including nurses) for example patients with Diabetes mellitus, cerebrovascular accidents, COPD and chronic bowel diseases.

P621 Validity and reliability of the European Heart Failure Self-Care Behavior Scale -Japanese version

N. Kato, N. Ito, K. Kinugawa, A. Yao, K. Kazuma. *The University of Tokyo, Department of Adult Nursing/Palliative Care, Tokyo, Japan*

Purpose: In Japan the frequency of readmission among patients with heart failure (HF) is very high, which emphasizes the need to improve self-care behavior. To support the self-care behavior of HF patients, we need to evaluate their behavior accurately using an instrument designed for HF patients. Reviewing the literature, we found the European Heart Failure Self-Care Behavior Scale (EHFScBS), developed by Jaarsma et al. The EHFScBS is a 12-item, self-administrated questionnaire, which has been tested for validity and reliability. Therefore, the purpose of this study was to evaluate the validity and reliability of the EHFScBS-Japanese version (EHFScBS-J).
Methods: After we received permission from the author to translate the EHFScBS into Japanese, it was translated according to a general translating step of the scale, and the EHFScBS-J was discussed with our team. It was necessary for some items to be modified to suit to the Japanese environment, and the author gave us permission to do so. After some patients confirmed the face validity of the EHFScBS-J, we carried out the main survey. Subjects were outpatients diagnosed with HF (aged at least 20 years old), who were asked to complete a questionnaire including the EHFScBS-J. Subject's physical condition (e.g. brain natriuretic peptide) and demographic attributes (e.g. age) were obtained from medical records. Validity was assessed through factor validity, concurrent validity, and internal consistency. Concurrent validity was assessed using spearman's rank correlation coefficient between the EHFScBS-J and the Self-Care Agency questionnaire for patients with chronic illness. Reliability was assessed by test-retest reliability.
Results: A total of 125 patients provided written informed consent to participate in the survey and responses were obtained from 116 of them (94.3%). The mean age was 64.6±15.3 years, and males accounted for 70.7% of the respondents. The result of exploratory factor analysis and confirmatory factor analysis confirmed the one dimensionality of the EHFScBS-J, in concordance with the result of the author. The contribution to one factor was 77.2%. Cronbach's alpha was 0.71. Spearman's correlation coefficient between the EHFScBS-J and the instrument for concurrent validity was -0.29 ($p<0.05$). The intraclass correlation coefficient of the scale was 0.69 and the weighted kappa of each item ranged from 0.33 to 0.87.
Conclusion: The EHFScBS-J was a valid and reliable scale for measuring the self-care behavior of HF patients.

P622 Telephone support by heart failure nurses has a significant impact on readmission rate and survival

C.M.H.B. Lucas, G.V.J. Cleuren. *Rijnland Hospital, cardiology, Leiderdorp, Netherlands*

Purpose: Intensified care programs nowadays include care given by heart failure nurses.One of their tasks is being responsible for supplying telephone back-up support for CHF-patients. Therefore it is interesting to see which patients particularly use this support and whether or not it has an impact on readmission rate and survival.
Methods: From 2000 a multidisciplinairy HF-program has been running involving 2 dedicated HF-nurses. Patients were instructed to call the CHF-nurses in case of questions and/or problems. Patient characteristics have been collected prospectively from 2000 until 2005 and put into a database.
Results: From 2000-2005 totally 1036 individual patients have been admitted for HF. Totally 339 (33%) patients or their partners or family of this group made telephone calls to the nurse. Characteristics of the patients calling have been compared to the characteristics of the non-callers. Significant differences were seen between callers and non-callers in those living at home (89% vs 82%), having been admitted before 2000 with HF (20% vs 16%) having an LVEF $<$ 45% (57% vs 49%). There was no difference between callers and non-callers in mean age nor in persons living alone vs living with partner or family. Interestingly 36% of the callers died versus 39% of the non-callers (p=0.001). In addition 5% of the callers have been readmitted once or more times versus 13% of the non-callers (p=0.000).
Conclusion: As shown by the numbers many CHF-patients being admitted with HF use telephone back-up support provided bij CHF-nurses as a means to increase selfsupport. As shown those patients calling do better looking at mortality data and readmission data. Therefore in our opinion the telephone back-up support given by CHF-nurses is an important part of their work with significant positive effects. Probably because in this way imminent deterioration in physical condition of the patient can be prevented at an earlier stage.

P623 Assessing concerns about elective cardiac catheterization: the CATH Concern Questionnaire

P.H. Caldwell[1], H.M. Arthur[2], C. Francoeur[3], M. Natarajan[2], S.S. Anand[2] on behalf of CARING Network. [1]*McMaster University, Faculty of Health Sciences, Hamilton, Canada;* [2]*McMaster University, Hamilton, Canada;* [3]*University of Waterloo, Waterloo, Canada*

Purpose: Fears and beliefs about invasive cardiac procedures may affect perception of risk and in turn, influence consent to undergo interventions such as cardiac catheterization (CATH). This study examined the utility of the CATH Concern Questionnaire (CCQ) and explored differences in concerns by gender.
Methods: The 23 item CCQ was administered to 102 consecutive patients (51 women and 51 men) on a waiting list for an elective CATH. The CCQ was administered at the pre-CATH appointment (T1), which was approximately one week prior to the booked procedure, and again at home one day before the CATH (T2).
Results: The CCQ was found to have a high internal consistency (Cronbach's alpha = 0.84- 0.85). At T1, seven individual items showed significant gender differences (see table). In all cases but one, women had significantly greater psychosocial concerns than men. Men and women reported an increase in concern between T1 and T2 (t= -2.09, p=0.04). Women reported an overall greater degree of concern than men (higher total scale score), however this difference was not statistically significant.

Gender Differences in CATH Concerns

Item	t[1]	p value
I believe this is a high risk procedure.	-2.74	0.001
It bothers me that I have not met the doctor who will do the procedure	-2.09	0.04
I am concerned that I will not be able to lie flat and/or still for a long period of time	-2.53	0.01
*I am worried about being away from work	4.16	>.001
I worry about how I will cope with this procedure.	-2.11	0.04
I fear this procedure will cause a heart attack.	-3.062	>.001
It is important for me to feel in control.	-2.05	0.04

*males higher mean score 1 – unpaired t-test.

Conclusions: Gender differences were found in concerns about undergoing elective CATH. Preliminary testing of the CCQ suggests that gender differences are focused primarily on psychosocial concerns. Additional testing of the CCQ, with a larger sample, is required to confirm the psychometric properties of the CCQ and the extent of observed gender differences. If confirmed, the findings may provide insight into gender differences related to CATH decision making and highlight opportunities for supporting patients' coping strategies prior to or during cardiac procedures.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P624 Patients experiences of driving restrictions during treatment with implantable cardioverter defibrillator

A. Stromberg, F. Blixt, F. Andersson, I. Johansson. *Linkoping University Hospital, Department of Cardiology, Linkoping, Sweden*

Introduction: According to international and national guidelines and clinical practice, patients with Implantable Cardioverter Defibrillator (ICD) are often given driving restriction during a period of 6 months after implantation or shocks. Not being allowed to drive during a period of time is likely to affect the individual negatively in daily life, but there is little data exploring the patients' reactions, perceptions and experiences. Aim: To describe how patients with an ICD experience driving restrictions.
Method: A qualitative design was applied. Twenty two strategically chosen ICD patients between 43 and 82 years with different ICD indications were interviewed. All patients were driving regularly and had a valid driving licence. All patients had experienced driving restriction after implantation and some also after shocks. The analysis was inspired by phenomenography and data analysed in 7 steps: familiarisation, compilation, condensation, grouping, comparison, labelling and contrasting.
Results: The analyses revealed that the meaning and significance of driving was individual and differed significantly between the informants. The first information about driving restriction was perceived in many different ways and the reactions ranged from great shock, anger, lack of understanding to agreement and comprehension. The patients perceived that the information about driving restrictions was sometimes insufficient, unclear or given at the wrong occasion. The patients' experiences during the period of driving restriction varied. Many patients felt handicapped, dependent and locked in, but most patients accepted this and reasoned that health and safety was more important than having the freedom to drive by themselves. They also stated that it was an obligation toward the physician not to drive when they had been given this restriction and had a mutual agreement. The respondent had different views on driving in the future. Some had no fears or uncertainty of their driving abilities while others were afraid of getting arrhythmias and shocks while driving and some feared getting a permanent driving restriction.
Conclusion: Handling driving restrictions after ICD implantation and shocks is a complex and delicate issue in clinical practice. More individualised advices, education and support should be given according to the patients' perceptions and needs, since there is a great variety how driving restriction affects a patient emotionally and in daily life.

P625 Angina specialist nurse service reduces readmission rates for acute coronary syndrome in patients with chronic stable angina and newly diagnosed angina

A.O. Molajo, J. Caton, C. Metcalfe-Pearson. *Royal Albert Edward Infirmary, Cardiology, Wigan, United Kingdom*

Purpose: The National Health Service provision for service delivery to angina patients is inadequate. Service delivery systems vary between and within tiers of care. Review intervals are inflexible. There is delay in identifying the onset of angina instability. The Angina Specialist Nurse Service was set up to address this deficiency.
Method: An angina specialist nurse with coronary care experience was appointed in 2000. Mapping of patient journey through the National Health Service identified deficiencies. Delivery was reconfigured to rectify the deficiencies. Patients were seen before discharge and follow up visit scheduled. In addition, the nurse provided patients with telephone number for contact between clinic visits. She provided fast track chest pain clinic and exercise test for patients with new onset of symptoms from primary care and non cardiologists in secondary care. We audited the service.
Result: Admissions were 797, 686, 785, 785, 755, 700 and 672 patients from 1999 to 2005 respectively. Referrals to the angina specialist nurse service were 350, 264, 324, 362, 331, 320 and 304 from 2000 to 2005 respectively. Readmissions were 20%, 20%, 22% 15%, 10%, 5% and 3% from 1999 to 2005 respectively. Interventions occurred in 10%, 9%, 18% and 16% from 2002 to 2005 respectively.

Conclusion: The mapping of the journey of care of angina patients in the National Health Service, identified deficiencies in service delivery. The reconfigured Service is an efficient low cost method of addressing these deficiencies. The morbidity of readmissions was reduced by the service. The Angina Specialist Service is an effective method of optimizing care delivery for angina patients in the United Kingdom.

P626 Current status and role of nurses in heart failure units in Spain

E. Zamora, J. Lupon. *Hospital Universitari Germans Trias i Pujol, Badalona, Spain*

Introduction: Heart failure is one of the major health clinical problems in developed countries. Heart failure units offer a more comprehensive care to patients with this syndrome. Their implementation in hospitals differs clearly among countries of the European Union. Actual data on heart failure units in Spain and the role that nurses play in them were not available until now.
Objective and Method: To know the current implementation in Spain of hospital heart failure units, their characteristics and the role that nurses play in them. We performed a short questionnaire (12 items) that has been answered by 110 Spanish hospitals.
Results: 45 out of the 110 hospitals (41%) have a heart failure unit. This percentage varied significantly according to the technological level of the hospital, ranging from 8% in hospitals of level 1 (lowest) to 38% in hospitals of level 2, and to 76% in those of level 3 (highest). The great majority (91%) of heart failure units are run mainly by Cardiology Departments. Cardiologists are also the physicians most frequently participating in the units (98%), followed by geriatricians (22%), internal medicine doctors (11%) and rehabilitation professionals (9%). These units mainly take care of ambulatory patients (98%), although 67% of them take also care of hospitalized patients. In about 78% of the reporting units, nurses are involved in the care of heart failure patients, most of them only with partial-time dedication (63%); their task is mainly educative intervention (66%), although in 34% of cases they perform only tasks of basic support to doctors (vital constants and EKG); only in 37% of cases nurses performed their own visits. When asked about the number or nurses involved in each unit, the majority of hospitals with heart failure unit answered that one (26%) or two (26%) nurses were involved, 20% answered more than two and 28% did not answered the question. Heart failure rehabilitation programs are scarcely expanded in Spain as only about 31% of heart failure units have such kind of program.
Conclusions: Despite the increasing evidence of the beneficial effect of heart failure units, only 41% of Spanish hospitals have such kind of units, although in hospitals of high technological level this percentage increased up to 76%. Involvement of nurses specifically and with full-time dedication to the unit is quite low.

RISK FACTORS IN THE ELDERLY: ARE THEY IMPORTANT?

P627 Statin treatment and mortality risk of cardiovascular patients aged 75 years and older

T. Strandberg[1], K.H. Pitkala[2], R.S. Tilvis[1]. [1]*University of Oulu, Public Health and General Practice, Oulu, Finland;* [2]*University of Helsinki, Helsinki, Finland*

Purpose: Statin treatment has been repeatedly shown to reduce mortality and vascular events, but there are less data in the oldest patients, especially among those with comorbidities. We have followed-up a group of cardiovascular patients aged 75 years and older, and related their 6-year mortality to baseline statin use.
Methods: In the DEBATE study mailed questionnaires, sent to a random sample of individuals aged 75 and over, were used to retrieve 400 home-living patients with cardiovascular diseases. At baseline in 2000, they underwent clinical examinations and laboratory testing. Baseline drug treatments were recorded. Mini Mental State Examination (MMSE) score below 24 points was considered to indicate cognitive impairment. The Dutch risk score (including age, gender, blood pressure, pulse rate, body mass index, hypertension, diabetes, history of myocardial infarction) was calculated to reflect total risk. 15D instrument was used to assess health-related quality of life (HRQoL). Total mortality up to July 31, 2006 was collected from national registers. Hierarchical Cox regression was used to determine independent predictors of mortality expressed as a risk ratio (RR) with 95% confidence interval (CI).
Results: Average age at baseline was 80 years and 65.3% (n= 261) were women. Of the patients, 80.8% (n= 323), 36.5% (n=146) and 13.8% (n=55) had a history of coronary heart disease, cerebrovascular disorders, or peripheral artery disease, respectively. In addition, a substantial proportion of patients had a history of malignant, thyroid, pulmonary or gastrointestinal diseases. Median MMSE score was 27 (interquartile range 25-28) and 60 individuals had a score below 24 points. At baseline, 83 patients (20.8%) were using statins. During the 6-year follow up 129 (32.3%) individuals died. Baseline statin treatment was associated with a 45% reduced total mortality risk (RR 0.55, 95% 0.33-0.93) after adjustment for baseline risk score, cognitive function and HRQoL.
Conclusions: Statin treatment denotes reduced mortality risk even in 75+ cardiovascular patients with comorbidities. The survival benefit is of the same magnitude as observed in a few other observational studies among oldest patients.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P628 Myocardial function and structure by echocardiography/Doppler and tissue Doppler in pre-diabetic and diabetic elderly subjects in two population-based cohorts

M. Leosdottir[1], R. Willenheimer[1], J. Plehn[2], T.B. Harris[3], R. Borgquist[2], P. Gudmundsson[2], L.J. Launer[3], H. Bjornsdottir[4], P. Nilsson[3], V. Gudnason[2]. *[1]Malmo University Hospital, Dept of Cardiology, Malmo, Sweden; [2]George Washington University, Dept of Medicine, Washington Dc, United States of America; [3]National Institute on Ageing, Bethesda, United States of America; [4]Icelandic Heart Association, Kopavogur, Iceland*

Purpose: Young and middle-aged diabetic patients without known heart disease are known to have depressed left ventricular (LV) function and LV hypertrophy, when compared to non-diabetics. A significant association between LV diastolic dysfunction, measured with tissue Doppler imaging (TDI), and fasting glucose (FG) below the diabetes threshold has also been shown. However, there are no studies of older subjects. We examined the association between glucometabolic status and LV function and LV mass index (LVMI) in two independent population-based elderly cohorts: the AGES-Reykjavik Study (AGES, n=841, 76±6 yrs, 48% men) and the Malmo Preventive Project (MPP, n=1169, 70±4 yrs, 64% men).
Methods: Using multivariable regression analysis adjusted for covariates, FG, HbA1c and HOMA index (the latter in AGES only) were compared to indices of LV function: pulsed Doppler early (E) and late (A) maximum transmitral flow velocities, E/A ratio and transmitral deceleration time; TDI septal (sept) and lateral (lat) LV wall maximum systolic (Sm), early (Em) and late (Am) diastolic velocities and Em/Am ratio; LV ejection fraction (EF); and LVMI. Subjects were also stratified into 6 groups by glucometabolic status: 1) FG ≤5.0 mmol/l; 2) 5.1-5.5 mmol/l; 3) 5.6-6.0 mmol/l; 4) impaired fasting glucose; 5) new-onset diabetes; and 6) prevalent diabetes. These were compared with regard to LV functional parameters and LVMI.
Results: In the AGES cohort, no significant associations were observed between FG and measures of LV function or LVMI. HOMA index was weakly positively correlated with transmitral E (F=4.1; p=0.045). HbA1c was positively correlated with LVMI (F=11.6; p=0.001) and negatively with Em sept (F=4.6; p=0.03). LV function indices and LVMI did not differ between glucometabolic groups. In MPP, FG and HbA1c were not associated with TDI measures of LV function, LVMI or EF. Significant trends towards depressed diastolic function by means of increased Am lat (F=4.3; p=0.04), Am sept (F=11.6; p=0.001) and reduced Em/Am ratio sept (F=4.4; p=0.04) with higher glucometabolic group were observed. When subjects were divided into younger (n=370) and older (n=320) than 70 years, these associations remained significant only in the younger group.
Conclusions: Contrary to previous reports in younger subjects, no general associations between glucometabolic status and LV function or LVMI were observed in two large independent cohorts of older persons. Age-related changes in LV function and LVMI might be more important than glucose metabolism in older subjects and these should be explored as potentially explaining the observed results.

P629 Cholesterol fractions and apolipoprotiens are strong predictors of heart disease mortality in older men

R. Clarke[1], J.R. Emberson[1], S. Parish[1], M. Shipley[2], P. Linksted[1], P. Sherliker[1], S. Clark[1], J. Armitage[1], A. Fletcher[3], R. Collins[1]. *[1]Clinical Trial Service Unit, Nuffield Department of Clinical Medicine, Oxford, United Kingdom; [2]University College London Medical School, London, United Kingdom; [3]London School of Hygiene & Tropical Medicine, London School of Hygiene & Tropical Medicine, London, United Kingdom*

Purpose: The relevance of blood lipids for prediction of ischaemic heart disease (IHD) in older people is uncertain and hence cholesterol-lowering therapy is not routinely prescribed in the elderly. The aim of this study was to compare IHD mortality associations with plasma levels of total cholesterol, LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), apolipoprotein B (Apo B), and apolipoprotein A_1 (Apo A_1), measured in older men with or without prior CVD.
Methods: IHD mortality risks were assessed in a 7-year follow-up of a cohort of 5344 men (mean age 77 years), including 26% with and 74% without diagnosed cardiovascular disease (CVD).
Main Outcome Measure: Hazard ratios (HR) for IHD deaths (n=447) were estimated for a 2 standard deviation difference in usual plasma lipids.
Results: IHD mortality was not significantly associated with total cholesterol in all men (HR: 1.05), but a significant positive association in men without CVD and a slight, non-significant inverse association in men with CVD was observed (HR: 1.47 vs 0.84). The patterns were similar for LDL-C (HR: 1.50 vs 0.98) and Apo B (HR:1.68 vs 0.93). IHD risks were inversely associated with HDL and with Apo A_1 in men with and without CVD. IHD risks were strongly associated with total/HDL-C (HR 1.57) and Apo B/Apo A_1 (HR: 1.54), in all men and remained strongly predictive at all ages.
Conclusion: Blood lipids other than total cholesterol are strong predictors of IHD in older men. Differences in lipids that are achievable by statins were associated with about one-third lower risk of IHD, irrespective of age.

Table

Lipid	No prior CVD HR (95% CI) per 2 SD higher usual level (n=215 cases)	Prior CVD HR (95% CI) per 2 SD higher usual level (n=232 cases)
LDL (mmol/L)	1.50 (1.10, 2.03)	0.98 (0.73, 1.31)
Apo B (g/L)	1.68 (1.26, 2.26)	0.93 (0.68, 1.26)
HDL (mmol/L)	0.74 (0.54, 1.01)	0.69 (0.50, 0.95)
Apo A1 (g/L)	0.87 (0.62, 1.21)	0.62 (0.44, 0.88)
Total cholesterol(mmol/L)	1.47 (1.08, 1.98)	0.84 (0.63, 1.13)
Total/HDL	1.71 (1.31, 2.23)	1.21 (0.94, 1.54)
Apo B/Apo A1	1.70 (1.29, 2.24)	1.11 (0.84, 1.47)

P630 Effects of diabetes mellitus on total life expectancy and llife expectancy with and without cardiovascular disease

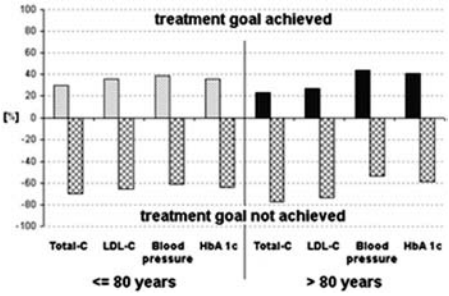
O.H. Franco Duran[1], E.W. Steyerberg[2], F.B. Hu[3], J. Mackenbach[4], W. Nusselder[2]. *[1]Unilever, Corporate Research, Sharnbrook, United Kingdom; [2]Erasmus MC, Public Health, Rotterdam, Netherlands; [3]Harvard University, School of Public Health, Boston, United States of America; [4]ErasmusMC, Public Health, Rotterdam, Netherlands*

Background: Diabetes mellitus is a recognized risk factor for cardiovascular disease and mortality. However, limited information exists on the effect of diabetes on life expectancy with and without cardiovascular disease. We aimed to calculate the effect of diabetes after age 50 on life expectancy and the number of years lived with and without cardiovascular disease.
Methods: Using data from the Framingham Heart study, we built life tables to calculate the effects of having diabetes on life expectancy and years spent with and without cardiovascular disease among populations aged 50 years and over. For the life table calculations, we used hazard ratios for three transitions (healthy to death, healthy to cardiovascular disease, cardiovascular disease to death), by presence of diabetes at baseline and adjusted for age and confounders.
Results: Having diabetes significantly increased the risk of developing cardiovascular disease (HR 2.5 for women and 2.4 for men) and of dying once cardiovascular disease was present (HR 2.2 for women and 1.7 for men). Diabetic men and women at age 50 years lived on average 7.5 (95% CI: 5.5; 9.5) and 8.2 (95% CI: 6.1; 10.4) years less than their non-diabetic equivalents. The differences in life expectancy free of cardiovascular disease were similar (7.8 and 8.4 years respectively).
Conclusions: The increase in the risk of cardiovascular disease and mortality from diabetes represents a very important loss in life expectancy and life expectancy free from cardiovascular disease. Prevention of diabetes is a fundamental task facing today's society pursuing healthy aging of the population.

P631 Guideline based therapy of coronary artery disease: differences in octogenarians? Results from the German Coronary Risk Management (CoRiMa) Study

K. Pels[1], S. Cassens[2], U. Keil[3], J. Bernarding[4], M. Prien[1], M. Brosz[2], H.-P. Schultheiss[5], J.C. Geller[6]. *[1]Charite, Campus Benjamin Franklin, Med. Clinic 2- Cardiology, Berlin, Germany; [2]Karlsruhe, Germany; [3]Muenster, Germany; [4]Magdeburg, Germany; [5]Berlin, Germany; [6]Bad Berka, Germany*

Background: Optimal secondary prevention is critically for the reduction of morbidity and mortality in patients with Coronary Artery Disease (CAD). The elderly patients do benefit in the same way as younger patients from a guideline based therapy of CAD. The aim of this study was to investigate if CAD therapy is practiced as efficient in patients older than 80 years (y) than in younger patients.
Methods: Data from CAD patients of physician offices in Germany, seen between January 1998 and June 2005 were identified. The data were exported anonymously and transferred into the project database. Age, sex, blood pressure, serum analysis data (cholesterol (c), HbA_{1c}) levels were analyzed. The last office visit of each patient from both groups (< 80y or > 80y) was used for the analysis of treatment goals based on reference values stated in current guidelines.
Results: 64.265 patients with CAD were included in the study. 10.508 of these patients were >80y at the last office visit and 36% of those had also diabetes mellitus (DM). In patients without DM there was no age dependent difference in achievement of treatment goals. The results of the high risk subgroup of patients with CAD and DM are presented in the following graph (difference for all parameters significant, p<0.001)
Conclusion: (1) In CAD patients without DM treatment efficacy is overall low, particularly regarding hyperlipidemia (80% did not achieve treatment goals for total



CAD patients with DM

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

C and LDL-C), independent of age. (2) In the high risk subgroup of CAD patients with DM achievement of treatment goals was in general higher than in non diabetic patients and significant lower in octogenarians regarding hyperlipidemia but higher regarding efficacy of blood pressure and DM treatment in comparison to younger patients.

P632 Metabolic, cardiovascular and autonomic improvement induced by exercise training in female LDL-knockout mice submitted to ovarian hormones deprivation

M.V. Heeren[1], J. Paulini[2], L.E. De Sousa[2], K. Flues[2], E.D. Moreira[2], K. De Angelis[3], M.C. Irigoyen[3] on behalf of Human Moviment Laboratory. *[1]Sao Paulo, Brazil; [2]Sao Paulo University, Physical Education, Sao Paulo, Brazil; [3]Sao Judas University, Physical Education, Sao Paulo, Brazil*

Purpose: alterations in lipidic profile and autonomic function are frequently observed after menopause, increasing women cardiovascular risk. On the other hand, exercise training has been recognized as a non pharmacological treatment for metabolic and cardiovascular diseases. The aim of the present study was to investigate the effects of exercise training on arterial pressure (AP), baroreflex sensitivity and metabolic parameters in ovariectomized LDL-knockout mice.
Methods: Female ovariectomized (bilateral ovaries removal) LDL-knockout (Oko) mice were divided into 2 groups: sedentary (SOko) and trained (TOko). One week after ovariectomy, the TOKO was submitted to an exercise training protocol on a treadmill for 4 weeks (1h/day; 5 days/week; 50-65% VO2 max.). Plasmatic triglycerides and cholesterol were measured at the end of the protocol. AP signals were recorded, in conscious animals, and processed using an data acquisition system (CODAS, 2KHz). Baroreflex sensitivity was evaluated by tachycardic and bradycardic responses to AP changes induced by sodium nitroprusside and phenylephrine.
Results: Maximal exercise capacity was increased in TOko as compared to SOko. Body weight and plasmatic triglycerides were not different between studied groups. The plasmatic cholesterol was diminished in TOko rats (191 $\pm$8mg/dl) when compared to SOko rats (250$\pm$9mg/dl). The systolic, diastolic and mean AP were reduced in TOko group (MAP: 101$\pm$3mmHg) when compared with SOko group (MAP: 125$\pm$3mmHg). Exercise training induced improvement in bradycardic reflex response to AP rises in TOko animals (-4.24 $\pm$0.62 bpm/mmHg) in relation to SOko animals (-1.49$\pm$0.15 bpm/mmHg); however, tachycardic reflex responses to AP falls were similar between studied groups. In conclusion, trained LDL-knockout ovariectomized mice showed an exercise training-induced improvement in basal metabolic and hemodynamic parameters, as well as on autonomic control of circulation, suggesting an important role of this non-pharmacological treatment in the rehabilitation of post-menopause women with dislipidemia. Supported by FAPESP (06/53739-0), Sao Judas Tadeu University

CORONARY ARTERY DESEASE IN THE ELDERLY: IS THERE A DIFFERENCE COMPARED TO THE YOUNG?

P633 Six-month clinical outcome of elderly patients with ST-elevation MI according to reperfusion: data from the French FAST-MI registry

N. Boudou[1], V. Bataille[1], T. Simon[2], G. Amat[3], P. Bareiss[4], J.P. Cambou[3], D. Carrie[3], N. Danchin[5]. *[1]CHU Rangueil, Cardiology B, Toulouse, France; [2]Hopital Saint-Antoine, Paris, France; [3]Centre Hospitalier, Cardiology, Vichy, France; [4]CHU Hautepierre, Cardiology, Strasbourg, France; [5]Hopital Georges Pompidou, Cardiology, Paris, France*

Background: Demographic changes in Western countries population have resulted in an increase in the number of elderly patients hospitalized for STEMI. There is a wide gap between the proportion of myocardial infarction patients aged 75 years or older in Western countries and their enrolment in randomized controlled trials on ACS
Objective: To assess 6-month mortality of STEMI patients $\geq$ 75 years old in the French registry of Acute ST elevation or non-ST-elevation Myocardial Infarction (FAST-MI).
Methods: FAST-MI is a prospective multicentre study (223 French institutions, university teaching hospitals, general and regional hospitals and private clinics with intensive care units), including all patients admitted to UCIs for AMI over a 1-month period in November 2005.
Results: 453 STEMI patients admitted within 48 hours after symptoms onset were $\geq$ 75 years old (26.4% of the STEMI population (n=1714). Mean age was 82.02$\pm$5.0 and 51.6% were women. Only 44.5% of the patients were treated by reperfusion therapy: 27.1% underwent primary angioplasty; 10.6% pre-hospital thrombolysis, 6.9% in-hospital thrombolysis. Six-month mortality rate was: 17.8% after angioplasty; 13% after pre-hospital lysis, 23.3% after in-hospital lysis and 30.2% for patients without reperfusion therapy, p= 0.016. By multivariate analysis, independent predictors of 6-month mortality were: smoking (or prior) (OR= 2.45, 95% CI= 1.3-4.6, p=0.005), heart failure (OR= 4.8, 95% CI= 2.5-9.2, p$<$0.0001), presence of co-morbidity (OR= 2.1, 95% CI= 1.03-4.1,p=0.04), anterior location of MI (OR= 2.2, 95% CI= 1.3-3.95, p=0.005), systolic pressure at admission (OR=0.98, 95% CI= 0.97-0.99,p$<$0.0001), primary angioplasty (OR= 0.3, 95% CI= 0.16-0.65, p=0.002), pre-hospital thrombolysis (OR= 0.4, 95% CI= 0.15-1.19, ns), hospital thrombolysis (OR= 0.77, 95% CI= 0.26-2.3, ns).
Conclusion: In the absence of specific guidelines on treatment of elderly patients with STEMI, these real-world data show that reperfusion therapy is associated with improved survival at 6 months.

P634 Young patients with acute coronary syndromes have different clinical characteristics and better outcomes than older patients. The Global Registry of Acute Coronary Events

A. Budaj[1], F. Van De Werf[2], H.S. Lim[3], R.G. Goldberg[4], G. Montalescot[5], J.M. Gore[6], R. Dedrick[5], D. Brieger[7] on behalf of GRACE. *[1]Grochowski Hospital, Cardiology Dept., Warsaw, Poland; [2]Universitair Ziekenhuis Gasthuisberg, Leuven, Belgium; [3]Austin Hospital, Melbourne, Australia; [4]Brown University, Providence, United States of America; [5]Pitie-Salpetriere Hospital, Paris, France; [6]UMASS Medical School, Worcester, United States of America; [7]Concord Hospital, Sydney, Australia*

Purpose: Recognition of clinical characteristics and risk factors for developing an acute coronary syndrome (ACS) at a young age may facilitate primary prevention in this population.
Methods: Data were analysed from unselected patients with an ACS enrolled in the Global Registry of Acute Coronary Events (GRACE) between 1999 and 2006. Patients were categorized as either 'young' ($<$40 years; n=1525; 2.7%) or 'older' ($\geq$40 years; n=54,507). Logistic regression analysis was utilized to examine differences in clinical characteristics and hospital and long-term outcomes between young and older patients.
Results: Young patients were more likely than older patients to present with ST-segment elevation myocardial infarction (50% vs 36%, P$<$0.001) and to have a percutaneous coronary intervention in hospital (47% vs 37%, P$<$0.0001). In-hospital and 6-month mortality rates were lower in young than older patients (1.8% vs 5.1% and 1.4% vs 5.1%, respectively). The odds ratio (95% confidence interval) for dying during hospitalization, adjusted for GRACE prognostic factors other than age, was 0.31 (0.19-0.36; P$<$0.0001) and for 6-month post-discharge mortality was 0.13 (95% CI 0.06-0.28; P$<$0.0001). Multivariable factors for ACS at a young age are shown in the Table.

Variables for young vs older patients

Multivariable factor	Odds ratio	95% CI	P value
Killip (class I vs IV)	4.15	1.32-13.04	$<$0.0001
Systolic blood pressure (low vs high)	2.52	2.05-3.11	$<$0.0001
Diastolic blood pressure (high vs low)	2.00	1.61-2.44	$<$0.0001
No previous hypertension	2.00	1.75-2.32	$<$0.0001
Smoking (current or former vs non)	1.94	1.67-2.26	$<$0.0001
Pulse (high vs low)	1.69	1.43-2.00	$<$0.0001
Previous renal insufficiency	1.56	1.17-2.08	$<$0.01
No previous diabetes mellitus	1.47	1.22-1.79	$<$0.0001
Male sex	1.36	1.51-1.60	$<$0.001
Delay from symptom onset to hospitalization (short vs long)	1.22	1.05-1.42	0.001

Conclusion: Young patients presenting with ACS have different clinical characteristics to older patients, but have better clinical outcomes.

P635 Myocardial infarction in the young: a gender-based comparison

F.B. Sozzi[1], G.B. Danzi[1], L. Foco[2], M. Ferlini[2], M. Tubaro[3], M. Galli[4], P. Celli[3], P.M. Mannucci[2]. *[1]IRCCS Maggiore Hospital, M.R.E. Foundation, Cardiology, Milan, Italy; [2]Health Sciences Dept., Medical Statistics, Pavia, Italy; [3]San Filippo Neri Hospital, Rome, Italy; [4]San Camillo Hospital, Rome, Italy*

Background: A relative paucity of informations concerns the natural history, clinical features and coronary anatomy in young patients with acute myocardial infarction. In particular, a dearth of data exists relating to gender differences in young patients.
Objective: To evaluate whether or not there are correlations between the clinical characteristics and the extent and localization of coronary artery lesions in young men compared with young women.
Methods: The study population consisted of 1646 young patients (87% men, 13% women) [mean age 39$\pm$5 years] with a first acute myocardial infarction admitted to one of the 125 Coronary Care Unit of Italy in a period of 3 years. Clinical data were collected. All patients underwent coronary angiography during hospitalization.
Results: Smoking, hypercholesterolemia and obesity were significantly more prevalent in men than in women; physical inactivity was significantly more prevalent among women. Hemodynamically significant coronary stenosis occurred in 82% of patients and were more frequent in men than in women (p $<$0.05). Women more frequently had single-vessel disease and no coronary lesions at all (58% vs 47% and 24% vs 9% women vs men respectively, both p $<$0.05). Men more frequently had multivessel disease (38% vs 13%, p $<$0.05). Significant stenosis mainly affected the left anterior descending artery (52%) with no gender-related difference; men more likely had lesions of the left circumflex or right coronary artery (p $<$0.05).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusion: In young patients with a first acute myocardial infarction risk factors profile and extent of coronary artery lesions were significantly different between genders.

P636 Prognostic implications of elevated cardiac Troponin T (cTnT) in the extreme elderly group of patients

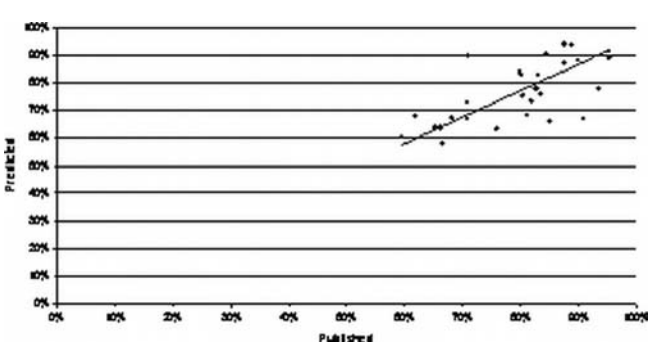
J.J. Gohil, D.Y.C. Leung, J.K. French, G. Le, T. Nguyen, C.P. Juergens. *Liverpool Health Service, Cardiology Department, Sydney, Australia*

Background: Elevation of cardiac Troponin T (cTnT), a specific and prognostic marker of myonecrosis in acute coronary syndrome, has been reported in other conditions. However, the prognostic implications of an elevated cTnT in unselected patients aged 80 years or older are unclear.
Methods and results: We studied 236 consecutive patients ≥80 years of age (mean age 85±4 years, 144 women) admitted to our tertiary centre who had cTnT measured. 117 patients (49.6%) had elevated cTnT (>0.03μg/L) and 115 patients did not. There were 66 (28%) patients with diabetes, 47 (20%) with chronic renal failure, 71 (30%) with history of heart failure (HF). 48(20%) were current smokers, 16(7%) had history of malignancy, and 143 (61%) patients were discharged on diuretics. During their hospital stay, 5 had cardiogenic shock, 52 (22%) had HF, 34 (14%) patients developed acute renal failure and 8 (3%) had major bleeding. Discharge diagnosis was non-cardiac in 131 (60%) and cardiac in 104 (40%) patients. 30 days mortality was 30% in the cTnT elevated and 10% in the cTnT non-elevated group (P<0.001). 1year mortality was 43% and 20% (P<0.001) in cTnT elevated and non-elevated groups respectively. Mean survival for cTnT elevated patients was 822 + 84 days versus 1364 + 72 days in the cTnT non-elevated group (P<0.001). After exclusion of patients with cardiogenic shock, univariate predictors of mortality were current smoker (P=0.009), history of HF (P=0.002), malignancy (P=0.002), bleeding (P=0.035), diuretics on discharge (P=0.01), HF during admission (P<0.001), acute renal failure (P=0.007) and cTnT elevation (P=0.001). Multivariate predictors of long term mortality were HF during admission (OR 3.26, 95%CI 2.26-4.69), cTnT elevation (OR 3.91, 95%CI 2.15-7.11), malignancy (OR 6.80, 95%CI 3.47-13.31) and bleeding (OR 7.92, 95%CI 2.62-23.92) and acute renal failure (OR 5.26, 95%CI 3.25-8.50).
Conclusion: Our results showed that an elevated cTnT in unselected consecutive patients 80 years or older admitted into hospital has significant independent prognostic implications.

P637 Can we predict survival following a myocardial infarction sufficiently well?

J.J. Caro[1], K. Migliaccio-Walle[1], K.J. Ishak[2]. *[1]Caro Research, Concord, United States of America; [2]Caro Research, Montreal, Quebec, Canada*

Purpose: Understanding life expectancy after myocardial infarction (MI) is vital for prognosis, projecting treatment impact and informing health policy. This study compared literature-reported actual survival up to one year with rates predicted using a published equation to assess the added value of further mortality studies.
Methods: Patient characteristics, medical history and observed survival (at 30-day, 1, 3, 5 years) were extracted from each article identified in a MEDLINE search for studies of survival following MI published 1/1/2000 to 31/3/2005 reporting population-, community- or hospital-based non-trial data collected 1/11/85 to 31/12/1995. The corresponding predicted survival was calculated using published Saskatchewan equations, accounting for age, sex, diabetes, prior MI, CABG, prior stroke, hypertension and hyperlipidemia. Linear and logit regression examined the accuracy of the prediction and the additional effect of other factors not in the equation.
Results: Data from 41 articles representing 14 countries were used in this analysis following a review of 115 articles identified from 690 abstracts. Published 1-year survival ranged from 55.7 94.9% vs 59.4 95.2% predicted. Predictive ability was excellent (Figure, p<0.0001). At 30 days, published survival ranged from 44.6-97.6% vs 74.3-98.0% predicted. Two major outliers were studies of 1st MI. When removed, the predictive ability was very good (p=0.049) with no additional factors entered.
Conclusions: The equations demonstrate very good predictive validity. New research efforts ought to focus on survival in special populations (e.g., renal disease) following MI rather than continuing to study unselected MI patients.



1-year survival post-MI

P638 Percutaneous coronary intervention for acute myocardial infarction in the elderly: comparison on clinical outcome between younger patients, septuagenarians and octogenarians

S. Nakamura, E. Tada, K. Fujiwara, O. Kakuda, N. Kurita, M. Hirose, S. Nakamura, S. Tahara, K. Hozawa, O. Hirashima. *New Tokyo Hospital, Department of Cardiology, Matsudo, Japan*

Background: Previous studies have suggested that the elderly patients have worse outcomes of percutaneous coronary interventions (PCI). However, contemporary outcomes of PCI in those patients with acute myocardial infarction (AMI) are still unclear.
Methods: We studied clinical, angiographical results of 430 consecutive octogenarians (mean age 84.6 years, 56.7% male), 672 septuagenarians (mean age 75.4 years, 64.0% male) and 2,100 younger patients (mean age 58.8 years, 74.0% male) undergoing emergent PCI for AMI from Apr. 1999 to Mar. 2004. The octogenarians had a higher incidence of cardiogenic shock and congestive heart failure.
Result: See table.

	Younger patients (<70 years)	Septuagenarians (70-79 years)	Octogenarians (≥80 years)	p
Number of patients	2,100	672	430	–
Clinical success (%)	98.5	96.7	94.2	NS
In-hospital				
Cardiogenic shock (%)	8.0	9.8	16.7**	0.01
Death (%)	0.6	1.9	4.9*	0.05
12-month				
Re-infarction (%)	6.9	7.9	12.8*	0.05
Re-heart failure (%)	8.0	7.9	14.0*	0.05
Death (%)	0.2	0.7	3.5*	0.05
TLR: re-PCI (%)	18.1	18.9	18.8	NS
Any events (%)	24.6	27.2	40.0*	0.05

**p<0.01, *p<0.05 Octogenarians vs Younger patients and Septuagenarians.

Conclusion: In octogenarians, emergent PCI in patients with AMI can be performed with high success rate, albeit with high incidence of in-hospital and long-term mortality, and adverse clinical events.

ELECTRICITY AND THE ELDERLY

P639 Prevention of thromboembolic events associated with atrial fibrillation in the elderly

K. Abdel-Aziz[1], T. Thirugnanachandran[1], M. Aldawoud[2], J. Robson[2], K. Sarsfield[1]. *[1]St James University Hospital, Elderly Medicine, Leeds, United Kingdom; [2]Bradford Royal Infirmary, Elderly medicine, Bradford, United Kingdom*

Purpose: Atrial fibrillation (AF) is the commonest arrhythmia affecting the elderly and is a significant risk factor for thromboembolic stroke. Several risk stratification systems have been evaluated and found to reliably identify patients at highest risk. In the UK, the national institute for clinical excellence (NICE) published guidelines in 2006 to identify which patients should be offered thromboprophylaxis. All patients over 75 with an additional risk factor should be considered for anticoagulation. We aimed to establish current thromboprophylaxis practice in the elderly and whether those at highest risk were receiving anticoagulation following the introduction of new guidelines.
Methods: A retrospective analysis of 562 patients on elderly wards in two teaching hospitals was performed. 85 patients with a diagnosis of chronic AF were identified. Risk scores using the $CHADS^2$ system were generated and thromboprophylaxis regime recorded.
Results: 85 patients were included (range 70 – 98; mean 86 years). Thromboprophylaxis regimes are tabulated below. Contraindications to anticoagulation were documented in only 8 patients. 3 patients declined anticoagulation.

Table 1. Summary of current thromboprophylaxis practice in our elderly patients

$CHADS^2$ score	No. of patients	Adjusted annual stroke rate (95% CI)	Warfarin	300mg aspirin	150mg aspirin	75mg aspirin	75mg clopidogrel	none
0	0	1.9 (1.2-3.0)	0	0	0	0	0	0
1	11	2.8 (2.0-3.8)	3	1	0	6	0	1
2	36	4.0 (3.1-5.1)	15	4	0	12	1	4
3	24	5.9 (4.6-7.3)	8	4	1	9	1	1
4	10	8.5 (6.3-11.1)	2	1	0	7	0	0
5	4	12.5 (8.2-17.5)	1	0	0	3	0	0
6	0	18.2 (10.5-27.4)	0	0	0	0	0	0
Total number of patients	85		29	10	1	37	2	6

Conclusions: Over half of the patients at moderate to high risk of stroke ($CHADS^2$ ≥2) were not warfarinised. Low dose aspirin was used preferentially

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

to full dose aspirin. Only a small proportion of patients had documented contraindications to anticoagulation. Our study suggests antiplatlet therapy is still being prescribed at sub-optimal doses and that warfarin is underused in the elderly despite new guidelines.

P640 Pacing in the very elderly: evidence of age discrimination?

J.M. Mccomb[1], C.J. Plummer[2], R.G. Charles[1], M.W. Cunningham[1], A.D. Cunningham[1] on behalf of Cardiac Network Device Survey Group. *[1]Freeman Hospital, Cardiology Dept., Newcastle Upon Tyne, United Kingdom; [2]Newcastle Upon Tyne, United Kingdom*

Purpose: The requirement for permanent pacing increases with age. It has been suggested that there is discrimination against the elderly, in that they receive less complex pacing modes than do younger patients. We investigated this at national level, using the National Pacemaker Database (NDP).
Methods: All pacemaker implants in the years 2003 and 2004 were reported to the NPD, and all registrations have been checked for completeness. Data recorded include age, pacing indication, mode of pacing and post code.
Results: The permanent pacemaker implantation rate in men over 85 years of age in 2003 and 2004 was 7,228/million, and in women 3,016/million. It is unlikely that indications for pacing, and in particular the prevalence of atrial fibrillation (AF) will vary regionally within the UK, although an increased prevalence of AF in the elderly may impact on pacemaker mode, favouring single chamber rate responsive (VVI/R) pacemakers. 2,933 patients (7.3% of all pacemaker recipients) over 90 years of age received pacemakers during these 2 years. Of these, the indication for pacing was AF in 24%, compared with 23.9% for all recipients regardless of age; complete heart block (CHB) in 33% (26.3% in all ages); and sick sinus syndrome (SSS) in 19% (28.4% in all ages). 23.9% of those $>$ 90 years old received dual chamber and 34.3% VVIR pacemakers, in comparison with 56.1%% and 25.3% respectively of all pacemaker recipients, regardless of age. The variation in proportion of very elderly patients receiving dual chamber versus VVI pacemakers in this age group ranged regionally from 5% to 39%. The proportion reciving dual chamber pacemakers for CHB varied from 0-71.4% and for SSS 5.9-88%.
Conclusion: A greater proprtion of very elderly patients do not receive complex (and nationally recommended) pacing modes in comparison with younger patients. This is not explained by the prevalence of AF, nor by the estimated quarter of patients who receive VVI/R pacemakers because of other co-morbidities. Co-morbidities may more often preclude dual chamber pacing in the very elderly, but the wide regional variation suggests that very elderly patients are treated differently in different areas, suggesting policies which discriminate against age.

P641 Cinical data of elderly patients with paroxysmal supraventricular tachycardia

B. Brembilla-Perrot[1], O. Yangni N'da[2], O. Huttin[1], F. Duhoux[1], C. Tatar[1], F. Chometon[1], S. Ammar[1], L. Groben[1], J. Bertrand[1], D. Beurrier[1]. *[1]Chu De Brabois, Departement De Cardiologie, Vandoeuvre Les Nancy, France; [2]Vandoeuvre Les Nancy, France*

The purpose of the study was to evaluate the incidence of supraventricular tachycardias (SVT) among patients aged more than 70 years, their clinical and electrophysiological data and their management. At least 12% of european population are currently 70 years and older. Heart failure, ischemic heart disease and atrial fibrillation (AF) are common causes of hospitalization. Less is known on other arrhythmias as SVT.
Methods: 820 patients aged from 8 to 93 years were consecutively recruited in our department for recurrent SVT's; 145 of them were aged from 70 to 93 years (mean 76$\pm$5) (group I); 675 patients had less than 70 years (group II) (45$\pm$8). They had no preexcitation syndrome on ECG. Intracardiac or esophageal electrophysiologic study (EPS) included programmed atrial stimulation up to 2 extrastimuli in control state and if necessary after isoproterenol.
Results: Advanced heart disease was present in 22 group I patients (15%), 11 group II patients (1.6%) ($p<0.05$). Syncope was as frequent in group I as in group II (16%). Atrioventricular node re-entrant tachycardia (AVNRT) was noted in 105 group I patients (72%), 498 group II patients (74%) (NS). AV re-entrant tachycardia in a concealed accessory pathway was noted in 10 group I patients (7%), 59 group II patients (9%) (NS). Atypical AVNRT was noted in 14 group I patients (10%), 26 group II patients (4%) ($p< 0.05$); the mechanism was undetermined in other patients. Radiofrequency catheter ablation of slow pathway or accessory pathway was required in 106 group I patients (73%) and 385 group II patients (57%) ($p<0.01$); the complications were more frequent in group I (10%) than in group II (2.5%) patients ($p< 0.05$). A permanent AF occurred during EPS or ablation in 19% of group I patients and 5% of group II patients ($p<0.01$).
Conclusions: Age higher than 69 years was noted in 18% of patients without preexcitation syndrome admitted for paroxysmal SVT. The electrophysiological mechanism was similar in old and younger patients except for the atypical AVNRT, which was more frequent in old patients. Radiofrequency ablation of SVT was required more frequently in elderly patients than in younger patients. However, the complications of ablation were more frequent and the occurrence of AF was not rare (19%) in elderly patients.

P642 Incidence, clinical and electrophysiological data of Wolff-Parkinson-White syndrome in elderly patients

B. Brembilla-Perrot[1], O. Yangni N'da[2], O. Huttin[1], F. Duhoux[1], F. Chometon[1], S. Ammar[1], J. Bertrand[1], N. Zhang[1], J. Cedano[1], D. Beurrier[1]. *[1]Chu De Brabois, Departement De Cardiologie, Vandoeuvre Les Nancy, France; [2]Vandoeuvre Les Nancy, France*

The purpose of the study was to evaluate the clinical and electrophysiological data of elderly patients with a patent Wolff-Parkinson-White (WPW) syndrome. The study of WPW syndrome is recommended in children and young adults. Less is known in the elderly patients. Atrioventricular (AV) accessory pathway (AP) refractory period and conduction velocity and the risk of atrial fibrillation (AF) are known to increase with age.
Methods: 461 consecutive patients aged from 6 to 81 years were recruited for overt WPW syndrome and tachycardias (n=242) or syncope (n=55); other patients were asymptomatic (n=164); 32 patients (7%), 16 males, 16 females, were aged from 60 to 81 years (mean 68$\pm$4) (group I). Clinical data and results of intracardiac or esophageal electrophysiologic study (EPS) were collected in group I and compared to those of patients younger than 60 years (group II): atrial pacing and programmed atrial stimulation were performed in control state and after isoproterenol.
Results: Patients were asymptomatic as frequently in group I than in group II (34% vs 35.5%) and male sex was not different (50% in group I vs 60% in group II). Three group I patients (9%) and 19 group II patients (4%) (NS) had another heart disease. The AP wa s more frequently left sided in group I (54%) than in group II (40.5%) ($p<0.05$). The maximal rate conducted though AP was similar in group I and in group II (186$\pm$59 vs 195$\pm$62 b/min in control state, 278$\pm$25 vs 247$\pm$64 b/min after isoproterenol). AV reentrant tachycardia (AVRT) was induced as frequently in group I (50%) than in group II (58%); AF was induced more frequently in group I (34%) than in group I (20%) ($p<0.05$). Five group I patients (16%) and 55 group II patients (13%)(NS) had the criteria of a malignant form of WPW with the induction of AF conducted through the AP at a rate $>$ 220 b/min in control state and $>$ 290 b/min after isoproterenol. Two group I patients developed spontaneous malignant arrhythmias. Radiofrequency (RF) catheter ablation of AP was unsuccessful in 5 of 14 patients of group I (36%) and only 6 of 70 group II patients (8.5%) ($p< 0.01$) with a left sided AP, because arterial retrograde catheterism was difficult.
Conclusion: The presence of a WPW syndrome in a patient aged of more 59 years is rare (7% of the total population with a WPW), but is often related to a left-sided AP which is is still capable to conduct rapidly to the ventricles. Spontaneous and induced AF is frequent. Therefore, the evaluation of these patients is recommended. However, RF ablation can be difficult in elderly patients.

P643 Telecardiology for acute myocardial infarction diagnosis in the elderly

N.D. Brunetti[1], G. Amodio[2], G. Dellegrottaglie[3], L. De Gennaro[3], P.L. Pellegrino[3], M. Di Biase[3], G. Antonelli[1]. *[1]University of Foggia, Cardiology Department, Foggia, Italy; [2]Azienda Ospedaliera Policlinico, Emergency Cardiology Department, Bari, Italy; [3]Cardio-on-line Europe S.r.l., Bari, Italy*

Aim acute: myocardial infarction in elderly patients might show an atypical presentation, with symptoms other than chest or epigastric pain. A timely and correct diagnosis might thus be neglected or delayed with dramatic clinical and survival consequences in this setting of patients characterized by a higher incidence of adverse events.
Methods: 27841 patients from all over Apulia (19.362 Km^2, 4 millions inhabitants), referred since October 2004 until April 2006 to public emergency health care number "118" and underwent ECG evaluation. Data recorded were transmitted with a mobile telephone support to a telecardiology "hub" active 24-hours a day. Hospitalization or further examinations were disposed by emergency physicians on basis of ECG diagnosis and consultation.
Results: 39% of patients referred chest or epigastric pain, 26% loss of consciousness, 10% breathlessness, 7% palpitations. ST elevation acute myocardial infarction (STEMI) was diagnosed in 1.92% of patients enrolled. 65.54% of patients with STEMI were male, 47.44% were older than 70 years, 49.60% of patient older than 70 years were male. Mean age of male patients with STEMI was 64.64$\pm$13.82 vs 74.76$\pm$12.82 for females ($p<0.001$), with a bimodal distribution for two genders. Among patients with STEMI $<$70 years old chest or epigastric pain was present in 88.81% of subjects while atypical presentation (breathlessness, loss of consciousness, palpitations, other symptoms) was detected in remaining 11.19% (10.81% for males vs 12.73% for females, p n.s.). Elderly patients ($>$70 years old) showed atypical presentation of STEMI in 32% of cases (34.92% for females vs 29.03% for males, p n.s.) ($p<0.001$ in comparison to younger patients). Rate of atypical misleading presentation of STEMI rose up from a 9.17% in the class of age 60-69 years to 25.56% in the class 70-79, to 35.24% in the class 80-89, and to 46.15% in the class $>$89 ($p<0.01$ in all cases); dramatic errors or delay of diagnosis were thus avoided thanks to an immediate home ECG in a significant number of patients.
Conclusions: Telecardiology home ECG diagnosis could significantly help in avoiding errors and delay of STEMI diagnosis in elderly patients with an increased prevalence of atypical presentations.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P644 Muscle metaboreflex contribution to resting limb hemodynamic control is preserved in older individuals

J.P. Ribeiro, B.T. Roseguini, C.N. Alves, G.R. Chiappa, R. Stein.
Hospital De Clinicas De Porto Alegre, Cardiology Division, Porto Alegre, Brazil

Background: Aging is associated with tonic elevations in basal sympathetic vasoconstrictor outflow to skeletal muscle and a parallel decline in vascular function. The effects of aging on the activity of muscle metabosensitive afferents are poorly understood.
Objective: The purpose of this study was to test the hypothesis that older individuals exhibit attenuated calf vascular resistance responses to muscle metaboreflex activation in comparison with young subjects.
Methods: Forteen young (mean ± SD age 23±3 years) and 13 older (62±7 years) sedentary subjects participated in the study. Functional capacity was evaluated by cardiopulmonary exercise testing. To evaluate muscle metaboreflex, we measured heart rate, mean blood pressure, calf blood flow (venous occlusion plethysmography), and calf vascular resistance responses to static handgrip exercise at 30% of maximal voluntary contraction, followed by recovery with or without circulatory occlusion.
Results: Mean resting blood pressure was higher in the older group (95±9 vs 86±7) and peak oxygen uptake was lower (27±8 vs 43±1 mL/kg.min). Maximal handgrip voluntary contraction was not significantly different between the groups (31±7 vs 36±9 N). Mean blood pressure and calf vascular resistance increased significantly (ANOVA $p<0.05$) throughout exercise and remained elevated during the circulatory occlusion period (PECO+) when compared with control situation (PECO-) in both groups. There were no differences between the two groups in blood pressure and calf vascular resistance relative changes from baseline during the entire protocol in both trials. Calf blood flow responses were also similar in the young and older subjects, except for the first minute of exercise, where young subjects had higher calf blood flow responses. Heart rate increased less (ANOVA $p<0.05$) at the end of exercise in the older group. In contrast to the young group, heart rate remained slightly elevated during PECO+ when compared with PECO- in older subjects.
Conclusion: Our results demonstrate that old subjects have similar blood pressure and calf hemodynamic responses to static handgrip exercise and selective action of the muscle metaboreflex when compared with young subjects, compatible with preserved muscle metaboreflex contribution to resting limb hemodynamic control with aging in humans.

P645 Prevalence of atrial fibrillation in former and still active long term endurance cross-country skiers. A twenty eight to thirty years follow-up study

J. Grimsmo[1], I. Grundvold[2], H. Arnesen[2], S. Maehlum[3].
[1]*Feiringklinikken A/S, Cardiac Rehabilitation Dept, Feiring, Norway;*
[2]*Ulleval University Hospital, Department of Cardiology, Oslo, Norway;*
[3]*Norwegian Institute of Sports Medicine, NIMI Ringerike, Hoenefoss, Norway*

Objectives: The prevalence of atrial fibrillation is approximately 0,4% in the general population and increases with age to probably more than 10% at ages over 75-80 years. Atrial fibrillation in athletes may be more common than in the general population at the same age. This question is still unresolved. We studied a group of endurance cross-country skiers after 28-30 years in a follow-up study. The aim of the study was to find the prevalence of atrial fibrillation in this population.
Methods: The population was previously first studied in 1976 and consisted of 122 long-time active, highly trained cross-country skiers belonging to three preselected age groups (group I 26-33 years, group II 43-50 years, group III 58-64 years). In a follow-up study in 1981 117 participated. All now living men were invited to participate in our 28-30 years follow-up study. Out of the initial 122 men 36 (29,5%) had died, with 1/35 in group I, 7/48 in group II and 28/39 in group III. Of the 86 still living 78 responded (90,7%). The tests included a resting ECG, maximal treadmill test with VO2 max and exercise ECG (not group III), echocardiography and two questionnares.
Results: 13 (16,7%) had developed paroxysmal or permanent atrial fibrillation with 6/33 (18,2%) in group 1, 5/37 (13,5%) in group II and 2/8 (25%) in group III. 11 (14,1%) seems to have developed atrial fibrillation with the first appearance at the average age of 57,8 years (38 – 72), without known structural heart disease at the time of appearance. 2 out of 6 with still paroxysmal atrial fibrillation had only had 1 and 3 episodes respectively. 2 (87 and 80 years old) developed permanent atrial fibrillation in 2004 and 2005 after many years with coronary heart disease.
Conclusion: Atrial fibrillation is quite common in this population. The findings support the assumption that long term endurance exercise at this level predispose to atrial fibrillation.

INFLUENCE OF GENDER ON CARDIOVASCULAR DESEASE

P646 The aging process of the heart: impact of gender on cardiac remodeling - results of the longitudinal population-based MONICA/KORA Survey

J. Stritzke[1], M.R.P. Markus[1], B. Mayer[1], W. Lieb[1], A. Luchner[2], A. Doering[3], U. Keil[4], H.-W. Hense[2], H. Schunkert[4] on behalf of KORA Investigators. [1]*Universitaetsklinikum Schleswig-Holstein, Medizinische Klinik Ii, Campus Luebeck, Luebeck, Germany;* [2]*Universitaetsklinikum Regensburg, Klinik und Poliklinik fuer Innere Medizin II, Regensburg, Germany;* [3]*GSF Nationales Forschungszentrum fuer Umwelt, Institut fuer Epidemiologie, Neuherberg, Germany;* [4]*Universitaetsklinikum Muenster, Institut fuer Epidemiologie und Sozialmedizin, Muenster, Germany*

Background: Left ventricular (LV) geometry reflects physiological requirements imposed by body size and load. Previous studies demonstrated that pathological LV remodeling is a strong prognostic factor for impaired cardiovascular outcome. Taking advantage of the longitudinal design of this study we evaluated for the first time gender-specific adaptations of cardiac remodeling during the aging process by sequential echocardiographic investigations in a population based sample.
Methods: Subjects (474 men and 531 women, aged 25 to 74 years) who originated from a gender and age stratified random sample of German residents of the Augsburg area were examined by standardized echocardiography at baseline and after ten years of follow-up. The effect of aging on changes of left ventricular enddiastolic diameter (LVEDD), and wall thickness (WT, sum of septal und posterior wall thickness) was assessed by comparison of five age groups.
Results: During the 10 year follow-up, in general, we observed an increase in wall thickness as well as an increase in LVEDD. However, comparing men and women as well as women in different age groups marked differences in the remodeling process were detectable. Comparing the youngest (25-34 years at baseline) with the oldest (65-74 years) subgroup we observed a significant acceleration of the increase in WT during ten years of follow-up (males: +5.9% [95%-CI 3.1, 8.7] vs. +16.8% [12.8, 20.7], $p<0.001$; females: +1.6% [-1.5, 4.6] vs. +8.5% [4.2, 12,8], p=0.012). A slight increase of LVEDD over time was observable in men of all age groups. In contrast, females until the age of 44 years displayed with a slight increase of LVEDD over time whereas women in older categories demonstrated a slight decrease of LVEDD (+1.6% [-0.2, 3.3] vs. -1.7% [-4.1, 0.8] (25-34 vs. 65-74 years), p=0.034). Comparing men and women with the age of 45 years and above there were significant differences in the change of LVEDD (+1.8% [0.4, 3.3] vs. -1.3% [-2.5, 0.0] (men vs. women, 45-54 years), p=0.002).
Conclusions: We observed with increasing age substantial gender differences in cardiac remodeling. While male individuals display a significant trend towards an eccentric remodeling (increase in LVEDD), women are characterized by a tendency towards concentric remodeling (decrease in LVEDD) with aging. Especially the decrease in LVEDD in elderly women may have implications for diastolic filling of the ventricle that is clinically known to display gender-specific deteriorations in this group.

P647 Anticonceptive drug use and pro-atherogenesis: population evidence from ASKLEPIOS

E.R. Rietzschel[1], M.L. De Buyzere[1], D. De Bacquer[2], S. Bekaert[1], P. Segers[2], P. Cassiman[3], P. Verdonck[3], G.G. De Backer[2], T.C. Gillebert[3] on behalf of the ASKLEPIOS investigators.
[1]*University Hospital Ghent, Department of Cardiovascular Diseases, Ghent, Belgium;* [2]*Ghent University, Department of Public Health, Ghent, Belgium;* [3]*Asklepios Primary Care Physicians VOF, Asklepios Primary Care Physicians, Erpe-Mere/Nieuwerkerken, Belgium*

Purpose: Combination therapy with the female hormones estrogen (E) and progestins are among the most frequently used drugs in the world with approximately 100 million women worldwide taking oral contraceptives (OC). Data from recent large trials have cast serious doubt on the cardiovascular safety of hormonal replacement therapy (HRT). In contrast to the active controversy surrounding HRT, very little attention has been focused on OC, a drug therapy using 10 to 100 fold higher levels of estrogen than HRT. We describe the population correlates of OC exposure in subjects free from overt cardiovascular disease.
Methods: The Asklepios study is a representative sample (2524 apparently healthy M/F volunteers, aged 35-55 years) from the Belgian general population. The subjects were extensively screened (biochemistry, lifestyle data, cardiac and vascular echography, arterial tonometry). Vascular echography of the carotid and femoral arteries was systematically performed and atherosclerosis was defined by presence of carotid or femoral plaque.
Results: Of 1301 women (median age 45.7 y), 27.4% were actively taking OC and 10.0% were taking HRT. In contrast, past use of OC is far more prevalent with 81% of women having taken OC for at least 1 year. The median duration of exposition in these women was 13 years. After multivariate adjustment for age, smoking, blood pressure, total & HDL-cholesterol, obesity, diabetes, physical activity, fruit, vegetable and alcohol intake, educational achievement and drug therapy (lipid-lowering, antihypertensive, aspirin), use of OC was associated with a significant increase in carotid or femoral unilateral plaque. Odds ratio's (OR) per 10 years of OC exposure were: carotid plaque 1.17 (1.00-1.33) and femoral plaque 1.28

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(1.10-1.47). We further looked at the prevalence of bilateral disease (involvement of right and left carotid/femoral artery) as a more specific and stringent phenotype of atherosclerosis. OR per 10 years OC exposure were: carotid plaque 1.42 (1.03-1.84); femoral plaque 1.34 (1.05-1.63).
Interpretation: Use of hormonal contraceptive therapy is very common and associated with an unexpected increase in the prevalence of carotid and femoral atherosclerosis in otherwise young, apparently healthy women. Our results suggest a 20-30% increased prevalence of plaque in the carotid and femoral arteries per 10 years of OC exposure. In the light of widespread (>80% of our population sample; > 100 million women globally) and usually prolonged OC use (>10 years) these results suggest OC use could be an important factor in the global atherosclerotic burden.

P648 Young women with ST-elevation myocardial infarction - Coronary Stenoses as often as men but three times higher early mortality

A.S.E. Sederholm Lawesson[1], U. Stenestrand[1], L. Wallentin[2], E. Swahn[1]. *[1]Department of Cardiology, Linkoping, Sweden; [2]Uppsala Clinical Research Center, Uppsala, Sweden*

Purpose: Myocardial infarction (MI) in patients < 46 years is unusual but important with a risk of premature death. As it is previously indicated that there is a sex-difference in mortality after MI most pronounced in young age-groups, we wanted to assess the impact of sex on in-hospital mortality after multivariate adjustments in a young ST-elevation MI (STEMI) population. We also wanted to compare results of coronary angiography between sexes in order to test the hypothesis that a non-atherosclerotic aetiology is more common in young women than in young men with STEMI.
Methods: All STEMI patients admitted 1995-2004 to CCUs in Sweden registered in the prospective observational Register of Information and Knowledge about Swedish Heart Intensive care Admissions (RIKS-HIA) were included. Diabetes, hypertension, smoking, reperfusion therapy, previous MI, angioplasty or bypass surgery were used as co-variates in logistic regression analyses of mortality.
Results: 397 women and 1868 men were included, mean age 41(±4) vs. 40(±5) yrs. 66% of women vs. 64% of men (p=NS) were investigated with coronary angiography (Table 1). In-hospital death was 1% vs. 3%, crude odds ratio for women, 3.20 (95% confidence interval (CI) 1.53-6.69), multivariate adjusted odds ratio 3.42 (95% CI 1.58-7.38).

Baseline characteristics

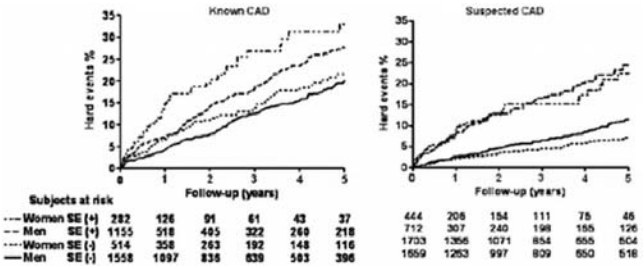
	Men (%)	Women (%)	p-value
≥1 ischemic heart disease risk factor	72	79	0.006
≥2 ischemic heart disease risk factor	19	26	0.002
Diabetes Mellitus	12	18	0.003
Hypertension	15	21	0.002
Current smoker	57	66	0.002
Normal coronary angiogram	9	9	0.95
One vessel disease	56	72	<0.001
Multivessel/left main disease	35	20	<0.001

Conclusions: Young STEMI women have a great MI risk burden. We did not find evidence for a sex difference in non-atherosclerotic aetiology of STEMI as there was no sex difference in normal coronary angiograms. The multivariate adjusted risk of in-hospital mortality was > 3 times higher in women, i.e. female sex seems to be an independent predictor of death in young STEMI patients.

P649 Prognostic value of stress echocardiography in men and women with known or suspected coronary artery disease

L. Cortigiani[1], R. Sicari[2], R. Bigi[3], F. Bovenzi[2], E. Picano[1]. *[1]Lucca Hospital, Lucca, Italy; [2]Cnr, Institute of Clinical Physiology, Pisa, Italy; [3]University School of Medicine, Milan, Italy*

Background: Research continues to report underrecognition and underdiagnosis of CAD as contributory to high mortality rates in women. Indeed, once the diagnosis is made, it does appear that current treatments are equally effective at reducing risk in both women and men. Aim. To compare the prognostic implication of stress echocardiography result in men and women with known or suspected coronary artery disease (CAD).
Methods: We analyzed the data of 8028 patients (5084 men, 2944 women; age 62±11 years) who underwent stress echocardiography (377 exercise, 5799 dipyridamole, and 1852 dobutamine) for evaluation of known (n=3509) or suspected (n=4519) CAD. Patients were followed-up for the occurrence of death or myocardial infarction.
Results: During a median follow-up of 25 months, there were 965 events (649 deaths, 316 infarctions). Additionally 2187 patients underwent revascularization and were censored. The rate of revascularization was higher in men than in women with both known (p<0.0001) or suspected CAD (p<0.0001). Considering patients with known CAD, 5-year event rate was 28% in men and 33% in women with ischemia (p=0.10), and 20% in men and 21% in women without ischemia (p=0.69). Considering patients with suspected CAD, 5-year event rate was 24% in men and 22% in women with ischemia (p=0.52), and 11% in men and 7% in women without ischemia (p=0.0001).



Conclusion: Ischemia at stress echocardiography predicts similar prognosis in men and women with both known and suspected CAD. Moreover, a nonischemic test is associated with comparable event rate in men and women with known CAD. In these conditions, revascularization procedures should be evenly used in the two sexes.

P650 ER-alpha is expressed in cardiac stem cells and supports self-renewal after cardiac ischemic injury in rats

J. Li, M. Brinckmann, M. Timm, E. Kaschina, A. Grzesiak, C. Curato, C. Birka, T. Unger. *Center for Cardiovascular Research, Charite, University Medicine Berlin, Berlin, Germany*

Several lines of clinical and experimental evidence suggest a protective role of estrodiol in response to cardiac ischemic injury although the mechanisms underlying this cardioprotection have not yet been clearly defined. Estradiol exerts its actions through the activation of two estrogen receptors (ER): ER-alpha and ER-beta. In adult rats, ER-alpha increases in an age-dependent manner and remains relatively high, suggesting its role in heart maturation. We assessed the regulation of cardiac ER-alpha in response to ischemic injury in rats. Seven days after myocardial infarction, both real-time RT-PCR and immunofluorescence staining revealed that ER-alpha was upregulated. Double immunofluorescence staining showed that ER-alpha was mainly detected in BrdU incorporating nuclei of new Sca-1+ cells, accumulating in peri-infarct zone. Further, we isolated and purified the c-kit+ cell population from rat infarcted hearts by modified MACS technology and FACS sorting.These ex vivo cardiac c-kit+ cells expressed both sca-1/ER-alpha and maintained a stable phenotype under in vitro conditions for more than 16 months after their isolation. In rat undifferentiated embryo myoblasts (H9C2), which are characterized by their diffentiation potential into myocyte-like cells and predominant ER a expression, exogenous 17 b-estrodiol (E2) treatment supported self-renewal. In addition, real-time RT-PCR showed that E2 induced Akt and Tbx-3 but suppressed GATA-4 gene. By contrast, estrogen receptor blocker ICI 182780 abolished these in vitro effects of E2. Together, the present findings demonstrate that ER-alpha may support self-renewal of cardiac stem cells in response to cardiac ischemic injury in rats.

P651 Erectile performance as estimated with penile Doppler is related to aortic stiffness and carotid wall thickness

N. Ioakeimidis, C. Vlachopoulos, K. Aznaouridis, K. Rokkas, A. Tsokanis, D. Tsekoura, K. Baou, C. Masoura, A. Askitis, C. Stefanadis. *Athens Medical School, Hippokration Hospital, 1st Department of Cardiology, Athens, Greece*

Purpose: Erectile dysfunction (ED) has been reported as the first sign of a generalized vascular disease. Intima-media thickness (IMT) and aortic stiffness are markers and prognosticators of cardiovascular risk. The association between ED, IMT and aortic stiffness has not been investigated.
Methods: A total of 112 men with ED were evaluated for penile vascular disease by penile Doppler ultrasound: 40 men (aged 61±9 yrs) with coronary artery disease (CAD) and 72 men (aged 59±11 yrs) without CAD. IMT of common carotid arteries, carotid-femoral pulse wave velocity (PWV, an index of aortic stiffness) and pharmacologically stimulated peak systolic velocity (PSV) of cavernous arteries were used to assess vascular damage.
Results: Patients with CAD had decreased PSV (27.2 vs 33.8 cm/s, P=0.01), increased IMT (0.98 vs 0.86 mm, P<0.01) and increased PWV (8.9 vs 8.2 m/s, P<0.01) compared with men without CAD. PSV was inversely correlated with age (r= -0.24, P<0.05), pulse pressure (r= -0.25, P<0.05), Framingham score (r= -0.28, P<0.05), IMT, PWV and high sensitivity C-reactive protein (hsCRP) (figure). After adjusting for potential confounding factors such as age, mean pressure, body-mass index, total cholesterol, HDL, hsCRP and intensity of smoking in

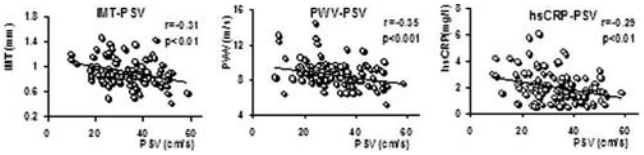


Figure 1

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

multivariate linear regression models, penile PSV was independently associated with both IMT (b= -0.35, P<0.01) and PWV (b= -0.27, P=0.02) (adjusted R2 of models 0.27 and 0.25 respectively).
Conclusions: Carotid IMT and aortic stiffness are associated with impaired erectile function as estimated by penile PSV. This finding provides further insights into the pathophysiology of ED and may have implications for the cardiovascular risk in these patients.

P652 Endogenous androgens and vascular markers of atherosclerosis in healthy postmenopausal women

G. Georgiopoulos[1], I. Lambrinoudaki[2], K. Stamatelopoulos[1], G. Christodoulakos[2], K. Kyrkou[1], D. Rizos[2], I. Karnezis[1], S. Rokas[1], G. Creatsas[2], C. Papamichael[1]. *[1]Alexandra University Hospital, Clinical Therapeutics, Athens, Greece; [2]University of Athens Aretaieio Hospital, 2nd Department of Obstetrics and Gynecology, Athens, Greece*

Objective: Women after menopause exhibit a significant increase in cardiovascular morbidity and mortality. While several studies have underlined the postmenopausal estrogen decline as a pivotal cause for this phenomenon few and controversial data exist about the role of serum androgen levels in this setting. The present study aims to examine the relationship between levels of endogenous androgens with functional and structural vascular markers of early atherosclerosis in postmenopausal women not on hormone therapy.
Methods/Design: Thirty seven healthy postmenopausal (age 56.7±4.8 years, years in menopause 8.3±5.4 years) women without receiving exogenous hormone administration were consecutively enrolled in a university menopause clinic. Blood lipid profile, glucose level, estradiol (E2), total testosterone (T) levels and sex-hormone binding protein (SHBG) were measured in all participants. The free androgen index (FAI) was calculated by the equation FAI=T*3.47* 100/SHBG. Flow-mediated dilatation (FMD) as a marker of endothelial function, mean carotid and femoral intima-media thickness (IMT) as a marker of generalized atherosclerosis, and carotid-femoral pulse wave velocity (PWV) as a marker of aortic stiffness were measured in all individuals in one session. Abdominal preperitoneal (PPT) and subcutaneous (SCFT) fat thickness were also measured ultrasonographically. E2, SHBG and FAI were divided into tertiles and differences between groups were assessed by ANOVA.
Results: Age and the duration of menopause were not significantly different across tertiles of all 3 examined parameters. PPFT (p=0.014) and LDL cholesterol (p=0.013) progressively increased and HDL cholesterol (p=0.004) progressively decreased across E2 tertiles. BMI (p=0.009), SCFT (p=0.035) and mean carotid IMT (p=0.05) progressively increased across tertiles of SHBG. Systolic blood pressure (p=0.047), diastolic blood pressure (p=0.065) and mean carotid IMT (p=0.1) progressively increased across tertiles of FAI although DBP and IMT did not reach statistical significance. No differences were observed among groups in FMD, PWV and femoral IMT.
Conclusions: Increased androgenicity, indicated by low SHBG and increased FAI, may be associated with increased arterial blood pressure and accelerated atherosclerosis as this is expressed by increased IMT in healthy postmenopausal women. The observed proatherogenic profile in women with high endogenous estrogens may indicate an indirect androgen effect, as the production of estradiol in postmenopausal women is mainly determined by circulating androgens, which serve as precursor steroids.

P653 Are coronary event rates declining slower in women than in men?

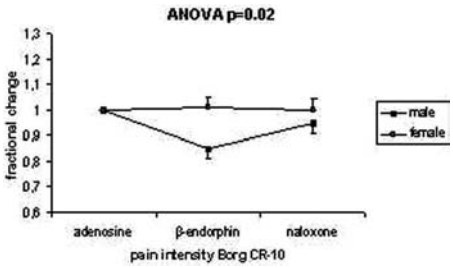
H.-R. Lehto[1], S. Lehto[2], A.S. Havulinna[3], M. Ketonen[4], Y.A. Kesaniemi[5], J. Airaksinen[5], V. Salomaa[2] on behalf of FINAMI Study Group. *[1]University Hospital of Turku, Turku, Finland; [2]University Hospital of Kuopio, Kuopio, Finland; [3]KTL-National Public Health Institute, Helsinki, Finland; [4]Joensuu Central Hospital, Joensuu, Finland; [5]Oulu University Hospital and Biocentre Oulu, Oulu, Finland*

Purpose: To examine whether the incidence, attack rate and mortality of myocardial infarction (MI) events have declined less in women than in men.
Methods: We used data from two large population-based MI registers, the FINAMI registers and the Finnish Cardiovascular Disease Register (CVDR). The former is based on detailed review of hospital documents and death certificates in four geographical areas. The latter is based on administrative data but covers the whole country. The event rates in men and women aged >35 years were compared for two time periods, 1994-1996 and 2000-2002. We computed Poisson regression models, where the gender by time period interaction was the main outcome of interest. The effect of troponins on the diagnostics was taken into account by using correction coefficients derived from our previous work.
Results: In the FINAMI register 5252 events were included in the analyses among men and 4898 among women. In the CVDR the corresponding numbers were 78709 in men and 70464 in women. In the FINAMI register the age-standardized incidence and attack rate of MI events did not change in women, but declined significantly in men. In CVDR declining incidence and attack rate were observed in both genders but the declines seemed steeper in men than in women. A significant mortality decline was observed in FINAMI data among men and in CVDR data among both genders. In Poisson regression models of the FINAMI data the gender by time period-interaction was significant for incidence (p=0.024), attack rate (p=0.012) and mortality (p=0.046) suggesting smaller declines in women than in men. In CVDR data the findings were consistent with FINAMI and all corresponding p-values were <0.0001 due to the large number of events. However, when the incidence and attack rate models were corrected for the effect of troponins, the gender by time period interactions became nonsignificant. For mortality, the troponin correction was not meaningful, since much of the mortality takes place out-of-hospital and troponins have not changed much the diagnostics of fatal MI events.
Conclusions: The incidence and attack rate of MI events have declined more slowly in women than in men. The data suggested this difference was explained by the adoption of troponins causing a bigger increase in the event rates among women than among men. However, the slower decline in coronary mortality among women than among men cannot be easily explained by technical reasons. Further studies on gender differences in case fatality and treatment of MI events are warranted to elucidate the reasons for the slower mortality decline in women.

P654 Beta-endorphin modulates adenosine provoked chest pain in men, but not in women - a comparison between patients with ischemic heart disease and healthy volunteers

B. Sadigh[1], M. Berglund[2], R.B. Fillingim[3], D. Sheps[3], C. Sylven[1]. *[1]Karolinska University Hospital, Huddinge, Dept of Cardiology, Stockholm, Sweden; [2]Karolinska university hospital, Huddinge, Dept of Cardiology, Stockholm, Sweden; [3]University of Florida, Gainsville, Dept of Cardiology, Gainsville, United States of America*

Introduction: Increasing evidence suggests the existence of sex differences in pain perception. Adenosine, an early messenger for myocardial ischemia induces angina pectoris-like symptoms in healthy volunteers and in patients with ischemic heart disease.
Aims: To study whether gender influences adenosine-provoked chest pain and the analgesic effect of the opioid receptor agonist β-endorphin.
Materials and methods: 20 patients (10 male and 10 female) with significant coronary artery disease and 20 healthy volunteers (10 male and 10 female) were studied. Both the hand algometer and Borg CR-10 scale were used to estimate chest pain. Chest pain was provoked double-blind by injections of placebo, 1/3, 2/3, 3/3 of maximal tolerable dose of adenosine twice in randomized order. This procedure was repeated after bolus injection of β-endorphin followed by infusion and repeated a third time after bolus injection of naloxone 0.8 mg. Central chest pain and physiological responses were quantified using hemodynamic and psychophysical methods.
Results: Pain estimate by hand algometer and the Borg CR-10 scale correlated (r=0.77, p<0.001). Both sexes reported a dose-dependent increase of adenosine-provoked chest pain with no differences for maximum tolerable dose of adenosine per kilogram. β-endorphin administration lowered adenosine-provoked pain in both male patients and male healthy volunteers (p=0.02) but not in women. Naloxone tended to increase the pain perception in male patients (p=0.052) and male healthy volunteers (p=0.054) but did not have any significant effect on pain modalities in female.



Conclusions: In conclusion, women were resistant to β-endorphin modulation of adenosine- provoked chest pain. In male subjects β-endorphin induced analgesia.

P655 The effects of hormone replacement therapy on the myocardial velocities and myocardial performance index

M.A. Duzenli[1], K. Ozdemir[2], A. Sokmen[3], A. Soylu[1], K. Gezginc[1], C. Celik[1], M. Tokac[1], B. Altunkeser[1]. *[1]Selcuk University Meram Faculty of Medicine, Cardiology Department, Konya, Turkey; [2]Konya, Turkey; [3]Maras, Turkey*

The results of the studies, in which the effect of hormone replacement therapy (HRT) on cardiac functions have been evaluated, are rather disputable. In these studies, cardiac functions were evaluated with conventional echocardiography methods. This study was planned in order to investigate the effects of HRT on tissue Doppler echocardiography (TDE) parameters and myocardial performance index (MPI).
Method: In a prospective controlled study 60 healty postmenopausal women

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

were randomly assigned to 2 groups (32 in the HRT group and 28 in the control group). After conventional echocardiographyic paramaters were measured, TDE recordings obtained of the mitral and tricuspid annulus. Systolic velocity (Sm), early and late diostolic velocities (Em and Am) and time intervals were measured and MPI was calculated. Sequentially symptom limited exercise stress test was performed. After 3 and 6 months of HRT (oral 0.625 mg conjugated estrogen and 2.5 mg medroxyprogesteron acetate/day), same processes were repeated. The effect of HRT on myocardial velocities, MPI and exercise time were evaluated at the 3rd and 6th month.

Results: On the sixth month of the study, no change in E/A ratio was observed in the control group whereas a significant increase in the HRT group was determined. There was no change in segmental and mean LV Sm, and RV Sm of both groups throughout the study. However, LV Em/Am, RV Em/Am ratios of the HRT group had significantly increased on the sixth month. After 6 months of HRT, LV and RV MPI values were observed to decrease significantly. Additionally significant increase in exercise period and METS values were observed after 3 and 6 months of HRT (table).

	HRT		Control		p	
	bazal	6 month	bazal	6 month	bazal	6 month
E/A	0.89±0.24	0.99±0.24	0.83±0.16	0.82±0.18	NS	.01
Em/Am	0.96±0.20	1.08±0.21	0.95±0.21	0.94±0.20	NS	.001
LV MPI %	57±10	51±6	56±11	56±0.8	NS	.02
RV MPI%	55±20	44±07	53±14	51±11	NS	.006
Exercise duration (min)	7.8±2.2	8.9±2.4	7.6±1.9	7.6±1.8	NS	.03
METS	9.1±1.2	10.2±2.5	9.0±1.8	8.8±2.0	NS	.02

Conclusion: Data obtained in this study suggests that HRT is not only effective for treating menopausal complaints, but also increases cardiovascular performance by improving especially diastolic functions.

P656 The effects of menopause on the myocardial velocities and myocardial performance index

M.A. Duzenli[1], K. Ozdemir[2], A. Sokmen[3], A. Soylu[4], N. Aygul[1], M. Tokac[1]. *[1]Selcuk University Meram Faculty of Medicine, Cardiology Department, Konya, Turkey; [2]selcuk university of medical faculty, cardiology, Konya, Turkey; [3]Maras, Turkey; [4]Konya, Turkey*

Objectives: In previous studies, the effect of menopause on cardiac functions was investigated by standard echocardiography. The significant age difference between pre- and postmenopausal women in these studies have caused dispute among investigators as to whether these cardiac structural and functional changes were related to aging or menopause.This study was planned in order to investigate the effect of menopause on cardiac functions by tissue Doppler echocardiography (TDE) and myocardial performance index (MPI) in age-matched pre-post menopausal women.

Method: Seventy-two premenopausal and 71 age-matched postmenopausal women were enrolled the study. After conventional echocardiographic paramaters were measured, TDE recordings were obtained at the septal, lateral, anterior and inferior side of the mitral annulus, and tricuspid lateral annulus. Systolic velocity (Sm), early and late diastolic velocities (Em and Am) and isovolumetric contraction (ICT), relaxation time (IRT), ejection time (ET) were measured and MPI was calculated by Formula (ICT +IRT/ET). Sequentially symptom limited exercise stress test was performed.

Results: Age, heart rate, systolic and diastolic blood pressure, body mass index were similiar in both groups. While left ventricular (LV) ejection fraction and end-diastolic and end-systolic diameter were similiar in both groups, LV septum and posterior wall thickness were higher in postmenopausal women (9.1mm±1.2 vs 8.9mm±1.0 $p<0.001$ and 8.2mm±1.0 vs 7.4mm±1.0 $p<0.001$ respectively). Mitral E wave and mitral E/A ratio were significantly lower in postmenopausal women compared to premenopausal women (0.64m/s±0.15vs 0.70m/s±0.12 $p<0.01$ and 0.96±0.25 vs 1.07±0.24 $p<0.005$ respectively). LVSm, LV and RVEm/Am ratios were lower in postmenopausal women (9.1cm/s±1.2 vs 10.2cm/s±1.3 $p<0.001$ and 0.91±0.22 vs 1.02±0.20 $p<0.005$ and 079±0.20 vs 0.89±0.20 $p<0.005$ respectively). MPI calculated by TDE significantly increased in postmenopausal women (0.59±0.11 vs 54±0.7 p=0.02). In addition, exercise duration and METS values were significantly lower in postmenopausal women than in premenopausal women ((7.4 min ± 2.4 vs 9.0 min ±1.7 $p<0.01$ and 8.8 METS ±2.4 vs 10.1 METS ± 1.8 $p<0.05$ respectively).

Conclusion: Menopause affects MPI and myocardial velocities, which provide more quantitative data abouth myocardial functions, negatively. These findings indicate that the hormonal changes in menopause impair LV systolic and diastolic functions and RV diastolic function.

P657 Are there gender disparities in the treatment of Non-ST elevation and ST-elevation acute coronary syndromes in the Middle East? Observations from the SMART registry

A. Hammoudeh[1], H. Tarawneh[2], R. Tabbalat[2], A. Harassis[2], I. Alhaddad[3], E. Almousa[4], Y. Ismail[5], M. Izraiq[4], A. Nammas[6] on behalf of SMART Registry Investigators. *[1]Al-Essra Hospital, Cardiology, Amman, Jordan; [2]Khalidi Medical Center, Amman, Jordan; [3]Jordan Hospital Medical Center, Amman, Jordan; [4]Istiklal Hospital, Amman, Jordan; [5]Jordan University Hospital, Amman, Jordan; [6]Islamic Hospital, Amman, Jordan*

Background and methods: Data from the west indicate that women do not receive the same level of care as men do when they are admitted with acute coronary syndrome (ACS). To determine if such a gender-specific disparities also exist in the Middle East we evaluated the utilization of medications and diagnostic and revascularization procedures in ACS women and men admitted to 10 tertiary care centers in Amman from June 2005 to June 2006.

Results: Of 2765 ACS patients, 554 (20%) were women. Mean age of women was 64 and of men 55 years. Compared with men, women had more prevalence of diabetes (57% vs. 38%, $p<0.0001$), hypertension (69% vs. 50%, $p<0.0001$) and dyslipidemia (34% vs. 29%, $p<0.014$), but they were less likely to be smokers (24% vs. 63%, $p<0.0001$). Women were more likely to have unstable angina than men (70% vs. 65%, $p<0.03$), less ST-elevation myocardial infarction (STEMI) (17% vs. 22%, $p<0.03$), and similar rate of non-ST elevation MI (NSTEMI) (13% vs. 13%, p=NS). No significant differences (p=NS) existed between women and men in the use of aspirin (95% vs. 96%), statins (86% vs. 87%) or beta blockers (34% vs. 29%), but ACE inhibitors/angiotensin II blockers were used more often among women than men (40% vs. 34%, p=0.003). Despite a similar rate of using unfractionated and low molecular weight heparins in women and men (83% vs. 81%, respectively); women were less likely to receive clopidogrel (60% vs. 66%, p=0.01) and glycoprotein IIb/IIIa inhibitors (33% vs. 42%, $p<0.001$) compared with men. Coronary angiography was less utilized in women than men with NSTE ACS (76% vs. 82%, p=0.003) and STEMI (79% vs. 88%, p=0.034). Moreover, less women underwent percutaneous coronary intervention (PCI) than men whether they had NSTE ACS (50% vs. 58%, p=0.004) or STEMI (57% vs. 72%, p=0.005). No significant difference was found in the utilization of coronary bypass surgery in both genders (5.2% in women vs. in 6.8% men, p=0.17) despite a trend of lower rate in women sustaining NSTE ACS (4.2% vs. 6.6%, p=0.06) and a trend of higher rate in women sustaining STEMI (10% vs. 7.5%, p=0.44) compared with men.

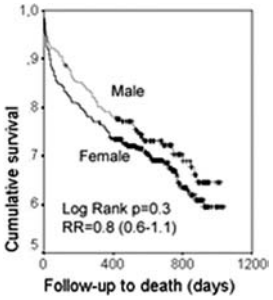
Conclusion: In this Middle Eastern ACS population, women were older, had more comorbidities, more unstable angina and less STEMI compared with men. The use of aspirin, beta blockers, ACE inhibitors/angiotensin II blockers and statins was comparable to that in men, but women were less likely to receive other antiplatelet agents. Despite performing coronary angiography for about 8 of 10 and PCI for 5 of 10 women, these rates were significantly lower than those in men.

P658 Women and heart failure with preserved left ventricular ejection fraction: is their long-term outcome worse than men?

L. Perez De Isla[1], J. Zamorano[2], V. Canadas[2], L. Contreras[2], C. Almeria[2], J.L. Rodrigo[2], V. Serra[2], L. Mataix[2], D. Herrera[2], C. Macaya[2]. *[1]Hosp.Clinico San Carlos,Instituto Cardiovasc., Unidad De Imagen Cardiovascular, Madrid, Spain; [2]Hospital Clinico San Carlos, Cardiology, Madrid, Spain*

Prognostic factors regarding heart failure (HF) with preserved left ventricular ejection fraction (LVEF) are still not well described and we still do not know if there is any difference in patients' prognosis depending on their gender. Our aim is to show the influence of patients' gender in the long-term outcome after a first admission due to HF with preserved LVEF.

Methods: 771 consecutive patients with a first admission to hospital because of HF with preserved LVEF between January 2002 and September 2003 comprised our study group. Cardiovascular risk factors, clinical, electrical and echocardiographic variables were studied. In all patients, long-term follow-up was performed by means of clinical revisions and telephone contact. Death was the primary end-



Survival curves

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

point. Kaplan Meier curves were constructed and Cox regression analysis was performed.
Results: There were 551 women (66.3%). Mean age was 82.6±43.6 (women: 85.2±52.7; men: 77.5±12.4; p=0.021). Mean follow up was 564.5±298.3 days. Variables in both groups were similar except for age, presence of mitral regurgitation, history of hypertension and atrial fibrillation (more frequent in women), smoking, renal failure, and history of ischemic heart disease (more frequent in men) and the end-diastolic and end-systolic volumes and interventricular septum thickness (greater in men). Gender was not found as a marker of long-term bad outcome (Log Rank p=0.3; RR=0.8;95%CI:0.6-1.1;p=0.2) neither in the uni nor in the multivariate analysis after statistic adjustment for the potentially confounding factors (RR=0.7;95%CI:0.4-1.2;p=0.23) (see figure).
Conclusions: Gender is not a marker of increased mortality in patients after a first admission because of heart failure with preserved LVEF.

P659 Renal function and mortality in the Glasgow population

C.A. Murphy[1], T. Mc Donagh[2], H.J. Dargie[2]. *[1]Western Infirmary, Cardiology Department, Glasgow, United Kingdom; [2]Royal Brompton Hospital, Cardiology, London, United Kingdom*

The link between chronic kidney disease (CKD) and cardiovascular death is under increasing scrutiny. We report on our findings from epidemiological studies started in 1990's.
Methods: The MONICA epidemiology study of 1992 investigated 1640 volunteers from the general population, with subsequent rescreening in 1995, 2002 and 2004. The ELDERLY study (n=1009) of 1995 was of similar design, but only included volunteers over 55 years old. Rescreening occurred in 1998, 2002 and 2004.
All deaths up to and including 2006 were collated from the General Register Office for Scotland.
Results: Earliest available data on renal function for the MONICA population was for 853 patients from the 1995 rescreen. Those people deceased (n =117) by 2006 had significantly lower eGFRs than survivors (72.1ml.min v 78.8ml/min, $p<0.001$). Women had significantly lower eGFRs than men (72.8 ml/min v 83.3ml/min, $p<0.001$). 74.5% of individuals with stage 3 CKD (eGFR <60ml/min) or worse were female.
For the ELDERLY population, the earliest available renal data was for 576 volunteers in the 1998 rescreen, of which 107 had died by 2006. There was no difference between deceased and survivors in mean eGFR, although significantly fewer survivors had CKD stage 4 (eGFR<45ml/min). As with MONICA, women had significantly lower eGFR (67.0ml/min v 73.3ml/min, $p<0.001$) and 71.5% of individuals with CKD stage 3 or worse were female.
Outcome: In the MONICA cohort, all cause mortality for men and women were 16% and 9.2% respectively. Cardiovascular (CVS) death rates were 6.2% and 5.1% respectively. For both all cause mortality and CVS mortality in men, those with eGFR < 80ml/min had death rates higher than the mean. In women, mortality rates (both all cause and CVS) above the mean were seen in those with eGFR of < 70ml/min.
In the ELDERLY cohort, all cause mortality rates for men and women were 23.2% and 13.7% respectively. CVS death rates were 11.6% and 6.0% respectively. For both men and women, all cause mortality rates were significantly higher than the mean in those individuals with eGFR <50ml/min. In both gender groups, CVS mortality rates higher than the mean were seen in those with eGFR<70ml/min.
Conclusion: Current classification of CKD does not take age or gender into consideration. The cut-off in eGFR for increased mortality rates differs between men and women, and also between different age groups. Our data suggests that age and gender have a bearing on what constitutes renal "impairment" in terms of outcome.

P660 Do gender differences still exist in the recent era? In-hospital and one year outcome after myocardial infarction

M. Godin, H. Eltchaninoff, E. Gauliard, C. Tron, D. Brunet, A. Cribier. *Rouen University Hospital, Cardiology, Rouen, France*

Background: Gender differences have been described in various studies demonstrating a worse outcome in women in comparison with men after myocardial infarction (MI) and/or myocardial revascularization.
Methods: The aim of our study was to evaluate possible gender differences in patients (Pts) hospitalized with acute MI in the recent era. We conducted a prospective study between december 2004 and may 2005 including 209 Pts admitted to our institution with the diagnosis of acute ST or non ST MI. Presentation, clinical history, risk factors, treatment, in-hospital, one-month and one-year clinical outcomes (death, MI, stroke, target lesion revascularization after PCI) were compared between women and men. All patients were contacted by phone for follow-up.
Results: The population included 209 Pts (33% women), 42% with ST MI. Women were older (72.3 vs 65.5 yrs, p=0,012) with more frequent hypertension (81% vs 50%, p<0,001) and less smokers (24% vs 81%, p<0,001). Chest pain was less frequent in women in the setting of ST+ MI (68% vs 87%, p=0,037). Delay for admission after onset of symptoms was comparable; however coronary angiography was performed later in women (3.11 vs 2.05 days, p=0.004). 89% of men and 81% of women had coronary angiography during hospital stay, p=NS. Extent of coronary disease was similar as well as ejection fraction. Success of PCI was lower in women: 87% vs 96%, p=0.02. Women received more often a drug eluting stent (39% vs 21%, p<0.05). Hospital stay was longer in women (10.7 vs 7.7 days, p<0.0001). 97.4% of patients could be contacted for follow-up. Composite endpoint of death, MI, stroke and target lesion revascularization was comparable at one-month (6.6 vs 7.1%, p=NS) and at one-year (18.5 vs 17.7%, p=NS). Female gender was not identified as a predictor of worst outcome at one-month and at one year.
Conclusions: Our results compare favorably with previous data concerning differences in clinical characteristics and presentation of women in comparison to men. However, one-month and one-year clinical outcomes were comparable and female gender was not identified as a predictor of worse outcome.

P661 Women with palpitations of pregnancy associated with symptoms have significantly higher incidence of cardiac arrhythmias

A. Dhawan, J. Singh, P.S. Lewis. *stepping hill hospital, Stockport, United Kingdom*

Introduction: Palpitations is one of the most common reasons for cardiac consultations during pregnancy generally attributed to benign cardiac arrhythmias of pregnancy. Commonest complaint in these women is an awareness of fast heartbeat without any associated symptoms. However there is a small proportion in whom palpitations are associated with significant symptoms like, chest tightness, dyspnoea, sweating, dizziness and syncope. We compared symptomatic palpitations with asymptomatic palpitations.
Methods: We studied 180 pregnant women referred for further assessment of palpitations during pregnancy. Out of these 118 women had associated symptoms and 62 were asymptomatic. Both groups had no evidence of any prior known structural abnormalities of the heart. All women were extensively investigated for potential underlying causes of palpitations. All had detailed history, examination, baseline blood tests including Thyroid Function Test, 12 lead electrocardiogram, echocardiogram, holter monitor, and regular follow ups.
Results: Women with symptoms were older in age (33.1±4.2 vs 30.1±6.0, p = 0.005) and had significantly higher incidence of anaemia (p= 0.014). Women with symptoms were more likely to have a significant cardiac arrhythmia noted on Holter recording, (22/118 vs 2/62, p=0.008).Using a multivariate binary logistic model including age, symptoms and presence of anaemia; only age (OR1.14, 95% CI: 1.03-1.27 p=0.011) and symptoms (95% CI: 1.30-26.3 p= 0.022) were significant independent contributors to the final diagnosis.
Conclusion: This study shows that not all palpitations of pregnancy are benign and that the presence of symptoms is associated with a higher incidence of significant cardiac arrhythmias. Anaemia significantly contributes towards symptoms but not towards final diagnosis.

INFLAMMATION AND BIOMARKERS FOR CARDIOVASCULAR DISEASE IN THE ELDERLY

P662 Lower levels of fetuin A is associated with valvular calcification and stenosis progression in the elderly patients with aortic stenosis

D. Mohty, P. Pibarot, J.P. Despres, A. Cartier, B. Arsenault, P. Mathieu. *Hopital Laval, Cardiology, Quebec, Canada*

Introduction: Aortic stenosis (AS) is a disease process involving an active calcification of the aortic valve. Its prevalence increases markedly with aging. There remain uncertainties as to whether mechanisms leading the development and progression of AS in elderly subjects are similar to those in the younger population. We hypothesized that the blood level of fetuin A, an important circulating protein with anti-calcifying properties, would be involved in pathophysiology of AS in the elderly population.
Methods: In 114 patients operated for AS, the plasma level of fetuin A as well as complete blood lipid profile including the size of LDL particles were determined. Calcium content of the aortic valve was measured. In a subset of patients (n=55) for whom at least two transthoracic echocardiography (TTE) separated by at least 6 months were available pre-operatively, the annualized hemodynamic progression rate of the stenosis was calculated.
Results: In the elderly patients (divided in age quartile) the low-density lipoprotein cholesterol (LDL-C) (p=0.03), triglyceride (p=0.01), LDL-C content in small size LDL particles ($LDL\text{-}C_{<255Å}$) (p=0.007), apoB/ApoA-I ratio (p=0.01), and fetuin A (p=0.004), were all significantly lower compared to younger patients. In the highest age quartile group (≥77 years), lower level of fetuin A was associated with increased valvular calcium content (p=0.03) and with faster hemodynamic progression rate as measured by the annualized maximum aortic transvalvular gradient (p=0.04). In this quartile, low fetuin A level remained significantly associated with valvular calcium (p=0.02) and preoperative progression rate of gradient (p=0.02) after adjustment for covariables. In the whole cohort of patients, fetuin A levels was negatively correlated with age(r=-0.34; p=0.0002) and CRP (r=-0.19; p=0.05), whereas it was positively correlated with triglyceride levels (r=0.21;

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

p=0.02). On multivariate analysis, age was the only variable associated with decreasing concentration of circulating fetuin A.
Conclusion: The elderly patients had a less atherogenic lipid profile. However, this positive effect may be counterbalanced by the age-related reduction in fetuin A, which in turn may contribute to enhanced valvular calcification and disease progression in the elderly.

P663 The detrimental effect of age on urinary albumin excretion and arterial stiffness in essential hypertensive subjects: assessing the inflammatory component of cardiovascular aging

C. Tsioufis, K. Dimitriadis, M. Selima, D. Tsiachris, D. Tousoulis, P. Toutouzas, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: Evidence suggests that subclinical inflammation may be a link between aging and diffuse vascular dysfunction, while urinary albumin excretion and arterial stiffening are associated with subclinical atherosclerosis. In the present study, we examined the interrelationships between aging, high-sensitivity C-reactive protein (hs-CRP), urinary albumin excretion expressed as the albumin to creatinine ratio (ACR), and arterial stiffness in essential hypertensive patients.
Methods: 295 newly diagnosed untreated non-diabetic patients with stage I to II essential hypertension [192 men, mean age=50±8 years, office blood pressure (BP)=148/95 mmHg] were divided into two groups according to age: Older group (mean age >or=60 years, n=43) and younger group (mean age<60 years, n=252). In all subjects a rterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method (Complior SP), while ACR values were determined as the mean of two non-consecutive morning spot urine samples.
Results: Older compared to younger group had lower office and 24-h diastolic BP (90±8 vs 96±9 mmHg and 74±9 vs 83±9 mmHg, respectively; $p<0.0001$ for both), and greater left ventricular mass index (114.3±15 vs 105.2±11 g/m^2, $p<0.05$) while did not differ regarding sex, body mass index and metabolic profile (p=NS). Moreover, older compared to younger patients exhibited increased levels of hs-CRP (3.2±0.7 vs 2.1±0.7 mg/l, $p<0.05$), ACR (36.5±12 vs 22.8±7 mg/g, $p<0.05$) and PWV (8.8±1.5 vs 7.9±1.2 m/sec, p=0.001). In the entire population, age was associated with hs-CRP (r=0.120, $p<0.05$), ACR (r=0.221, $p<0.05$), and PWV (r=0.399, $p<0.0001$), while it was negatively related to 24-h diastolic BP (r=-0.319, $p<0.0001$). Furthermore, hs-CRP was correlated with body mass index (r=0.281, $p<0.0001$) ACR (r=0.631, $p<0.0001$) and PWV (r=0.233, $p<0.05$). In multiple regression analysis, age and hs-CRP were independent predictors of both PWV and ACR ($p<0.05$). Analysis of covariance revealed that hs-CRP, ACR and PWV concentrations were significantly different between groups after adjusting for confounders ($p<0.05$ for all).
Conclusions: Hypertensive patients of more than 60 years of age are characterized by increased levels of hs-CRP, ACR and PWV, whereas the main determinants of early renal dysfunction and arterial stiffness are age and low-grade inflammation. These findings provide an insight into the accelerated atherosclerotic mechanisms of cardiovascular aging.

P664 Improvement of aging-associated cardiovascular dysfunction by copper(II) aspirinate complex

T. Radovits[1], S. Loganathan[1], H. Sakurai[2], T. Hoppe-Tichy[2], M. Karck[2], G. Szabo[2]. [1]*University of Heidelberg, Department of Cardiac Surgery, Heidelberg, Germany;* [2]*Kyoto Pharmaceutical University, Dept. of Analytical and Bioorganic Chemistry, Kyoto, Japan*

Purpose: Overproduction of free radicals in aging tissues causes oxidative stress, which play an important role in the pathogenesis of cardiovascular dysfunction associated with advanced aging. It has been recently reported, that the copper(II) aspirinate complex exerts not only the well-known anti-inflammatory and platelet anti-aggregating effects of aspirin, but due to its superoxide dismutase (SOD) mimetic activity, it acts as a potent antioxidant as well. In this study we investigated the effects of copper(II) aspirinate on aging-associated myocardial and endothelial dysfunction.
Methods: Aging (24 month old) and young (3 months old) rats were treated for 3 weeks with vehicle (controls), or with copper(II) aspirinate (200mg/kg/d) per os. Left ventricular pressure-volume relations were measured by using a microtip Millar pressure-volume conductance catheter, and indexes of contractility (e.g. slope of ESPVR (Emax), and dP/dtmax-EDV) were calculated. In organ bath experiments for isometric tension with isolated aortic rings, endothelium-dependent and –independent vasorelaxation were investigated by using acetylcholine (ACh) and sodium nitroprusside (SNP).
Results: When compared to the young controls, aging rats showed impaired left ventricular contractility (Emax: 0.51±0.04 vs. 2.16±0.28mmHg/μl; dP/dtmax-EDV: 10.71±2.02 vs. 37.23±4.18mmHg/s/μl; $p<0.05$) and a marked endothelial dysfunction (maximal relaxation to ACh: 66.66±1.30 vs. 87.09±1.35%; $p<0.05$). Treatment with the copper(II) aspirinate complex resulted in a significantly improved cardiac function (Emax: 1.21±0.17 vs. 0.51±0.04mmHg/μl; dP/dtmax-EDV: 23.40±3.34 vs. 10.71±2.02mmHg/s/μl; $p<0.05$) and higher vasorelaxation to ACh in aging animals (94.83±0.73 vs. 66.66±1.30%; $p<0.05$), while the endothelium-independent vasorelaxation to SNP was enhanced only to a lower extent. The treatment did not significantly influenced the myocardial and vascular functions of young rats.
Conclusions: The current results demonstrate that oxidative stress and inflammatory pathways contribute to the pathogenesis of cardiovascular dysfunction in the aging organism, which can be reversed by copper(II) aspirinate.

P665 Association between methylenetetrahydrofolate reductase and inflammatory markers in the inCHIANTI study

A.M. Gori[1], B. Giusti[1], A.M. Corsi[1], I. Sestini[1], C. Saracini[1], F. Lauretani[2], S. Bandinelli[3], L. Ferrucci[4], G.F. Gensini[4], R. Abbate[4]. [1]*University of Florence, Department of Medical and Surgical Critical Area, Florence, Italy;* [2]*Tuscany Regional Health Agency, Florence, Italy;* [3]*Azienda Sanitaria di Firenze, Geriatric Rehabilitation, Florence, Italy;* [4]*National Institute on Aging, Gerontology Research Center, Baltimore, United States of America*

Pourpose: Homocysteine plasma levels (Hcy) have been shown to depend on both environmental and genetic factors, and to be associated with the risk of developing atherosclerosis.
Methods: Aim of this study was to evaluate the association between C-reactive protein (CRP) or interleukin-6 (IL-6) serum levels and genetic polymorphisms both of methionine metabolism enzymes [5, 10-methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C, methionine synthase (MTR) A2756G gene polymorphisms] and of inflammatory gene polymorphisms [CRP 1059 G/C and IL-6 -174 G/C] in the InCHIANTI Study, a prospective population-based Italian study of risk factors for disability in late life. We studied 586 men (78% aged ≥ 65 years) and 784 women (81% aged ≥ 65 years) randomly selected from people living near Florence.
Results: A significant genotype-phenotype association ($p<0.01$) between CRP or IL-6 levels and C677T MTHFR polymorphisms was observed; no significant association with A1298C MTHFR or A2756G MTR polymorphisms was found. Adjusting for age, sex, BMI, smoking habit, physical activity and creatinine levels, CRP serum levels were significantly ($p<0.001$) higher in TT compared to CC and CT genotypes of C677T MTHFR polymorphism [CC: 2.29 (2.03-2.58) mg/L; CT: 2.24 (2.07-2.42) mg/L; TT: 2.92 (2.58-3.30) mg/L]. This association was maintained in older subjects (≥ 65years) [CC: 2.59 (2.27-2.95) mg/L; CT: 2.52 (2.31-2.75) mg/L; TT: 3.42 (2.97-3.93) mg/L; $p<0.001$]., but not in those with age < 65 years [CC: 1.47 (1.11-1.95) mg/L; CT: 1.48 (1.24-1.75) mg/L; TT: 1.63 (1.25-2.11) mg/L]. IL-6 serum levels were significantly ($p<0.001$) higher in subjects carrying 677 TT genotype than in subjects with 677CT and 677CC genotypes [CC: 1.19 (1.08-1.31) pg/mL; CT: 1.21 (1.13-1.29) pg/mL; TT: 1.44 (1.31-1.59) pg/mL] after controlling for the aforementioned confounders. This phenotype-genotype association was observed in older subjects (≥ 65years) [CC: 1.31 (1.18-1.46) pg/mL; CT: 1.42 (1.32-1.52) pg/mL; TT: 1.64 (1.47-1.83) pg/mL] but not in subjects with age< 65 years [CC: 0.89 (0.71-1.12) pg/mL; CT: 0.69 (0.60-0.79) pg/mL; TT: 0.87 (0.71-1.08) pg/mL]. In the InChianti participants we did not observe a significant association between CRP 1059 G/C polymorphism, IL-6 -174 G/C polymorphism and CRP, IL-6 and homocysteine levels.
Conclusions: Our results indicate that homocysteine-related polymorphisms may be implicated in mechanisms that modulate the inflammatory response.

P666 Bone marrow derived cells contribute to cell turnover in ageing murine hearts

H. Moellmann[1], H. Nef[1], S. Kostin[2], S. Voss[2], C. Troidl[2], S. Sass[2], M. Weber[1], C. Hamm[1], A. Elsasser[1]. [1]*Kerckhoff Heart Centre, Dept of Cardiology, Bad Nauheim, Germany;* [2]*Max-Planck-Institute, Bad Nauheim, Germany*

Purpose: The paradigm that cardiac myocytes are non-proliferating and terminally differentiated cells has recently been challenged since some studies reported the ability of bone marrow derived cells to transdifferentiate into cardiomyocytes after myocardial damage. However, the physiological role of bone marrow derived cells during the lifespan of an undamaged heart is widely unknown. We therefore examined the quantity and phenotype of bone marrow derived cells in aged murine hearts.
Methods: 12-week-old mice (n=20) were sublethally irradiated and bone marrow from enhanced green fluorescent-transgenic (eGFP) littermates was transplanted. After 1 month 5 mice were sacrificed and served as control. The remaining mice were sacrificed after 18.2±1.1 months. Hearts were retrogradely perfused with formalin and stored in liquid nitrogen. Immunohistochemical staining was performed using titin and connexin 43 antibodies to identify cardiomyocytes, vimentin for fibroblasts, vimentin and α-smooth muscle actin for myofibroblasts, α-smooth muscle actin for smooth muscle cells, and F4/80 for macrophages. Endothelial cells were stained by BS 1 and CD31. Additionally, anti-eGFP immunostaining was used to exclude autofluorescence. Sections were analyzed using fluorescence microscopy and confocal laser microscopy.
Results: Bone marrow transplantation was successful as FACS analysis showed 92±5% eGFP expressing leukocytes after 1 month and 81±6% after 18 months. Numerous eGFP-positive cells were found in left ventricular sections. Quantification revealed 9.3±3.3 cells/mm^2 to be derived from bone marrow cells. Most of these cells were fibroblasts and myofibroblasts. In addition, numerous endothe-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

lial cells contributing to neoangiogenesis were detected. Few eGFP-positive cardiomyocytes could be identified.
Conclusion: The present study demonstrates for the first time a substantial recruitment and accumulation of bone marrow derived cells in the ageing myocardium suggesting their contribution in cell turnover of the heart during the lifespan of mice.

ADULT CONGENITAL HEART DISEASE

P667 The Ross procedure in the young. Long term clinical and echocardiographic follow up

M. Delgado Ortega, D. Mesa Rubio, M. Ruiz Ortiz, E. Romo Penas, J.L. Bonilla, A. Gamez, P. Alados, J. Casares Mediavilla, M. Concha, J. Suarez De Lezo. *Hospital Reina Sofia, Cardiology Dept., Cordoba, Spain*

Background and Aim: The Ross procedure is an alternative to mechanical aortic valve replacement in the young. An exhaustive echocardiographic analysis is absolutely necessary for candidates selection and follow up. The aim of this study is to analyze long term clinical and echocardiographic follow up of patients who underwent Ross procedure.
Patients and Methods: Since November 1997 until December 2006, 96 patients (aged 30±12 years, 72% male) underwent Ross procedure. All of them had a preoperative and postoperative echocardiographic examination, and at least an anual echocardiographic study in the follow up.
Results: Indication for Ross operation was aortic regurgitation in 44%, aortic stenosis in 23% ad mixed lesion in 33%. Etiology was congenital in 66% of cases, rheumatic in 17%, degenerative in 10%, postinfectious in 3% and other etiologies in 3%. Associated lesions included mitral regurgitations (10%), aortic coartation (5%) and left ventricular tract obstruction in 8 cases (7 subaortic stenosis, 1 Shone sindrome). Median follow up was 63 ±30 months. There were 2 deaths (1 perioperative death and 1 late death at 36 months of follow up) and 3 infectious endocarditis (1 of the homograft, medically managed and 2 of the autograft, who were reoperated for autograft failure). In echocardiographic follow up there were 15 homograft stenosis with peak doppler gradient>50 mmHg (1 patient had percutaneous angioplasty, 2 underwent stent implantation and 1 had reoperation), 8 autograft regurgitations (5 needed mechanical aortic valve replacement), 1 moderate autograft stenosis and 2 autograft pseudoaneurisms (both underwent surgery). Probability of event free survival at 6 years of follow up was 87%.
Conclusions: Late outcome for the Ross procedure is excellent in terms of global and event free survival. However, autograft regurgitation and homograft stenosis are two possible complications that can appear in the long term. A close echocardiographic follow up is needed to allow an early diagnosis and treatment.

P668 Safety, survival and complications of systemic atrioventricular valve surgery in patients with a dilated systemic right ventricle

R.W.C. Scherptong, H.W. Vliegen, M.G. Hazekamp. *Leiden University Medical Centre, Department of Heart Disease, Leiden, Netherlands*

Purpose: There is a lack of data on safety, short-term complications and survival of systemic atrioventricular valve (SAV) surgery in patients with a systemic right ventricle. In this study, survival and post-operative complications of SAV repair, was investigated in patients with a Mustard/Senning correction for transposition of the great arteries (TGA) or a congenitally corrected TGA (cTGA), with a dilated right ventricle and moderate to severe SAV regurgitation (SAVR).
Methods: All adult patients with either TGA or cTGA, who underwent SAV plasty or replacement between 1999 and 2006, were included in the analysis. The files of patients were checked for severity of SAVR, post operative complications, length of in hospital stay (IHS) and 1-year survival. Complications were categorized as: Hemodynamic, rhythm-related, respiratory, infectious, or re-operation.
Results: 11 Adult patients were operated. Patient characteristics are summarized in Table 1. Patients without post-operative complications (N=4) had a mean IHS of 10 days. Patients (N=2) with 1 complication (infectious, rhythm related) had a mean IHS of 14 days. The 5 patients with multiple complications had a mean IHS of 35 days. 1 Patient was re-operated for stomach perforation. All complications were treated successfully and the 1-year survival rate was 100%.

Patient characteristics

Characteristics	No. of Patients
Gender (male/female)	4/7
cTGA/TGA	5/6
Severity of SAVR 3–3/4–4	5–2–4
Age at time of operation	35.3±13.3 yrs
Plasty/Replacement	8/3

Conclusion: Although there is a risk of (treatable) short-term complications, SAV surgery for regurgitation in patients with a dilated systemic right ventricle, is a safe operation with an excellent survival rate in our hospital.

P669 Effects of ramipril on endothelial function and proinflammatory cytokines in normotensive patients with successfully repaired coarctation of the aorta: a randomized cross-over trial

S. Brili, D. Tousoulis, C. Antoniades, M. Karali, N. Papageorgiou, E. Stefanadi, N. Ioakeimidis, C. Stefanadis. *Athens, Greece*

Coarctation of the aorta leads to impaired endothelial function in the pre-coarctation arterial tree and increased inflammatory process, which persists many years after successful surgical repair. Aim. We examined the effect of ramipril on endothelial function and inflammatory process in young normotensive subjects with successfully repaired coarctation of the aorta.
Methods: Twenty normotensive subjects with successfully repaired coarctation of the aorta 11.4±1.3 years ago, were randomised to receive ramipril 5mg/d or no treatment for 4 weeks, in a randomised cross-over prospective trial with a 4 weeks washout period between interventions. Endothelial function was evaluated by gauge-strain plethysmography and endothelium dependent dilation (EDD) was determined. Values were expressed as means±SEM or median(25th-75th percentile) as appropriate.
Results: EDD was significantly improved after ramipril treatment (from 39.8±2.9% to 49.0±3.1% $p<0.05$) but not after no treatment (from 42.0±2.2% to 44.1±2.1% p=NS). Maximum hyperaemic flow was also increased after ramipril (from 7.21±1.1 ml/100ml tissue/min to 8.9±1.0 ml/100ml tissue/min $p<0.05$) while remained unchanged in controls (from 8.04±1.4 to 7.8±1.2ml/100ml tissue/min, p=NS). Serum IL-6 was decreased after ramipril treatment (from 2.33[1.35-4.36] to 1.59[0.89-2.15] $p<0.05$) while remained unchanged in controls (from 1.14[0.87-4.19] to 1.45[0.92-4.43] p=NS). Serum IL-1b and CRP were slightly but not significantly decreased by ramipril (from 0.28[0.19-1.41] and 1.64[0.24-3.52] to 0.23[0.13-0.27] and 1.05[0.33-2.31] respectively, p=NS for both). Similarly, EID remained unchanged after both treatment with ramipril (from 56.6±5.6% to 58.3±10.1% p=NS) or after no treatment (from 59.2±14.2% to 57.7±10.1% p=NS).
Conclusions: Ramipril significantly improves endothelium dependent dilation and decreases the expression of interleuin-6 in young normotensive subjects with successfully repaired coarctation of the aorta. Therefore, ramipril may have direct beneficial effects on vascular function and inflammatory process in patients with successfully repaired coarctation of the aorta.

P670 Medium term results of stenting of coarctation of the aorta in children and adults

L. Hudsmith[1], J. De Giovanni[2], O. Stumper[1], S.A. Thorne[2], P. Clift[2]. *[1]The Queen Elizabeth Hospital, Cardiology Dept, Birmingham, United Kingdom; [2]Birmingham Children's Hospital, Birmingham, United Kingdom*

Purpose: Coarctation of the aorta is seen in 1 in 12000 live births in the UK. Untreated there is significant morbidity related to accelerated atherosclerotic disease, stroke disease and a risk of aneurysm formation and aortic rupture. Treatment is usually surgical in the neonate but in children and adults, the use of percutaneous balloon dilatation has become common place although the long term results of such procedures are not yet fully established. We present a large series of paediatric and adult patients who underwent angioplasty±stenting of aortic coarctations.
Methods: Cases were identified from our records. Patients were reviewed in outpatient clinic to assess current haemodynamic status and the patency of the stent was assessed by multi slice CT scanning in the adults and by transthoracic echocardiography and angiography in the children. Catheter laboratory records were reviewed to obtain procedural information.
Results: 103 patients (mean age 25 (9-64 years) with aortic coarctations were stented between July 1998 and December 2006. 69% had native coarctations and 31% were treated for recoarctation. In 80% of procedures an aortic stent was implanted (77% Jomed, 10% CP covered, 5% Palmaz). The mean stent length was 42±12 mm (17-58mm) with a diameter of 15±3 mm (10-23mm). Following the procedure, there was a significant reduction in systolic blood pressure (pre-procedure 150±18 mmHg to 132 mmHg ± 16, $p<0.001$) with an 82% reduction in gradient (pre 29.8±12 mmHg, post 5.0±5 mmHg, $p<0.001$). Mean fluoroscopy time was 12.5±8 minutes (2.3 to 36 minutes, median 10 mins).The median length of stay in hospital was 2 nights. There were no patient deaths. There were 2 discrete aortic dissections which were managed conservatively and one stroke with full recovery on follow-up. One patient subsequently developed haemoptysis and a broncho-aortic fistula was successfully treated percutaneously with a covered stent and one patient had haematemesis and a aorto-oesophageal fistula was treated with a covered stent followed by surgery.
Conclusions: Balloon angioplasty±stenting is a safe and reliable treatment for patients with aortic coarctation, avoiding the need for surgery and is associated with a short inpatient hospital stay, a low incidence of significant complications and a significant reduction in systolic blood pressure.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P671 Arrhythmia burden in adults with Congenital Heart Disease in a level 2 GUCH Centre

P.A.M. Felix[1], S. Howard[2], L.J. Freeman[2]. *[1]Norfolk and Norwich University Hospital, Cardiology, Norwich, United Kingdom; [2]Norwich, United Kingdom*

Purpose: The number of patients born with congenital heart disease (CHD) surviving to adult life is increasing exponentially. Our institution is an intermediate (level 2) GUCH centre with a dedicated clinic for adults with congenital heart disease started in 1993. The patient population has increased from 330 in 1998 to 632 in 2004 (820 in 2006). We have sought to determine the arrhythmia burden in a secondary care hospital which is likely to be reflected through many institutions. This has not previously been established.
Methods: The grown-up congenital heart disease (GUCH) clinic database was used for patient demographics and to analyse the frequency and types of arrhythmias in different groups and their management. Certain patient groups have annual ambulatory 24hr Holter monitoring (e.g. TGA, Fallot) whilst in others this is triggered by symptoms. Routine exercise testing may occur in certain groups (e.g. TGA, Fallot with pulmonary regurgitation) or for pre-pregnancy assessment which may highlight arrhythmias.
Patient Population: There are 632 patients in the clinic with an average age of 36 years (range 10-80 years). Operative intervention has been performed in 468 (74%) with 96 (15.2%) requiring a second operation and 39 (6.2%) a third operation. Our clinic serves a catchment population of around 700,000.
Results: Of the 632 patients, 16.1% (102) had a documented arrhythmia. Conditions with the highest arrhythmia load were secundum ASD 39% (27/69), TGA 50% (10/20), Ebstein 57% (4/7), complex CHD 32% (8/25). Fallot's tetralogy surprisingly had infrequent arrhythmias (10/56). All other groups have incidence less than 18%. 22.3% of these underwent EPS and ablation, whilst 16.5% had permanent pacemaker (PPM) insertion.
Routine screening detected 16% of arrhythmias in simple CHD compared with 38% in complex CHD. The number of congenital heart disease patients admitted with arrhythmia over the last 4 years is 33 (5.2%). 20 patients have died; of these 8 patients had SCD at home.
Conclusion: 16.1% of this heterogeneous group of adults have arrhythmias; this is the first report documenting the arrhythmia burden in a secondary care setting in UK. Screening as a tool for identifying these arrhythmias is more useful in complex congenital heart disease- where resources for screening should be directed. The arrhythmogenic substrate in adults with CHD is complex. Supra regional EPS centres for this group with complex anatomy need to be increased to deal with this demand often related to incisional re-entrant tachycardia. This is an important area that needs specialist recognition and funding.

P672 Is speckle tracking a useful tool in the evaluation of right ventricular systolic function in tetralogy of Fallot with transannular patch repair?

E.S. Zegers, J.C. Constandse, A.P.J. Van Dijk. *Radboud University Medical Centre, Cardiology, Nijmegen, Netherlands*

Purpose: To compare RV function in adults with transannular patch repair in tetralogy of Fallot (TOF) assessed with cardiac magnetic resonance imaging (CMR) and RV free wall strain and strain rate by speckle tracking.
Methods: retrospective study in repaired TOF, the endsystolic and enddiastolic RV volumes and ejection fraction (RVEF) were assessed by CMR. During the same period the RV free wall was imaged in the 4-chamber view. 2 D strain and strain rate in the basal, middle and apical segments of the RV free wall were analyzed by speckle tracking. Longitudinal maximum systolic strain (SL Peak S), maximum systolic strain rate (Sr Peak S), maximum early filling strain rate (Sr Peak E) and late filling strain rate (Sr Peak A) were derived.
Results: 14 repaired TOF with mean age 28 yrs, 85% male, were investigated. RV volumes and RVEF were correlated with strain and strain rate. There was only a significant correlation between RVEF and Sr Peak S of the apical segment (Pearson 0,609, $p < 0.05$). There was no significant correlation between CMR and Sr peak S of the basal and middle segment. Also there was no significant correlation in the measurements of SL Peak S, Sr peak E or Sr Peak A.

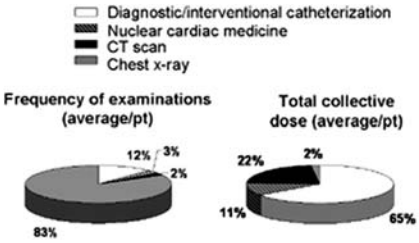
	RV EDV (ml)	RV ESV (ml)	RVEF (%)	S mean (%)	SR mean (1/s)	E mean (1/s)	A mean (1/s)
Mean	196.79	123.14	38.29	-19.41	-1.15	1.18	0.49
Std. deviation	90.72	64.86	13.22	5.54	0.21	0.99	0.29

Conclusion: RV systolic function in TOF with transannular patch repair assessed with CMR and 2 D strain and strain rate by speckle tracking showed no significant correlation. The influence of the often large non-contractile RV outflowtract patch on RV volumes may be the explanation for this lack in correlation. As in these cases strain and strainrate are more directly related to RV function, determination of strain and strain rate may be a more useful tool for the evaluation of RV function in TOF patients with transannular patch repair, especially in those scheduled for pulmonary valve implantation.

P673 Cumulative radiation dose from medical testing in grown-up patients with congenital heart disease

L. Ait-Ali[1], N. Botto[1], M.G. Andreassi[1], P. Festa[1], E. Picano[2]. *[1]Pasquinucci Hospital, Massa, Italy; [2]Cnr, Institute of Clinical Physiology, Pisa, Italy*

Background: The "Biological effects of Ionizing Radiation" (BEIR VII,2005) underlines "the need of studies of infant who are exposed to diagnostic radiation". Aim: to assess the individual cumulative lifetime radiological dose in grown up congenital heart disease (GUCH) patients.
Methods: In 41 consecutive operated GUCH patient (24 males, age= 27±9 years old), followed in our outpatient clinic, a cumulative radiological history was collected with a structured questionnaire and access to a lifetime hospital records. All patient underwent at least one surgical intervention during the infancy for Tetralogy of Fallot (n=18), Aortic coarctation (n=10), anatomical/functional univentricular heart (n=8), other congenital heart disease (n=5) The cumulative exposure was expressed in milliSievert and derived from average effective dose values of individual examinations proposed by the European Commission Medical Imaging Guidelines (2001) and most recent peer reviewed literature. The associated cancer risk was estimated from BEIR VII, 2005 document.
Results: On average, cumulative exposure was 22.3±12.4 (mean±SD) mSv per patient equivalent to about 1115±620 chest x-rays. Diagnostic and interventional catheterization accounted for the most important sources of exposure (65% of total collective effective dose, see figure). The median cumulative dose gave an average extra-risk of cancer of about 1 out of 200 patients (range, 1 in 448 to 1 out of 58).



Conclusion: the average contemporary GUCH patient is exposed to a significant cumulative radiological effective dose, from diagnostic and therapeutic interventions. Every effort should be done to justify the indications and to optimise dose delivery during ionizing testing, especially in children, in order to minimize the associated cancer risk.

P674 Joint cardiac and obstetric management of repaired and native maternal coarctation during pregnancy

S. Bowater, L. Hudsmith, E. Knox, P. Clift, P. Thompson, S.A. Thorne. *The Queen Elizabeth Hospital, Birmingham, Birmingham, United Kingdom*

Aortic coarctation is generally well tolerated in pregnancy. In cardiac obstetric practice, the majority of mothers with coarctation will have had previous intervention. Important complications are significant coarctation/ recoarctation, aneurysm formation at the repair site and hypertension.
Methods: We retrospectively reviewed notes of patients under the Adult Congenital Heart Disease Clinic with a diagnosis of aortic coarctation over a five year period (2001-2006). Female patients with third trimester pregnancies were included. Our current practice recommends normal vaginal delivery at a local hospital in the absence of complications. Patients with native coarctation, an aneurysm or a tight recoarctation require tertiary centre management with regular review in a joint Obstetric and Cardiac clinic with an elective caesarean section advised. In the presence of hypertension or modest recoarctation, we recommend vaginal delivery with a short second stage in our tertiary centre. All women should receive pre-conception counselling and assessment including aortic imaging with MRI.
Results: 24 pregnancies in 19 women (mean age at pregnancy 25±6 years, range of 1-3 pregnancies per patient) resulted in 24 live births. All except one had previous repair of their coarctation: 83% surgical and 17% primary balloon dilatation ± stent, median age at repair 9 months (range 9 days – 23 years). 10 patients had at least one complication of their coarctation repair: 42% systemic hypertension, 32% recoarctation (peak velocity range 1.8m/s2 to 3.1m/s2 on MRI) monitored throughout pregnancy and 16% aneurysm formation at the repair site. 9 patients had associated cardiovascular comorbidities including significant aortic valve disease (26%). 5 patients had required a reoperation (all prior to pregnancy). 7 (37%) patients were treated with beta-blockers for systemic hypertension during pregnancy. All deliveries occurred between 35-41 weeks gestation. 16/24 (67%) of deliveries were performed at a tertiary centre, 50% (8/16) caesarean section, 7 planned (2 for obstetric reasons and 5 for cardiac) and 1 emergency. 3/8 vaginal deliveries required instrumentation. Second stage ranged from 22 to 155 minutes (median 67 minutes). There were no fetal or maternal deaths in the peripartum period.
Conclusion: Women with a history of coarctation contemplating pregnancy should have formal haemodynamic and aortic imaging assessment of the coarc-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

tation site, preferably before conception to enable appropriate risk stratification with consultation with obstetric and anaesthetic colleagues.

P675 Assessment of Ebstein's anomaly by cardiovascular magnetic resonance

B. Bouzas, P.J. Kilner, A. Pijuan, A. Uebing, S. Babu-Narayan, W. Li, M.A. Gatzoulis. *Royal Brompton Hospital, CMR and ACHD Unit, London, United Kingdom*

Purpose: To evaluate patients with Ebstein's anomaly by cardiovascular magnetic resonance (CMR), relating patient's functional capacity with CMR measurements of the size and contractility of the functional part of the right ventricle (RV) and of tricuspid regurgitation (TR).
Methods: We assessed 35 consecutive patients and 10 matched controls using a 1.5 Tesla Siemens Sonata CMR system. Steady state free precession cines were acquired in transaxial as well as short axis stacks (7 mm slice thickness and 3 mm gap) covering both ventricles, and in oblique slices including right ventricular outflow tract (RVOT) views for measuring the diameter of the RVOT 1cm below the pulmonary valve, with oblique cine and velocity map acquisitions to delineate the tricuspid valve and its regurgitant jet. Volumes and function of right and left ventricles where calculated by planimetry. Cardiopulmonary exercise testing was performed on a treadmill according to a modified Bruce protocol.
Results: CMR provided excellent views of the varied abnormalities of right heart structure and function in the Ebstein patients, with transaxial cines being more suitable than short axis for visualising tricuspid valve structures and measuring RV volumes. Compared to normals, patients had higher RV end diastolic volume index (RVEDVi) ($p=0.006$), RV end systolic volume index (RVEDVi) ($p<0.001$) and RV stroke volume index (RVSVi) ($p<0.001$) and lower ejection fraction (RV EF) ($p=0.007$). Left ventricular (LV) stroke volume index (LVSVi) was lower in patients than in normals ($p=0.03$) and there was a trend, although non significant, towards lower LV end diastolic volume index (LVEDVi) ($p=0.07$). RVOT diameter was wider in patients than in controls (31.4 ± 7.0 vs 23.9 ± 3.7, $p=0.02$). TR was absent in 1 patient, mild in 7, moderate in 8 and severe in 19. Eighteen patients were in NYHA functional class I, 13 in class II and 4 in class III. There was a significant reduction of RV EF ($p=0.03$), peak oxygen consumption (MVO2) ($p=0.02$) and percentage of predicted MVO2 (%MVO2) ($p=0.005$) with higher NYHA functional class. No correlation was found between TR and RV EF or NYHA functional class. RV EF correlated with LV EF ($r=0.52$, $p<0.001$).
Conclusions: In spite of atrialisation of the inlet portion, functional RV volumes were higher in Ebstein's patients than controls, while RV EF and LV volumes were lower. RV EF, peak MVO2 and %MVO2 were associated with functional capacity. There was correlation between RV EF and LV EF suggestive of ventricular-ventricular interaction.

P676 Impact of shunt location, size, direction, state of repair and anatomy on long-term survival of adults with pulmonary hypertension associated with cardiac defects

P. Gallego Garcia De Vinuesa[1], J. Oliver Ruiz[2], E. Diaz-Carballo[2], A. Gonzalez Garcia[2]. [1]*Sevilla, Spain;* [2]*Adult Congenital Heart Disease Hosp. La Paz, Madrid, Spain*

Background: Pulmonary arterial hypertension (PAH) associated with congenital systemic to pulmonary shunts (CSPS) in adults includes a very heterogenous group of patients. In order to determine populations with similar prognosis, we sought to analyse the effect of shunt location (supra or infratricuspid), size, direction or state of repair and anatomy (simple or complex) of the underlying cardiac defect (CHD) on overall mortality (M) and actuarial survival curves of different groups of patients.
Methods: A total of 93 patients $>$ 18 years old with severe PAH (Doppler subpulmonary AV valve regurgitation flow velocity $>$ 3.5 m/s without pulmonary outflow tract stenosis or left heart abnormalities) and CSPS, followed-up for 11 ± 9 years, were identified. PAH was confirmed at cardiac catheterization in all cases. Mean age was 44 ± 19 years old and 67% were female. 60 patients had simple and 33 complex anatomy and the location of shunt was supratricuspid in 32 and infratricuspid in 61. Left-to-right shunt was present in 49 and right to left in 44 cases. PAH with restrictive or repaired shunt was found in 16 patients and non-restrictive/non-repaired shunts in 66.
Results: Overall M was 24% (22 patients), mean age at death $44\pm$ 21 years old and survival at 15 years (S_{15}) was 75%. Outcome was significantly worse in supratricuspid (M 33%, S_{15} 50%) than in infratricuspid shunts (M 18%, S_{15} 85%, log rank 12.5, $p=0.0004$); in left-to-right (M 33%, S_{15} 40%) than in right-to-left shunts (M 14%, S_{15} 90%, log rank 18, $p=0.0001$); in restrictive/repaired (M 56%, S_{15} 35%) than in non-restrictive/non-repaired shunts (M 20%, S_{15} 80%). Despite no differences in M and survival between simple and complex CHD in the global population, patients with right-to-left shunt and complex CHD had a higher M (20% vs 0%) and a worse S_{15} (85% vs 100%) than simple CHD (log rank 5.01, p=0,025).
Conclusions: PH with restrictive or repaired shunts has the most unfavourable prognosis. Supratricuspid or left-to-right shunts have a worse outcome than infratricuspid with right-to-left shunts. Complex CHD is associated with worse prognosis in right-to-left shunts.

P677 Clinical management of pulmonary arterial hypertension in adult patients with congenital heart disease

M. D'alto[1], B. Sarubbi[1], P. Argiento[1], E. Romeo[1], D. Alfano[1], M. Palma[1], G. Santoro[1], C.D. Vizza[2], M.G. Russo[1], R. Calabro'[1]. [1]*Second University of Naples, Monaldi Hospital, Chair of Cardiology, Naples, Italy;* [2]*University La Sapienza, Cardiology, Rome, Italy*

Background: Pulmonary arterial hypertension (PAH) due to congenital heart disease (CHD), is hampered by high mortality and morbidity. Therapeutic medical advances over the past two decades have resulted in significant improvements in quality of life and survival in patients with PAH.
Aim: To evaluate the therapeutical options in adults with PAH CHD-related.
Methods: Between 2001-2006 we observed 41 patients with PAH CHD-related (21 M, 20 F, mean age 38.4 ± 13.5). Fifteen had ventricular septal defect (VSD), 9 atrio-ventricular canal, 5 single ventricle, 5 atrial septal defect, 3 pulmonary atresia with VSD, 2 trasposition of great arteries with VSD, 2 persistent ductus arteriosus. The NYHA class at firs observation was II for 8 patients, III for 20 patients and IV for 13 patients. The O_2 saturation at rest was 81.3 ± 11.8%. The systolic pulmonary pression evaluated non-invasively with echocardiography was 90.1 ± 22.4 mmHg. Twenty-eight/41 patients underwent right heart catheterization: the mean pulmonary arterial pression (mPAP) was 72.4 ± 24.6 mmHg; the mean indexed pulmonary vessel resistances (iPVR) was 7.8 ± 5.8 Wood Unit/m^2; the mean QP/QS was 0.9 ± 0.7.
Results: At 3.6 ± 2.1 year follow-up one patient died suddenly. Twenty-five pts are under therapy with loop diuretics, 19 with digoxin, 14 with spironolactone, 9 with aspirin, 11 with warfarin. Three patients are under therapy with oral sildenafil (25 mg x 3 or 4/die), 2 with e.v. epoprostenol (9.5ng/kg/min), 25 with oral bosentan (125 mg x b.i.d. or 62.5 mg b.i.d.). Three patients underwent periodic "blood-letting" for hematocrit $>$70%. One patient was scheduled for heart-lung and one for lung transplantation. The NYHA class was improved in 25/40 (63%) survived patients, in fact the actual NYHA class is II for 20 patients, III for 16 patients and IV for 4 patients.
Conclusion: A complex therapeutical management is required for patient with PAH CHD-related. In our experience bosentan, sildenafil and epoprostenol treatments, associated to background therapy, were safe and well tolerated in adults patients with PAH CHD-related.

P678 Abnormal aortic elastic properties in adults with congenital valvular aortic stenosis

S.-C. Yap, A. Nemes, F.J. Meijboom, T.W. Galema, M.L. Geleijnse, F.J. Ten Cate, M.L. Simoons, J.W. Roos-Hesselink. *Erasmus MC, Cardiology, Rotterdam, Netherlands*

Purpose: Abnormalities of the aortic root are common in patients with a bicuspid aortic valve. Our aim was to investigate the elastic properties of the aortic root in patients with congenital aortic valvular stenosis (AS) in comparison with age- and gender-matched controls, and to investigate the influence of stenosis severity and aortic size on aortic root elasticity.
Methods: Thirty-two adults with congenital AS without previous cardiovascular surgery were prospectively studied. Aortic root elasticity indices such as aortic stiffness index (ASI), aortic root distensibility (ARD), and aortic strain were calculated with the use of M-mode echocardiography.
Results: ASI was significantly higher in patients compared to controls, 8.5 ± 8.5 versus 4.0 ± 1.4, respectively ($P<0.01$). Other indices of aortic root elasticity were similar between patients and controls (Table 1). Correlations were found between aortic size and indices of aortic elasticity ($r=-0.40$ ($P=0.02$) and $r=-0.47$ ($P<0.01$) for aortic strain and ARD, respectively), denoting that an increased aortic dimension results in a stiffer aorta. Interestingly, no correlations were found between indices of severity of AS and aortic elasticity, suggesting that an abnormal aortic elasticity is independent of stenosis severity.

Table 1

Characteristic	Controls (n=32)	Patients (n=32)	P-value
Age (yrs)	30.5 ± 8.2	30.4 ± 7.5	NS
Gender (male/female)	22/10	22/10	NS
LV mass index (g/m^2)	75.4 ± 15.7	106.0 ± 30.4	<0.001
Peak aortic gradient (mmHg)	–	57.6 ± 22.3	–
Aortic valve area (cm^2)	–	1.34 ± 0.59	–
Pulse pressure (mmHg)	49.0 ± 10.4	52.1 ± 15.5	NS
Aortic systolic diameter (cm)	2.65 ± 0.29	3.41 ± 0.56	<0.001
Aortic diastolic diameter (cm)	2.34 ± 0.28	3.05 ± 0.53	<0.001
Aortic strain (%)	13.5 ± 5.0	12.4 ± 9.6	NS
Aortic distensibility (10^{-6} cm^2/dynes)	4.3 ± 1.9	4.2 ± 3.6	NS
Aortic stiffness index	4.0 ± 1.4	8.5 ± 8.5	<0.01

Conclusions: Congenital AS results in abnormal aortic elastic properties, independent of stenosis severity. Furthermore, there seems to be a relationship between aortic dimensions and aortic stiffness.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P679 Outcome after percutaneous closure of a patent foramen ovale using a new generation closure device: a multi-centre study

J.G.L.M. Luermans[1], M.C. Post[1], R. Schrader[2], T. Sluysmans[3], T. Vydt[4], M. Chessa[5], E. Onorato[6], J. Goy[7], W.I.H.L. Budts[8]. [1]*St. Antonius Hospital, Cardiology, Nieuwegein, Netherlands;* [2]*Markuskrankenhaus, Cardiology, Frankfurt, Germany;* [3]*St. Luc, Paediatric Cardiology, Brussels, Belgium;* [4]*Middelheim Hospital, Cardiology, Antwerpen, Belgium;* [5]*Policlinico San Donato, Paediatric Cardiology, Milan, Italy;* [6]*Gavazzeni Hospital, Cardiology, Bergamo, Italy;* [7]*Clinique Cecil, Cardiology, Lausanne, Switzerland;* [8]*University Hospital Gasthuisberg, Cardiology, Leuven, Belgium*

Purpose: Patent foramen ovale (PFO) has been associated with paradoxical embolism and cryptogenic stroke. Moreover, percutaneous PFO closure seems to reduce the risk for recurrent thrombo-embolic events. Currently, different devices are used for PFO closure. In this large multi-centre study, safety and efficacy of percutaneous PFO closure, using a new generation closure device, are reported.
Methods: Patients, who underwent between July 2002 and September 2006 a percutaneous PFO closure with the new generation closure device (double umbrella device with 2 fold 6 stranded wire arms and articulated configuration), were included in the study. The primary endpoint was defined as re-occurrence of stroke, transient ischemic attack (TIA), or peripheral thrombo-embolism. Peri-procedural and mid-term complications were reported.
Results: Four-hundred and thirty patients (mean age 50.7±13.0 years, 231 men) could be included in the study. Indications for closure were cryptogenic stroke (69.8%), TIA (23.5%), peripheral embolism (3.3%), migraine (3.0%) and other (0.5%). The primary endpoint occurred in 0.5% for stroke, in 2.5% for TIA, and in none for peripheral embolism for a median follow-up time of 0.8 years, range 3.9 years. Peri-procedural complications were reported in 11.5% of cases, from which only 0.2% was defined as major. No severe complications occurred during mid-term follow-up. During follow-up, a residual right-to-left shunt was present in 12.5% of patients who did not suffer from a recurrent event, compared to 36.4% of patients who reached the primary endpoint (p=0.04).
Conclusions: In this multi-centre study, percutaneous closure of a symptomatic PFO with the new generation device is a safe and effective procedure to prevent the recurrence of paradoxical thrombo-embolic events.

P680 Echocardiographic evaluation of systolic right ventricle function in repaired right ventricular outflow tracts: a comparative study with MRI

M. Ladouceur[1], A. Redheuil[1], E. Mousseaux[1], Y. Boudjemline[2], L. Iserin[1]. [1]*Hopital Europeen Georges Pompidou, Cardiology Department, Paris, France;* [2]*Hopital Necker Enfants Malades, Paris, France*

Background: Pulmonary regurgitation (PR) is a frequent sequaellae of congenital heart surgery on right ventricular outflow tract. Timing of pulmonary valve replacement (PVR) for PR is based on criteria of right ventricle (RV) function and dilatation assessed by MRI. Today, pulmonary valve replacement is indicated before irreversible RV dysfunction. However, echocardiographic evaluation of RV remains difficult.
Purpose: tocompare echocardiographic criteria of RV function with systolic RV function assessed by magnetic resonance imaging.
Methods and Results: 20 patients (28±6 y.o.; 10 women) with a repaired RVOT (12 Fallot, 3 pulmonary atresia with ventricular septal defect, 4 pulmonary stenosis and 1 double outlet right ventricle) were explored. Most of them were asymptomatic (80% NYHA 1 versus 10% NYHA 3) and only one patient had congestive right heart failure. All patients were in sinus rhythm during evaluation. During the same day, transthoracic echocardiography and MRI were performed. On echocardiography: Right Ventricle Ejection Fraction (RVEF) by the Simpson method, pulsed DTI measurement of maximal velocity (S max), RV fractional area change, Tei index and myocardial acceleration during isovolumic contraction (IVA) were measured. During MRI, RVEF (41±9%) and regurgitation fraction of PR were calculated. 50% of patients had a moderate to mean PR (regurgitation fraction between 25 and 50%) and 35% had a severe PR. A mild tricuspid regurgitation (T.R) was found in 15% of the cases; and there was no severe TR. Only Tei index (0.25±0.09, r=0.91, p≤ 0.01) and RVEF by Simpson method (48±17%, r=0.45, p≤0.05) were significantly correlated with RVEF assessed by MRI. RV fractional area change tended to be correlated with RVEF by MRI but it was not significant (39.2±11.6%, r=0.35, NS) A Tei index superior or equal to 0.36 corresponded to a RVEF ≤ 35% by MRI (sensibility =50%, specificity=93%, PPV=66%, NPV=87%, p≤0.05).
Conclusion: Systolic RV function must be regularly followed up in PR to indicate a pulmonary valve replacement before severe RV dysfunction. Echocardiographic assessements of Tei index and RVEF by Simpson method are significantly correlated with the systolic RV function assessed by MRI; they can be used to schedule regular MRI during long term follow up of patients with congenital heart disease.

P681 Quality of life and exercise capacity in 497 patients with congenital heart disease

A. Gratz, J. Hess, A. Hager. *Deutsches Herzzentrum Munich, TU Munich, Pediatric Cardiology and CHD, Munich, Germany*

Purpose: to compare self reported health related quality of life with objective exercise performance in patients with congenital heart disease.
Patients and methods: 497 patients (219 female, 14-73 years old) with various congenital heart defects (52 shunt, 62 left heart obstruction, 29 right heart obstruction, 42 Ebstein, 86 Fallot, 84 TGA after atrial switch, 40 other TGA, 30 Fontan, 18 palliated/native cyanotic, 54 others) as well as a group of 52 healthy controls (18 females, 14-57 years old) completed a health related quality of life questionnaire (SF-36). Then they performed a symptom limited cardiopulmonary exercise test with measurement of oxygen uptake on a bicycle in a sitting position. As patient groups differed in sex and age all measured values were normalized to published sex and age related reference values.
Results: Despite severe limitations at the exercise test, there was only reduced quality of life in the scales of physical functioning ($p<0.0005$) and general health ($p<0.0005$). This could be confirmed in all diagnosis subgroups. There was very good correlation of self estimated physical function ($r=0.402$, $p<0.0005$), physical role ($r=0.157$, $p<0.0005$), general health ($r=0.302$, $p<0.0005$), vitality ($r=0.173$, $p<0.0005$) and social functioning ($r=0.159$, $p<0.0005$) with peak oxygen uptake. Bodily pain, emotional role, mental health and health transition showed no significant relation.
Conclusion: Patients with congenital heart defects are only impaired in their physical functioning and their general health in respect to their quality of life. This is also true for severe heart defects such as Fontan or palliated cyanotic defects. The amount of impairment correlates directly to the exercise performance.

P682 Risk of complications during pregnancy in women with atrial septal defects

S.-C. Yap[1], W. Drenthen[2], J.W. Roos-Hesselink[1], P. Moons[3], B.J.M. Mulder[4], H.W. Vliegen[5], A.P.J. Van Dijk[6], F.J. Meijboom[2], P.G. Pieper[5] on behalf of ZAHARA Investigators. [1]*Erasmus MC, Cardiology, Rotterdam, Netherlands;* [2]*University Medical Centre Groningen, Cardiology, Groningen, Netherlands;* [3]*University Hospitals Leuven, Cardiology, Leuven, Belgium;* [4]*Academic Medical Centre, Cardiology, Amsterdam, Netherlands;* [5]*Leiden University Medical Centre, Cardiology, Leiden, Netherlands;* [6]*University Medical Centre Nijmegen, Cardiology, Nijmegen, Netherlands*

Purpose: Atrial septal defect (ASD) is the most common congenital heart disease at adult age. However, the information on the outcome of pregnancy in women with ASD is limited to small series. Our aim was to investigate the magnitude and determinants of cardiac, obstetric and neonatal complications during pregnancy in women with (un)repaired ASD.
Methods: Using the Dutch CONCOR registry and a local Belgium tertiary center database, 188 ASD women were enrolled. A total of 100 women had 243 pregnancies, including 49 miscarriages (20.2%) and 6 elective abortions. Detailed recordings of each completed pregnancy (n=188, 98 women) were obtained.
Results: Cardiovascular events (i.e. arrhythmias, transient ischemic attack) were observed during 4.8% of the completed pregnancies. Obstetric complications included: hypertension-related disorders (10.6%), postpartum hemorrhage (10.6%), premature rupture of membranes (5.9%), and premature labor (5.9%). Importantly, the percentage of small-for-gestational-age children (18.2%) and fetal/neonatal mortality (1.6 and 1.0%, respectively) were high. Women >30 years appear to be at greater risk for both cardiac and obstetric complications (Table 1). Furthermore, repair prior to pregnancy was associated with less neonatal events.

Table 1. Predictors of events

Baseline characteristic	Cardiac events (n=9, 4.8%)	Obstetric events (n=47, 25.0%)	Neonatal events (n=47, 24.5%)
Prior repair of ASD	0.68 (0.14-3.38)	1.18 (0.58-2.42)	0.34 (0.14-0.82)*
History of arrhythmia	2.94 (0.69-12.5)	0.95 (0.38-2.38)	0.93 (0.37-2.33)
Previous completed pregnancy	0.53 (0.13-2.18)	1.33 (0.69-2.58)	1.18 (0.61-2.28)
Smoking before pregnancy	1.68 (0.40-7.03)	0.72 (0.32-1.63)	1.35 (0.64-2.86)
Smoking during pregnancy	0.94 (0.11-7.89)	0.64 (0.20-1.98)	0.84 (0.29-2.40)
Presence of RV dilatation	1.37 (0.16-11.7	1.41 (0.46-4.28)	0.69 (0.19-2.54)
Maternal age >30 years	7.12 (1.43-35.3)*	2.18 (1.11-4.29)*	0.74 (0.36-1.50)

Data are presented as odds ratios (95%CI). Cardiac events (i.e., heart failure, stroke, TIA, arrhythmias, endocarditis), obstetric events (i.e., PIH, preeclampsia, eclampsia, HELLP syndrome, premature labor, postpartum hemorrhage), neonatal events (i.e., premature delivery, small-for-gestational age, fetal mortality, neonatal mortality). *P<0.05.

Conclusions: Pregnancy is generally well tolerated in repaired ASD patients, but in unrepaired ASD patients neonatal events were encountered more frequently. Maternal complications were seen more often in women >30 years.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P683 Percutaneous closure of patent foramen ovale with different devices: long-term results

S. Staubach, W. Zimmermann, N. Wawra, C. Heinisch, N. Majunke, A. Baranowski, M. Reschke, C. Bussmann, N. Wunderlich, H. Sievert. *CardioVascular Center, Cardiology Department, Frankfurt, Germany*

Purpose: Patent foramen ovale for prevention of paradoxical embolism is practiced in many centers today. We report the long-term results of one of the largest single center series in using different closure devices.
Methods: Between August 1994 and December 2006 1381 patients underwent percutaneous PFO-closure at our center with one of the in Europe approved devices. The age ranged from 17 to 85 (mean 49.9 years). Before intervention 730 patients had a TIA, 688 a stroke and 58 a peripheral embolism. 113 patients had both, TIA and stroke (recurrent embolic event rate 22,6%/year). The following devices were implanted: 533 Amplatzer, 380 Helex, 270 CardioSEAL-STARflex, 116 Premere, 26 SIDERIS, 23 CardioSEAL, 19 AngelWings, 10 ASDOS, 4 PFO-Star. Follow-up was done at 1, 3 and 6 months, thereafter if clinically indicated and by questionnaires.
Results: Device implantation was technically successful in all patients. In 4 patients the occluder embolized during or shortly after the procedure, the occluder was retrieved by catheter techniques, the PFO closed by a new occluder. 43 patients received a second device due to residual shunt, 2 patients a third device. The procedure time averaged 34.8min (±17.35min), the mean fluoroscopy time was 6.1min (±5.09min).
Mean follow up was 2546 patient years. At their last follow-up (≥6months - 10years), 835 out of 898 patients in whom a TEE was performed had complete closure. 2 patients died due to device related complications. 19 patients developed thrombi, 45 atrial fibrillation. During follow-up 11 patients suffered from a TIA and 16 patients from a stroke (annual embolic event rate 1,1%, annual stroke rate 0,6%).
Conclusions: Our long-term results of percutaneous PFO-Closure over 12 years confirm that it is feasible and safe. Severe complications may occur but they are very rare. PFO closure seems to be effective in preventing embolic stroke.

P684 Aortic wall abnormalities associated with the bicuspid aortic valve

R. Proietti, A. Milazzo, S. Mazzetti, F. De Chiara, C. Russo, F. Mauri, E. Vitali. *Niguarda Hospital, Cadiovascolare De Gasperis, Milano, Italy*

Background: The aim of this study was to determine the long-term occurrence of ascending aorta dilation and dissection in patients who had undergone isolated aortic valve replacement for clinically significant pathologies of the native bicuspid or tricuspid aortic valves with no ascending aorta enlargement at the time of surgery.
Methods: Clinical and echocardiographical follow-up (mean period 260±46 months) on 100 patients who had undergone isolated aortic valve replacement was performed. Patients were divided into two equally numbered groups, according to native valve morphology: bicuspid or tricuspid. The two groups were matched for: patient age, type of surgery, follow-up period and size and type of protheses. Ascending aorta diameter was assessed at the time of surgery and described in all cases as normal- less than 4.5 cm.The differences in the mean values at each level of ascending aorta (annulus, valsalva junction, sinotubular junction and ascending aorta) were evaluated by t-student test with a p-value < 0,05.
Results: During follow-up, 12 acute aortic syndrome and sudden cardiac deaths were registered among patients with bicuspid aortic valves, while no deaths were reported among patients with tricuspid aortic valves (p=0,0001). Five patients in the bicuspid native aortic valve group died due to aortic dissection, while no aortic dissections were detected in the tricuspid native aortic valve patients. Follow-up including echocardiography revealed significant differences between the two groups for diameter enlargement at the valsalva junction and ascending aorta ($p<0.05$).
Conclusion: With its long-term follow-up, this study found that aortic dissection and sudden cardiac death occurred more frequently in patients with native bicuspid aortic valves. These patients have significant enlargements in their ascending aorta diameters compared to subjects with native tricuspid aortic valves. With regard to bicuspid aortic valve patients, aortic dilatation is out of proportion to the coexistent valvular lesion and occurs even after aortic valve replacement. This situation is most likely determined by an abnormal enzymatic predisposition of the arterial wall. The conclusion of this study is that echocardiography performed during bicuspid aortic valve patient follow-up can detect ascending aorta enlargement,and in turn, aid in predicting the occurrence of adverse outcome.

P685 Type A aortic arch interruption in adult patients: percutaneous approach

M. Pan Alvarez-Osorio[1], J. Suarez De Lezo[1], M. Romero[1], C. Duran[1], J. Suarez De Lezo Jr[2], F. Esteban[2], D.J. Pavlovic[2], A. Medina[1], J. Segura[2], S. Ojeda[2]. *[1]Reina Sofia Hospital, Cardiology, Cordoba, Spain; [2]Dr. Negrin Hospital, Cardiology, Las Palmas, Spain*

Purpose: Interruption of the aortic arch is an extremely rare entity in adults (12 reports in the medical literature up to 2002). Surgical repair is associated with high morbidity and mortality. We analyze the results of percutaneous treatment in patients with type A aortic arch interruption.
Methods: From February 1994 to February 2007, 92 patients over 6 years of age were admitted to our institution for percutaneous stent treatment of coarctation of the aorta; at angiography, 5 showed a loss of luminal continuity between the aortic arch and the descending aorta distal to the left subclavian artery, and constituted the focus of this study. There were 3 men and 2 women in this study group, with ages ranging from 17 to 66 years (mean 44±22). All patients had severe hypertension and 2 had functional class III heart failure. As compared with the overall series, patients with aortic arch interruption had a larger ascending aorta diameter as matched by age (49±21 mm vs 29±10 mm), had a higher ascending-to-descending aorta gradient (64±35 mmHg vs 39±12 mmHg), and were older (44±122vs 22±13 years). A simultaneous approach for the left brachial artery and femoral artery was undertaken in all 5 patients. The length of the occluded segment (after simultaneous injection in ascending and descending aorta) was 6±7mm (range 2-18mm).
Results: The interruption was recanalized anterogradely in 2 patients and retrogradely in the remaining 3. Recanalization of the occluded segment was performed with a 0.014" dedicated stiff guide-wire for coronary occlusion (3 of them were radiofrequency guides). After crossing with the wire, a coronary balloon was used for predilation. The procedure was completed with conventional wires and balloons. Final stent diameter was 19±2mm (15-20mm). Primary success with no complications was achieved in all 5 patients. The gradient between ascending and descending aorta changed from 64±35 mmHg to 5±3 mmHg. Two patients underwent elective, delayed surgical replacement of the ascending aorta due to aneurysmal dilation (> 55 mm). After a mean follow-up of 22±24 months, 4 patients remain asymptomatic in functional class I- II. The remaining patient died from heart failure 5 years after the procedure at the age of 71.
Conclusion: Percutaneous approach for type A aortic arch interruption is feasible and may provide an alternative to surgical treatment.

P686 Strong and independent prognostic value of peak circulatory power in adults with congenital heart disease

A. Giardini, S. Specchia, A. Donti, F. Sciarra, M. Bonvicini, F.M. Picchio. *Pediatric Cardiology, Bologna, Italy*

Background: The identification of adult congenital heart disease (ACHD) patients that are at higher risk of death is challenging. Peak circulatory power (CircP, expressed as peak exercise oxygen uptake multiplied for peak mean arterial blood pressure) is a strong predictor of death in adults with acquired heart disease. We sought to establish the distribution and the prognostic value of peak CircP across a wide spectrum of ACHD patients.
Methods: Four-hundred thirty two consecutive ACHD patients of varying diagnosis and 98 healthy controls underwent cardiopulmonary exercise testing at a single laboratory between 1996 and 2005. Patient age was 32±10 years.
Results: A gradual decline in peak CircP was found across the spectrum of congenital heart defects ($p<0.0001$ at ANOVA). Reduced peak CircP values were associated with presence of heart failure symptoms ($p<0.0001$), absence of sinus rhythm (p=0.010), and use of antiarrhythmic medications (p=0.0013). At a follow-up of 4.4±2.4 years, 23 patients (5.3%) had died. Peak CircP was a strong predictor of mortality at univariate analysis and the strongest independent predictor of mortality among exercise parameters. A peak CircP inferior to 1406 mmHg·ml $O_2 \cdot min^{-1} \cdot kg^{-2}$ was associated with a 14-fold increase in the risk of death (24% at 5 years of follow-up).
Conclusions: Peak CircP is abnormal across the spectrum of ACHD patients. Peak CircP appears as the strongest predictor of adverse outcome in ACHD patients.

PEDIATRIC CARDIOLOGY

P687 Direct hemodynamic and late echocardiographic results of balloon pulmonary valvuloplasty in children with pulmonary valve stenosis

P. Werynski, A. Rudzinski, W. Krol-Jawien. *University Children's Hospital of Cracow, Pediatric Cardiology, Krakow, Poland*

Since 1982, balloon pulmonary valvuloplasty (BPV) is the treatment of choice for pulmonary valve stenosis (PVS). Scarce data are, however, available on BPV results in the aspect of immediate hemodynamic and late echo findings. Objective: to assess the selected hemodynamic parameters in PVS children immediately pre and post-BPV and late follow-up echocardiographic studies.
Material: 137 (76M+61F) children, aged 1 month–16.3 years (x=5.3±4.8), weighing 3.2-69 kg (x=21±14.9) with isolated PVS, qualified to BPV between 28.03.1988-31.12.2004, based on echo studies (Doppler gradient: x=76.5±19.7mm Hg). Newborns with critical PVS were excluded from the study.
Methods: All the patients subjected to hemodynamic and angiocardiographic studies pre and post-BPV (applied balloon/PV annulus ratio: x=1.3±0.1) were divided into three groups depending on the right ventricular systolic to systemic pressure ratio (RVSP/SP: <2/3, >2/3 - <1, >1). Selected hemodynamic parameters pre (1) and post-BPV (2) and the assessment of late follow-up (x=6.1±3.4

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Abstract P687 – Table 1

Group/No of patients	RVSP mmHg X		RVEDP mmHg X		SPG mmHg X		PASP mmHg X		Efficacy /No of late restenosis/ type of procedures	SPG Doppler mmHg X
	1	2	1	2	1	2	1	2		
1/(58)	65.3±10.3	28.6±7.6	6.2±3.0	5.6±2.2	49.3±11.1	12.5±7.6	15.8±1.1	16.8±0.9	58/58/(0)	13.4±6.9
2/(41)	91.7±11.6	35.0±14	6.3±3.0	5.5±2.9	75.6±12.3	17.0±13	15.8±1.2	17.8±1.3	40/41/(0)1 - valvotomy	16.9±12.1
3/(38)	133.3±27.3	38.4±19.2	8.5±3.0	7.2±2.3	117.3±28	17.9±15.5	14.5±1.3	19.4±2.1	38/38/(6) 4 –re BPV2- valvotomy	17.1±12.2

years) echo systolic-pressure-gradient (SPG) in pts free of reintervention were compared.

Results: Results are presented in the table. After BPV, in all but one patient, significant ($p<0.001$) reduction of RVSP, RVEDP, SPG as well as PASP increase in Group 3 were observed. Although the early results of BPV in most pts were satisfactory, six Group 3 pts developed restenosis requiring additional treatment in late follow-up.

Conclusions: In most severe form of PVS, the outcome of BPV may not be completely satisfactory in relation to hemodynamic residuals and possibility of defect recurrence.

P688 Anti-inflammatory effects of hmg-coa reductase inhibitor (statin) on acute coronary arteritis in a rabbit model of Kawasaki disease

S.I. Ozawa, M. Fujii, T. Yahata, A. Niboshi, K. Hamaoka. *Kyoto Prefectural University of Medicine Grad, Department of Pediatric Cardiology And Nephro, Kyoto, Japan*

Introduction: Recently, it has been demonstrated that HMG-CoA reductase inhibitors (statins) significantly reduce major coronary events. In addition, recent observations also suggest that some of the clinical benefits associated with statin therapy may be pleiotropic; that is, they are independent of their cholesterol-inhibiting action. In this study, we tried to evaluate the availability of statins mediated through their anti-inflammatory effects on coronary arteritis in a rabbit model of Kawasaki disease (KD).

Methods: Japanese white male rabbits (age; 5~7 weeks of age, weight; 900-1,000g) were used in this study. Coronary arteritis was induced by the intravenous administration of horse serum twice into juvenile rabbits. Furthermore, the rabbit models with coronary arteritis were divided into 3 groups as follows: the rabbit group without any other treatment (A), those treated with Fluvastatin (20mg/kg) (B) and those treated with Pravastatin (10mg/kg) (C) daily from the day after the second administration of horse serum. Then the animals were sacrified and the hearts were removed at day 3, 5 and 7 after the second administration of horse serum. To evaluate the anti-inflammatory effect of the statins on coronary arteritis, we investigated the serial process of the histopathological features during the acute phase of the coronary arteritis in these three groups.

Results: In group A, histological examinations demonstrated severe panvasculitis with endothelial destruction, marked mononuclear cell infiltration in all layers and edematous thickening of the medial layer. These inflammatory findings were the most prominent at the day 3 and same to the histopathological features in KD. On the other hand, in both groups B and C, the inflammatory findings were significantly suppressed even at day 3 in comparison with those in group A. Edematous thickening in the medial layer was not significant in the groups B and C, too.

Conclusions: In this study, it was revealed that statins had the significant anti-inflammatory effects on acute coronary arteritis shown in the rabbit model of KD. It is suggested that statins have good possibilities of being effective for preventing the development of coronary aneurysmal changes.

P689 Presence of accessory AV pathways in human fetuses, substrate for fetal supraventricular tachycardias

N.D. Hahurij[1], N.A. Blom[1], D.P. Kolditz[1], M.C.E.F. Wijffels[1], R. Bokenkamp[1], R.R. Markwald[2], M.J. Schalij[1], R.E. Poelmann[1], A.C. Gittenberger-De Groot[1]. *[1]Leiden University Medical Center, Department of Paediatric Cardiology, Leiden, Netherlands; [2]Medical University of South Carolina, Cell Biology, Charleston, United States of America*

Purpose: Fetal and neonatal atrioventricular reentrant tachycardias can be life threatening but resolve in the majority of cases during the first year of life. The temporary presence of accessory atrioventricular (AV) myocardial connections during the normal process of AV junction isolation may explain this phenomenon.

Methods: We studied 44 human embryonic (n=6), fetal (n=34) and neonatal (n=4) sectioned hearts with an age range of 4 to 36 weeks of development. Immunohistochemical markers were used to identify myocardium and connective tissue including antibodies against MLC-2a, HHF-35, collagenVI and periostin. The accessory AV myocardial connections were quantified and categorized according to their specific location in the AV sulcus and 3D AMIRA reconstructions of the AV nodal area were made.

Results: Up to 6 weeks of development, atrial and ventricular myocardium was continuous at the AV junction. Between 6 and 10 weeks, numerous AV myocardial connections were observed at the left (45%), right (35%) and septal (20%) region of the AV junction. Whereas most right sided connections were identified as distinct myocardial strands, left sided connections comprised larger areas of myocardium. Between 10 and 20 weeks, all AV connections consisted of discrete myocardial strands that gradually decreased in number. The majority of AV connections (67%) were observed at the right AV junction, most of them located at the lateral aspect (45%) in close contact with the so-called right atrioventricular ring bundle. At the left AV junction and the septal area only 17% and 16% of the AV connections were observed, respectively. The 3D reconstructions of the AV nodal area at these stages also showed several myocardial AV connections related to the developing AV node. From 20 weeks until birth and in neonatal hearts no accessory connections were observed anymore.

Conclusions: The isolation of the AV junction is a gradual and ongoing process and particularly right lateral AV connections are commonly found at later stages of normal human cardiac development. These transitory accessory myocardial connections may act as substrate for atrioventricular reentrant tachycardias in the fetus or neonate.

P690 Cardiovascular manifestations in 150 patients with williams beuren syndrome: new findings

A. Del Pasqua[1], G. Rinelli[2], A. Toscano[1], R. Iacobelli[1], C. Digilio[1], L. Pasquini[1], S.P. Sanders[1], A. De Zorzi[1]. *[1]Universita' degli Studi, Cardiology, Siena, Italy; [2]Ospedale Pediatrico Bambino Gesu', Cardiology, Rome, Italy*

Purpose: Williams syndrome (WS) is a complex genetic disorder including typical cardiovascular defects, mental retardation, a peculiar cognitive profile, and a typical dysmorphic facies. Data collected from cardiac follow-up were studied to determine the prevalence and the types of cardiovascular abnormalities in a large population of patients referred to our institution with the diagnosis of WS confirmed by FISH.

Methods: We retrospectively reviewed the files of 150 patients, 83 male, age range 7 months-45.4 years (mean 14.8 yrs, median 13.9 yrs) to determine the cardiac diagnosis, interventions, and clinical status.

Results: 113 of the 150 pts (75%) had a cardiac abnormality. Of the 117 patients with a cardiac abnormality, 98 continue to be followed at our institution, with a mean follow-up duration of 6.4 years (range 6 mo to 25 years). 94 patients (83%) had a defect(s) typical for WS including supravalvar aortic stenosis (73 pts, 65%), supravalvar/peripheral pulmonary stenosis (51 pts, 45%), coarctation (7 pts, 6%), and mitral valve prolapse (7 pts, 6%). In 67 pts lesions were isolated while in 27 were associated. 19 pts (17%) had defects atypical for WS, in 12 pts were associated with typical lesions and in 7 the defect was isolated. The most frequent non typical defect was interventricular septal defect (9 pts, 8%). There were also 2 pts with tetralogy of Fallot, 1 with aortic insufficiency, 1 with mitral insufficiency and 2 with bicuspid aortic valve. 33 pts (22% of the total population) had systemic hypertension and 25 patients are under treatment with anti-hypertensive therapy. Only 10 of those have achieved long-term control of blood pressure. 24 pts underwent presurgical cardiac catheterization and 6 interventional catheter procedures were performed in 5 pts. 30 surgical procedures were performed in 26 pts, 17(3 redo) for supravalvar aortic stenosis, 4 for supravalvular pulmonary stenosis and/or pulmonary branches stenosis, 5 for coarctation, 4 for the others. 2 deaths occurred among the 98 pts.

Conclusion: As in previous studies we found a high prevalence of typical cardiovascular abnormalities in WS patients. The new finding is the high prevalence (17%) of atypical defect with the most frequent being the interventricular septal defect. Moreover hypertension seems to represent a significant problem in the long-term management of these patients.

P691 Idiopathic restrictive cardiomyopathy in children is caused by mutations in cardiac sarcomere protein genes

J.P. Kaski[1], P. Syrris[2], M. Burch[1], M.T. Tome Esteban[1], M. Christiansen[3], P.S. Andersen[2], N. Sebire[1], M. Ashworth[1], W.J. Mckenna[1], P.M. Elliott[1]. *[1]Great Ormond Street Hospital, Cardiology Dept., London, United Kingdom; [2]University College London, Medicine, London, United Kingdom; [3]Statens Serum Institut, Copenhagen, Denmark*

Background: Restrictive cardiomyopathy (RCM) in children is associated with rapid disease progression and a poor prognosis. Approximately 30% of patients have a family history of cardiomyopathy, but few causative genetic mutations have been identified and the majority of cases are thought to be idiopathic. Mutations in the gene encoding cardiac troponin I have been identified in adults with RCM, but the prevalence of sarcomeric protein gene mutations in children with RCM is unknown.

Methods and Results: Fifteen patients (11 females, median age 5.5 years) with idiopathic RCM referred between 1991 and August 2006 underwent detailed clini-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

cal and genetic evaluation. Twelve had received orthotopic transplants at the time of the study. The entire coding sequences of the genes encoding eight cardiac sarcomere proteins and desmin were screened for mutations. Familial evaluation was performed on first-degree relatives. Five patients (33%) had a family history of cardiomyopathy: RCM (n=2); hypertrophic cardiomyopathy (n=1); dilated cardiomyopathy (n=1) and left ventricular noncompaction (n=1). Sarcomere protein gene mutations were identified in six patients (40%): 3 in the cardiac troponin I gene (TNNI3) and 1 each in the troponin T (TNNT2), beta-myosin heavy chain (MYH7) and alpha-cardiac actin (ACTC) genes. Three were de novo mutations and 5 were novel mutations. All mutations occurred in functionally important and conserved regions of the genes.
Conclusions: This study shows that mutations in sarcomere protein genes are an important cause of apparently idiopathic RCM in childhood, accounting for 40% of cases, and reports the first cases of familial RCM caused by mutations in MYH7 and ACTC. Familial disease was present in a third of cases, and 50% of the sarcomeric protein mutations were inherited, suggesting that screening of relatives, including children, for RCM is warranted.

P692 Epicardium-Derived-Cells in annulus fibrosis development and persistence of accessory atrioventricular pathways

D.P. Kolditz[1], M.C.E.F. Wijffels[1], A. Van Der Laarse[1], R.R. Markwald[2], A.C. Gittenberger-De Groot[1], M.J. Schalij[1]. *[1]Leiden University Medical Center, Cardiology Dept., Leiden, Netherlands; [2]Medical University of South Carolina, Cell Biology and Anatomy, Charleston, South Carolina, United States of America*

Background: The developmental mechanisms fundamenting the appearance of accessory atrioventricular (AV) pathways have remained mainly unknown. In this study the role of Epicardium-Derived-Cells (EPDCs) in formation of the isolating annulus fibrosis was investigated.
Methods: On the 3rd day of incubation (HH16), migration of EPDCs was mechanically inhibited by in-ovo microsurgery in quail embryos. In-ovo electrocardiograms (ECGs) were recorded in wildtype (n=12) and EPDC-inhibited (n=12) post-septated hearts at HH stages 38 to 42. Subsequently, in these EPDC-inhibited hearts (n=12) and in wildtype hearts (n=45)(HH38-42) ex-ovo extracellular electrograms were recorded. Electrodes were positioned on the left atrium, right ventricular base, left ventricular base and left ventricular apex. Electrophysiological data was correlated with morphology (MLC2a).
Results: In-ovo ECGs showed significantly shorter PR-intervals in EPDC-inhibited hearts (43±11ms) compared to wildtype hearts (57±7ms) (p=0.001), while the mean RR (259±37 bpm vs. 264±21 bpm) and QRS-intervals (26±13ms vs. 19±4ms) did not differ (p=0.723 and p=0.074, respectively). The ventricular activation sequence, as deducted from the ex-ovo electrogram recordings, was found to differ significantly between EPDC-inhibited versus wildtype hearts ($p<0.001$); while the right or left ventricular base was the location of earliest ventricular activation in 20/45 (44%) of wildtype embryonic hearts (heart rate 114±18 bpm), all EPDC-inhibited hearts (heart rate 125±35 bpm) showed premature activation of the ventricular base (100%). Moreover, EPDC-inhibited hearts displayed significantly shorter AV-intervals (62±12ms) compared to wildtype hearts (79±25ms) (p=0.033). Morphologically, small MLC2a-positive myocardial AV-continuities were found in mainly the right posteroseptal region of both wildtype and EPDC-inhibited hearts. Interestingly however, in EPDC-inhibited hearts multiple broad accessory AV-pathways were also found in the right and left lateral free wall region coursing through marked isolation defects in the annulus fibrosis. In retrospect electrophysiological measurements could structurally be directly related to the broadest accessory pathway present.
Conclusions: EPDCs play an important role in formation of the annulus fibrosis. Absence of or a delay in EPDC-migration causes marked defects in the annulus fibrosis with persistence of broad accessory myocardial AV-connections, functionally resulting in premature ventricular activation. These persistent accessory AV-connections may provide a substrate for postnatally persistent reentrant arrhythmias.

P693 NYHA class predicts mortality in long term survivors after atrial switch surgery for D-Transposition of the Great Arteries (TGA)

R.K. Mohindra, S. Giridhar, J. O'sullivan, M. Chaudhri. *Freeman Hospital, DEpartment of Cardiology, Newcastle Upon Tyne, United Kingdom*

Purpose: Does NHYA class predict late mortality in patients who have undergone an atrial switch operation for TGA?
Methods: Retrospective observational study. Review of medical records in the setting of a Tertiary Referral Centre.
Results: We identified 123 patients who had undergone an atrial switch operation at our hospital or elsewhere in the UK. 71 (57%) patients had simple TGA. The rest had TGA associated with other cardiac lesions. Breakdown by procedure type: 58 (47%) Mustard, 49 (40%) Senning, 16 (13%) unknown. Population age profile by operation type (median, mean interquartile): Mustard (28.8y, 7.97y), Senning (18.9y, 6.1y), unknown (19.2 y, 9.1y). Mortality was 16% (20/123) with 5 cases of late sudden death. Cumulative probability of survival at 10, 20, 30 and 40 years was 92%, 89%, 86% and 66% respectively. Age did not significantly correlate with late mortality.
NYHA class information was available in 91 patients. Of the rest there were 4 early deaths, 4 had significant non-cardiac disability and 4 were lost to follow up. In 7 survivors NYHA class was not formally recorded but each had had formal exercise testing (mean 17.4 (range 12-21) minutes modified Bruce protocol). These were not included in the NYHA analysis. Data was not obtainable in 13 (10.5%) patients. NYHA class tended to increase with age. All but 2/30 patients older than 30 years were in NYHA class II or above. Excluding patients where NYHA class was not available NYHA class correlated significantly with mortality. The mortality rate was 5.3% (4/75) in NYHA I/II and 53.3% (8/15) in NYHA III/IV ($p<0.0005$). 61% (75/123) of survivors were in NYHA I/II.

Number Alive + Number Dead by Age Group

NYHA Class	Age (y)								Total
	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	
I	–	1+0	1+1	14+0	9+0	6+0	–	2+0	–	34
II	0+1	–	1+1	10+0	7+0	5+1	6+0	7+0	–	39
III	0+3	–	-	2+2	–	1+0	2+1	1+0	–	12
IV	1+0	–	-	–	-	–	0+1	–	0+1	3
Total	5	1	4	28	16	13	10	10	1	88

Excludes 3 living patients in NYHA II (ages 16y, 22y and 24y) whose NYHA class assessment date was unavailable.

Conclusion: The strong association between NYHA class and mortality suggests that patients who are older than 30 years old and are in NYHA II or above should be closely followed and may need additional intervention.

P694 3-dimensional echocardiography in prenatal diagnosis of congenital heart disease

Y. Mivelaz[1], K. Francini[1], S. Di Bernardo[1], N. Sekarski[1], Y. Vial[1], E.J. Meijboom[2]. *[1]Lausanne, Switzerland; [2]Centre Hospitalier Universitaire Vaudois, Division of Pediatric Cardiology, Lausanne, Switzerland*

Objective: The development of new echocardiographic techniques has been a corner of prenatal diagnosis of congenital heart disease; real-time 3D colour Doppler echocardiography (4D) is no exemption. We used a systemic real time 4D (STIC) to imae the fetal heart. The aim of the study was to prove that 3D cardiac volumes obtained from the four-chamber view can adequately visualise the different cardiac parts and correlated this with 2D Doppler studies of CHD to examine its function as a prenatal screening tool for CHD.
Methods: This study included foetal STIC investigations performed between 2004-2005. The acquisition varied in angle between 20-30° and took 10-15 seconds. Two groups were analysed, a normal fetal population and a group of fetuses with CHD. The first group was analysed to evaluate the image availability of the different cardiac structures, in the second the efficacy of diagnosis based on 4D evaluations was compared to 2D results and post-natal outcome.
Results: 47 cardiac volumes with the 4-chamber view as starting point during the acquisition were analysed. 37 fetuses with normal cardiac anatomy (30 between 17-24/52, 17 between 25 and 36/52). An inexperienced investigator with a basic formation in echography reviewed the data for the views required for a standard fetal cardiac evaluation. Visualisation in 17-24 and 25-36 weeks GA: 4-Chamb 96-100%, Septum 96-100%, AV-valves 100%, Pulm. Art 91-100%, Ao 91-100%, Duct. Art. 57-79%, Ao arch 35-21% Pulm Ven. 25-21%
The 10 STIC studies of fetuses with CHD were obtained between 14-36 weeks gestation (mean: 27). Cardiac analysis was possible in 95%, complete diagnosis in 74%, partial in 16%, requiring modification in 5% (1 study) and unobtainable in 5%. In 1 case an associated diagnosis of complex CHD, which was missed before, could be diagnosed and was confirmed postnatally.
Conclusion: The use of STIC volumes allows inexperienced investigators to obtain the different views necessary for a complete cardiac exam in an offline fashion. Secondly the achieved good correlation between direct 2D and indirect offline STIC diagnosis suggests that this new technique can be reliably used for the prenatal screening of CHD in the hands of experienced fetal cardiologists.

P695 Two novel prenatal treatment strategies for experimental left ventricular hypoplasia

D. Sedmera[1], A. Dealmeida[2], T. Mcquinn[2]. *[1]1.Lf Uk, Anatomy, Prague, Czech Republic; [2]MUSC, Cell Biology and Anatomy, Charleston, Sc, United States of America*

Purpose: To verify the possibility of prenatal surgical treatment and gene therapy for amelioration of experimental left ventricular hypoplasia in the chick embryo.
Methods: In control embryos and those with established phenotype of left ventricular hypoplasia induced by left atrial ligation at ED4, we performed 1) right atrial clipping to shunt more blood to developing left ventricle at ED8, or 2) injection of GFP/FGF2 expressing adenoviruses at ED7, with the aim to induce myocyte proliferation in normal or hypoplastic myocardium in loading-dependent and independent manner. Sampling was performed at ED9, and included appropriate controls with $N \geq 5$ embryos per group.
Results: High-frequency echocardiography confirmed that partial right atrial clip-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

ping resulted in a significant increase in left ventricular end-diastolic volume. Both procedures resulted in significantly increased myocyte proliferation in both control and hypoplastic left ventricles; in the clipping model this effect was global (+38 and +27%, respectively) and resulted in a significant increase of myocardial volume of the hypoplastic left ventricle (in absolute numbers $2.4x10^6$ more myocytes). while in adenoviral injection increased myocyte proliferation (+45 and +39%) was limited to infected area, identified by GFP fluorescence and with documented 2-3 fold human FGF2 overexpression. No increase in apoptosis, or midterm adverse effects, were noted with the viral vectors.
Conclusions: we have shown in an in vivo model of left heart hypoplasia that 1) atrial level surgery can increase blood flow to the hypoplastic left ventricle, resulting in increased myocyte proliferation and numbers, and 2) localized transfection with FGF2 via adenoviral vector can induce fetal myocyte proliferation in loading-independent manner. This data provides support for current experimental human fetal procedures aimed on selected cases of congenital heart disease that are hard to manage postnatally.
Supported by NIH RR16434, MoD 5-FY02-269, MoE CR VZ 206100-3, IRP AVOZ50450515 from the AXCR, and Purkinje Fellowship from the ASCR.

P696 Incidence of anteroseptal location of atrioventricular accessory pathway in Wolff-Parkinson-White syndrome according to the age of the patient

B. Brembilla-Perrot[1], O. Huttin[2], F. Chometon[1], J. Bertrand[1], D. Beurrier[1], S. Ammar[1], N. Zhang[1], M. Abbas[1], L. Groben[1], F. Marcon[1]. [1]*Chu De Brabois, Departement De Cardiologie, Vandoeuvre Les Nancy, France;* [2]*Cardiology, CHU of Brabois, Vandoeuvre Les Nancy, France*

The purpose of the study was to evaluate the incidence of anteroseptal (AS) location in Wolff-Parkinson-White syndrome (WPW) according to the age of the patient and the clinical data of these patients. The radiofrequency ablation of atrioventricular accessory pathway (AP) which is now currently used, remains associated with a risk of complete AV block in the case of AS location and can be debated.
Methods: Electrophysiologic study (EPS) was performed in 459 patients aged from 6 to 81 years (36±17), 269 men,190 women, recruited for a patent WPW syndrome. The location of AP was determined on a 12 lead ECG during atrial pacing in maximal preexcitation according to classical criteria. The location was confirmed by the site of AP catheter ablation in half of the patients; 5 patients were excluded because the location remained not clearly defined. EPS was indicated for suspected or documented tachycardias (n=251), syncope (n= 48) or was systematic in asymptomatic patients (n= 155).
Results: AS AP location was identified in 28 patients aged 8 to 51 years (6%). Their mean age was younger than the age of remaining population (26±12 vs 37±17, $p < 0.001$). The incidence of asymptomatic WPW was similar in AS location (11/28; 39%) and in other locations (144/431, 33%) (NS). The maximal rate conducted over AP did not differ significantly (188±55 vs 195±60 b/min); the number of potentially malignant form of WPW at EPS was similar in AS location (4/28, 14%) and in other locations (60/431, 14%). According to the age, the incidence of AS location was significantly higher in children and adolescents (11%) than after 40 years (4%) ($p < 0.01$). The incidence by range of age was 12/106 (11%) between 8 and 19 years, 4/76 (5%) from 20 to 29 years, 7/91 (8%) from 30 to 39 years, 4/70 (6%) from 40 to 49 years, 1 aged 51 years/62 (1.6%) from 50 to 59 years, 0 after 60 years (n=54).
Conclusions: AS AP location in WPW syndrome was more frequent in children than in adults. The clinical and electrophysiological data did not differ significantly in these patients from patients with other AP location. The incidence decreased after 40 years; AS AP location was never noted after 51 years in our population. This spontaneous disappearance with age should be taken into account for the indications of AS AP ablation.

P697 Losartan in the prophylaxis of aortic aneurysm in Marfan syndrome children

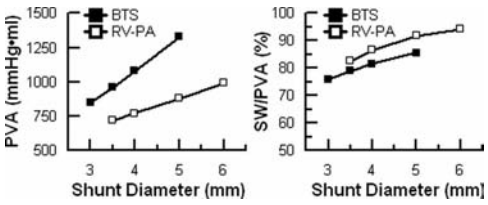
A. Pini[1], G. Trifiro[2], M. Rigoldi[1], M. Viecca[1]. [1]*MarfanClinic - Sacco Hospital, Cardiology, Milan, Italy;* [2]*Pediatry-Neonatology San Giuseppe Hospital, Pediatry, Milan, Italy*

Purpose: Marfan syndrome is a systemic connective tissue characterized by autosomal dominant inheritance. The primary underlying defects are mutations in FBN1 which codes for the extracellular structural protein, fibrillin. Recently has been pointed out the hypotheses that fibrillin could stimulate an overexpression of TGF-beta receptors and therefore an excess of this growth factor. Losartan has been sperimentally tested and has been observed a reverse of the early aorta damage in Marfan mice by blocking TGF-beta expression. Inasmuch, betablocker therapy does not significantly alter the rate od aortic dilation in children with Marfan syndrome.
Methods: We assessed the aortic diameter in a pediatric population with MFS: 31 patients (12 M, 17 F; 14 prepubertal), all fulfilling Gand criteria. Echocardiographic evaluation was performed every three months by the same operator after the replacement of betablocker treatment with losartan therapy (1 mg/kg/day). Data of the aortic diameter increase during the first 9 months of losartan therapy were compared with those observed during previous 9 month of betablockers therapy. Statistical analysis was performed by two-tailed Student's t-test.
Results: Betablocker therapy was gradually discontinued while Losartan treatment was gradually introduced in order to avoid wash-out. The target dose of losartan (1 mg/kg/die) was reached in all children within one month. No clinically symptomatic hypotension was observed. The mean increase in the aortic diameter at the level of sinus of Valsalva during betablocker treatment was 1.01±0.04 mm vs 0.05±0.01 mm during losartan treatment ($p<0.001$)
Conclusions: Losartan therapy seems to reduce significantly the rate of change of aortic root dilatation as compared with betablocker treatment in Marfan syndrome children. Based to these preliminary data, the recommendation of lifetime losartan therapy instituted during childhood should be considered.

P698 Right ventricle-pulmonary artery shunt for Norwood procedure is beneficial in reducing pressure-volume area and myocardial oxygen consumption compared to Blalock-Taussig Shunt: an in-silico analysis

S. Shimizu[1], T. Shishido[1], K. Uemura[1], A. Kamiya[1], T. Kawada[1], S. Sano[2], M. Sugimachi[1]. [1]*National Cardiovascular Center RI, Cardiovascular Dynamics, Osaka, Japan;* [2]*Okayama University, Cardiovascular Surgery, Okayama, Japan*

Purpose: Systemic circulation has been reconstructed (Norwood procedure) with right ventricle in hypoplastic left heart syndrome. Recent use of the shunt to maintain pulmonary circulation from right ventricle (RV-PA) for Blalock-Taussig shunt (BTS) may have contributed to the clinical dramatic improvement in 20 years. With potential merits (decreased systemic-to-pulmonary diastolic run off) and demerits (PA-to-RV diastolic regurgitation), we hypothesized that the net advantage resulted in reducing myocardial oxygen consumption in RV-PA.
Methods: A computer model of the postoperative cardiovascular dynamics of Norwood procedure either with BTS or with RV-PA was developed, with a time-varying elastance chamber model and modified three-element Windkessel vascular model. Shunt pressure (P)-flow (Q) relation was described as $P=\{aQ+bQ^2/D^4\}$ (D, shunt diameter). We estimated systemic and pulmonary blood flow (Qs, Qp), systemic and pulmonary arterial pressure (SAP, PAP), right ventricular end-diastolic volume (EDV), stroke work (SW), and pressure-volume area (PVA) for various shunt diameters.
Results: When heart rate, mean SAP and Qs were fixed for each shunt diameter, Qp, mean PAP, and systolic SAP were higher in BTS than RV-PA. These values increased with shunt diameter except systolic SAP in RV-PA. Diastolic SAP in RV-PA was higher (by 5-10mmHg) than BTS. Possible diastolic regurgitation notwithstanding, the preload of RV (EDV) was smaller (~18%) in RV-PA. These resulted in lower PVA (~30%) and larger SW/PVA (~6%) in RV-PA.



PVA & SW/PVA

Conclusions: A higher diastolic SAP and prevention of excessive Qp increase in RV-PA are favorable for single ventricular circulation. With adequate pulmonary circulation in RV-PA, RV delivers larger SW for lower PVA, i.e., lower myocardial oxygen consumption.

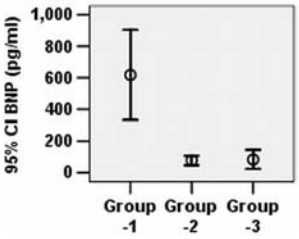
P699 Diagnostic value of BNP plasma levels in neonates with haemodynamically significant left to right shunts

A. Davlouros[1], A.K. Karatza[2], A.G. Georgiopoulou[2], D.A. Alexopoulos[2]. [1]*Patras University Hospital, Cardiology, Patras, Greece;* [2]*Patras University Hospital, Paediatrics, Patras, Greece*

Introduction: Haemodynamically significant heart disease, constitutes a diagnostic dilemma in Neonatal Intensive Care Units (NICU). Most newborns with heart disease have a Left-to-Right (LtR)shunt (ASD, VSD, PDA). Cardiac ultrasound is diagnostic; however it is not always available. We investigated the possible diagnostic value of plasma BNP levels in neonates with suspected heart disease and a Left-to-Right (LtR)shunt.
Methods: Plasma BNP levels were determined in 26 neonates with and 14 neonates without heart disease respectively, admitted in our NICU. Heart disease was suspected if there was a heart murmur, or respiratory distress and confirmed with heart ultrasound. Only neonates with any kind of LtR shunt were included in the study. A haemodynamically significant LtR shunt was defined as a $Qp/Qs \geq 1.5$.
Results: Thirteen neonates (group 1) had a haemodynamically significant LtR shunt, 13 (group 2) had a non-significant shunt and 14 (group 3) did not have heart disease. Plasma BNP levels were significantly higher in group-1 vs. groups 2 and 3, whereas did not differ between the latter two groups (Figure) (617,4±473.1 pg/mlvs. 78,6±50,8 pg/mlvs. 83,8± 105,4 pg/mlANOVA $p<0.001$). ROCcurveanalysisshowedthataplasmaBNP > 336 pg/mlhas 77% sensitivityand

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

100% specificity for diagnosing haemodynamically significant LtR shunts. BNP levels < 120 pg/ml had 92,3% sensitivity and 74% specificity (92.3% accuracy) respectively.



Conclusion: Plasma BNP levels in neonates with suspected heart disease, may be a useful bedside test for diagnosing haemodynamically significant RtL shunts. These neonates may need medical, invasive or surgical treatment. An echocardiogram is mandatory and if not available, transfer to a centre with paediatric cardiology facilities should be scheduled.

P700 Reduced aortic elasticity and dilatation are associated with aortic regurgitation and left ventricular dysfunction after the arterial switch operation

H.B. Grotenhuis, D. Fontein, J. Ottenkamp, M.G. Hazekamp, H.W. Vliegen, L.J.M. Kroft, A. De Roos. *Leiden University Medical Center, Radiology Department, Leiden, Netherlands*

Purpose: To assess dimensions and elasticity of the aorta and their impact on aortic valve competence and left ventricular (LV) function in transposition of the great arteries (TGA) patients corrected with the arterial switch operation (ASO).
Methods: MRI was performed in 15 ASO patients (mean±SD age (yrs.): 16±4) and 15 matched controls.
Results: ASO patients frequently showed aortic root dilatation as compared to controls (mean difference 5.7-9.4mm, P≤0.007 at 3 predefined levels). ASO patients showed reduced aortic elasticity, as indicated by increased pulse wave velocity (PWV) in the aortic arch (5.1m/s±1.2 vs. 3.9m/s±0.7, P=0.004) and reduced root distensibility (2.2*10-3mmHg-1±1.8 vs. 4.9*10-3mmHg-1±2.9, P<0.01). Minor degrees of aortic regurgitation (AR) were present in 6 patients (AR fraction 5%±3 vs. 1%±1, P<0.001). In addition, LV ejection fraction (LV EF) was decreased in ASO patients (51%±6 vs. 58%±5, P=0.003) and LV dimensions were enlarged with LV end-diastolic volume 112mL/m^2±13 vs. 95mL/m^2±16 (P=0.007) and LV end-systolic volume 54mL/m^2±11 vs. 39mL/m^2±7 (P<0.001). AR fraction was correlated with increased PWV in the aortic arch (r=0.39, P=0.03), reduced root distensibility (r=0.45, P=0.01) and aortic root dilatation (r 0.32-0.66, P≤0.01 for all levels). Degree of AR predicted decreased LV EF (r=0.41, P=0.026) and was correlated with increased LV dimensions (r=0.48, P=0.008; r=0.67, P<0.001; respectively).
Conclusions: Aortic root dilatation and reduced elasticity of the proximal aorta were frequently present in ASO patients. Dilatation of the aortic root and reduced proximal aortic wall elasticity were associated with degree of AR, while AR was correlated with LV systolic dysfunction and increased LV dimensions after ASO.

P701 Regional myocardial function in children with aortic regurgitation

B. Goebel[1], R. Arnold[2], S. Ley[3], J. Eichhorn[4], H.E. Ulmer[3], C. Schmidt-Winter[4], H.R. Figulla[4], T.C. Poerner[4]. *[1]University Hospital of Jena, 1st Dept. of Medicine, Jena, Germany; [2]University Hospital of Freiburg, Dept. of Pediatric Cardiology, Freiburg, Germany; [3]German Cancer Research Centre, Dept. of Radiology, Heidelberg, Germany; [4]University Hospital of Heidelberg, Dept. of Pediatric Cardiology, Heidelberg, Germany*

Aim of the study was to determine the influence of volume overload on regional myocardial function in children with aortic regurgitation (AR) using Tissue Doppler and Strain rate imaging (TDI/SRI).
Methods: According to standard echocardiographic criteria, thirty children with AR (21 male, mean age 15±6 years) were divided into three groups: mild AR (n = 6), moderate AR (n = 15), severe AR (n = 9). All patients and 30 age and gender matched healthy controls underwent echocardiography with TDI/SRI using a dedicated software for a 16-segment LV model. The following parameters were extracted: displacement (D), peak systolic (VS) and diastolic (VE) velocities, peak strain (S), peak systolic (SRS) and diastolic strain rate (SRE) While D, VS and VE were obtained in the basal segments, strain and strain rate were expressed as mean values between all LV segments.
Results: Results for standard echocardiographic and TDI/SRI measurements are shown in Table 1.
Conclusion: All children with AR presented with significant reduced long-axis diastolic motion (VE). But according to the SRI parameters, there was no evidence for alteration of systolic contraction or diastolic relaxation.

Abstract P701 – Table 1

	Controls (n = 30)	AR mild (n = 6)	AR moderate (n = 15)	AR severe (n = 9)
Echo endiastolic LV volume (ml)	–	77±17	82±15	96±18†
Echo regurgitationfraction (%)	–	15±9	26±6†	45±11†‡
Radial-axis D (mm)	6±2	7±2	8±2	8±2
Radial-axis V_S (mm/s)	39±12	38±6	42±7	45±11
Radial-axisV_E (mm/s)	-69±29	-66±28	-72±29	-73±30
Radial-axis S (%)	56±12	49±15	49±15	43±17
Radial-axis SR_S (1/s)	4.23±1.11	3.96±1.16	4.27±1.29	3.78±1.10
Radial-axis SR_E (1/s)	-8.83±3.03	-7.52±2.25	-9.07±6.13	-7.66±3.04
Long-axis D (mm)	11±3	10±3	10±2	9±3§
Long-axis V_S (mm/s)	64±18	53±13	57±14	49±13§
Long-axis V_E (mm/s)	-119±20	-85±24§	-95±29§	-89±34§
Long-axis S (%)	-26±9	-25±8	-27±11	-27±13
Long-axis SR_S (1/s)	-2.31±1.26	-2.15±1.09	-2.11±1.16	-2.13±1.08
Long-axis SR_E (1/s)	3.71±1.85	3.00±1.60	3.22±1.90	3.22±1.61

Comparison between the groups: § p < 0.05 vs. controlls, † p < 0.05 vs. AR I, ‡ p < 0.05 vs. AR II, * p < 0.05 vs. AR III.

P702 Role of cardiovascular magnetic resonance in detection of myocardial inflammation and coronary artery involvement during the acute phase of Kawasaki disease

S. Mavrogeni[1], G. Papadopoulos[2], E. Karanasios[1], D. Georgakopoulos[1], M. Douskou[3], D.V. Cokkinos[3]. *[1]Onassis Cardiac Surgery Center, Athens, Greece; [2]Aghia Sophia Childrens' Hospital, Athens, Greece; [3]Bioiatriki MRI Unit, Athens, Greece*

Kawasaki disease (KD) is an acute vasculitis of unknown etiology. Infants and children may show myocarditis and/or pericarditis with coronary artery aneurysms (CAA), causing both short- and long-term morbidity and mortality. Thirteen patients, aged 3-7 yrs with Kawasaki disease, during the acute phase, were assessed by cardiovascular magnetic resonance for simultaneous evaluation of coronary arteries, myocardial function and the presence of myocardial inflammation. Coronary Magnetic Resonance Angiography (MRA) was performed using a 1.5T system. Evaluation of myocardial inflammation was performed using T2-weighted (T2-w), T1-weighted (T1-w) before and after contrast media injection and late enhanced images. Evaluation of images was performed according to previously described protocols. Left ventricular ejection fraction was also calculated from short-axis cine.
Coronary arteryectasia (CAE) was documented in all patients, while discrete aneurysms only in five. RCA aneurysms were identified in 3 patients (5± 2 mm in diameter) and LAD aneurysms in 2 patients (7±3 mm in diameter). Myocardial inflammation was identified in 4 cases (30.8%). In these patients in the T2-w images the signal ratio of myocardium to skeletal muscle (latissimus dorsi) was 2.85±0.34 (normal values 1.28±0.05), indicative of myocardial oedema. From the T1-w images the relative myocardial enhancement was 28±5 (normal values 2.3±0.69), indicative of myocardial inflammation. No late gadolinium enhanced areas were identified. Ejection fraction of left ventricle was mildly decreased (EDV=76±0.6 ml, ESV=38±0.4, EF=48±2%). Myocardial inflammation was present in 3 patients with CAE and only in one patient with CAA.
CAE is a common finding during the acute phase of the disease. Myocardial inflammation with mild decrease of LV function is also a frequent finding. Cardiovascular magnetic resonance can easily identify these entities and can be of value for treatment guidance and follow-up.

P703 Utilization of newly developed tissue doppler derived techniques in the evaluation of patients with pulmonary stenosis pre and post balloon pulmonary valvuloplasty

T. Abuarab[1], M. El Sayed[2], A. El Feki[1], H. Attia[1]. *[1]Ain Shams University, Ain Shams Hospitals, Cardiology Department, Cairo, Egypt; [2]Ain Shams university hospitals, cardiology, Cairo, Egypt*

Purpose: To use strain and strain rate imaging techniques in the assessment of the right ventricular regional functions in patients with congenital valvular pulmonary stenosis pre balloon dilatation and to assess the same functions in the immediate and short term periods following balloon dilatation.
Methods: The study was conducted on 30 patients with isolated congenital valvular pulmonary stenosis who were referred for balloon pulmonary valvuloplasty. For each patient full echocardiographic study was done including assessment of regional right ventricular function and myocardial deformation properties using strain (S) and strain rate (SR) imaging and analysis techniques in the basal (b), mid (m) and apical (a) segment of right ventricle free wall pre balloon dilatation, immediately post balloon, one month following balloon pulmonary valvuloplasty.
Results: All patients had underwent successful balloon pulmonary valvuloplsty with drop of peak systolic pressure gradient across pulmonary valve immediately and short term post balloon (75.53±20.2 to 26.77±9.88 to 21.77±7.15 mmHg P-value < 0.001 highly significant). This was associated with significant improvement in systolic(SSR) and diastolic strain rate (E & A)and systolic strain (SS) parameters in the basal, mid and apical segments of the right ventricle free wall

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

immediately (2) and short term (3) post balloon in comparison to preprocedural (1) parameteres.

An example of the results

	Mean	Std. deviation	Paired t-test	P-value (significance)
SSR a1 (s^{-1})	-2.02	±0.51	10.2	<0.001 (highly significant)
SSR a2	-3.01	±0.71		
E a1 (s^{-1})	2.5	±0.72	-6.6	<0.001 (highly significant)
E a2	3.5	±0.86		
A a1 (s^{-1})	3.1	±0.9	-3.66	<0.05 (significant)
A a2	3.1	±0.77	-3.66	
S a1 (%)	-21.5	±8.1	6.5	<0.001 (highly significant)
S a2	-30.5	±9		

This is a comparison between systolic strain rate (SSR), diastolic strain rate (E,A) and systolic strain (SS) pre (1) and immediately post BPV (2) at the apical (a) segment of RV free wall.

Conclusion: Using strain and strain rate deformation properties in assessment of regional longitudinal right ventricular function in cases of of congenital valvular pulmonary stenosis pre and post balloon pulmonary valvuloplasty are considered a good tool in early and accurate recognition of improvemnet of right ventricular regional function.

P704 Impact of three dimensional echocardiography in defining complex congenital heart diseases compared to two dimensional echocardiography: the surgical view

A. Del Pasqua[1], G. Rinelli[2], A. Toscano[1], R. Iacobelli[1], L. Pasquini[1], M. Marzilli[2], S.P. Sanders[1]. *[1]university of siena, cardiology, Siena, Italy; [2]bambino gesu pediatric hospital, cardiology, Rome, Italy*

Purpose: Three-Dimensional Echocardiography (3D echo) offers a nearly infinite number of cutting planes through the 3-D data set, many impossible to obtain with 2D Echo, and previously shown to be of value in simple defects like ASD or VSD. Our aim was to assess whether 3D echo can better define anatomy and interrelations between structures in Complex Congenital Heart Defects (CCHD) and to verify the surgical impact of this technology.
Methods: From March 2006 to October 2006, we enrolled 43 patients (53.4% male) with CCHD. Mean age was 4.6 months (median 0.5, range: 1 day- 5 years), mean weight was 4.8 kg (median 3, range 1.5-19). After the 2D echo, we obtained 3D acquisitions in full volume and live Real Time(RT) 3D. Technical quality was classified as excellent, satisfactory or poor. 3D acquisitions were defined as "very useful" if new information was added, "useful" if only better anatomical definition was obtained and "not useful" if nothing was added to 2D. Images were reviewed by cardiologists and surgeons before surgical correction and the echocardiographic findings were compared with the surgical findings.
Results: For each patient the mean acquisition time for the standard 2D Echo was 30±10 min and for 3D was 8±3 min. RT3D acquisitions were successfully accomplished in all patients; 60.4%(26/43) were excellent, 30.2%(13/43) satisfactory and 9.3%(4/43) poor quality. Reconstruction time (mean 20±8 min) was measured after gaining considerable experience with the work station and software. 3D acquisitions were very useful in 30.2% (13/43), specifically in: Ebstein's anomaly with vascular ring, truncus, double outlet right ventricle, transposition of the great arteries, asplenia syndrome with left aortic arch and right ductus, type B aortic interruption, polysplenia, malposition of the great arteries, criss-cross heart. The 3D acquisitions were useful in 37.2% (16/43) and not useful in 32.5% (14/43). Surgical colleagues reported a remarkable correspondence between the 3D images and the actual anatomy in all cases.
Conclusions: The routine use of 3D echo in addition to the 2D is feasible in most children and useful in about 1/3 of cases of CCHD. Although no new diagnoses were made using 3D echo, the 3D images provided a more comprehensive view of the anatomy and a clearer understanding of the interrelations between structures. Association of 2D and 3D echo has a high reliability (100% of correlation with surgical findings). Evidently 3D reconstruction can be obtained only by selection of the optimum 2D cut plane which is experience-related and requires a learning curve.

MECHANISMS OF ATHEROGENESIS

P705 Altered fibrin clot structure and function 3 months after myocardial infarction

T. Mwambingu, P.J. Grant, E.M. Scott. *University of Leeds, Academic Unit of Molecular Vascular Medicine, Leeds, United Kingdom*

Purpose: Myocardial Infarction (MI) is one of the most serious clinical complications of atherosclerotic disease. The structure and function of the fibrin clot is believed to be important in the clinical manifestation of arterial thrombotic occlusion. Following an acute MI, secondary prevention of further coronary events involves the regular prescription of anti-thrombotic as well as several other cardioprotective drugs. We performed a case-control study to investigate the structure and function of ex-vivo fibrin clots from male subjects under the age of 65 years who were 3 months post MI and on regular secondary prevention therapy.
Methods: The ex-vivo fibrin clot structure of 91 male subjects 3 months post MI and 91 age matched control subjects was assessed by measurement of clot turbidity (lag phase and maximum absorbency [max abs]) and clot lysis time [corr t]). The lag phase represents the length of time required for fibrin protofibrils to grow to sufficient length to allow lateral aggregation, the shorter this is the quicker the clots begin to form. Max Abs reflects the average fibrin fibre size and the number of protofibrils per fibre, the greater it is, the thicker the fibres. The shorter the clot lysis time, the easier it is to dissolve the clot with lytic agents.
Results: Max abs was significantly greater in the MI group, 0.58 (0.56-0.60) versus 0.54 (0.52-0.56) in controls ($p<0.005$). Clot lysis time (corr t) was also significantly longer in the MI group, 2405 (2069-2742) seconds versus 1917 (1804-2030) seconds in the control group ($p<0.001$). There was no significant difference in lag phase between the two groups.
Conclusions: Despite taking secondary prevention drugs, including antithrombotic therapy, male subjects 3 months post MI form fibrin clots ex-vivo that have thicker fibres and are more resistant to fibrinolysis than those of control subjects. This may have implications for the development of subsequent cardiovascular events.

P707 Ultrasensitive confocal imaging of C-reactive protein binding to Fcgamma-receptors on monocytic cells

D.E. Manolov[1], K. Tron[2], C. Roecker[1], M. Kaechele[3], G.U. Nienhaus[1], J. Torzewski[2]. *[1]University of Ulm, Internal Medicine II, Internal Medicine II - Cardiology, Ulm, Germany; [2]University of Ulm, Department of Biophysics, Department of Biophysics, Ulm, Germany; [3]University of Ulm, Internal Medicine II, Internal Medicine II - Cardiology, Ulm, Germany*

Background: C-reactive protein (CRP), the prototype human acute phase protein, is widely regarded as a key player in cardiovascular disease. The cellular CRP receptor is still under debate. Since 1999, Fcgamma-receptors (FcgammaRIIa and FcgammaRI) have been controversially discussed as potential CRP receptors. Use of anti-CRP-antibodies or radioactively labeled CRP and FACS analysis have led to false positive results. Recently, we have confirmed that CRP binds to FcgammaRIIa (CD32) and FcgammaRI (CD64) on transfected COS-7 cells using ultrasensitive confocal fluorescence microscopy.
Purpose: Characterization of CRP-binding to Fcgamma-receptors on monocytic cells and to FcgammaRIII on transfected cells.
Methods: Binding studies of gently labelled CRP to Fcgamma-receptors-transfected COS-7 cells or to monocytic cells; applying of highly sensitive confocal fluorescence microscopy; Incubations and observations performed on single native cells.
Results: CRP binds to FcgammaRIIa and FcgammaRI but not to FcgammaRIII (CD16) on transfected COS-7 cells. The calculated avidity for FcgammaRI is similar to that estimated for FcgammaRIIa. In presence of the gamma-chain (functional counterpart of FcgammaRI) avidity increases by 30-fold. Dissociation of CRP from the cell surface can not be detected over the time course of several hours and is thus extremely slow. MonoMac 6 cells (a macrophage cell line), display clear FcgammaRI- and FcgammaRIIa-, but not FcgammaRIII-expression. In MonoMac 6 cells, CRP avidly binds to the cell surface, and binding is blockable by human IgG.
Conclusion: As CRP shares functional similarities with IgGs and interacts with Fc-receptors we hypothesize that Fcgamma-receptors may have originated from CRP-receptors in the evolution of the immune system. Multivalent binding and receptor clustering are involved in the interaction of CRP with Fcgamma-receptors. These studies may contribute to the development of CRP-receptor blockers for the treatment of cardiovascular disease.

P708 The cannabinoid receptor CB2 is not associated with myocardial infarction

W. Reinhard, K. Stark, A. Baessler, M. Fischer, K. Sedlacek, C. Hengstenberg. *University Hospital Regensburg, Cardiology, Regensburg, Germany*

The peripheral cannabinoid receptor CB2 is primarily expressed in immune tissues and has been implicated in mediating anti-atherosclerotic effects in vivo. In epidemiologic studies, the importance of inflammatory reactions in atherosclerosis has been clearly demonstrated. However, the role of CB2 in the pathogenesis of coronary artery disease remains unclear. We therefore hypothesized that genetic variations within the CB2 gene are associated with the development of myocardial infarction (MI).
Methods: We analysed 13 SNPs covering the CB2 gene and adjacent genes with a mean inter-SNP distance of 13 kb in a case-control sample of 2.151 individuals from the Regensburg MI Family Study and the population stratified MONICA-Augsburg survey III (76.3% male, 1.118 cases with MI <60 years of age, 1.033 unrelated controls).
Results: The minor allele frequency of all SNPs was ≥ 10% and all SNPs were in Hardy-Weinberg equilibrium. In allelic and genomic models of the total sample, none of the examined SNPs showed significant association with MI. Comparison of case-control allele frequencies in men and women separately did not show relevant evidence for a relation between common genetic variations within the CB2 gene and MI. Furthermore, we examined the control group for association of the CB2 gene variations with cardiovascular risk factors, such as arterial hypertension, dyslipidemia or obesity. No such association was observed.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusion: In a very large case-control sample, common variations within the CB2 gene were not associated with MI. Furthermore, in the normal control sample, no association between these CB2 gene variants and common cardiovascular risk factors was observed.

P709 Serum PON-1 activity and TBARS levels correlate with angiographic extent and severity of coronary artery disease

A. Arat-Ozkan, T. Gurmen, A. Kaya, Z. Yigit, M. Ersanli, S. Kucukoglu.
Institute of Cardiology, Istanbul University, Cardiology, Istanbul, Turkey

Background: Paraoxanase-1 (PON-1), an HDL- associated enzyme protects LDL against oxidation by blocking the accumulation of lipidperoxides in LDL, thus having an antiatherogenic effect.
This study is designed to examine the association of activity and lipidperoxide levels with the extent and severity of coronary artery disease (CAD).
Method: We studied PON-1 activity and lipidperoxid levels, expressed as TBARS in 105 consecutive patients (72 men, 33 women, mean age 57.7± 11.6) with known or suspected CAD referred for a first coronary angiography. Based on angiographic findings subjects were classified to no or mild CAD (<50% stenosis), one-vessel- and multivessel -disease groups.Gensini scores were calculated for each subject to define the severity and extent of the disease.
Results: Serum PON-1 activity of the one vessel- (227±81) and multivessel-disease (226±90) groups were significantly lower compared to controls (279±80, p 0.03 and p 0.01 respectively). TBARS levels of one-vessel (7.5±3.7, $p<0.04$) and multivessl disease (9.5±3.1, $p<0.001$) were significantly higher than subjects without disease (5.3±1.7). Gensini scores correlated with PON-1 activity (r= -0.43, $p<0.0001$), TBARS levels (r = +0.42, $p<0.001$) and HDL levels (r = -0.55, $p<0.001$).
Conclusion: PON-1 activity and lipidperoxide levels expressed as TBARS correlate well with the angiographic extent and severity of CAD.

P710 Evaluation of systemic inflammatory markers improves the prediction of coronary calcifications

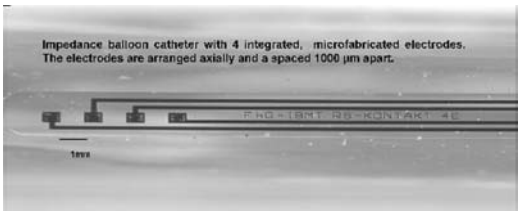
C.D. Garlichs[1], A. Yilmaz[1], T. Frank[1], D. Raaz[1], I. Cicha[1], S. Achenbach[1], P. Lewczuk[2], J. Wiltfang[1], W.G. Daniel[2]. *[1]University Hospital Erlangen, Department of Cardiology, Medical Clinic 2, Erlangen, Germany; [2]University Clinic for Psychiatry, Erlangen, Germany*

Background: Coronary calcification is a marker of coronary atherosclerosis. Since atherosclerosis is a chronic inflammatory disease, we investigated whether the evaluation of systemic inflammatory parameters can predict coronary calcification and improve the predictive value of lipids and age for coronary calcification.
Methods: Plasma was obtained from 230 patients (~60 years, 146 male, 84 female) with clinical indication for performing cardiac computer tomography, and analysed with a Luminex Laser-based Fluorescence Analyser. Quantification of coronary calcification was performed by applying the Agatston Score to the MDCT data. To identify predictive biomarkers, we compared 144 coronary calcifications patients (CAC) with a control group (C; n=86).
Results: CAC had significantly enhanced plasma concentrations of IL-7 (10.92 vs 7.60 pg/mL in C; p=0,009) and IL-13 (60.55 vs 48.20 pg/mL; p63 years showed a 5-fold elevated risk of coronary calcifications as compared to patients 121 pg/mL the risk was increased 4-fold as compared to patients with a IP-10 63 years and IP-10 concentration >121 pg/mL was ~30-fold increased as compared to patients <56 years and an IP-10 concentration <79 pg/mL. The established biomarkers, lipids, hsCRP, and IL-6 did not show significant differences between C and CAC.
Conclusions: The inflammatory parameters IL-7, IL-13, and IP-10 allow the prediction of coronary calcification independent of age and serum lipids. In combination with age, IL-7 and IL-13 showed a strong association with elevated risk for coronary calcification. The biomarker lipids, hsCRP and IL-6 did not predict coronary calcium.

P711 Electric impedance spectroscopy of human atherosclerotic lesions using a new impedance catheter system

I. Streitner[1], M. Goldhofer[1], S. Cho[2], H. Thielecke[3], R. Kinscherf[4], J. Metz[4], F. Streitner[3], R. Grobholz[3], K.K. Haase[5], T. Sueselbeck[4]. *[1]University Hospital of Mannheim, First Departement of Medicine, Mannheim, Germany; [2]Fraunhofer Institute for Biomedical Engineeri, Department of Biohybride Systems, St. Ingbert, Germany; [3]Fraunhofer Institut for Biomedical Engineerin, Department of Biohybride Systems, St. Ingbert, Germany; [4]University of Heidelberg, Department of Anatomy and Cell Biology III, Heidelberg, Germany; [5]Klinikum am Steinenberg, Departement of Cardiology, Reutlingen, Germany*

Newer techniques are required to identify atherosclerotic lesions that are prone to rupture. Electric impedance spectroscopy (EIS) can characterize biological tissues by measuring the electrical impedance. We tested a newly designed impedance catheter (IC) (abstract picture) by measuring the impedance of different stages of atherosclerosis on human arteries.
Method: Electrical impedance measurements (EIM) were performed on 7 aortic and 6 femoral arteries at 132 spots. The arteries were obtained at 13 autopsy procedures, stored at 4 C in saline (0.9%) solution. The arteries were cut in small segments (1x3cm) and the measurement spots were marked with an adventitial cross of threads in advance. The impedance was measured at 100 kHz and compared with the corresponding histomorphometric data of each vessel segment.
Result: According to the classification of Stary et al. we found the following mean impedance of different plaque types: Plaque I (PI, n=33) 375±47 Ω, Plaque II (PII, n=34) 358±63 Ω, Plaque III (PIII, n=21) 342±52 Ω, Plaque IV (PIV, n=21) 356±41 Ω, Plaque Va (PVa, n=13) 455±66 Ω, Plaque Vb (PVb, n=10) 698±239 Ω. The mean impedance of PVa and PVb were significantly higher in comparison to PI, PII, PIII, PIV ($p\leq0,05$) and PVb showed a significantly higher impedance than PVa (<0,05).



Impedance Balloon Catheter

Conclusion: EIS could be successfully performed by using a newly designed microelectrode on human atherosclerotic lesions. In this experimental study high grade atherosclerotic lesions (PIV, PVa, PVb) could be differentiated and PVa, PVb showed significantly higher impedance in comparison to early stages of atherosclerosis.

P713 Expression of the transcription factor EGR-1 in atherosclerotic lesions correlates with a stable plaque phenotype and higher collagen expression

P.T.G. Bot[1], M.J. Goumans[2], J. Sluiter[2], P. Van Vliet[2], A. Smits[2], A.F. Mol[3], J.P. De Vries[4], J.J. Piek[1], G. Pasterkamp[3], I. Hoefer[3]. *[1]Academic Medical Center Amsterdam, Cardiology, Amsterdam, Netherlands; [2]University Medical Center Utrecht, Utrecht, Netherlands; [3]University Medical Center, Utrecht, Netherlands; [4]Antonius Hospital, Nieuwegein, Netherlands*

Background: Atherosclerotic plaque formation is an inflammatory disease of the vessel wall. Unstable plaques, more prone to rupture and to cause clinical events, are characterized by an increased macrophage accumulation and a reduced smooth muscle cell (SMCs) and collagen content. Early Growth Response-1 (EGR-1) is a transcription factor downstream of Transforming Growth Factor-beta (TGF-beta), stimulating SMC proliferation and collagen synthesis. In atherosclerotic lesions, EGR-1 is mainly expressed by SMCs. We therefore hypothesized that increased EGR-1 and TGF-beta expression levels correlate with a stable plaque phenotype.
Methods and Results: Human carotid atherosclerotic plaques (n=103) were collected from patients undergoing carotid endarterectomy. Plaque characteristics, i.e. collagen, macrophage and SMC content and thrombus formation were analyzed histologically. Higher EGR-1 protein levels, as determined by Western Blotting, correlated positively with plaque stability as well as TGF-beta signaling. Increased intraplaque TGF-beta, as determined by ELISA, as well as EGR-1 levels were associated with a significant increase in expression of the EMMPRIN variant of 45 kD, which has been shown to correlate with less matrix degradation and hence a more stable phenotype. Furthermore, a negative correlation between TGF-beta and MMP9 was observed. In vitro, EGR-1 overexpression stimulated collagen synthesis and diminished levels of the TGF-beta transcription factors pSMAD2/3. Inhibition of the TGF-beta co-receptor endoglin also resulted in a significantly decreased EGR-1 expression, indicating a feedback loop controlled EGR-1 regulation by TGF-beta.
Conclusions: Higher EGR-1 levels are associated with a stable plaque phenotype and higher collagen content in human carotid plaques. Furthermore, both EGR-1 and TGF-beta could shift the balance towards less matrix degradation by induction of EMMPRIN45kD and a decrease in the expression of MMP-9. In vitro inhibition of TGF-beta signaling leads to diminished expression of EGR-1, while overexpression of EGR-1 inhibits TGF-beta signaling. We would like to introduce a pathway of TGF-beta signaling in atherosclerotic plaques, which by increasing EGR-1 expression through both pSmad2/3 as well as endoglin leads to more collagen production, less matrix degradation and more smooth muscle cell proliferation. The TGF-beta/EGR-1 pathway might serve as a novel target to stabilize atherosclerotic plaques.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P714 Nebivolol reduces VCAM-1 and MCP-1 expression in human endothelial cells and prevents foam cells formation via inhibition of protein kinase C beta

A. Kuroedov[1], E. Osto[1], P. Mocharla[1], M. Volpe[2], T.F. Luscher[2], F. Cosentino[1]. *[1]Cardiology, University Hospital, Cardiovascular Research, Zurich, Switzerland; [2]Cardiology, 2nd Faculty of Medicine, Cardiovascular Research, Rome, Italy*

Background: We recently demonstrated, that nebivolol, a selective b $_1$ -blocker, but not atenolol, improves endothelial function in apoE-deficient mice. A histological analysis of atherosclerotic plaques showed higher number of smooth muscle cells in plaque's shoulder and a thicker fibrous cap in nebivolol-treated animals. However, the molecular mechanisms of antiatherosclerotic properties of nebivolol remain unclear.
Materials and Results: Human aortic endothelial cells (HAECs) were stimulated with IL-1β (10 ng/mL) after 2 hours of pretreatment with nebivolol or atenolol (5 $\times$ 10^{-6} mol/L). IL-1β (10 ng/mL) increased VCAM-1 expression in HAEC as assessed by Western blotting (826±52% versus control; n=4; $p < 0.01$). Pretretment with nebivolol resulted in a significant attenuation of IL-1β-induced VCAM-1 expression (n=4; $p < 0.01$ versus IL-1 b alone). Increase of MCP-1 in culture medium after stimulation with IL-1β was completely abolished by nebivolol. In contrast, atenolol did not affect nether VCAM-1 nor MCP-1 expression. Western blotting with antibodies against phosphorylated PKCβ_2 isoform revealed that incubation of the cells with IL-1β increased ser-660 residue phosphorylation. Nebivolol blunted IL-1β-induced ser-660 phosphorylation.
THP-1cells, a human monocytic cell line, were differentiated in to macrophages after 24 h exposure to phorbol ester (PMA, 0.1μmol/L) or to IL-1β (10 ng/mL). Pretreatment with nebivolol or atenolol was performed 1 hour before PMA or IL-1β exposure. Indeed we observed an upregulation of CD14 expression, a marker of monocyte transdifferentiation (285±42% versus control; n=3; $p < 0.05$). Nebivolol (5 $\times$ 10^{-6} mol/L) abolished such IL-1β-induced CD14 upregulation. Furthermore, the monocyte-derived macrophages were incubated up to 48 hours with 10 μg/mL DiI-labeled acLDL. Nebivolol significantly decreased uptake of acLDL as assessed by flow cytometry (443 ±57 fluorescent units versus 717±113 fluorescent units in control; n=5; $p < 0.01$). Atenolol did not affect acLDL uptake. Western blotting with an antibody against phosphorylated PKC β_1 revealed that incubation of cells with PMA/acLDL increased thr-642 phosphorylation. Accordingly, only nebivolol blunted PMA/acLDL-induced thr-642 phosphorylation.
Conclusion: Our results show that nebivolol exerts its antiatherosclerotic effect via inhibition of PKCβ-induced intracellular signaling in endothelial cells and macrophages.

P715 Lipid-altering efficacy and tolerability profile of extended release niacin/laropiprant in patients with primary hypercholesterolemia or mixed hyperlipidemia

D. Maccubbin[1], W. Sirah[1], A. Betteridge[1], Q. Yu[1], C. Mccrary Sisk[1], H. Bays[2], A.G. Olsson[3], J. Paolini[2]. *[1]Merck Research Laboratories, Rahway, New Jersey, United States of America; [2]Louisville Metabolic & Atherosclerosis Res Ct, Louisville, Kentucky, United States of America; [3]Stockholm Heart Center, Stockholm, Sweden*

Purpose: Niacin has proven lipid-modifying efficacy and cardiovascular benefit, but is underutilized due to flushing, a process mediated by prostaglandin D2 (PGD2). Laropiprant (LRPT) is a PGD2 receptor antagonist that reduces flushing with extended release niacin (ERN). We evaluated the lipid efficacy and flushing profile of ERN/LRPT (fixed dose tablet containing 1g ERN and 20 mg LRPT) as monotherapy or added to statins.
Methods: In this double-blind, 24-wk study, dyslipidemic patients (pts) (66% on statins), were randomized to ERN/LRPT 1g (n=800), ERN 1g (n=543), or PBO (n=270). After 4 wks, active treatments were doubled to 2g (2 tablets) for 20 wks. Endpoints included effects of ERN/LRPT 2g vs. PBO on lipids/lipoproteins, and of ERN/LRPT vs. ERN on patient-reported flushing symptoms.
Results: ERN/LRPT significantly reduced LDL-C, triglycerides, non-HDL-C, and Apo B, and increased HDL-C and Apo A-I in the total population (Table) and in statin naïve pts. ERN/LRPT produced significantly less flushing than ERN during initiation (Week 1) and chronic therapy for all prespecified endpoints (incidence, intensity, bothersomeness, sleep difficulty, discontinuation). ERN pts reported more moderate or greater flushing than ERN/LRPT pts during the 24 wk treatment ($p<0.001$ across wks 6-24). By wk 24, the frequency of moderate or greater flushing was 0.7 days/wk among ERN pts vs. 0.2 days/wk for ERN/LRPT and PBO pts. ERN/LRPT was well tolerated.
Conclusions: ERN/LRPT 2g, given alone or with a statin, produced significant, durable improvements in multiple lipoprotein parameters. The improved tolerability of ERN/LRPT supports a simplified 1g→2g dosing regimen and should allow more pts to reach and maintain a 2g therapeutic dose.

% Change from Baseline in Lipids across Weeks 12 through 24*

	LS Mean (95% CI)		
Lipid Parameter	ERN/LRPT 2g	Placebo	Difference
LDL-C	-18.9 (-21.0, -16.8)	-0.5 (-3.3, 2.4)	-18.4 (-21.4, -15.4)
HDL-C	18.8 (17.2, 20.4)	-1.2 (-3.4, 1.0)	20.0 (17.7, 22.3)
TG, median	-21.7 (-23.9, -19.5)	3.6 (-0.5, 7.6)	-25.8 (-29.5, -22.1)
Non HDL-C	-19.0 (-20.8, -17.2)	0.8 (-1.6, 3.3)	-19.8 (-22.4, -17.3)
Apo B	-16.4 (-18.0, -14.7)	2.5 (0.2, 4.7)	-18.8 (-21.2, -16.5)
Apo A-I	11.2 (10.1, 12.4)	4.3 (2.7, 5.9)	6.9 (5.3, 8.6)

*Patients with at least one post-titration measurement included in the analysis.

P716 Enhanced expression of immunoproteasomes and CD8+ T-cells in atherosclerotic lesions - implications for the involvement of MHC class I antigen presentation

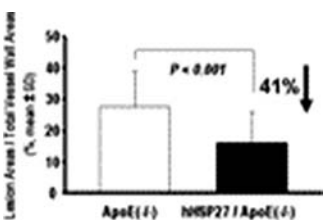
S. Meiners[1], A. Nittmann[2], H. Kunte[1], L. Harms[1], G. Baumann[1], V. Stangl[1], K. Stangl[1]. *[1]Charite - Universitaetsmedizin Berlin CCM, Kardiologisches Forschungslabor, Berlin, Germany; [2]Charite - Universitaetsmedizin Berlin, CCM, Berlin, Germany*

Background: Inflammatory mechanisms and humoral immune responses have been implicated in the pathogenesis of atherosclerosis. However, little is known about the contribution of MHC class I antigen presentation, which involves proteolytic processing of endogenous proteins by the proteasome, subsequent presentation of the generated epitopes in the context of MHC class I molecules, and eventually induction of cytotoxic CD8+T-cell responses. In this study, we analyzed expression of immunoproteasomes and counted the number of CD8+ T-cells in weak and severe atherosclerotic lesions of carotid arteries.
Methods and Results: Paraffin-embedded material of the carotid artery of thrombendarterectomized patients was immunohistochemically analyzed for expression of the immunoproteasomal subunit LMP7 and for the presence of CD8+ T-cells using the LSAB method. We studied a cohort of 65 patients with matched weak and severe lesions and correlated our expression data with patients' data. Comprehensive quantitative analysis of CD8+ T cells in these lesions revealed a positive correlation of CD8+ T-cells and lesion severity; i.e. the more severe the lesions, the more CD8+ T-cells were present. Similarly, expression of the immunoproteasomal subunit LMP7, which is a major catalytic subunit of the proteasome and is known to be induced by cytokines, was increased in more severe lesions. Interestingly, smokers had a significantly increased number of CD8+ T cells in weak lesions compared to non-smokers.
Conclusion: Our data show for the first time a possible involvement of MHC class I antigen presentation in atherosclerosis. It is tempting to speculate that enhanced oxidative stress as observed in smokers might alter generation of antigenic MHC class I epitopes thus contributing to lesion progression by activation of a cytotoxic T-cell response within the atherosclerotic plaque.

P717 Overexpression of the estrogen receptor beta associated protein, Heat Shock Protein 27, is atheroprotective

E.R. O'brien, X. Zhoa, Y.-C. Chen. *University of Ottawa Heart Institute, Cardiology, Ottawa, Canada*

Recently, we discovered that Heat Shock Protein 27 (HSP27) is an estrogen receptor associated protein that represses estrogen mediated transcription (Miller et al, ATVB 2005). Moreover, in human coronary arteries, the expression of HSP27 decreases with the progression of atherosclerotic disease stage and serum levels are >3-fold higher in normal controls compared to patients with angiographic evidence of coronary artery disease.
Purpose: To determine if HSP27 is in fact protective against the development of atherosclerosis.
Methods: Female mice over-expressing human HSP27 (hHSP27) were crossbred with atherosclerosis-prone apoE null mice (apoE) to yield hHSP27apoE mice (n=6), and compared to apoE mice (n=6) for aortic lesion development. All mice were fed a cholesterol supplemented diet for 4 weeks, and euthanized at age 10 weeks.
Results: All mice were viable, and showed no difference in body weight or length. Similarly, cholesterol levels were similar (approximately 1100 mg/dL). The percentage aortic lesion area, measured by quantitative histomorphology of en face specimens, was reduced by 41% in the hHSP27apoE vs. apoE mice ($p<0.001$). Moreover, there was a decrease in the degree of vessel wall lipid deposition and inflammation in the hHSP27apoE vs. apoE mice.



Conclusions: Over-expression of HSP27 is associated with attenuated atherogenesis. Coupled with human data on this protein, HSP27 appears to be a novel biomarker for atherosclerosis.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P718 Liver X receptor-dependent regulation of vascular smooth muscle cell proliferation and migration

F. Blaschke[1], M. Umetani[2], O. Leppanen[3], Y. Takata[4], E. Caglayan[2], D.J. Mangelsdorf[1], P. Tontonoz[2], W.A. Hsueh[2], R.K. Tangirala[2]. *[1]Charite, Humboldt University, Clinical And Molecular Cardiology, Berlin, Germany; [2]Dallas, United States of America; [3]Uppsala, Finland; [4]Los Angeles, United States of America*

Liver X receptors (LXRs), members of the nuclear hormone receptor superfamily, consist of two isoforms, LXRα and LXRβ. Previous studies established LXRs as key modulators of both lipid and glucose metabolism and inflammatory signaling. Activation of vascular smooth muscle cells (VSMCs) is not only associated with enhanced cell growth and migration, but also with increased expression of chemoattractants and extracellular matrix proteins. To determine the functional relevance of LXRs in VSMC growth, we used primary aortic VSMCs isolated from LXRα-, LXRβ- and LXRαβ-deficient and littermate wildtype mice. The synthetic LXR agonist (T1317) dose-dependently attenuated proliferation of wildtype VSMCs, whereas no effect of T1317 on cell growth was observed in LXRαβ-deficient VSMCs. While T1317 inhibited proliferation of LXRα-deficient VSMCs, the inhibition was completely lost in LXRβ-deficient VSMCs. Compared to wildtype cells, LXRαβ-deficient VSMCs proliferated slowly and also showed decreased migration in response to plateled-derived growth factor (PDGF-BB). Immunohistochemistry of cross-sections from the uninjured aorta of wildtype and LXRαβ-deficient mice showed a similar number of elastic and smooth muscle cell layers, indicating that arteries in LXRαβ-deficient mice are structurally normal. The in vivo role of LXRs in the control of VSMC proliferation was examined by using a femoral arterial-injury mouse model. Neointimal thickness was significantly decreased in LXRαβ-deficient mice compared to LXR wildtype mice. In addition, neointima formation was drastically decreased in LXR wildtype mice treated with T1317, but not in LXRαβ-deficient animals. Von Willebrand factor immnunostaining showed no difference in reendothelialization four weeks after arterial injury. Next we examined the role of LXRs in cytokine-induced expression of genes, which have been implicated in the pathogenesis of neointima formation. Real-time RT-PCR experiments demonstrated that plasminogen activator inhibitor-1 (PAI-1) expression was significantly higher in LXRαβ-deficient mice, whereas osteopontin expression was lower compared to littermate wildtype mice. In summary, our results demonstrate that LXR ligands attenuate cell growth and neointima formation in a LXRβ-dependent manner. Decreased proliferation and migration of LXRαβ-deficient VSMCs is, at least in part, mediated by a modulation of osteopontin and PAI-1 expression. Thus, LXRβ, but not LXRα plays an important role in VSMC growth and may constitute a novel therapeutic target for the treatment of proliferative vascular diseases.

P719 Aging induces a decreased vascular remodeling response in LDLr-/- mice: identification of quaking as a new player in vascular homeostasis

A.O. Kraaijeveld[1], R. De Nooijer[2], E.E. Van Der Wall[3], J.W. Jukema[3], T.J.C. Van Berkel[2], E.A.L. Biessen[2]. *[1]Lacdr, Biopharmaceutics Dept., Leiden, Netherlands; [2]LACDR, Leiden, Netherlands; [3]Leiden University Medical Centre, Cardiology, Leiden, Netherlands*

Objective: Aging is regarded as a major risk factor for atherosclerosis. It is still unclear if it directly and/or indirectly impacts the process of atherogenesis, and by which genetic pathways this is regulated specifically. Therefore, we not only evaluated the effect of aging in collar induced atherosclerosis on lesion size, composition and vascular remodeling, but also tried to identify differentially regulated genetic pathways in the context of atherosclerosis upon vascular aging.
Methods: Atherosclerotic lesions were elicited in carotid arteries of young (12 weeks, n=16) and aged (52 weeks, n=15) LDLr-/- mice by bilateral perivascular collar placement after six weeks of Western type diet. Six weeks later, left carotid arteries as well as aortic roots were harvested and analyzed histologically. In addition, micro-array analysis was performed on the right carotid arteries.
Results: Carotid plaque (40,500 vs. 14,800 μm^2, $P<0.04$) and media areas (52,300 vs. 33,600 μm^2, $P<0.02$) were larger in young vs. aged mice. In line with this finding, aortic root plaque area was larger in young mice ($7{,}38x10^5$ vs. $5{,}06x10^5$ μm^2, $P<0.03$). Intriguingly, due to a substantial outward remodeling in younger mice (total vessel area 179,400 vs. 113,500 μm^2, $P<0.04$), carotid lumen areas were increased compared to aged mice (86,572 vs. 65,122 μm^2, $P<0.04$). No differences were seen in plaque composition, suggesting that age per se is not a causal factor in plaque stability. Micro-array analysis revealed a significant up-regulation of the vasculogenesis pathway in aged mice, with specific up-regulation of the Quaking (Qk) gene. Qk protein was detected in carotid and aortic root plaques and mainly observed in endothelial cells and macrophages. Qk function was subsequently assessed in vitro; gene silencing with Qk siRNA caused an increased wound healing response after scratching an endothelial cell monolayer (P=0.02), indicative of an important role of Qk in cell proliferation and/or migration.
Conclusions: Decreased atherogenesis and outward remodeling accompany increasing age in our collar induced atherosclerosis model. Qk seems to be an important player in age-dependent vascular homeostasis.

P720 Potential membrane adaptors for atypical GPI-anchored T-cadherin

D. Ivanov[1], M. Philippova[1], M. Joshi[1], P. Erne[2], T. Resink[1]. *[1]Basel University Hospital, Department of Research, Basel, Switzerland; [2]Kantonsspital Luzern, Division of Cardiology, Luzern, Switzerland*

T-cadherin (T-cad) is an atypical GPI-anchored member of the cadherin superfamily. In the cardiovascular system T-cad is upregulated on endothelial and smooth muscle cells in pathological conditions. Overexpression of T-cad and it's ligation stimulate angiogenesis as well as endothelial cell proliferation, migration and survival. Membrane adaptors transmitting signals from the cell surface T-cad to its intracellular targets are not known. The aim of our study was to identify membrane signalling partners of T-cad. HUVEC were infected with adenoviral vector encoding chimeric T-cad with c-myc tag on the N-terminus, lysed with Triton X-114, and T-cad/c-myc protein was precipitated with anti-c-myc antibodies. The samples were separated on gradient SDS-PAGE, and proteins coprecipitated with T-cad/c-myc were subjected by Nanoflow liquid chromatography-tandem mass spectrometry. The following proteins were identified: glucose-related protein GRP-78, GABA receptor alfa-1 subunit, integrin beta-3 and two hypothetical proteins LOC124245 and FLJ32070. Integrin beta-3 and GRP-78 are good candidates for the role of membrane adaptors of T-cad-dependent signalling since they are involved in control of angiogenesis and survival. Colocalization of integrin beta-3 and GRP-78 with T-cad was confirmed by immunoblotting of precipitates with specific anti-integrin beta-3 and anti-GRP-78 antibodies and by confocal microscopy. We also show that blocking anti-GRP78 antibodies reduce phosphorylation levels of Akt and GSK3 proteins suggesting that GRP78 may mediate T-cad effects on Akt pathway.
Conclusion: We identified integrin beta-3 and GRP-78 as potential molecular adaptors that may mediate T-cad signalling effects in vascular endothelial cells.

P721 Homocysteine induces VCAM-1 gene expression through NF-kB and NAD(P)H oxidase activation: protective role of Mediterranean diet polyphenolic antioxidants

M.A. Carluccio[1], M. Massaro[1], M. Carluccio[1], E. Scoditti[1], C. Storelli[2], A. Distante[1], R. De Caterina[3]. *[1]CNR-Institute of Clinical Physiology, Institute of Clinical Physiology, Lecce, Italy; [2]University of Lecce, Laboratory of General Physiology, Lecce, Italy; [3]G. d'Annunzio University, Institute of Cardiology, Chieti, Italy*

Introduction: Hyperhomocysteinemia is a recognized risk factor for atherosclerotic vascular disease, but molecular mechanisms are no completely understood. Because VCAM-1 expression is crucial in monocyte adhesiveness, we evaluated the NF-κB-related induction of VCAM-1 by homocysteine (Hcy) and the possible inhibitory effect of specific dietetic polyphenolic antioxidants, such as trans-resveratrol (RSV) and hydroxytyrosol (HT).
Methods and Results: We found that in human umbilical vein endothelial cells (HUVEC), Hcy, at $\geq$50 μmol/L, but not cysteine, induced VCAM-1 expression at protein and mRNA levels, at enzyme immunoassay and Northern blot, respectively. Transfection studies with deletional VCAM-1 promoter constructs demonstrated that two tandem NF-κB motives in VCAM-1 promoter are necessary for Hcy induced VCAM-1 gene expression. This was confirmed by Hcy induced NF-kB activation at EMSA and the nuclear translocation of its p65 (Rel A) subunit and the degradation of both inhibitors(I)kB-α and -b at Western analysis. Hcy increased intracellular ROS, measured with dichlorofluoresceine fluorescence assays, in HUVEC, by NAD(P)H oxidase activation, determined through the membrane translocation of its p47phox subunit. Antioxidants, NF-κB and NAD(P)H oxidase inhibitors decreased the Hcy inducted intracellular ROS and VCAM-1 expression. Previously, we found that antioxidants RSV and HT inhibited NF-κB mediated VCAM-1 induction by LPS or TNFα. Here we shown that nutritionally relevant concentrations of RSV and HT, but not folate and B vitamins, reduced (>60% inhibition at 10^{-6} mol/L) Hcy-induced VCAM-1 expression and monocytoid cell adhesion to the endothelium.
Conclusions: These data point out that pathophysiologically relevant Hcy concentrations induce VCAM-1 expression through NF-κB-mediated pro-oxidant mechanism. This can be inhibited by natural Mediterranean diet antioxidants, suggesting a their possible therapeutic role in Hcy-induced vascular damage.

P722 Heart rate reduction by If-current inhibition reduces atherosclerosis and improves endothelial as well as erectile function in ApoE-/- mice

F. Custodis[1], M. Baumhaekel[2], N. Schlimmer[2], F. List[2], M. Boehm[2], U. Laufs[2]. *[1]Uniklinik des Saarlandes, Cardiology Dept., Homburg, Germany; [2]Uniklinik des Saarlandes, Cardiology, Homburg/Saar, Germany*

Purpose: Elevated resting heart rate has been shown to be associated with increased risk for cardiovascular morbidity and mortality. Erectile dysfunction is related to endothelial dysfunction and atherosclerosis due to very similar risk factors. Therefore we hypothesized that heart rate reduction may influence endothelial- and erectile function and tested the effects of the I_f -current inhibitor ivabradine in high-cholesterol fed ApoE-/- mice.
Methods and Results: Male ApoE-/- mice were treated with the I_f -current in-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

hibitor Ivabradine (10 mg/kg/d p.o.) or vehicle in parallel with a high-cholesterol diet for 7 weeks to induce atherosclerosis. Treatment with ivabradine led to a marked heart rate reduction (ivabradine: 472±9 bpm vs vehicle: 545±11 bpm, $p<0.01$). Plasma cholesterol levels as well as systolic blood pressure were not different between groups. Atherosclerotic lesions were quantified by standardized protocols after oil-red O staining. High cholesterol feeding led to severe atherosclerotic lesion formation in the aortic sinus and the aorta. Ivabradine reduced atherosclerotic plaque size to 24±2% (vs 50±5%, $p<0.05$). Endothelial function of aortic rings and erectile function in corpora cavernosa (CCS) were determined in an organ bath chamber under physiological conditions (pH 7.4, 37°C). Endothelium dependent relaxation of aortic rings and the corpora cavernosa to carbachol was significantly improved in ivabradine fed ApoE-/- mice compared to controls ($p<0.01$). Endothelium independent relaxation of CCS and aortic rings to nitroglycerin was not different between groups. Real-time PCR analysis showed significant upregulation of vascular eNOS to 156±11% ($p<0,05$) in aortic rings after ivabradine treatement. Lipidperoxidation as marker of chronic oxidative stress was reduced in the vasculature of the ivabradine group by 30±8% compared to vehicle treated mice ($p<0.05$).

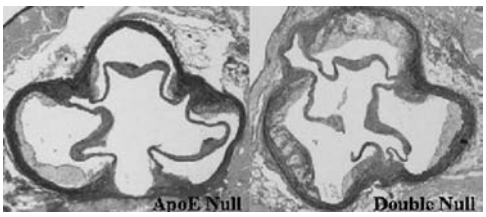
Conclusions: Reduction of resting heart rate in cholesterol-fed ApoE-/- mice treated with ivabradine reduces atherosclerotic lesion formation, improves endothelial function, upregulates eNOS expression and reduces vascular lipid peroxidation. These vasculoprotective effects are associated with improved erectile function. These results support the importance of heart rate reduction in vascular prevention and warrant further clinical testing.

P723 Deletion of tumour necrosis factor-related apoptosis-inducing ligand attenuates development of atherosclerosis in ApoE null mice

V. Watt[1], S. Francis[2], D. Crossman[1]. *[1]University of Sheffield, Cardiovascular Research Unit, Sheffield, United Kingdom; [2]University of Sheffield, Cardiovascular Research Unit, Sheffield, United Kingdom*

Purpose & Methods: The role of TRAIL (TNFSF10) in atherosclerosis has not been fully elucidated. Recent research suggests that administration of TRAIL leads to a reduction in lesion size in diabetic ApoE null mice. In order to determine if TRAIL has any effect on atherosclerotic lesion formation, we generated a double knockout (TRAIL null, ApoE null) mouse colony by cross-breeding. Mice were fed chow or a cholate-free Western diet for 8 & 12 weeks (56 mice in total, n=6-8 for each group). En face whole aortae stained with oil red O & paraffin sections of the aortic sinus & brachiocephalic artery were analyzed by histomorphometry. Data were compared to ApoE null mice.

Results: Double null mice fed on western diet (8 weeks) or chow (12 weeks) had larger lesions in the en face aorta preparations than controls ($p<0.05$, $p<0.0001$ respectively). Similar data were seen in the aortic sinus sections: double null mice fed chow or western diet for 8 weeks had larger lesions compared to ApoE null controls ($p<0.05$, $p<0.001$, see figure). Interestingly, there was no difference between the groups at 12 weeks. In the brachiocephalic artery lesions, no difference in size was seen at the 8 week timepoint. At 12 weeks, double null mice fed chow, again had larger lesions when compared to ApoE null mice on the same diet ($p<0.05$).



Aortic Sinus after 8 weeks Western diet

Conclusion: Taken together, these results indicate that the presence of TRAIL attenuates the development of atherosclerotic lesions in atherosclerosis-prone mice. Further work is now underway to determine the effect of TRAIL deletion on the cellular content of these lesions.

P724 High glucose inhibits nitric oxide production through increased osmolarity, without inducing the surface expression of adhesion molecules in human endothelial cells

R. Madonna[1], M. Zurro[2], E. Montebello[2], G. Lazzerini[3], R. De Caterina[4]. *[1]"G. d'Annunzio" University, Chair of Cardiology, Chieti, Italy; [2]Cheti, Italy; [3]CNR, Institute of Clinical Physiology, Pisa, Italy; [4]Chieti, Italy*

Introduction: Previous research has suggested that high glucose induces endothelial dysfunction in terms of decreased nitric oxide (NO) availability and increased endothelial adhesion molecule expression. We investigated the contribution of hyperosmolarity in the regulation of NO production and adhesion molecules expression in human endothelial cells exposed to high glucose.

Methods: Human umbilical vein endothelial cells (HUVEC) were exposed to 5.5 mmol/L glucose (control), high glucose (HG, 30 mmol/L) and hyperosmolar control (glucose 5.5 mmol/L plus mannitol 25 mmol/l). Analyses of Ser1146-phosphorylated nitric oxide synthase (Ser1146-eNOS), the expression of adhesion molecules VCAM-1, ICAM-1 and E-Selectin (by enzyme immunoassay and immunoblotting), and the adhesion of U937 cells to the endothelium (rotational adhesion assay), after short-term (0, 12, 24, 48, 72 h) and long-term incubation (1 and 2 weeks), were performed. NO production was measured by the Griess assay.

Results: Both the short- and long-term exposure to either HG or the hyperosmolar condition increased the total cellular content of VCAM-1, ICAM-1 and E-Selectin (densitometric units), but did not exert any significant effect on their surface expression or on U937 cell adhesion. After short- and long-term incubations to both HG and to the hyperosmolar condition, a downregulation of Ser1146-eNOS (densitometric units) and NO production (micromol/100.000 cells) were observed (Table).

	48 h			1 week		
	Basal	HG	High Mannitol	Basal	HG	High Mannitol
VCAM-1	7±0.5	25±5*	40±7*	15±5	60±10°	95±12°
ICAM-1	50±10	170±10*	185±21*	78±20	200±25°	225±35°
E-Selectin	10±5	30±7*	45±5*	17±8	55±4°	70±7°
Nitrite	11.4±0.3	4.3±0.9*	3.6±0.3*	13.3±1	4.4±0.5°	2.8±0.5°
Ser^{1146}-eNOS	50±5	20±5*	17±4*	53±10	13±4°	10±3°

Mean ± SD; *$p<0.05$ vs 48 hours basal; °$p<0.05$ vs 1 week basal; units of measures: densitometric units (for expression of VCAM-1, ICAM-1, E-Selectin and Ser1146-eNOS at immunoblotting) and micromol/100.000 cells (for nitrite production).

Conclusion: High glucose decreases NO avaliability through a mechanism mediated by hyperosmolarity, thus contributing to detrimental vascular consequences of hyperglycaemic states.

VASCULAR BIOLOGY AND ATHEROSCLEROSIS

P725 DNA-variants in cell cycle inhibitors CDKN1C and CDKN1B increase the risk of myocardial infarction

I. Rodriguez, E. Coto, J.R. Reguero, P. Gonzalez, P. Roman, I. Lozano, M. Martin, V. Alvarez, C. Moris. *Hospital Universitario Central de Asturias, Genetica Molecular, Oviedo, Spain*

Purpose: Atherosclerosis is characterised by excessive proliferation of leukocytes and vascular smooth muscle cells within the arthery wall. In mice, manipulation of cyclin dependent kinase inhibitors (CKIs) such as CDKN1A (p21) and CDKN1B (p27) modifies the risk of atherosclerosis. In humans, CDKN1A, CDKN1B, and CDKN1C (p57) are differentially expressed in normal vs. atherosclerotic vessels. The aim of this study was to determine the role of DNA polymorphisms in these CKIs in the risk of suffering myocardial infarction (MI).

Methods: A total of 332 MI-patients (all men and younger than 55 years), and 329 healthy controls were studied. We genotyped 10 polymorphisms in the coding and promoter regions of CDKN1A, CDKN1B, CDKN1C, and CDKN2A through PCR followed by digestion with restriction enzymes (RFLP) or electrophoresis on polyacrilamide gels (SSCA). Allele and genotype frequencies were compared by means of a chi-squared test.

Results: For the microsatellite repeat in the CDKN1C gene we found a significantly increased frequency of the 11/13 and 11/12 repeats in patients, while the frequency of 11/11 homozygotes was decreased in patients (OR=0.62; P=0.002). This suggests that long repeat alleles (12 and 13) could confer a higher risk of developing MI, while the 11/11 genotype could be protective. A CDKN1B promoter polymorphism (–838 C/A) was previously associated with MI and affected gene expression in vitro. We found a synergistic effect for the -838 AA + 11/13 repeats or AA + 11/12 repeats in the risk for MI, compared to either genotype alone. We did not find any significant difference in the allelic or genotype frequencies of the four polymorphisms of p21 and the four of p16, between patients and controls.

Conclusions: Two polymorphisms in CDKN1B and CDKN1C genes were associated with MI-risk in our population, in a synergistic way for the -838 C/A (CDKN1B) and promoter microsatellite (CDKN1C). Our work supported a role for the cell cycle inhibitor genes in atherosclerosis and MI, making them valuable therapeutical targets for treating this disease.

P726 Cholesterol rich plasma milieu independently induces select phenotype endothelial microparticles expression and alters endothelial progenitors proliferative capacity

M. Calfa, L. Mauro, A. Ferreira, H. Dodson, K. Lens, W. Jy, Y. Ahn, J. Jimenez, E. De Marchena. *University of Miami, Division of Cardiology, Miami, United States of America*

Background: Endothelial microparticles (EMP) antigenic profile was recognized to mirror the endothelial cellular (EC) injury. Distinct EMP CD 31+/42b- > CD 62E+ phenotype was identified in EC apoptosis. Elevated EMP counts have been observed with multiple cardiac risk factors. In contrast, EC repair associated circulating endothelial progenitors (CEPC) were determined at decreased levels.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

The link between cholesterol and EMP, EC injury pattern respectively CEPC was not independently studied. Therefore, we analyzed in patients with no interfering risk factors the impact of high (HC) versus normal cholesterol (NC) on EMP release, CEPC proliferation, circulating levels and correlation with HC and low-density lipoprotein (LDL).
Methods: Subjects were age, gender matched. Flow cytometry with human anti-CD31, 42b, 62E identified EMP. HC, NC group derived CEPC underwent colony formation assay (CFU). Acquired coronary artery endothelial cells (CAEC), CEPC from NC subjects were cultured with plasma from each group. All methods were previously reported ($p<0.05$ significant).
Results (table): Cholesterol, LDL were higher in the HC group (p=0.001 each). Circulating CD31+/42b- EMP but not CD 62E+ were increased in HC plasma as opposed to NC (p=0.001). HC induced cultured CAEC, CD 31+/42b-release unlike NC (p=0.01). There was no induction on CD 62E+ (p=0.62). Correlation between cholesterol, LDL and EMP count revealed a significant positive association only with CD 31+/42b- but not CD 62E+. NC subjects derived CEPC proliferation was less when exposed to HC compared to NC plasma (p=0.002). CEPC levels from HC patients were lower in contrast to NC (p=0.001). CEPC relation with HC was negative and similarly to EMP.

Results

n=17 (age < 45 years)	High cholesterol	Normal cholesterol
Cholesterol level (mg/dL)	242.35±44.09	140.00±17.59
LDL level (mg/dL)	182.07±13.76	85.57±11.34
CD31+/42b- level (x10^6/mL)	1.19±0.61	0.34±0.08
CD62E+ level (x10^6/mL)	0.29±0.10	0.26±0.11
CAEC CD31+/42b- release count (x10^6/mL)	0.75±0.24	0.23±0.1 Negative control 0.19±0.07
CAEC CD 62E+ release count (x10^6/mL)	0.26±0.07	0.24±0.6 Negative control 0.21±0.4
CEPC proliferation assay (CEPC CFU)	12±4	25±4
CEPC level (CEPC CFU)	10±2	25±4
Correlation Analysis CD31+/42b- relation	positive with Cholesterol R=0.60 p=0.001	positive with LDL R=0.71 p=0.0001
Correlation Analysis CD 62E+ relation	no relation with Cholesterol R=0.12 p=0.49	and with LDL R=0.25 p=0.19
Correlation Analysis CEPC relation	negative with Cholesterol R= -0.87 p=0.001	negative with EMP CD31+/42b- R= -0.51 p=0.004

Conclusion: Cholesterol rich plasma decreases CEPC proliferative capacity also induces select phenotype EMP release, suggestive for EC apoptosis. In addition, with HC milieu the elevated EMP count, measure for increased EC injury reveals a negative relation with the low CEPC level, marker for diminished repair potential. Therefore, HC plasma milieu demonstrates an independent, dual target impact as reflected by circulating EMP, CEPC analysis.

P727 Contribution of KLOTHO and osteoprotegerin gene polymorphism to coronary artery stenosis and calcification

S.H. Jo, S.G. Kim, N.R. Joo, S.R. Choi, E.J. Kim, H.S. Kim, G.Y. Cho, H.J. Kim, C.Y. Rhim, Y.J. Choi. *Hallym University Sacred Heart Hospital, Division of Cardiology, Internal Medicine, Anyang, Gyeonggi-Do, Korea, Republic of*

Background: KLOTHO gene variant has been reported to be associated with human aging, stroke and longevity and serum level of osteoprotegerin (OPG) has been suggested to be associated with osteoporosis, early coronary artery disease and coronary calcification. However, there was few study on relation of the coronary artery disease and calcification with KLOTHO and OPG gene mutation.
Methods and Results: Four hundreds and thirty four patients referred for coronary angiography due to their chest pain were enrolled. All the patients have undergone coronary angiography. The genotype of G395A polymorphism for KLOTHO and A163G, G209A, T245G, T950C for OPG gene polymorphism were investigated. Of the patients received coronary angiography, 51.8% (225/434) patients had a coronary artery stenosis defined as $\geq$ 50% diameter stenosis at no less than one coronary artery by coronary angiography. Homozygote or heterozygote for G395A allele of KLOTHO were significantly more frequent in patients with coronary artery disease (CAD) than in non-CAD group (30.3% vs 21.5%, p=0.039). In subgroups of age $<$ 60, the G396A mutant is more frequent in CAD group (35.3% [24/68] vs 18.8% [19/101], p=0.016) but in patients $\geq$ 60 years old, there was no difference (29.0% vs 31.7%, p=0.473). After multivariate analysis using multiple logistic regression model, the age, dyslipidemia, smoking, elevated serum creatinine and KLOTHO gene G395A mutant was the independent risk factors for CAD (OR =1.649, CI [1.030-2.639], p=0.037). The allele frequency and polymorphisms in the 4 promoter region of OPG gene were not different between CAD and non-CAD patients (at least 1 mutant among 4 polymorphisms, 67.6% vs 65.6%, respectively, p=0.658) and were not associated with the coronary calcification. In combined analysis of KLOTHO and OPG genes mutations in age $<$70 years old, the concomitant KLOTHO and OPG (at least one mutant among 4 polymorphism) mutation was significantly more frequent in CAD patients than in non-CAD group (20.6% vs 10.1% respectively, p=0.011).
Conclusions: The KLOTHO gene G395A allele carrier state was identified as a novel risk factor of coronary artery disease and OPG gene mutation was not related with coronary artery calcification or stenosis in Korean population.

P728 Intrauterine exposure to maternal hypercholesterolemia increases the susceptibility to development of atherosclerosis in adult life

F.E. Alkemade[1], A.C. Gittenberger-De Groot[1], A.E. Schiel[1], J.C. Vanmunsteren[1], B. Hogers[1], L.M. Havekes[2], K. Willems Van Dijk[1], M.C. Deruiter[1]. *[1]Leiden University Medical Center, Anatomy And Embryology Dept., Leiden, Netherlands; [2]TNO Quality of life, Leiden, Netherlands*

Purpose: Maternal hypercholesterolemia in the human population is associated with a higher incidence and faster progression of atherosclerotic lesions in neonatal offspring. We hypothesized that intrauterine exposure of a genetically non-affected fetus to maternal hypercholesterolemia leads to accelerated development of atherosclerosis in adult life.
Methods: To exclusively investigate the epigenetic in utero effect we generated genetically identical heterozygous apoE-deficient offspring from mothers with a normocholesterolemic wild type or hypercholesterolemic apoE-deficient background. At embryonic day 17.5 the carotid arteries of the offspring from apoE-deficient mothers were analyzed morphologically and compared with offspring from wild type mothers. In adult female progeny on a high fat diet, a constrictive collar was placed around the left common carotid artery to trigger neointima formation.
Results: A significant loss of endothelial cell volume (24.81±1.11x10E4 vs. 18.81±1.54x10E4 μm^3) was observed in fetal life but no fatty streak formation. Spontaneous vascular lesions were not detected in the adult period. Four weeks after collar placement severe neointima formation was detected in offspring of hypercholesterolemic mothers (5.04±1.65x10E6 μm^3; 9/10) compared with only minor lesions in offspring of wild type mothers (0.28±0.18x10E6 μm^3; 2/10).
Conclusions: The susceptibility to atherosclerosis of morphologically normal adult vessels is already imprinted during prenatal development and is not genetically determined in our model. Thus, in our model with both prenatal and postnatal risk factors, vascular pathology in adult life is aggravated. Future research will concentrate on the mechanisms involved in this priming process as well as on prevention strategies.

P729 HIF-1alpha expression is associated with an atheromatous inflammatory plaque phenotype and upregulated in activated macrophages

A. Vink, A.H. Schoneveld, D. Lamers, A.J.S. Houben, P. Van Der Groep, P.J. Van Diest, G. Pasterkamp. *University Medical Center Utrecht, Pathology Department, Utrecht, Netherlands*

Purpose: Neoangiogenesis and inflammation are important features in atherosclerotic plaque destabilization. The transcription factor hypoxia inducible factor-1 alpha (HIF-1α) is a key regulator of angiogenesis and also involved in inflammatory reactions. We aimed to explore a role for HIF-1α in atherosclerotic plaque destabilization.
Methods and Results: Immunohistochemical HIF-1α expression was observed in 18/37 (49%) carotid and in 9/15 (60%) femoral endarterectomy specimens. HIF-1α staining was predominantly present in macrophages and macrophage derived foam cells and to a lesser extent in smooth muscle cells. Expression of HIF-1α was associated with presence of a large extra cellular lipid core (P=0.03) and macrophages (P=0.02). A strong association was observed between expression levels of HIF-1α and vascular endothelial growth factor (VEGF), an important down stream target of HIF-1α (P=0.006). In addition, expression of HIF-1α co-localized with VEGF expression. The average number of plaque microvessels was higher in plaques with no or minor HIF-1α staining than in plaques with moderate or heavy HIF-1α staining (P=0.006). In human macrophages, lipopolysaccharide activation induced HIF-1α expression under normoxic conditions.
Conclusions: In atherosclerotic plaque, the transcription factor HIF-1α is associated with an atheromatous inflammatory plaque phenotype and with VEGF expression. HIF-1α expression is upregulated in activated macrophages under normoxic conditions. These results provide evidence for a link between atherosclerotic inflammatory reactions and plaque angiogenesis.

P730 Chlamydia pneumoniae infection initiates the development of atherosclerosis in OLETF and LETO rats - the role of platelet-derived growth factor-B

S.-W. Jang, K. Chang, W.-S. Shin, S.-H. Kim, H.-J. Park, C.-S. Park, D.-B. Kim, P.J. Kim, S.-H. Ihm, K.-B. Seung. *College of Medicine, Catholic University, Cardiology, Seoul, Korea, Republic of*

Purpose: There is an increasing body of evidence that Chlamydia pneumoniae is linked with atherosclerosis. Animal studies have shown that C. pneumoniae contributes to the acceleration of atherosclerotic lesions. However, studies on the initiation of atherosclerosis are sparse and limited to rabbit. It has been reported that C. pneumoniae infection of endothelial cells activates platelet-derived growth factor-B (PDGF-B), which leads to proliferation and migration of smooth muscle cells. The aim of this study was to investigate the role of C. pneumoniae infection in initiating the atherosclerotic lesions in rat models.
Methods: Thirty 11-week-old Otsuka Long-Evans Tokushima Fatty (OLETF) rats, type 2 diabetic rats, and thirty age-matched Long-Evans Tokushima Otsuka

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(LETO) rats were either mock-inoculated or inoculated with C. pneumoniae intranasally at 11, 13 and 15 weeks of age and maintained on a high-cholesterol diet. The serum levels of lipid profiles, plasminogen activator inhibitor-1 (PAI-1), monocyte chemoattractant protein-1 (MCP-1) and C-reactive protein (CRP) were measured by ELISA at 24 weeks and 40 weeks of age. Atherosclerotic lesion areas (ALA) were measured and immunohistochemical staining with Chlamydia genus-specific monoclonal antibody, anti-human alpha smooth muscle actin and anti-rabbit PDGF-B were performed on the ascending aorta at 40 weeks of age.
Results: Chlamydial antigens were detected in C. pneumonia-infected OLETF and LET rats. The mean serum PAI-1 level of OLETF rats was higher than that of LETO rats ($p < 0.05$) regardless of C. pneumoniae infection state. However, there were no differences in the serum MCP-1 and CRP levels between OLETF and LETO rats. While no atherosclerotic lesion was observed in mock-infected LETO rats, mock-infected OLETF rats showed moderate atherosclerotic lesions. C. pneumoniae-infected OLETF rats showed greater ALA than the other groups (mock-infected LETO, 0 mm^2; C. pneumoniae-infected LETO, 3.29 ± 1.23 mm^2; mock-infected OLETF, 4.91 ± 2.11 mm^2; C. pneumoniae-infected OLETF, 9.20 ± 4.62 mm^2, $p < 0.05$). Characteristically, atherosclerotic lesions in rats were intimal thickening mainly composed of smooth muscle cells. ALA positively correlated with the presence and the extent of PDGF-B expression in the aortic wall ($p < 0.01$).
Conclusion: We observed that chronic infection of C. pneumoniae initiated the development of atherosclerosis in the LETO rats and accelerated the atherosclerosis in the OLETF rats. C. pneumoniae might induce smooth muscle proliferation and resultant intimal thickening through modulation of PDGF-B.

P731 Fungal rDNA signatures in coronary atherosclerotic plaques

N.E. El Mokhtari[1], A. Rehman[2], P. Rosenstiel[1], M. Lins[3], S. Schreiber[1], R. Simon[3], S.J. Ott[2]. *[1]University-Hospital Schleswig-Holstein, Department of Cardiology, Kiel, Germany; [2]Christian-Albrechts-University Kiel, Institute for Clinical Molecular Biology, Kiel, Germany; [3]University-Hospital Schleswig-Holstein„ Department of Cardiology, Kiel, Germany*

Bacterial DNA has been found in coronary plaques and it has therefore been concluded that bacteria may play a role as trigger factors in the chronic inflammatory process underlying coronary atherosclerosis. However, the microbial spectrum is complex and it is not known whether microorganisms other than bacteria are involved in coronary disease. Fungal 18S rDNA signatures were systematically investigated in atherosclerotic tissue obtained through catheter-based atherectomy of 38 patients and controls (unaffected coronary arteries) using clone libraries, denaturating gradient gel analysis (DGGE), in situ hybridization, and fluorescence in situ hybridization (FISH). Fungal DNA was found in 35 of 38 (92,11%) coronary heart disease patients by either PCR with universal primers or in-situ hybridization analysis (n=5), but not in any control sample. In a clone library with more than 350 sequenced clones from pooled patient DNA, an overall richness of 19 different fungal phylotypes could be observed. Fungal profiles of CHD patients obtained by DGGE analysis showed a median richness of fungal species of 5 (range from 2 to 9) with a high inter-individual variability (mean similarity 18.83%). For the first time, the presence of fungal components in atherosclerotic plaques has been demonstrated. Coronary atheromatous plaques harbour diverse and variable fungal communities suggesting a polymicrobial contribution to the chronic inflammatory etiology.

P732 Evidence for genetic regulation of endothelial progenitor cells and their role as biological markers of atherosclerotic susceptibility

A. Whittaker, J.S. Moore, M. Vasa, S. Stevens, N.J. Samani. *University of Leicester, Cardiovascular Sciences, Leicester, United Kingdom*

Objective: Endothelial progenitor cells (EPCs) are found in the peripheral circulation and are capable of endothelial repair and neovascularisation. EPC number and function are reduced in subjects with cardiovascular risk factors or proven coronary artery disease (CAD). We hypothesized that EPC number and/or function may be genetically regulated and may vary in healthy adult offspring depending on parental history of CAD.
Methods and results: 102 non-diabetic subjects, comprising 27 parents with angiographically proven premature CAD and 24 healthy controls, each with one healthy adult offspring were studied. We measured the number of circulating CD34+VEGFR-2+ and AC133+VEGFR-2+ EPCs, the number of EPCs grown in culture, and migration capacity of cultured EPCs towards vascular endothelial growth factor. There was significant correlation in the number of cultured EPCs between parents and offspring ($R = 0.642$, $p < 0.001$). Offspring of subjects with CAD had significantly higher numbers of circulating CD34+VEGFR-2+ and AC133+VEGFR-2+ cells ($p = 0.018$ and $p < 0.001$, respectively). There was no difference in migration capacity between groups.
Conclusions: Our results suggest that EPC number is, at least in part, genetically regulated. Circulating EPCs may represent biological markers of occult vascular damage in offspring with hereditary risk of CAD.

P733 Angiotensin II and PDGF utilise similar molecular mechanisms to induce coronary atherosclerosis

C.L. Allen[1], V.S. Mahadevan[2], M. Campbell[1], P.P. Mckeown[1], U. Bayraktutan[2]. *[1]University of Nottingham, Division of Stroke Medicine, Nottingham, United Kingdom; [2]Queen's University Belfast, Belfast, United Kingdom*

Platelet-derived growth factor (PDGF) and angiotensin II (ang II) have been implicated in atherogenesis. This study investigated whether these agents induce atherosclerosis through similar mechanisms i.e. enhanced oxidative stress, cell migration and proliferation using coronary artery smooth muscle cells (SMC). SMC were obtained from a commercial source and characterised by SM alpha-actin staining. The prooxidant [NAD(P)H oxidase] and antioxidant [eNOS, superoxide dismutase (SOD) and glutathione peroxidase (GPx)] enzyme activities were measured by specific assays. Both ang II and PDGF produced equal decreases ($\sim$50%, $p<0.05$) and increases (4 to 6-fold, $p<0.01$) in eNOS and total SOD activities, respectively. However, their effect on GPx activity was agent-specific in that ang II (5-50 nmol/L) significantly decreased GPx activity ($\sim$25%, $p<0.05$) while PDGF (5-50 ng/ml) failed to alter its activity. Chemotaxis experiments, using the Dunn chamber, revealed that both agents elicited a directed and comparable SMC migration which was dramatically inhibited by mevastatin (0.1μmol/L), enalapril (an angiotensin converting enzyme inhibitor; 1μmol/L), losartan (ang II type 1 receptor blocker; 1μmol/L) or MnTBAP (a cell-permeable SOD mimetic; 50 μmol/L). The impacts of ang II and PDGF on cell proliferation were examined using two independent methods based on the determination of total cellular protein levels and [3H]-thymidine incorporation rates. The data revealed that both agents generated dose- and time-dependent increases in SMC growth which were more prominent with ang II. For example, 442 ± 23 μg and 393 ± 21 μg of total proteins were detected at aforementioned higher doses of ang II and PDGF, respectively compared to untreated controls (303 ± 21 μg, $p<0.05$). Pretreatment of SMC with losartan (1 μmol/L), mevastatin (0.1 μmol/L) or a free radical scavenger, namely Tiron (50 μmol/L) attenuated both ang II- and PDGF-induced cell proliferation thereby indicating a pivotal role for free radicals in SMC growth. Experiments investigating the contributions of putative signal transduction pathways to ang II and/or PDGF-mediated changes demonstrated equal involvements of MAPK and protein kinase C in these changes. In conclusion, ang II and PDGF may promote atherosclerosis, at least in experimental conditions, through similar molecular mechanisms i.e. enhanced oxidative stress, SMC proliferation and migration that can be suppressed by statins, free radical scavengers and agents which regulate the synthesis and activity of ang II.

ATHEROSCLEROSIS – FROM BENCH TO BED

P734 High prevalence of subclinical atherosclerosis in psoriatic arthritis patients without clinically evident cardiovascular disease or classic atherosclerosis risk factors

C. Gonzalez Juanatey[1], M.A. Gonzalez-Gay[1], J. Llorca[2], J. Martin[3]. *[1]Hospital Xeral-Calde, Echocardiography Lab. Cardiology Department, Lugo, Spain; [2]University of Cantabria, Preventive Medicine and Public Health, Santander, Spain; [3]CSIC, Instituto de Parasitologia y Biomedicina, Granada, Spain*

Background: Information from series of patients attended to in referral centers indicates that individuals with psoriatic arthritis (PsA) have an increased mortality rate compared to the general population, and the mortality risk is related to disease severity at presentation to clinic.
Objective: To seek for the presence of subclinical atherosclerosis in PsA patients without clinically evident atherosclerosis or its complications and to assess whether demographic or clinical factors affect the development of atherosclerotic disease in a series of patients with PsA attended to in a community hospital.
Methods: Fifty-nine PsA patients that fulfilled the Moll and Wright criteria were recruited from our Hospital. Patients seen during the period of recruitment that had classic cardiovascular risk factors or had suffered cardiovascular or cerebrovascular events were excluded. Fifty-nine healthy matched controls were also studied. Carotid artery intima-media wall thickness (IMT) and carotid plaques were measured in the right common carotid artery. The study was performed using high-resolution B-mode ultrasound.
Results: PsA patients exhibited greater carotid artery IMT (0.699 ± 0.165 mm) than did matched controls (0.643 ± 0.111 mm) ($p= 0.031$; differences of means with a 95% confidence interval [CI]: 0.056, 95% CI: 0.005 - 0.108). Adjusted for age, the carotid IMT was correlated with age at the time of diagnosis of PsA (partial correlation coefficient (r)= -0.264, p= 0.04), disease duration (r= 0.264, p= 0.04), and total cholesterol (r= 0.233, p= 0.01) and LDL cholesterol (r= 0.243, p= 0.01).
Conclusions: The present study shows that PsA patients without cardiovascular risk factors or clinically evident cardiovascular disease have high prevalence of macrovascular disease in the form of increased carotid artery IMT compared with ethnically matched controls.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P735 The value of common carotid artery intima-media thickness in evaluating atherosclerosis

J. Tarjan[1], I. Vassanyi[2], B. Voros[2]. [1]*Hungarian Academy of Sciences, Endothel Working Group, Veszprem, Hungary;* [2]*Pannon University, Information System, Veszprem, Hungary*

Previous studies have shown a relationship between carotid intima-media thickness (CIMT) and global atherosclerosis. The aim of the present study was to examine the difference of the CIMT between controls (C) and patients (P) suffering of or being at risk (CVR) of getting cardiovascular diseases (CVD), as well as the relationship between CIMT and carotid plaque (CPL).

Methods: We evaluated 427 patients, (215 women and 212 men, 62±13 years, 338 with hypertension (HY), 142 with angina (A), 15 with previous myocardial infarction (MI), and 87 with HY+A and 124 control subjects without any CV disorder (59 women, 65 men, 41±14 years). The CVR were evaluated by SCORE risk stratification. Carotid ultrasonography was performed using a 7 MHz linear-array transducer, with Acuson 128XP/10c.The CIMT was measured at the far wall of the common carotid artery. For statistical analysis we used t-test, chi-square test, and standard data mining functions. We selected the dominant variables by information gain analysis, generated a classification (decision) tree using the dominant variables, and computed the ROC curves of the classification rules of the decision trees.

Results: Significantly higher mean values of CIMT were observed in P than in C (0,77±0,21 vs 0,57±0,13 $p<0,002$). In P the mean CIMT in women and man was 0,73±0,22 vs 0,77±0,17, respectively, p=0,001, while no significant difference was found in C (0,56±0,12 vs 0,56±0,11). The mean values of CIMT compared to the C group were: in HY 0,73±0,20 $p<0,001$, in A 0,70±0,20 $p<0,002$, in HY+A 0,78±0,24 $p<0,001$, respectively. The CIMT in C never exceeded 0.9 mm, but was also normal in 329 P (77%) and in 117 P with CPL (61%). The presence of CPL in patients exhibiting CIMT over 0,9 mm has 36% sensitivity and 88% specificity considering CVD. In CVD, the predictive value of CPL is decisively superior to that of CIMT, chi-square test 4,73 ($0.05>p>0.02$). The decision tree identified CPL, CIMT and age as most important variables for CVR. The areas under ROC curves are 0,85 (Low), 0,68 (Middle), and 0,78 (High) showing that the selected variables can best predict High and Low CVR.

Conclusions: CIMT by itself is not suitable to assess the severity of atherosclerosis in individual patients. If CPL is present, the probability of serious ASC is high. If CPL cannot be demonstrated, the impact of CIMT can only be evaluated together with other factors, like CVR, CVD, age and gender.

P736 Early atherosclerotic coronary lesions in Sudden Infant Death Syndrome

J. Milei[1], D.R. Grana[2], R. Perez[1], C. Navari[1], F. Azzato[1]. [1]*University of Buenos Aires-Conicet, Instituto De Investigaciones Cardiologicas, Buenos Aires, Argentina;* [2]*ININCA (UBA-Conicet), Buenos Aires, Argentina*

It has been known that initial atherosclerotic lesions of coronary arteries are recognizable in infancy. Recently, we have reported that preatherosclerotic intimal alterations of the coronary arteries are detectable in the prenatal period and are significantly associated with maternal smoking.

Purpose: To perform a morphologic characterization of early atherosclerotic lesions in autopsic materials belonging to sudden infant death syndrome (SIDS) in order to have an insight in the mechanisms involved in early atherogenesis.

Methods: We examined 52 SIDS victims (1 day to 1 year of age). Sixteen cases were used as control group, all dead of known causes. Serially cut sections of major epicardial coronary arteries were stained with hematoxylin-eosin, Azan, Alcian blue and acetic orceine, and were immunotypified for CD68, CD34 and α-SM-Actin. Endoluminal percentage involvement and maximal thickness of the lesion was obtained by histomorphometry (image analysis).

Results: In 44.2% of the SIDS group (23/52), and only in 6.3% of the control group (1/16) were found preatherosclerotic lesions (p=0.0062; Odds ratio=11.897). Alterations ranged from focal areas with mild myointimal thickening to early soft parietal plaques. Smooth muscle cells showed loss of polarity, infiltrating the subendothelium, mostly with rupture of the internal elastic lamina. No neoangiogenesis was observed. Morphometrically, endoluminal percentage involvement was 44.8±8.8%, and maximal thickness of the parietal lesion was 52.26±17.5 mm. Only one case showed a luminal obstruction of 43%, while in the others it was <10%.

Conclusions: Preatherosclerotic lesions developed very early in SIDS victims. From our findings, smooth muscle cells play and essential role in these lesions. Their proliferation and migration to the intima seems to be the touchstone of the process. The relationship between SIDS and atherosclerosis needs to be further investigated.

P738 Activated Factor XII Type A predicts cardiovascular outcome in patients admitted with chest pain

V. Poenitz[1], T. Brugger-Andersen[1], D. Pritchard[2], H. Grundt[2], H. Staines[3], D.W. Nilsen[3]. [1]*Stavanger University Hospital, Cardiology Department, Stavanger, Norway;* [2]*Axis-Shield, Dundee, United Kingdom;* [3]*University of Abertay, Dundee Business School, Dundee, United Kingdom*

Background: Activated Factor XII (XIIa) is a predictor of recurrent coronary ischaemic events in patients following a myocardial infarction (MI). Recently, novel in-vivo types of XIIa have been described. In the current investigation we assessed the relation between admission levels of activated factor XII type A (XIIaA) and a combined endpoint of mortality and recurrent TnT positive events at 12 months following hospitalisation in 871 patients admitted with chest pain suspected of having MI.

Methods: Blood samples for XIIaA determination were obtained immediately following admission. Plasma XIIaA concentrations were determined by ELISA. All cause mortality and recurrent TnT positive (>0.05ng/mL) events within each quartile of XIIaA were compared at 12 month follow-up.

Results: After a follow–up period of 12 months, 103 patients had died and 93 patients had suffered from a recurrent TnT positive event. The unadjusted risk ratio for the combined endpoint of patients with XIIaA in the highest quartile (Q4) was 2.75 (95% CI 1.63-4.64; $p<0.01$) compared with patients with XIIaA in Q1. In a logistic regression model, XIIaA (HR 2.67, 95% CI 1.44-4.98; $p<0.01$) added prognostic information for the combined endpoint of mortality and TnT positive events after adjustment for age, history of heart failure, BNP and early revascularization by PCI, i.e. factors associated with outcome in the multivariate model.

Conclusion: XIIaA is a powerful and independent predictor of cardiovascular outcome in patients admitted with chest pain and provides prognostic information additional to that provided by conventional risk factors.

P739 Near infrared imaging of lesion formation in ApoE-deficient mice

T. Dietrich[1], M. Tachezy[2], P. Stawowy[1], M. Graefe[1], K. Licha[3], P. Hauff[1], M. Schirner[1], E. Fleck[4], K. Graf[3]. [1]*German Heard Institute Berlin, Cardiology, Berlin, Germany;* [2]*German haeard Institut, cardiology, Berlin, Germany;* [3]*Bayer Schering Pharma AG, Optical Imaging & New Madalitis Research, Berlin, Germany;* [4]*German Heard institute Berlin, Cardiology, Berlin, Germany*

Ezetimibe (EZE), an inhibitor of cholesterol absorption, reduces atherosclerosis in Apo E deficient mice (ApoE(-/-)mice). It has been recently demonstrated that the angiogenic matrix protein ED-B fibronectin (ED-B) is upregulated in atherosclerotic lesions and can be imaged using antibody conjugates. In the present study we used a newly developed anti-ED-B scFv conjugated with a near infrared(NIR) fluorochrom for imaging of lesion formation in ApoE(-/-)mice treated with EZE in order to investigate the effect of EZE on the expression of ED-B and its use as a target for molecular imaging.

Methods: ApoE(-/-) mice were fed with high fat diet (21%fat) containing EZE(5μg/kg/d) or chow for 4, 6 and 8 month. ED-B imaging of the aortic lesions was performed after intravenous injection of ED-B-conjugate. Mice were sacrificed and aortas were analysed using a laser equipped NIR imaging system. Plaque lesion formation was analyzed by histology, immunohistochemistry and morphometry of the aorta and the supraaortic arteries.

Results: EZE treatment significantly reduced serum cholesterol levels over a period of 8 month. The aortic lesion formation detected by sudan staining and by NIR-EDB imaging was significantly reduced after 4, 6 and 8 month ($p>0.001$). ED-B imaging significantly correlated with the sudan stainings ($r=0.803$, $P<0.001$). Already after 2 months EZE treatment immunohistochemistry showed significant reduction in macrophages, ED-B immunoreactivity (both, $p<0.05$) and foam cell formation in aortic lesions. There was a significant correlation between ED-B and macrophage content in these lesions.

Conclusion: Ezetimibe significantly reduced atherosclerotic lesion formation and inflammation. Furthermore histological data revealed a reduced expression of ED-B and macrophages in the lesions. The results correlated with the data obtained with ED-B NIR imaging suggesting that this imaging tool can be used for monitoring atherosclerotic lesion formation in this experimental model.

P740 CD4+ CD28null lymphocytes, endothelial dysfunction and early atherosclerosis in patients with systemic lupus erythematosus

A. Recio Mayoral, S. Affinito, A. Qureshi, B. Zal, J. Axford, C. Babonian, J.C. Kaski. *St. George's Hospital Medical School, Division of Cardiac and Vascular Sciences, London, United Kingdom*

Purpose: Systemic lupus erythematosus (SLE) is associated with endothelial dysfunction, accelerated atherosclerosis and increased cardiovascular (CV) morbidity and mortality. The pathogenic mechanisms leading to CV disease in SLE are not known but chronic systemic inflammation and autoimmune mechanisms may play a role. We assessed whether an unusual subset of T-cells - the CD4+ CD28null T-lymphocytes- which have been shown to be increased in patients with

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

acute coronary syndrome, are associated with early atherosclerotic changes in patients with SLE.
Methods: The number of circulating CD4+CD28null cells was assessed using a validated method, as reported by our group previously, in 16 SLE patients (age 40±11 years; disease duration 11±5.8 years) without classical coronary risk factors and 15 age and gender matched normal volunteers (controls). In SLE patients, global damage index (SLICC/ACR score), disease activity and treatment-related parameters were assessed. In both patients and controls, carotid artery intima-media thickness (IMT) and systemic endothelial function (brachial artery flow mediated dilation (FMD)) were assessed.
Results: Total cholesterol levels were not significantly different in patients and controls (5.1±1.6 vs. 4.9±1.0 mmol/L, p=0.74). IMT was similar controls and patients (0.57±0.10 vs 0.54±0.11 mm, p=0.34). FMD, however, was significantly lower in SLE patients compared to controls (2.55±1.93 vs. 6.31±1.98, p<0.0001). Circulating CD4+CD28null cells were absent in the control group but present in 11 out of 16 patients. Of these, seven had persistent expansion of CD4+CD28null T cells constituting over 15% of the total CD4+ compartment. Patients with persistent expansion of CD4+ CD28null cells had a more pronounced decrease in brachial artery FMD compared to SLE patients, in whom the CD28 null population constituted <15% of the CD4+ T cells (1.38±1.9 vs 3.46±1.5, p=0.028). A significant positive correlation was found between number of CD4+CD28null cells and IMT values (r=0.86, p<0.0001) whereas there was a significant negative correlation between number of CD4+CD28null cells and FMD responses (r=-0.62, p=0.006) in SLE patients.
Conclusions: Circulating CD4+CD28null lymphocytes are increased in SLE patients, and these cells correlate with endothelial dysfunction and early atherosclerotic changes. Thus these T cells may contribute to CV disease in patients with SLE.

P741 Chronic renal failure is not associated with the prevalence and severity of coronary artery disease: analysis in 5641 consecutive patients

H.F.W. Alber, S. De Waha, M. Wanitschek, A. Ladurner, A. Suessenbacher, J. Doerler, M. Frick, H. Ulmer, O. Pachinger, F. Weidinger. *Innsbruck Medical University, Dept. of Cardiology, Innsbruck, Austria*

Background: Chronic renal failure (CRF) is associated with an increased incidence of cardiovascular events. However, few data exist on the relation between CRF and the prevalence and severity of coronary artery disease (CAD).
Methods: 5641 consecutive patients undergoing coronary angiography for the evaluation of chest pain were analysed. Cardiovascular risk factors were assessed by standardised questionnaire and routine blood chemistry. Severity of CAD was graded by visual estimation of lumen diameter stenosis. Significant stenoses were defined as lumen diameter reduction ≥70% in at least one major coronary artery. Coronary angiograms were graded as non-significant CAD, as 1-, 2- or 3-vessel disease (VD) or as non-CAD. Renal function was assessed by estimation of the glomerular filtration rate (GFR) using the abbreviated Modification of Diet in Renal Disease Equation (MDRD2). The GFR was then corrected for body surface area (Dubois formula).
Results: Overall, the GFR was lower in CAD (n=4124) compared to non-CAD patients (n=1517) (68.7±19.7 vs 72.8±20.0 ml/min; p<0.001), but was not different between 1-VD, 2-VD, 3-VD and non-significant CAD. CAD patients had lower HDL levels (51.9±15.3 vs 60.3±18.5mg/dl), were older (65.2±10.5 vs 59.9±11.4y), more often smokers (18.7 vs 16.5%), diabetics (19.9 vs 10.8%) and hypertensives (85.6 vs 69.6%) (all p<0.005), had similar LDL levels (124.5±38.3 vs 126.0±36.3mg/dl; p=NS) and were more frequently on chronic statin therapy (43.4 vs 27.9%; p<0.001). However, in multinomial logistic regression analysis (table) GFR was not independently associated with the presence and severity of CAD.

Table 1. Multinomial logistic regression analysis: CAD vs non-CAD

	Odds ratio	95%CI	Wald	p-value
Age	1.061	(1.053-1.068)	259.116	p<0.001
Gender	2.728	(2.352-3.165)	175.636	p<0.001
HDL	0.977	(0.973-0-982)	103.296	p<0.001
Hypertension	1.657	(0.795-1.434)	30.187	p<0.001
Diabetes	1.665	(1.355-2.047)	23.439	p<0.001
Smoking habit	1.795	(1.459-2.210)	30.526	p<0.001
GFR	1.001	(1.005-1.099)	0.512	p=NS

Conclusion: In this large consecutive patient cohort, CRF is not independently correlated with the angiographically documented prevalence and severity of CAD.

ECHO IN VALVULAR HEART DISEASE

P742 Echocardiographic assessment of prevalence, severity, progression and risk factors for paravalvular regurgitation (PVR) after heart valve replacement from the AVERT study

V.G. Davila-Roman[1], A.D. Waggoner[1], E. Kennard[2], L. Englberger[3], W.R.E. Jamieson[4], T.P. Carrel[5], H.V. Schaff[6] on behalf of AVERT investigators. *[1]Washington University School of Medicine, Cardiology, St. Louis, United States of America; [2]University of Pittsburgh, Department of Epidemiology, Pittsburgh, United States of America; [3]Cardiology, Berne, Switzerland; [4]Vancouver, Canada; [5]Cardiology, Berne, Switzerland; [6]Rochester, United States of America*

Objective: To determine prevalence, severity, progression and risk factors for PVR by echocardiography after heart valve replacement in the Artificial Valve Endocarditis Trial (AVERT).
Methods: Patients with aortic (AVR, n=221) &/or mitral (MVR, n=159) valve replacement had serial echocardiograms over a 7-year period. Large, asymmetric, or eccentric jets that originated outside of the sewing ring were considered indicative of PVR. A qualitative assessment defined the presence or absence of PVR, and a semiquantitative assessment defined the severity of PVR.
Results: A total of 1409 echocardiograms were performed: 800 AVR and 609 MVR. The mean number of studies/valve was 3.7 (range:1-10); mean echo follow-up was 5.7±1.5 years (2166 valve-years). The overall prevalence of PVR was 51 (13%): AVR 32 (14%) and MVR 19 (12%). For those with serial studies, AVR-PVR was mild in 66%, moderate in 34% and severe in 0%; MVR-PVR was mild in 74%, moderate in 5%; and severe in 21%. Severity of PVR increased in 21% of AVR-PVR and 13% of MVR-PVR. Clinical outcomes (valve replacement/repair, death) were similar for those with AVR-PVR compared to those without AVR-PVR; however, compared to those who did not have PVR, a significantly higher percentage of subjects in the MVR-PVR group underwent valve replacement &/or repair (11% vs. .7%, p<.05). Multivariate analysis identified carotid artery disease and everted suture as predictor of PVR, but not type or position of valve replacement.
Conclusions: After mechanical valve replacement the prevalence of echocardiographically-detected PVR in asymptomatic patients is rather low, PVR severity progression of low, and clinical outcomes are for the most part similar except in those with MVR-PVR, who have higher rates of valve replacement and/or repair.

P743 Real-time three-dimensional echocardiography: a new tool for assessing mitral valve regurgitation in a pediatric population

D.G. Latcu, S. Paranon, R. Bassil-Eter, J. Grosjean-Guitton, Y. Dulac, P. Acar. *Hopital des Enfants, Cardiology, Toulouse, France*

Purpose: Real-time three-dimensional echocardiography (RT3DE), commercially available nowadays, allows accurate left ventricular (LV) volumetric measurements without any geometric assumptions in adult patients. In pediatric patients three-dimensional LV volume measurement was validated only with an offline reconstruction technique. Our purpose is to validate this new method by measuring the stroke volume in a normal pediatric population. Then we use RT3DE to calculate regurgitant volume in pediatric patients with mitral regurgitation (MR).
Methods: Thirty-nine pediatric patients (aged one week to 16 years, median 6 years), with normal left ventricular outflow tracts and no ventricular septal defects (29 without MR and 10 with MR) had bi-dimensional echocardiography coupled with a RT3DE volumetric acquisition of the left ventricle (matrix probes, Philips). Stroke volume was calculated by the Doppler method at the aortic annulus (SVD). End-systolic and end-diastolic volumes of the LV were measured with the semi-automated method of QLab (Philips). Three-dimensional stroke volume (SV3D) was calculated as their difference. Mean time for measuring SV3D was 1 minute in patients with good endocardial detection and 3 minutes when manual corrections were needed. In the MR group regurgitant volume was calculated by the PISA method (VRPISA) and as the difference between SV3D and SVD (VR3D). Regurgitant fraction was also evaluated by the two methods (RFPISA and RF3D respectively).
Results: Measurements feasibility was 89% (impossible 3D acquisition due to agitation or poor quality acquisition). In the normal pediatric patients group, SV3D (27.9±18.1 ml) was highly correlated with SVD (30.7± 19.6 ml): r = 0.98, p < 0.0001, y = 0.90x + 0.08). Mean difference was 2.8±3.8 ml. The correlation was highly significant in both subgroups of patients with good endocardial detection (12 patients) and in those needing manual correction (13 patients), but was slightly better when no endocardial contour correction was needed (r = 0.97 and 0.94 respectively). In the MR group, VRPISA (20.7±16.9 ml) and VR3D (12.9±11.1 ml) are well correlated (r=0.92, p<0.001). Regurgitant fraction values are as also well correlated by the two methods: RFPISA=39.9±16.8, RF3D=32.8±17.0, r=0.79, p=0.006.
Conclusions: RT3DE is a simple, rapid and reliable method for evaluating stroke volume in children. Hence, its use may be of particular interest in evaluating regurgitant volume and fraction in MR. A larger population with volumetric overload (MR or ventricular shunt) is needed to reliably assess feasibility in this group.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P744 Real-time three-dimensional echocardiography in aortic stenosis: a novel method to improve accuracy in area calculation

J.L. Gutierrez-Chico[1], J.L. Zamorano Gomez[2], E. Prieto-Moriche[1], R.A. Hernandez-Antolin[1], M. Bravo-Amaro[2], L. Perez De Isla[1], M. Sanmartin-Fernandez[2], J.A. Baz-Alonso[2], A. Iniguez-Romo[2]. *[1]Hospital de Meixoeiro-MEDTEC, Department of Interventional Cardiology, Vigo, Spain; [2]Hospital Clinico San Carlos, Department of Cardiovascular Image, Madrid, Spain*

Objectives: Validation of a novel formula for aortic area, based on the principle of continuity equation (CE), that substitutes Doppler-derived stroke volume (SV) by SV directly measured with real-time 3D-echo (RT3D) and semiaoutomated border detection (SABD).
Background: RT3D has proven outstanding accuracy for LV volumes calculation. So far, however, neither this potential had been applied to hemodynamic assessment, nor RT3D had succeeded in the evaluation of aortic valve disease.
Methods: Aortic area was measured in 41 patients with aortic stenosis by Gorlin's equation, Hakki's formula, Doppler CE, 2D Simpson volumetric method, and by the novel RT3D method.
Results: RT3D has the best linear association and absolute agreement with Gorlin of all non-invasive methods (r=0.902, ICC=0.846), better than CE (r=0.646, ICC=0.626) and 2D volumetric method (r=0.627, ICC=0.378). Linear and Passing-Bablok regression show that RT3D fits better to Gorlin (r^2=0.814) than CE (r^2=0.417) and 2D (r^2=0.393). Its accuracy is comparable to Hakki's formula, routinely employed in cath-labs. Inter- and intraobserver agreements (ICC) were respectively 0.732 and 0.985, better than CE (0.662, 0.857). RT3D also grades most efficiently the severity of aortic stenosis as mild, moderate or severe (weighted kappa=0,932). RT3D underestimates aortic area (95% CI: 0.084-0.193 cm^2). ROC curves, however, show that the optimal cutoff point to consider aortic stenosis severe remains close to 1 cm^2 (1.06 cm^2).
Conclusions: RT3D is more accurate than CE and than 2D-based volumetric methods to calculate area and to grade severity of aortic stenosis. Area obtained by 3D echo is slightly underestimated, but its range is clinically negligible.

P745 Isolated mitral stenosis impaires atrial reservoir function in sinus rhythm and atrial fibrillation patients: strain and strain rate study

R. Ancona[1], P. Caso[2], S. Comenale Pinto[2], G. Di Salvo[1], I. Caso[1], S. Severino[2], R. Calabro[1]. *[1]Chair of Cardiology 2 University of Naples, Department of Cardiology Monaldi Hospital, Naples, Italy; [2]Complex operative unit of Cardiology Monaldi, Department of Cardiology Monaldi Hospital, Naples, Italy*

Background: Mitral stenosis(MS) causes left atrium (LA) enlargement-dysfunction and reduced LA flow velocity. Tissue Doppler imaging (TDI) assesses atrial function noninvasively; Strain (S) and Strain Rate (SR) imaging enables quantitative measurement of atrial reservoir function.
Aim of the study: to evaluate the effect of MS on right (RA) and LA reservoir function using S and SR and to compare atrial myocardial deformation properties in MS patients (pts) with sinus rhythm and atrial fibrillation(AF).
Methods: 65 healthy subjects comparable for age (53 years) and sex (55F,10M) with 65 pts with isolated MS: 20 with chronic AF and 45 in sinus rhythm, without other cardiac disease. Echocardiography System Seven GE with TVI function was used.We measured: mitral valve area, mean mitral gradient, LA and RA volumes, diameters, EF(%), right ventricle systolic pressure (PAPs). Peak systolic tissue atrial S and SR were evaluated in apical 4 and 2 chambers view at the level of the septal, lateral, anterior and inferior LA walls, and at level of the RA free wall, near the roof.
Results: MS pts had significantly: larger LA dimension(4,82 cm) than controls(3,5cm) and lower LA EF (28,75%) than controls (44,35%). LA maximal volume was greater in pts with MS(97,63 mL) than in controls(24,51 mL).The myocardial atrial S and SR were found to be significantly ($p<0.01$) lower for each atrial wall in pts with MS compared to controls (46±15 vs 75±18%). Pts with AF+MS showed significant ($p<0.01$) more impaired atrial myocardial deformation properties than MS pts in sinus rhythm (25 ±10 vs 55±18%). A significant direct correlation was found between LA S and PHT mitral valve area (P=0,03;R=0,51) and an inverse correlation between atrial S and mean mitral gradient (P=0,005;R=- 0,63). No correlation was found between RA S and SR and PAPs. RA S and SR show early impairement even in mild MS, when PAPs is low. During follow-up at 1 year 4 pts of 44 pts in sinus rhythm had at least one crisis of AF and 4 pts had cardiac asthma requiring hospitalization. At multivariate analysis (including atrial S, atrial maximal volume, PHT area, medium gradient, and PAPs) atrial S was an independent predictor of atrial fibrillation ($p<0,001$; coeff.=-0,31).
Conclusion: Strain Imaging is an echocardiography technique useful to study LA function in patients with MS noninvasively. Main result of our study is that atrial myocardial deformation properties are compromised in pts with MS, particularly in pts with MS+AF. Pts with low atrial strain values have an higher risk of AF and need careful follow-up.

P746 Strain analysis detects impaired left ventricular longitudinal function in candidates for aortic valve replacement due to severe aortic regurgitation

N.T. Olsen[1], P. Sogaard[1], J.P. Gotze[2], H.B. Larsson[3], T. Fritz-Hansen[1]. *[1]Gentofte Hospital, Cardiology Department, Copenhagen, Denmark; [2]Rigshospitalet, Biochemistry, Copenhagen, Denmark; [3]Glostrup Hospital, Center for functional MR, Copenhagen, Denmark*

Purpose: Detecting dysfunction of the left ventricle in aortic regurgitation is an important clinical challenge. Longitudinal systolic myocardial velocity has been proposed as a sensitive marker. To further examine this possibility, we analysed left ventricular longitudinal function (displacement, velocity, and strain) in patients with aortic regurgitation at different levels of symptoms and global left ventricular dysfunction.
Methods: 26 patients with isolated moderate to severe aortic regurgitation were examined in a prospective case-control design. Echocardiography was performed at inclusion. Global left ventricular function was assessed using Simpson's biplane method, measures of regional longitudinal left ventricular function was obtained by tissue Doppler imaging and speckle tracking. The presence of limiting symptoms, a depressed EF, and/or left ventricular end-systolic diameter above 25 mm/m^2 constituted indication for valve replacement. The patients were classified into two groups based on the absence (group A, n = 13) or presence (group B, n = 13) of indication for valve replacement.
Results: See table. Average systolic longitudinal strain was significantly lower in patients with aortic regurgitation who met criteria for valve replacement than in patients who did not. Systolic displacement and velocity were not significantly different in the two groups.

Comparison between groups

Mean ± SD	All patients	Group A (control)	Group B (+ AVR)	p value
n (% male)	26 (88%)	13 (84%)	13 (92%)	
Age, years	55±11	54±13	56±9	ns
LVEDV, ml	171±70	123±27	215±70	< 0.001
LVESV, ml	81±45	49±13	110±46	< 0.001
LVEF, %	55±9	60±5	50±9	< 0.01
Displacement, mm	11.3±2.0	11.8±1.3	10.8±2.4	ns
Systolic velocity, cm/sec	5.9±0.9	6.3±0.9	5.6±0.9	ns (0.07)
Systolic strain, %	-15.8±3.4	-17.9±2.3	-14.5±3.6	0.01

Group A: not candidates for AVR, Group B: candidates for AVR.

Conclusions: Left ventricular longitudinal function is affected in clinically severe aortic regurgitation. Strain is superior to velocity and displacement in detecting this. The finding of normal velocity and displacement should not be used to rule out left ventricular dysfunction in this group of patients.

P747 Not using the Pedof probe to measure transaortic flow velocity misclassifies twenty-five percent of patients with aortic stenosis

R. Marinigh, L.P. Badano, M. Cinello, D. Pavoni, N. Pezzutto, P. Gianfagna, P.M. Fioretti. *Az. Osp-Univers. S. Maria della Misericordia, Cardiopulmonary sciences, Udine, Italy*

Purpose: The constraint of time allotted to perform echo examinations, and continuous miniaturization and improvement of signal-to-noise ratio of modern combined imaging and Doppler transducers (steerable) have forced some echocardiographers to assess aortic jet velocity signal using only steerable transducers (ST). However, the accuracy of aortic jet peak velocity measured using modern ST in comparison with Pedof probe (PP) has never been tested.
Methods: Therefore, we studied 58 consecutive pts (62% males, 62 ±14 years) with moderate-severe AS (Peak gradient= 64±32 mm Hg, EOA= 0.92±0.35 cm^2). Each pt was searched for highest possible transaortic velocity using CW modality form apical and right parasternal approach using ST and PP in random order. Feasibility was 100% and 83% using ST and 93% using PP from apical and right parasternal approach, respectively.
Results: Results are summarized in Table. Using ST only, 3 pts out of 5 (60%) would have been misclassified as mild instead of moderate AS, and 10 pts out of 18 (55%) would have been misclassified as moderate instead of severe AS.

Table

	Steerable	Pedof	p Value
Vmax Apical (m/s)	3.76±0.8	3.66±0.8	0.02
Vmax Right Intercostal (m/s)	3.76±0.97	4.04±0.99	<0.0001
p Value	0.82°	<0.0001°	<0.0001°°
Peak Gradient Apex (mmHg)	53±24	52±26	0.68
Peak Gradient Right Intercostal (mmHg)	56±30	66±33	<0.0001
p Value	0.23°	<0.0001°	<0.0001°°
EOA Apex (cm^2)	0.96±0.36	0.99±0.38	0.034
EOA Right Intercostal (cm^2)	0.96±0.41	0.89±0.36	0.001
p Value	0.37°	<0.0001°	<0.0001°°

°Apical vs right intercostal approach; °°Steerable from apex vs Pedof from right intercostal approach.

Conclusions: PP and ST measure comparable peak flow velocities through the aortic valve from the apical approach. However, the PP allows recording of sig-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

nificantly higher velocities from right parasternal approach than the ST. Using the right intercostal approach and PP avoid misclassification of AS severity in 25% of pts with suspected AS.

P748 Validation of a new function corrected echocardiographic index of aortic stenosis severity

F. Antonini Canterin[1], M. Merlo[1], A. Pivetta[1], A. Aleksova[1], E. Leiballi[1], C.C. Beladan[2], R. Piazza[1], G.L. Nicolosi[1]. [1]*Azienda Ospedaliera S. Maria degli Angeli, Cardiologia, Pordenone, Italy;* [2]*Institute of Cardiovascular Diseases, Bucharest, Romania*

Purpose: A simplified index of aortic stenosis severity: "The Ejection Fraction-Velocity Ratio" has been recently validated. This index corrects the transvalvular gradient for ejection fraction (EF), a parameter of left ventricular (LV) function, as well as for transaortic flow. A theoretical limitation of this index is its utility in aortic stenosis patients with associated mitral regurgitation (MR), as in pts with MR ejection fraction is not a reliable parameter of LV systolic function. We aimed to test, in the same population, the reliability of a new index which corrects transaortic gradient for Doppler derived LV dP/dt, a less load dependent parameter of LV systolic function.
Methods: We evaluated by transthoracic echocardiography 84 pts (39 males, mean age 77±9 years) with aortic stenosis and associated MR. Continuity equation was used in all pts in order to assess aortic stenosis severity. LV dP/dt was calculated as the mean rate of Doppler derived LV pressure rise during early systole determined by the 1- and 3-m/sec velocity points on the rising segment of the continuous-wave mitral regurgitation velocity curve. Our new index represents the ratio between LV dP/dt and transaortic maximum gradient [dP/dt/4Vmax2]
Results: The mean aortic valve area was 1.17±0.47 cm^2. According to continuity equation aortic stenosis was severe (valve area $\leq$ 1 cm^2) in 37 pts and non-severe ($>$ 1 cm^2) in 47 pts. MR was mild in 39 pts, moderate in 29 pts and severe in 16 pts. The mean EF was 52±11% and the mean dP/dt was 1060±452 mmHg/s. The maximum transaortic Doppler flow velocity was 3.4±0.9 m/s. The mean value of the new index (dP/dt/maximum transaortic gradient) was 27±19 s^{-1}. ROC curve analysis showed a good accuracy of our new index in identifying pts with severe aortic stenosis: area under the ROC curve was 0.89 (95% CI 0.80-0.94; best cut off 20 s^{-1}). Using this cut-off there were 31 true positives, 40 true negatives, 7 false positives and 6 false negatives (84% sensibility and 85% specificity).
Conclusions: DP/dt/maximum transaortic gradient index has a good diagnostic accuracy in identifying pts with severe aortic stenosis. The new index, by correcting transaortic gradient for a less load dependent parameter of LV systolic function, could be useful in assessing pts with aortic stenosis and associated MR. Further studies are needed to assess the additional value of this new index in evaluating low gradient aortic stenosis pts with LV systolic dysfunction as the presence of contractile reserve represents a key point for the clinical decision making.

P749 Severity of carcinoid heart disease and relationship with NT-proBNP

S. Bhattacharyya, C. Toumpanakis, M. Caplin, J. Davar. *Royal Free Hospital, Department of Cardiology, London, United Kingdom*

Introduction: Carcinoid heart disease(CHD) is characterised by endocardial and valvular plaque deposition. Thickening of valve leaflets as well as chordae and sub-valvular apparatus causes reduced excursion, retraction and non co-aptation of valve leaflets associated with valvular regurgitation and stenosis. Valvular abnormalities can affect both the right and left sided cardiac valves. Severity of CHD affecting each valve as well as the number of heart valves involved varies. N Terminal Fragment Brain Natriuretic peptide (NT-proBNP) is raised in severe carcinoid heart disease. We assessed whether NT-proBNP correlates with the severity of carcinoid heart disease.
Methods: 21 patients with CHD underwent transthoracic echocardiography (TTE). Transoesphageal echocardiography(TEE) was undertaken if information on valve structure could not be obtained on TTE imaging. Each valve was individually scored for leaflet thickening,mobility,shortening and the degree of regurgitation or stenosis.The sum of all four valves produced a total carcinoid score. NT-proBNP was measured in all patients prior to echocardiography.
Results: Median carcinoid score was 25 (range 5 to 39). 33% of patients with CHD had one affected valve, 38% two valves, 19% three valves and 2 patients (10%) had all carcinoid involvement of all four cardiac valves. NT-proBNP positively correlated with carcinoid score. Spearman Rank Correlation Co-efficient r= 0.88, $p < 0.0001$ (figure 1).
Conclusion: There is a wide variation in severity of CHD. The majority of patients with CHD have involvement of one or two valves. NT-proBNP correlates with the severity of carcinoid heart disease. This may provide a medium for monitoring patients with carcinoid heart disease.

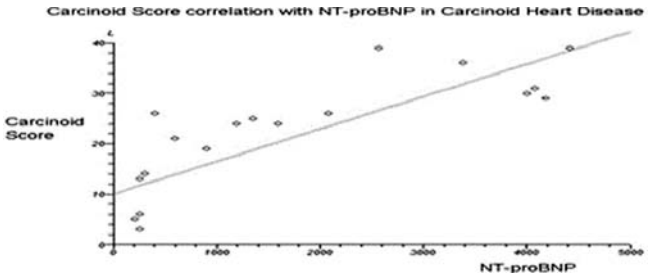


Figure 1

P750 Multi-planar reconstructive mode guided measurement of the degree of the papillary muscles displacement in functional mitral regurgitation; a novel method using real-time 3D echocardiography

J. Kwan, W.G. Choi, H.K. Yu, S.H. Kim, M.J. Jeon, D.H. Kim, K.S. Park, W.H. Lee. *Inha University Hospital, Cardiology Department, Inchon, Korea, Republic of*

Background and purpose: With recent development of 3D computer software, the multi-planar reconstructive (MPR) mode, for the 3D image analysis, it has become possible to identify the multiple cardiac structures separately and then put them all on a single plane for the geometrical measurement of them. The aim of the study is to suggest a new method to estimate the degree of the papillary muscle (PM) displacement accurately with the combined use of 3D echocardiography (3DE) and the commercially available MPR mode.
Methods: Thirty-three patients with functional mitral regurgitation (MR) (18: dilated cardiomyopathy, 15: ischemic cardiomyopathy with global LV remodeling) underwent real-time 3DE (Sonos 7500, Philips, Co.). MR severity was estimated by the regurgitant orifice area (ROA) by proximal isovelocity surface area (PISA) method. The degree of the PM displacement was defined by the distances from the each PM (ant-lat PM [3DAPM], post-med PM [3DPPM]) head to the anatomical reference marker, the medial junction of the aortic and mitral annuli (MJAM) during early-systole. Using the MPR mode, the MJAM, and the two heads of both PMs were identified and the distances were then measured. Both 3DAPM and 3DPPM were corrected (c) by the height of each patient. We also assessed the reproducibility of this new method with MPR mode and the conventional method with 2D echocardiography (2DE) in measuring PM displacement by repeating the measurement in two consecutive studies in 20 patients and then compared them with Bland-Altman analysis. 2DE assessment of PM displacement was done by measuring the distances from the mitral annulus to the ant-lat PM (2DAPM) and the post-med PM (2DPPM) on the apical 4 chamber and 2 chamber views.
Results: There was significant difference between the c3DPPM and c3DPPM (2.80±0.29 2.56±0.28 cm/m, p = 0.001). Both the c3DAPM (r=0.57) and c3DPPM (r= 0.62) showed significant correlations with ROA. In Bland-Altman plots, the mean differences of 2 measurements of the 3DAPM and 3DPPM were -0.04 and -0.04, and the 95% limits of agreement (mean ± 1.96SD) were -0.28/0.20 and -0.31/0.22, while those of the 2DAPM and 2DPPM were -0.08 and -0.13, and the 95% limits of agreement (mean ± 1.96SD) were -0.75/0.59 and -0.69/0.44.
Conclusions: The MPR mode guided c3DAPM and c3DPPM can be useful determinants of MR severity in functional MR. We suggest that the combined use of 3DE and the MPR mode can be a novel method to estimate the degree of displacement of both PMs accurately with providing better reproducibility than 2DE.

P751 Small left atrial volume is associated with good exercise capacity in patients with severe degenerative mitral regurgitation and normal left ventricular function

M. Vaturi[1], T. Hadar[2], Y. Shapira[3], D. Monakier[1], D.E. Weisenberg[1], M. Perlmutter-Weiser[1], N. Sela[1], A. Battler[1], A. Sagie[1]. [1]*Rabin Medical Center, Dept. of Cardiology, Petach-Tikva, Israel;* [2]*Sackler Faculty of Medicine, Tel Aviv Univers, Petac-Tikva, Israel;* [3]*Rabin Medical Center, Beilinson Hospital, Cardiology, Petac-Tikva, Israel*

Background: Left atrial volume (LAV) is a strong predictor of cardiovascular risk. When normal, it has a very high negative predictive value for ischemia in stress echocardiogram. However, the predictive value of LAV in mitral regurgitation (MR) still needs to be established.
Method: The Beilinson hospital 2004-2006 echocardiography database was queried. The study included patients with significant chronic degenerative MR (moderate to severe or more) that underwent treadmill exercise echocardiography. Resting LAV was measured using the bi-plane Simpson's method in apical 2- and 4-chamber views. The end-systolic value was indexed to body surface area (LAVi). Good exercise capacity was defined by >7 METS. Patients with other significant left-side valvular abnormalities, left ventricular dysfunction, exercise-induced ischemia and those with suboptimal images were excluded.
Results: Fifty two consecutive patients (age 60±14 yrs, 36 males) were selected. Two subgroups (19 vs. 33 patients), age- and sex-matched, were formed by LAVi cutoff of 40 ml/m^2 (30.8±5.8 vs. 63.7±16.4 ml/m^2 respectively, $p<0.01$). Those with greater LAVi had lower exercise capacity (9.1±3.6 vs. 12±2.1 METS, $p<0.001$), shorter exercise period (7.7±2 vs. 10.2±3.4 minutes, p=0.001) and higher tricuspid regurgitation grade ($p<0.01$) albeit similar RV systolic pressure, LVEDd and LVESd. The majority of patients with small LAVi had good exercise capacity (95% vs. 50%, $p<0.01$, Figure 1).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

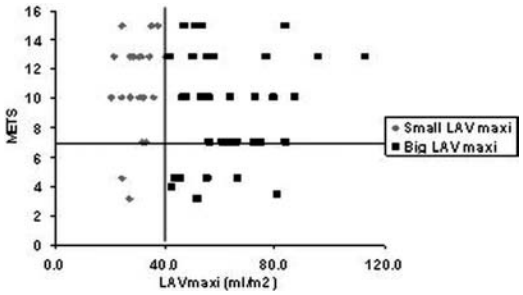


Figure 1

Conclusion: Small LAVi ($\leq$40 ml/m^2) is highly associated with good exercise capacity in patients with significant chronic MR and normal LV function. Decreased exercise capacity with larger LAVi may reflect factors such as LA compliance, illness duration, diastolic LV dysfunction and higher TR grade.

P752 Influence of female sex in the outcome of aortic regurgitation

A. Sambola, A. Evangelista, P. Tornos. *Hospital Vall d'Hebron, Barcelona, Spain*

Background: Several studies have suggested that women may have a worst postoperative outcome than men in chronic aortic regurgitation (AR). The factors involved in this different outcome are mainly unknown.
Purpose: 1) To analyze possible differences in postoperative outcomes between genders 2) Factors what may contribute to them.
Results: One hundred and forty-seven consecutive patients were operated for AR (107 men, aged 52$\pm$12 y and 33 women, 55$\pm$11 y) between 1982 and 2005. The percentage of patients undergoing surgery for symptoms was significantly higher among women than men: 34 women (92%) vs 74 men (67%), p=0.002. Twenty-two women (60%) were in FC III-IV vs 32 men (30%), p=0.0001. Preoperative raw LV diameters EDD (74$\pm$8 vs 68$\pm$8, p=0.0001) and ESD (54$\pm$9 vs 47$\pm$9, p=0.0001) were significantly lower in women, while indexed LV diameters for BSA were similar (IEDD 41$\pm$6 vs 42$\pm$4 mm/m^2, p=ns; IESD 29$\pm$6 vs 29$\pm$5 mm/m^2, p=ns). Preoperative EF did not show differences in both gender (47$\pm$12 vs 49$\pm$9, p=ns). Perioperative mortality was 4 women (10.8%) vs 3 men (2.7%), p=0.067. Late mortality (follow-up 7$\pm$5 years) did not show significant differences: 4 f (12%) vs 26 m (24%), p=ns.
Conclusions: Our data suggest that women are operated later than men, when most of them are severely symptomatic and there is a trend towards increased operative mortality. The use of raw LV diameters is likely underscore the preoperative risk thus delaying surgical indication.

P753 Echocardiographic evaluation of left atrial function in mitral regurgitation and its relation to patient clinical profile

H. Badran, A.K. Mostafa, A. Serage, H. Hassan, T. Gazy. *Shebin Elkom, Egypt*

Background: Left atrial (LA) performance has important clinical implications. Aim of this work was studying LA reservoir, conduit and contractile functions in chronic rheumatic MR using volumetric changes and Doppler tissue imaging (DTI) and examine its impact in patient clinical assessment.
Methods: 45 patients with rheumatic MR were included; 20M & 25 F with mean age 19$\pm$10 years. They were compared to 10 healthy subjects. LA volumes were measured using 2D echocardiography at mitral valve opening (maximal) (Vmax) and closure (minimal) (Vmin) and at onset of atrial systole (P wave of ECG) (Vp). LA passive emptying volume(PEV) & its fraction (PEF%) LA active emptying volume (AEV)& its fraction(AEF%) LA total emptying volume (TEV) & its fraction (TEF%) In addition DTI of the mitral annulus was used to assess LA contractile function(Aa).
Results: Despite the larger atrial volumes in MR group, the reservoir function using TEF% and conduit function using PEF% were significantly lower in MR group compared to control (59$\pm$13 vs 82$\pm$10, 38$\pm$9 vs 55$\pm$2) P $<$0.001, 0.01 respectively. The contractile function using both DTI and volumetric method (AEF%) were significantly reduced in MR group in comparison to control, (P value $<$0.001). LA functions showed strong inverse correlation to patient functional capacity, NYHA class, (r=- 0.90, -0.77, - 0.89) and the severity of MR (-0.37, -0.47, -0.57) respectively. In addition, LV function showed strong direct correlation to LA contractile and reservoir function, (r=0.51, 0.52 respectively) P value $<$0.001.
Conclusion: In rheumatic MR all LA functions were depressed despite increase in atrial volumes. Absence of compensatory increase in any of atrial function may be related to early LA involvement by rheumatic process. The determination of LA function in MR may help to optimize medical therapy could anticipate the proper timing of surgical interference.

P754 Strain and displacement before and after aortic valve replacement for aortic stenosis. A Speckle Tracking Echocardiography (STE) study

D. Cramariuc[1], E. Gerdts[1], L. Stangeland[2], L. Segadal[1], K.S. Andersen[1], E.S. Davidsen[1], K. Matre[2]. [1]*Institute of Medicine, University of Bergen, Department of Heart Disease, Bergen, Norway;* [2]*Haukeland University Hospital, Department of Thoracic Surgery, Bergen, Norway*

Purpose: To investigate whether STE can quantify abnormal motion of myocardial segments, including the interventricular septum, after aortic valve replacement for severe aortic stenosis.
Methods: STE was performed in 20 patients (13 women, mean age 74$\pm$8) with severe aortic valve stenosis 1 day before aortic valve replacement and 4-8 days postoperatively. Parasternal short-axis and apical 4-chamber views were used to assess peak and peak systolic circumferential, radial and longitudinal strain (CS, RS, LS), as well as radial, longitudinal and transverse displacement (RD, LD, TD), as mean values within each of 6 left ventricular wall segments.
Results: Patients presented increased relative wall thickness (0,55$\pm$0,21) and left ventricular mass index (131$\pm$29g/m^2), and normal ejection fraction (68% vs. 60%, p $<$ 0.01) pre- and post- aortic valve replacement. Septum and anteroseptum had similar pre- and postoperative RS, CS and LS, but lower RD (p$<$ 0.05), lower TD and LD (both p$<$ 0.001) with negative TD in basal and middle septum (Table). By contrast, the lateral wall had increased LD (15$\pm$9% vs. 32$\pm$17%) and TD (14$\pm$7% vs. 21$\pm$11%) (both p$<$ 0.05). RD did not change in other segments. The anterior and lateral walls had unchanged CS, LS, but lower RS (anterior: 33$\pm$13% vs. 26$\pm$14%, p$<$ 0.05; lateral: 35$\pm$15% vs. 29$\pm$17%, ns), while the posterior and inferior walls had unchanged RS but lower CS (posterior: -16$\pm$8% vs. -11$\pm$5%, p$<$ 0.05; inferior: 21$\pm$8% vs. 15$\pm$6%, p$<$ 0.01).

Table

	Pre-aortic valve replacement			Post- aortic valve replacement		
Septum	Basal	Middle	Apical	Basal	Middle	Apical
Peak LS (%)	-12$\pm$5	-17$\pm$4	-22$\pm$7	-13$\pm$6	-15$\pm$6	-19$\pm$8
LD (mm)	12$\pm$3	9$\pm$3	4$\pm$2	4$\pm$4*	1$\pm$3*	-1$\pm$2*
TD (mm)	3$\pm$3	6$\pm$3	5$\pm$3	-2$\pm$4*	-8$\pm$3*	1$\pm$2*
Peak CS (%)		-26$\pm$9			-27$\pm$9	
Peak RS (%)		30$\pm$14			25$\pm$13	
RD (mm)		5$\pm$4			3$\pm$2**	

*p$<$ 0.001, **p$<$ 0.05.

Conclusions: STE shows that abnormal motion of the interventricular septum post- aortic valve replacement is not due to strain alterations and thus to ischemia, but to negative transverse septal displacement combined with lower radial and longitudinal displacement.

P755 Prognostic impact of functional and morphological changes in patients with severe Aortic Valve Stenoses after Valve Replacement

S. Herrmann[1], J.M. Strotmann[1], M. Niemann[1], M. Beer[1], V. Lange[1], W. Voelker[1], G. Ertl[1], F. Weidemann[2]. [1]*Wuerzburg, Germany;* [2]*University Hospital, Medical Clinic, Dept. of Cardiology, Wurzburg, Germany*

The purpose of this clinical study was to investigate the clinical outcome in comparison to left ventricular (LV) function and myocardial structural changes in patients with severe aortic valve stenoses after aortic valve replacement (AVR).
Methods: Conventional echocardiography (for LV ejection fraction (EF)) and strain rate imaging (for peak systolic strain rate) were performed before (baseline) and 9 months after AVR in 27 patients with severe aortic stenoses. Radial myocardial function (peak systolic strain rate=SR) was assessed from the posterior wall and longitudinal function was assessed in the septal wall. Furthermore all patients underwent a magnetic resonance imaging study (MRI) with Gadolinium late enhancement technique (LE) to determine myocardial fibrosis. Cardiac biopsies were taken during AVR to evaluate interstitial fibrosis.
Results: Patients were assigned to three groups according to their NYHA-Class nine months after AVR (group 1 (n=5) NYHA–Class I; group 2 (n=9) NYHA-Class II; group 3 (n=13) NYHA–Class III or IV. For radial function systolic SR (group 1 =1.3$\pm$0.3 s-1; group 2=1.3$\pm$0.4 s-1; group 3=1.2$\pm$0.5 s-1; n.s) and EF (group 1=52$\pm$13%; group 2 =56$\pm$13%; group 3=53$\pm$13%; n.s.) were similar in the groups at baseline. In contrast, systolic longitudinal SR was higher in group 1 compared to group 3 (group 1 =-1,3$\pm$0,3 s-1 group 2=-0,9$\pm$0,3 s-1; group3=-0,8$\pm$0,3 s-1 p$<$0.05 vs. group 1). Parallel to the change of longitudinal systolic SR a significant higher rate of fibrosis in the cardiac biopsies and LE in MRI could be seen in Group 3.
Conclusions: These data suggest that regional longitudinal function and myocardial fibrosis may have an impact on clinical outcome after AVR in patients with severe aortic valve stenosis.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P756 Identification and exclusion of left atrial thrombi using contrast enhanced transesophageal echocardiography

P. Jung, J. Rieber, H.-Y. Sohn, H. Gross, F. Jander, A. Koenig, M. Leibig, K. Theisen, V. Klauss. *University of Munich, Cardiology Department, Munich, Germany*

Atrial fibrillation (AF) represents a major risk factor for the development of atrial thrombi, which can be detected by transesophageal echocardiography (TEE). However, TEE generates non distinctive results in a considerable number of patients. Newer transpulmonary contrast agents can precisely delineate the endocardial border but are primarily used for the left ventricle (LV). This study investigated the influence of contrast enhancement on the diagnostic value of TEE for the detection of left atrial (LA) thrombi in patients with AF.
Methods: TEE was performed in 40 consecutive patients (31 male, 63.8±14 years) with AF, who were planned to undergo electrical cardioversion (CV). Cineloops of 2 planes of the LA and LA appendage were stored digitally before and after intravenous bolus application of a transpulmonary contrast agent (SF36 microbubbles). Contrast artefacts were avoided by optimizing mechanical index and timing of image acquisition. Images were assessed offline and the diagnosis of LA thrombi was made semiquantitatively as follows: 1=present thrombus; 2=suspected thrombus; 3=no thrombus. Additionally, the presence of spontaneous echocontrast (SEC) and the flow velocitiy in the LA appendage (LAA-flow) were measured. After the TEE, patients were referred to CV at the discretion of the investigator.
Results: No adverse events occurred during both examination techniques. Atrial thrombi were diagnosed without doubt in 5 (10%) and 6 (12.5%) patients during native and contrast enhanced imaging, respectively. Of theese only only 3 revealed decreased LAA-flow (0.2, 0.25 and 0.17m/s) and SEC. Uncertain results (diagnosis 2) were significantly more frequent during conventional than with contrast enhanced TEE (n=16 vs. n=5, $p<0.01$). Thrombi were safely excluded in 20 patients (50%) during conventional vs in 28 patients (70%) during contrast enhanced TEE ($p<0.01$). The suspected thrombi during conventional TEE turned out to be an artefact due to an echodense crista terminalis or reverberations in 8 patients. CV was done subsequently in 20 patients without complications. Nonetheless, 1 patient without thrombus detection during both imaging techniques but marked SEC and low LAA-flow suffered a peripheral embolism 1 week after CV but admitted the discontinuation of his anticoagulation despite medical advice.
Conclusion: Contrast enhancement renders TEE images more interpretable and facilitates the exclusion of atrial thrombi in patients with AF planned for CV.

P757 Intraventricular gradients and systolic anterior movement of the mitral valve during exercise in athletes. Treatment with beta blockers. Fact or fantasy?

C. Cotrim[1], M.J. Loureiro[2], R. Miranda[1], S. Almeida[1], O. Simoes[1], L. Lopes[1], P. Cordeiro[1], M. Carrageta[1]. [1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal;* [2]*Hospital Garcia De Orta, Cardiology Department, Almada, Portugal*

Introduction: It is reported that the development of intraventricular gradients (IVG) on exertion seldom occurs. We performed exercise stress echocardiography (SE) in a 23-year-old athlete (AT) with a positive treadmill ECG and normal rest echocardiogram, and without angiographic coronary disease. During stress echocardiography he unexpectedly developed IVG of 105 mmHg and systolic anterior movement (SAM) of the mitral valve.
Purpose: To assess the occurrence of IVG and mitral valve SAM during exertion in athletes with "positive" screening results on cardiovascular evaluation for sports practice.
Methods: We evaluated 76 AT, mean aged 24±10 years (age ranged 12 to 56 years old), 64 of whom were males. 1 AT had non-obstructive hypertrophic cardiomyopathy (HCM) echocardiographic phenotype, 1 hypertensive AT had left ventricular hypertrophy (LVH) and 4 AT had mild mitral valve prolapse. The other 70 had normal resting echocardiograms. Clinical reasons for performing SE in these AT were: abnormal ECG in 15 AT, symptoms on exertion in 39 AT, abnormal treadmill ECG in 14 AT and family history of sudden death in 2 AT. They all underwent stress echocardiography with 2D and Doppler echographic evaluation before, during and after treadmill exercise. The 2 AT with LVH were excluded. In 18 (13 with symptoms) athletes the SE was repeated while treated with β blockers.
Results: In 30 (41%) of the AT studied the SE disclosed IVG ranging from 17 to 160 mmHg (84±36 mmHg). The IVG development was accompanied by SAM of the mitral valve in 21 AT (28%) and by symptoms in 17 AT. These findings persisted for less than 60 seconds after exercise test termination. From the 18 AT under β blockers, IVG disappeared in 11 and reduced in 7; from the 13 AT with symptoms, 9 AT became asymptomatic and 4 reported improvement of symptoms.
Conclusions: 1. A significant number of athletes referred for SE on the basis of clinical symptoms or abnormal cardiovascular tests develop mitral valve SAM and IVG during exercise. 2. This finding can only be disclosed during exertion and resolves rapidly after exercise termination. 3 The ocurrence of this phenomenon can be prevented or reduced with β blockers, which also produce effect on symptoms.

P758 Diagnostic usefulness and prognostic impact of tissue Doppler imaging in heart failure patients with secondary mitral regurgitation

C. Bruch, R. Gradaus, M. Grude, T. Wichter. *University of Muenster, Muenster, Germany*

Background/Aim: In patients (pts) with chronic heart failure (CHF), the presence of significant secondary mitral regurgitation (MR) is associated with increased morbidity and mortality. In such pts, the diagnostic usefulness and prognostic impact of tissue Doppler imaging (TDI) has not been studied.
Methods: This prospective study enrolled 370 pts with stable CHF (mean age 59±13 years, mean New York Heart Association (NYHA) functional class 2.6±0.5, mean ejection fraction (EF) 31±10%). Significant secondary MR defined as effective regurgitant orifice area $\geq$ 0.20 cm^2 was present in 92 patients (25%). Echo measurements comprised left ventricular dimensions/volumes, EF, mitral E/A-ratio, deceleration time and TDI derived mitral annular velocities (S', E', A', E/E'). During a follow-up of 790±450 days, all-cause mortality and re-hospitalization data were analyzed.
Results: Pts with or without significant MR did not differ with respect to age, medication, EF or mitral annular E' velocity, but MR pts were in a poorer NYHA functional class (2.8±0.4 vs. 2.6±0.5, p=0.01) and had a higher mitral E/E' ratio (15.5±9.7 vs. 12.5±6.1, p=0.001). During follow-up, 70 patients (18%) died and 134 patients (36%) were re-hospitalized due to worsening CHF. Mortality was significantly higher in patients with vs. without MR (33% vs. 14%, Chi square: 15.5, $p<0.001$). In the MR group, mortality was independently predicted by the mitral E/E' ratio (HR: 1.06, 95% CI 1.009-1.111, p=0.021) and age (HR: 1.043, 95% CI 1.01-1.077, p=0.011). In MR pts with an E/E' ratio $>$ 13.5 (cut-off value derived from ROC analysis, area under the ROC curve: 0.68±0.05), outcome was markedly worse in comparison to pts with an E/E' ratio $<$ 13.5 (event-free survival rate 31% vs. 64%, $p<0.001$). In the MR group, the E/E' ratio was the only clinical and echocardiographic variable with a significant association with re-hospitalization due to worsening CHF (HR: 1.04, 95% CI 1.005-1.081, p=0.026).
Conclusions: In CHF pts with significant secondary MR, a higher E/E' ratio is associated with increased morbidity and an adverse outcome. TDI may be a useful adjunct in the diagnostic work-up and risk stratification of such patients.

P759 The role of left ventricular long axis deformation in patients with asymptomatic non-ischemic mitral valve regurgitation and normal systolic function

S. Kyrzopoulos[1], D. Tsiapras[1], I.A. Paraskevaidis[2], V. Vartela[2], G. Domproglou[2], D.T. Kremastinos[1]. [1]*Onassis Cardiac Surgery Ctr., B' Cardiology, Athens, Greece;* [2]*Attikon University Hospital, Athens, Greece*

Purpose: Subclinical left ventricular (LV) dysfunction is often underestimated in patients with chronic mitral regurgitation (MR) due to the lack of a sensitive diagnostic index to monitor LV systolic function in those patients. We aimed to investigate the role of LV long axis deformation in patients with chronic asymptomatic non-ischemic MR.
Methods: Seventy patients (48 men, mean age 63.2±13.5 years) with chronic asymptomatic non-ischemic MR were enrolled. A standard echocardiographic, including tissue doppler imaging, study, an exercise radionuclide cineventriculography and a cardiac catheterization were performed. An increase of ejection fraction of $>$ 5% was considered a normal response at the exercise radionuclide cineventriculography.
Results: 42 of 70 patients (60%) had a normal response of LV ejection fraction to exercise. LV end-diastolic diameter and volume index were significantly higher in patients with an impaired LV response. Moreover, longitudinal strain rate (SR) was significantly reduced at the lateral wall in patients with an impaired LV response compared to those with normal LV response to exercise (1.27±0.22 vs 1.63±0.16, $p<0.001$) and at the inter-ventricular septum (1.22±0.26 vs 1.37±0.22, $p<0.02$). SR at the lateral wall was the index that best predicted LV response to exercise; while a cutoff value of 1.47 predicted an impaired LV response with a specificity and sensitivity of 100%. MR as defined by the width of vena contracta, was mild/moderate in 78.5% of patients with a SR at the lateral wall $>$1.47 and severe in 71.5% of patients with a SR at the lateral wall $<$1.47.
Conclusion: In patients with asymptomatic chronic MR, the evaluation of LV long axis deformation at rest can unmask a subnormal LV functional status.

ELECTROCARDIOGRAM ANALYSIS

P760 Combined criteria enhance the ECG diagnosis of left ventricular hypertrophy

I. Morrison[1], E. Clark[2], P.W. Macfarlane[1]. [1]*University of Glasgow, Cardiology, Glasgow, United Kingdom;* [2]*Royal Infirmary, Cardiology, Glasgow, United Kingdom*

Introduction: There are over 30 different ECG criteria that can be used to determine the presence of left ventricular hypertrophy (LVH). This study aimed to compare different criteria including the classical Sokolow-Lyon (SV1+maxRV5/6) and the relatively newer Cornell (SV3+RaVL) criteria both as voltage criteria per se and voltage x QRS duration products, as well as point scoring systems such

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

as the Romhilt Estes (RE), Perugia and the University of Glasgow age and sex modified Romhilt Estes (UGRE) score. Regression models for estimating LV mass from the ECG were also assessed.
Methods: Patients undergoing echocardiography (echo) were recruited from the Cardiology Department in Glasgow Royal Infirmary. The echo LV mass derived using the American Society of Echocardiography method was used as the gold standard. This was indexed to body surface area and, by using sex dependent cut offs of 116g/m^2 for males and 104g/m^2 for females, echo based LVH was determined. ECGs were processed by the University of Glasgow ECG analysis program permitting different LVH criteria to be assessed. Regression models were assessed using the Bland Altman method.
Results: 51 males and 76 females (mean age 60.3±18.5 years) were recruited as a test set. Of these, 33 males and 34 females had LVH by echo. For voltage only criteria, the Lewis index had the greatest sensitivity of 12%. However, when voltage criteria were adjusted to 95% specificity, the Cornell Index produced the greatest sensitivity at 19%. The best voltage duration product was that of Cornell, which gave 19% sensitivity adjusted to 95% specificity. The point scoring systems proved to be the most accurate with the Perugia being 22% and the UGRE score being 24% sensitive both at 95% specificity. ECG derived LV mass was found to have a wide variation from the echo derived LV mass and therefore was a poor predictor of LV mass. When the Cornell product was combined with UGRE score, sensitivity increased to 30% with a corresponding 93% specificity.
Conclusion: Voltage based ECG criteria for LVH are the worst performing while scoring systems are the best, with voltage duration products intermediate. However, the combination of the University of Glasgow modified RE score and the Cornell product gave the best overall result of 30% sensitivity and 93% specificity. This is the first such study to compare the combination of scoring systems and voltage duration products for detecting ECG LVH and it shows that the individual sensitivities can be improved relatively by 25% and 58% respectively, with little loss of specificity, when these strategies are combined.

P761 High throughput preclinical screening of the potential for QT prolongation by human pharmaceuticals utilizing mouse/rat magnetocardiogram system with a single-chip SQUID magnetometer array

K. Komamura[1], J. Kawai[2], M. Miyamoto[1], Y. Adachi[1], G. Uehara[1], Y. Haruta[3]. [1]*National Cardiovascular Center, Dept. of Cardiovascular Dynamics, Suita, Japan;* [2]*Kanazawa Institute of Technology, Applied Electronics Laboratory, Kanazawa, Japan;* [3]*Yokogawa Electric Co., MEG Center, Kanazawa, Japan*

Purpose: International conference on harmonization (ICH) guideline requires non-clinical evaluation of the potential for delayed ventricular reporalization, i.e. QT prolongation, for the development of novel human drugs in Europe, North America and Japan. ECG of hirsute small animals is time-consuming. Magnetocardiogram (MCG) has non-contact characteristics and is not interfered with lung filed. We newly developed and tested the validity of micro MCG for mouse and rat using superconducting quantum interference device (SQUID) on a single silicon chip.
Methods: Male ICR mice (n=7) were anesthetized with tribromoethanol, and then quinidine (60 mg/kg) was administered intraperitoneally. Male wister rats (n=7) were also anesthetized with pentobarbital and were given quinidine injection (60 mg/kg). At 3, 5, 7, 10 and 15 min after quinidine administration, MCG was recorded and QT interval was measured. According to the previous method, QT interval was defined as length from the onset of Q wave to the intersection of T wave and isomagnetic line. QT interval was corrected for RR interval (QTc) by the formula: QTc = QT/(RR/100)$^{\frac{1}{2}}$. In a separate experiment, we made regional (anterior, lateral, apex and posterior) myocardial injury with cryoprobe in the heart of anesthetized rats (n=6, each). One week after the surgery, the morphological patterns of MCG signal were compared to that of the normal control.
Results: Quinidine-induced QT prolongation over time was successfully measured by MCG in mice and rats. Mouse QTc was significantly prolonged from the baseline of 25.0±0.6 msec to 25.6±0.6 (3 min), 27.1±0.6* (5 min) 27.8±0.6* (7 min), 28.2±0.7* (10 min), 28.4±0.8* (15 min) msec (*p<0.05 vs. baseline). Rat QTc was significantly prolonged from the baseline of 26.2±0.7 msec to 26.7±0.8 (3 min), 27.7±0.7* (5 min) 28.8±0.7* (7 min), 29.3±0.8* (10 min), 29.5±0.9* (15 min) msec (*p<0.05 vs. baseline). In the second experiment, anterior myocardial injury created QS pattern of MCG, and posterior injury created QR pattern. Those two patterns were clearly different each other, and from the normal pattern.
Conclusions: Newly developed micro MCG for small animals with a single chip SQUID array enabled us to measure drug-induced QT prolongation by milliseconds. This system may facilitate the high throughput screening test and also basic scientific research of electromagnetic properties of the small animal heart.

P762 Body surface potential mapping in genotyped patients with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC-9): identification of new ECG-characteristics

M. Paul, C. Vahlhaus, H.-J. Bruns, C. Wollmann, E. Schulze-Bahr, L. Eckardt, G. Breithardt, T. Wichter. *Hospital of the University of Muenster, Cardiology and Angiology, Muenster, Germany*

Background: Presentation of patients (pts) with arrhythmogenic right ventricular cardiomyopathy (ARVC) and idiopathic right ventricular outflow-tract tachycardias (RVO-VT) may be similar. However, typical ECG features of ARVC are often subtle or absent and therefore do not always allow a clear differentiation between the two entities. Repolarization abnormalities in precordial ECG leads are also characteristic in ARVC. Thus, we analysed potential differences in the T-wave-integral (TWI) using a 120-channel body surface potential mapping (BSPM). Mutations in plakophilin-2 (PKP2) were identified in pts with ARVC (ARVC-9). Therefore, we additionally assessed the impact of genotype on TWI alterations.
Methods: ARVC pts were divided into 2 groups: those with a PKP2-mutation (PKP2-pos; n=5) and those without (PKP2-neg; n=5). In all pts, a BSPM with quantitative signal analyses of the TWI was performed. The results were compared to those obtained in 14 pts with RVO-VT and a control group of 12 healthy subjects. Age, body mass index as well as QRS-axis on surface ECG were not significantly different between the groups.
Results: All pts with ARVC had a significantly lower TWI in the right lower anterior region of the torso when compared to both pts with RVO-VT and controls (P<0.00001). These differences were especially pronounced in PKP2-pos in comparison to RVO-VT pts (P<0.00001) with a sensitivity of 91% and a specivicity of 90% respectively (area under curve: 0.98±0.13; P<0.00001). In addition, in PKP2-pos pts, TWI was significantly lower than in PKP2-neg pts (P<0.0001). Reciprocal changes were observed in the left upper posterior region of the torso. In all analyses, there were no significant differences between pts with RVO-VT and controls.
Conclusions: Apart from standard ECG lead positions new signal characteristics were identified with the help of BSPM. These allow a reliable differentiation between pts with ARVC and RVO-VT which has important implications for differential diagnosis and risk stratification. The repolarization abnormalities found were even more pronounced in PKP2-pos pts with ARVC.

P763 Is there still a role for ECG scoring systems in acute coronary syndromes?

R.A.P. Weir[1], A. Murphy[1], C.J. Petrie[1], E. Dick[1], S. Clements[1], T. Steedman[1], J.J.V. Mcmurray[1], H.J. Dargie[1], G.S. Wagner[2]. [1]*Western Infirmary, Cardiology, Glasgow, United Kingdom;* [2]*Duke University, Medical Center, Durham, United States of America*

Introduction: The Aldrich scoring system was validated in non-reperfused infarcts, and provided an electrocardiographic (ECG) estimate of "at risk" myocardium in acute myocardial infarction (MI), which correlated well with infarct size (IS) measured by Selvester scoring on the predischarge ECG. In reperfused infarcts, IS on ECG is generally lower than the Aldrich score, presumably reflecting myocardium salvaged by reperfusion therapy, although the applicability of Selvester scoring in the reperfusion era has been debated. Contrast-enhanced cardiac magnetic resonance imaging (ceMR) provides a gold-standard means of assessing IS. We hypothesised that, if the Selvester score correlated well with ceMR-measured IS, then the "success" of reperfusion in terms of percentage of myocardium salvaged could be estimated by comparing the admission ECG with a pre- or post-discharge ECG.
Methods: 38 patients (31 male, mean age 61±11 years) with incident ST-elevation MI (19 anterior, 19 inferior) – all successfully reperfused with thrombolytic - underwent ceMR at mean 4.1 days (range 1,7 days) after admission, and again at 3 months. The admission ECG was used to calculate the Aldrich score; ECGs at time of each ceMR were used to calculate the IS. Delayed enhancement images after gadolinium injection were used to measure IS on both ceMR scans.
Results: The median Aldrich score was 22.6% (min 8.7, max 36.6). IS on baseline ceMR was 22.2±10.1% (mean±SD) and on simultaneous ECG 18.4±9.3%; there was no significant correlation (r=0.21,p=0.28). There was, however, a significant relationship at 3 months: IS measured 16.2±8.7% on ceMR and 16.8±11.4% on ECG (r=0.43,p=0.032). When the 3 month results are viewed on a Bland Altman plot, the IS on ceMR is no longer consistently larger than that measured on ECG. IS on pre-discharge ECG correlated well with the 3 month ECG score (r=0.78,p<0.001).
Conclusion: IS on the acute ceMR generally exceeds the estimate on simultaneous ECG, but at 3 months there is a significant relationship. The early lack of correlation probably relates to difficulties in identifying the exact margins of the infarct zone - local oedema, microvascular obstruction and haemorrhagic transformation – which lead to overestimation of IS on ceMR but which have generally resolved by 3 months. The 3 month ceMR scan gives a more precise estimate of infarcted myocardium. These results suggest that the "success" of reperfusion may be estimated from simple comparison of 2 ECGs, using scoring systems derived largely in the pre-reperfusion era.

P764 Complexity and fractal measures of heart rate dynamics in patients undergoing direct PCI for acute myocardial infarction: impact of ischemia and reperfusion

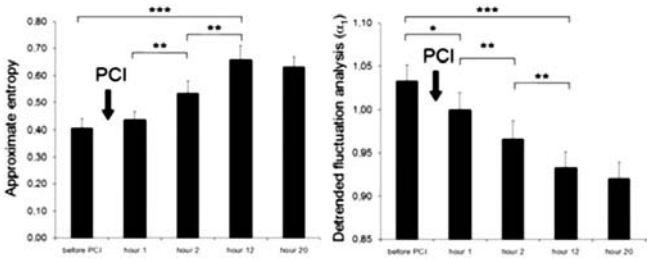
H. Bonnemeier[1], T. Demming[2], P. Scholten[3], M. Rouw[1], G. Van Oort[1], M. Barantke[2], J. Ortak[2], H. Schunkert[2]. [1]*Universitaet Zu Luebeck, Medizinische Klinik Ii, Luebeck, Germany;* [2]*Luebeck, Germany;* [3]*Arnhem, Netherlands*

Recently, analysis of non-linear heart rate dynamics has been applied to post

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

myocardial infarction (MI) risk stratification. The pathophysiological background of abnormal fractal heart rate behaviour in MI-patients has so far not been investigated. We hypothesized that reperfusion has significant effects on non-linear heart-rate dynamics and tested this assumption in patients undergoing direct PCI for acute MI.

Methods and Results: We investigated the most common non-linear indices [Detrended fluctuation analysis (DFA); power law slope (PLS); approximate entropy (APEn)] in 100 patients undergoing direct PCI for a first ST-segment elevation MI. DFA, PLS and APEn were determined before PCI, during the initial 2 hours after PCI, hours 12 and 20 after PCI from Holter-ECG-recordings started on hospital admission. DFA and PLS significantly decreased after PCI, exhibiting a constant further decline within 12 hours after PCI [DFA: before PCI 1.03 $\pm$0.3, hour 12 after PCI 0.93$\pm$0.03; $p<0.001$; PLS: before PCI -0.54$\pm$0.04, hour 12 after PCI -0.73$\pm$0.5; $p<0.001$), whereas APEn significantly increased within the same time period [APEn: before PCI 0.41$\pm$0.05, hour 12 after PCI 0.66$\pm$0.06; $p<0.001$].



*p<0.05; **p<0.01; ***p<0.001

Conclusion: Dynamical methods of heart rate dynamics based on fractals and complexity exhibit a characteristic time course after direct PCI for acute MI. The increase of APEn after reperfusion indicates an increase of the degree of irregular and complex heart rate fluctuations, suggestive for a recovery of cardiac vagal modulation.The decrease of DFA indicates both, a decline in sympathetic, as well as an increase in tonic vagal outflow. These observations provide novel evidence on reperfusion provoked autonomic reflexes that determine fractal organization in heart rate behavior.

CARDIAC COMPUTED TOMOGRAPHY

P765 Comparison of left atrium and pulmonary veins anatomy using 64-slice tomography in patients with Atrial Fibrillation and control subjects

I. Wozniak-Skowerska, M. Skowerski, A. Gola, M. Sosnowski, A. Wnuk-Wojnar, M. Trusz-Gluza. *Medical University of Silesia, I Department of Cardiology, Katowice, Poland*

Visualization of the left atria and pulmonary venous anatomy using multi-slice tomography (MSCT) is a new method useful for achieving better results and minimizing complications in patients (pts) undergoing catheter ablation (CA) for atrial fibrillation (AF). The aim of the study was to compare anatomy of the left atrium and pulmonary veins in pts with AF and the control subjects.

Methods: The MSCT scans performed with 64-slice Toshiba Multislice Aquilion System were done in 50 pts. The study group consisted of 33 pts (age: 48$\pm$9 yrs) with highly symptomatic drug refractory AF who were qualified to CA and 17 control subjects (C) without a history of AF matched for age and sex (age: 46$\pm$6 yrs). Left atrial and pulmonary vein (PV) anatomy was evaluated. Diameters of pulmonary vein ostia were measured in two directions -anterior-posterior (AP) and superior-inferior (SI). Venous ostium index (VOI) were calculated by dividing MSCT measurements in AP and SI directions.

Results: Common ostia of PV were detected in 13 AF pts (40%) and 3 pts (30%) from CG. Left and right common ostia of PV were observed in 10 (30%) pts and 3 (9%) pts with AF, respectively and in 2 (11%) pts and 1(6%) pt from CG, respectively. AP and SI diameters and VOI of PV ostia measured in AF and control pts are shown in the table. The diameter of left atrium was higher in AF pts than in the control group (39.2 mm vs. 35.2 mm, $p<0.005$).

AP and SI diameters and VOI of PV ostia

PV	PV - APAF (mm)	PV - APC (mm)	P	PV - SIAF (mm)	PV - SIC (mm)	P	VOIAF	VOIC	P
RS	17.7	14.9	**	15.3	13.7	NS	0.87	0.94	NS
RI	15.5	13.9	**	14.3	13.7	NS	0.92	1.02	*
LS	16.9	15.2	**	13.7	12.2	NS	0.82	0.81	NS
LI	15.9	13.8	**	12.5	10.4	NS	0.81	0.76	NS

** $p< 0.005$* $p< 0.05$.

Conclusions: MSCT visualization of pulmonary veins shows that variations in insertion of PV are present in AF pts and in control group. AF pts are characterized by larger ostial diameters than control subjects. We confirm an oval shape of pulmonary ostia, especially the left.

P766 Applicability of computational fluid dynamics for the in-vivo assessment of fluid tissue interactions in human coronary arteries

J. Rieber[1], K. Nikolaou[1], P. Jung[1], T. Potzger[1], H. Hetterich[1], A. Konig[1], B. Rogg[2], V. Klauss[2], N. Filipovic[3]. [1]*University of Munich, Medizinische Poliklinik, Cardiology Dept., Munich, Germany;* [2]*University of Bochum, Dep. of Mechanical engineering, Bochum, Germany;* [3]*University of Kragujevac, Dep. of supercomputing, Kragujevac, Serbia*

Beyond classic risk determinants local factors are involved in the initiation and progression of atherosclerotic lesions. These factors comprise multiple variables of tissue fluid interaction such as wall shear stress, equivalent stress and velocity distribution. The direct measurement of these factors in-vivo is difficult and restricted to animal models. However, using modern multislice computed tomography a detailed 3-D model of the epicardial coronary vessels can be obtained. Computational fluid dynamics (CFD) solver can be applied to calculate certain parameters of tissue fluid interactions. The aim of this study was to 1.) demonstrate the feasibility of in-vivo CFD calculation of human coronaries and 2.) to correlate the findings with radio frequency tissue information derived by intravascular ultrasound.

Methods and Results: We prospectively included 10 patients with suspected coronary artery disease who received a computed tomographic coronary angiography (CTA) (Dual source 64 slice CT) and invasive conventional coronary angiography within 4 weeks. In these patients intravascular ultrasound was attempted in all three epicardial vessels and ECG-triggered radio frequency tissue information was acquired simultaneously. The raw data of the axial slices obtained by CTA were transferred to a dedicated software package and a mesh model of the respective coronary artery was generated which was further used to calculate vessel wall shear stress, equivalent stress and velocity distribution. Calculation of CFD parameters was successfully performed in 24/30 coronary arteries. The remaining arteries were too small in diameter (n=2) or lacking of sufficient image quality (n=4). Seventeen coronary arteries (7 RCA, 5 LAD, 5 RCX) were assessed by intravascular ultrasound additionally. Vessel wall shear stress was inversely correlated with the presence of plaque (r= -0,62; $p<0.05$) as determined by intravascular ultrasound. However, no correlation of any CFD parameter with the radio frequency tissue information could be observed.

Conclusion: The findings of the present study demonstrate the feasibility of assessing fluid tissue interactions in human coronary arteries using modern multislice computed tomography non-invasively. The possible prognostic impact of this additional information has to be evaluated prospectively.

P767 Prevalence of coronary artery disease and plaque morphology by multi slice computed tomography in asymptomatic patients with type 2 diabetes

A.J.H.A. Scholte[1], J.D. Schuijf[1], A.V. Kharagjitsingh[2], J.W. Jukema[2], G. Pundziute[2], E.E. Wall Van Der[2], J.J. Bax[2]. [1]*Leiden, Netherlands;* [2]*Den Haag, Netherlands*

OBJECTIVE

Cardiovascular complications, including coronary artery disease (CAD), are the leading causes of morbidity and mortality in individuals with type 2 diabetes. The prevalence of CAD in asymptomatic patients with type 2 diabetes is unknown. The purpose of the study was to evaluate the prevalence of CAD as well as plaque morphology in this patient population using Multi Slice Computed Tomography (MSCT).

Methods: In 70 patients, 64-slice MSCT for coronary calcium scoring and coronary angiography was performed. Calcium score and number of diseased coronary segments was determined per patient; each diseased segment was classified as showing obstructive ($\geq$50% luminal narrowing) disease or not. In addition, plaque type (non-calcified, mixed and calcified) was determined.

Results: No or minimal calcium (calcium score $<$10) was observed in 31 (44%) patients. A calcium score of 10-100 was observed in 14 (20%) patients while a score of 101-400 or $>$400 was identified in respectively 12 (17%) and 13 (19%) patients.

On coronary angiography, a total of 56 (80%) patients showed CAD, of which 38 (54%) non-obstructive CAD and 18 (26%) obstructive CAD. In total, 322 coronary segments with plaque were identified, of which 132 (41%) contained non-calcified plaques, 65 (20%) mixed plaques and 125 (39%) calcified plaques.

While the percentage of patients with obstructive CAD paralleled increasing calcium score, the presence of CAD was also noted in 17 (55%) of patients with no or minimal calcium ($<$10).

Conclusions: MSCT angiography detected a high prevalence of CAD in asymptomatic patients with type 2 diabetes. The majority of detected plaques were either non-calcified or calcified. Importantly, a calcium score $<$ 10 did not exclude CAD in these patients. MSCT might be a useful technique to identify CAD in asymptomatic patients with type 2 diabetes.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P768 Predictors of major adverse cardiac events by multi-slice computed tomography

I. Pinto, R. Sasdelli, W. Ishikawa, M.P. Centemero, L.C. Souza, L.F. Tanajura, A. Sousa, J.E. Sousa, L.S. Piegas, A.D. Jatene. *Institute Dante Pazzanese - HCor, Sao Paulo, Brazil*

Purpose: Several authors have shown that multi-slice computed tomography (MSCT) allows the non-invasive evaluation of patients with coronary artery disease by permitting the calculation of the coronary calcium score and showing obstructions in the coronary tree. It is still unclear if data from MSCT may help in the prediction of the incidence of major adverse cardiac events (MACE) in the mid and long-term follow-up. The purpose of this study was to determine the MSCT predictors of MACE in a mid-term follow-up.
Methods: We selected 250 asymptomatic patients (pts) with, at least, 2 risk factors for coronary artery disease, that were undertaken to a 16 row MSCT. The scan included a series for calculation of the calcium score (CAS) and images acquired during the injection of 120 ml of iodine contrast media. Images analysis included the calculation of the CAS, the identification of coronary lesions, the quantification of vessel diameter (VD), the minimum vessel diameter (MVD) and the remodeling index (RI). The latter was defined as the vessel diameter at the lesion site divided by the VD. Lesions with RI >1 were considered as presenting positive remodeling. We also measured the mean coronary plaque attenuation coefficient. The patients were followed for three yrs.
Results: At the end of 3 yrs, 183 pts remained asymptomatic (Group I) while 67 (Group II) presented MACE (16 CABG, 44 Angioplasty and 7 had myocardial infarction). The mean number of risk factors, the mean age and the gender distribution were similar in both groups, but there were less diabetic patients in Group I (45, 25% vs. 34, 48%; p= 0.001).The mean CAS was higher in Group II (197$\pm$56 vs.48$\pm$26 in Group I, p=0.001), but the VD was similar between both groups (Group I 2.94$\pm$0.8 mm vs Group II 2.89$\pm$76 mm; p= 0.64). More patients had lesions of any degree in Group II (56, 83.6%) than in Group I (11, 16.3%; P=0.001). There were more patients with lesions presenting positive remodeling in Group II (44% vs. 82%, p= 0.049). The coronary artery plaque attenuation coefficient was significantly lower in Group II (165$\pm$53 vs. 62$\pm$58, p= 0.001) that also had more ulcerated plaques in Group II.
Conclusion: Diabetes, CAS, lesions of any degree, presence of positive remodeling and the plaque attenuation coefficient by MSCT were associated to MACE at the end of 3 years. Thus, the routine use of MSCT as a screening device may aid in the patient's risk calculation, adding relevant information to the currently standard methods for risk calculation.

P769 Quantitative parameters to compare image quality of non-invasive coronary angiography with 16-slice, 64-slice and dual source computed tomography

C. Burgstahler[1], A. Reimann[2], H. Brodoefel[1], I. Tsiflikas[1], M. Heuschmid[1], A.F. Kopp[1], S. Schroederl[2]. *[1]Eberhard-Karls-University, Department of Cardiology, Tuebingen, Germany; [2]Diagnostic Radiology, Tuebingen, Germany*

Background: Multi-slice computed tomography (MSCT) is a non-invasive modality to visualize coronary arteries with an overall good image quality. Improved spatial and temporal resolution of 64-slice and dual source computed tomography (DSCT) scanners are supposed to have positive impact on diagnostic accuracy and image quality. However, quantitative parameters to compare image quality of 16-slice, 64-slice MSCT and DSCT are missing.
Methods: A total of 256 CT scans were evaluated (Siemens, Sensation 16: n=90, Siemens Sensation 64: n=91, Siemens Definition: n=75). Mean Houndsfield Units were measured in the cavum of the left ventricle (LV), the ascending aorta (Ao), the left ventricular myocardium (My) and the proximal part of the left main (LM), the left anterior descending artery (LAD), the right coronary artery (RCA) and the circumflex artery (CX). Moreover, the ratio of intraluminal HU to myocardial contrast attenuation was assessed for all coronaries. Clinical data (body mass index (BMI), risk profile, gender, age, heat rate) were accessible for all patients.
Results: Mean contrast attenuation (CA) was significantly higher for DSCT in comparison to 64- and 16-slice MSCT within the RCA (347$\pm$13 vs. 254$\pm$14 [64-MSCT] vs. 233$\pm$11 [16-MSCT] HU), LM (362$\pm$11/275$\pm$12/262$\pm$9), LAD (332$\pm$17/248$\pm$19/219$\pm$14) and LCX (310$\pm$12/210$\pm$13/221$\pm$10, all $p<0.05$), whereas there was no significant difference between DSCT and 64-MSCT for the LV, the Ao and the My. The ratio of ventricular CA to myocardial CA was significantly better using DSCT (3.44$\pm$0.08 vs. 3.05$\pm$0.10 vs. 2.74$\pm$0.07, $p<0.05$) as well as the ratio of CA within the LAD to myocardial CA. Heart rate had a significant impact on CA in 16-slice and 64-slice CT ($p<0.05$) but did not affect DSCT. BMI had no impact on the contrast ratio in all CT generations.
Conclusion: Improved spatial and temporal resolution as well as reduced scan duration of dual source CT leads to a better CA within the coronaries and a better ratio within the ventricle and the LAD. DSCT is not affected by elevated heart rates in contrast to 64-slice and 16-slice MSCT. These advantages of DSCT might have positive impact on the diagnostic accuracy.

HEART FAILURE AND CARDIOVASCULAR MAGNETIC RESONNANCE

P770 Assessment of left ventricular dyssynchrony by 3D whole-heart MR tagging in patients with subacute myocardial infarctions

A.K. Rutz[1], S. Ryf[1], S. Plein[2], S. Kozerke[1], P. Boesiger[1], J. Schwitter[3]. *[1]Federal Institute of Technology, Institute of Biomedical Engineering, Zurich, Switzerland; [2]University of Leeds, Academic Unit of Cardiovascular Medicine, Leeds, United Kingdom; [3]University Hospital Zurich, Divivion of Cardiolog, Department of Internal Medicine Dim, Zurich, Switzerland*

Purpose: Individual responsiveness to cardiac resynchronization therapy (CRT) is not yet highly predictable. The aim was to quantify dyssynchrony in the whole heart in patients after myocardial infarctions (MI) and in controls applying a novel 3D MR tagging technique.
Methods: Ten patients with sub-acute MI and 5 controls were scanned with a 3D TFEPI CSPAMM sequence with a spatial/temporal resolution of 3.00x7.71x7.71mm^3/30ms in 3 breath-holds (1.5T, Philips, NL). For viability assessment, late enhancement images were acquired (Gadovist, 0.25 mmol/kg). Midwall circumferential fiber shortening (cFS) and time to maximum cFS (Tmax) were extracted from 48-60 segments/heart using a home-written peak-combination HARP software. The standard deviation (SD) of Tmax of all segments of the entire heart was calculated as a measure of dyssynchrony. In addition, for each segment the absolute time difference (Tdif) for maximum cFS relative to the mean Tmax of the entire heart was calculated and the sum of Tdif (total Tdif) was used as another marker of dyssynchrony.
Results: In patients and controls Tmax was not different (366$\pm$41ms vs 355$\pm$44ms p=ns). However, SD of Tmax was higher in patients (78$\pm$16ms vs 44$\pm$6ms, $p<0.001$). Total Tdif of 3.83$\pm$0.50 sec was also higher in patients than in controls (2.29$\pm$0.30 sec, $p<0.0001$). The location of increased Tmax correlated with scar (r=0.86; $p<0.001$, example in Fig. 1a: blue=decreased contraction; 1b: red=scar; 1c: blue=early contraction, red=delayed contraction, green=regular contraction).

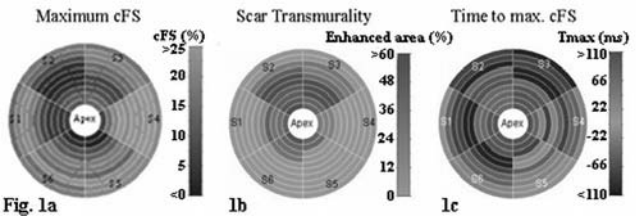


Fig 1. Function, Viability, Dyssynchrony

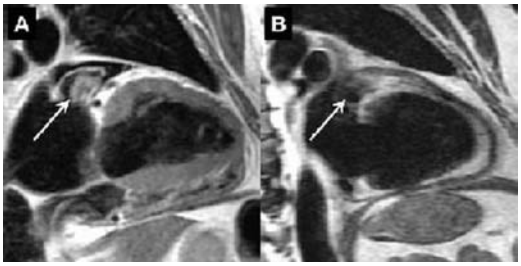
Conclusions: An accelerated 3D MR tagging acquisition yielded dyssynchrony information of the entire left ventricle. Together with MR-derived viability information, this MR approach shows potential to quantify both, dyssynchrony and scar and may guide CRT.

P771 Thrombogenic milieu assessed by cardiac magnetic resonance imaging in comparison to transesophageal echocardiography

P. Bernhardt[1], G. Pilz[2], M. Klos[1], R. Scheck[1], K. Haase[1], M. Wild[1], G. Braeuner[1], E. Ali[1], B. Hoefling[1]. *[1]University of Ulm, Internal Medicine Ii, Ulm, Germany; [2]Hospital Agatharied, Cardiac MRI, Hausham, Germany*

Background: Left atrial appendage (LAA) emptying velocities (LAAv), spontaneous echo contrast (SEC) and left atrial thrombi as determined by transesophageal echocardiography (TEE) are important predictors for cerebral embolism in patients with atrial fibrillation (AF). Aims of our study were to evaluate the ability of cardiac magnetic resonance imaging (CMR) to assess thrombogenic milieu in comparison to TEE findings by assessing LAA volume, ejection fraction and flow velocity as well as presence of left atrial thrombi.
Methods: Consecutive patients with AF scheduled for TEE prior to cardioversion were included to the study. Patients with sinus rhythm and TEE indication served as controls. All patients were scanned in a 1.5-T CMR scanner. Contiguous functional and T1-weighted images covering the entire LAA in long axes orientation (see Figure: (A) suspected thrombus/thrombogenic milieu [arrow] and (B) no thrombogenic milieu [arrow]) and phase contrast sequences orthogonal to the LAA orifice were acquired. CMR data were compared with TEE findings by experienced and blinded investigators.
Results: 59 patients (42 with AF and 17 with sinus rhythm) were included to the study. TEE determined LAAv highly correlated with LAA ejection fraction (κ=0.75), LAAv (κ=0.74) and with LAA dimension (κ=-0.76) evaluated by CMR as well as with degree of SEC (κ=-0.84). Our CMR algorithm yields in a sensitivity for detecting a thrombogenic milieu of 0.84, specificity of 0.88, positive predictive value of 0.76 and negative predictive value of 0.92.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020



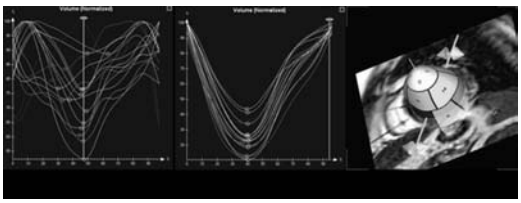
T1-weighted double-IR images

Conclusion: CMR is able to diagnose thrombogenic milieu consisting of reduced LAAv, dense SEC and/or left atrial thrombus determined by TEE. Thus, patients suspected to have an increased embolic risk may be evaluated by CMR examination.

P772 Assessment of mechanical dyssynchrony using cardiovascular magnetic resonance imaging and semi-automatic border detection: initial experience

R. Koos[1], M. Neitzel[1], G. Schummers[2], G.A. Krombach[3], T. Rassaf[2], R.W. Guenther[2], M. Kelm[2], H.P. Kuehl[2]. *[1]University hospital RWTH Aachen, Department of Cardiology, Aachen, Germany; [2]TomTec Imaging, Unterschleissheim, Germany; [3]University hospital RTWH Aachen, Department of Diagnostic Radiology, Aachen, Germany*

Background: The systolic dyssynchrony index (SDI) was introduced as a measure of mechanical asynchrony using 3D-echo (echo) to select patients (pts) who may benefit from CRT. However, 3D-echo may be inadequate in pts with suboptimal acoustic window. Thus, we aimed to compare the SDI in pts with reduced LV function and in healthy controls using cine cardiovascular magnetic resonance imaging (CMR).
Methods: 25 pts (65±7 years) with reduced LV function (EF 31±11%) and 10 control subjects (42±21 years, EF 70±11%) were included. For cine CMR a standard SSFP imaging sequence was used with a temporal resolution of 40 frames per RR-interval. A stack of 10 to 12 short-axis images covering the complete LV were acquired. Quantitative analysis was performed off-line using a preliminary semi-automatic border detection software adapted from 3D echo (4D MR-LV-Analysis). With this technique LV casts are calculated for each of the 40 time frames per RR interval providing global volume-time-curves. The casts can be further subdivided into 17 subsegments resulting in volume-time curves for each of these subsegments. Global volumes, EF and the SDI were calculated in each patient.
Results: Figure 1 gives an example for a patient with marked mechanical dyssynchrony (SDI 11%, left panel) and a normal control subject (SDI 3%, middle panel) as well as a view of the LV cast at end-diastole. The mean SDI differed significantly between pts (15±5%) and controls (5± 2%, $p<0.001$). A correlation between the EF and the SDI was observed ($r=0.83$; $p<0.001$).



Conclusions: The results of this preliminary study suggest that CMR with semi-automatic border detection may be useful for the assessment of mechanical dyssynchrony in pts with reduced LV function and poor echo image quality.

P773 Changes in left and right ventricular volumes and mass in patients with ischaemic heart disease and chronic heart failure during long term medical treatment: a cardiac magnetic resonance imaging study

C.V. Bourantas, H.P. Loh, E.I. Lukaschuk, L. Tin, J. Windram, A.C. Tweddel, A.L. Clark, N.P. Nikitin, J.F.G. Cleland. *Academic Cardiology, Castle Hill Hospital, Cottingham, United Kingdom*

Background and aims: ACE inhibitors and Beta-blockers are known to have initial favourable effects on left ventricular (LV) remodelling in patients with LV systolic dysfunction and dilatation due to ischemic heart disease. It is uncertain whether such effects persist, wax or wane during long-term follow-up.
Methods: 62 patients with ischaemic heart disease and left ventricular ejection fraction (LVEF) < 50% free of important valve or respiratory disease and already on stable treatment with ACE inhibitors and b-blockers for >9 months were enrolled. Each patient underwent Cardiac Magnetic Resonance Imaging (CMRI) at baseline and after a further year of follow-up. Body surface area (BSA) was used to index (I) volumes (V) and mass (M), measured at end-systole (ES) and end-diastole (ED) at baseline and follow-up in both left (LV) and right (RV) ventricles. Cardiac index (CI) was taken as the product of heart rate and stroke volume indexed to BSA (SVI). Statistical analysis was performed using the Wilcoxon test. A P value <0.01 was considered significant.
Results: Patients' mean age was 68±8 years, 84% were men, 15% were in NYHA class III/IV, 79% remained on ACE inhibitors and 87% beta-blockers at follow-up. 84% had a myocardial infarction, 18% had hypertension and 24% were diabetics. At baseline the mean LVEF was 32%, the mean RVEF was 44%. LVEF, LVEDVI, LVESVI, LVEDMI, LVESMI, LVSVI and LVCI were similar between the two examinations. However, there was progressive RV dilatation despite treatment (RVEDVI; 62.7 ± 10.5ml/m^2 vs. 72.5 ± 7.8ml/m^2, $p<0.0001$/RVESV: 26.3 ± 10.1ml/m^2 vs. 40.3 ± 15.1ml/m^2, $p<0.0001$). RVEF was preserved and RVEDMI, RVESMI, RVSVI and RVCI did not change between baseline and follow up. On Pearson correlation analysis only baseline RVEDVI ($r=0.46$, $p<0.001$ for change in RVEDVI and $r=0.46$, $p<0.001$ for change in RVESVI) and baseline RVESVI ($r=0.42$ $p<0.001$ for change in RVEDVI and $r=0.38$ $p<0.002$ for change in RVESVI) predicted RV dilatation.
Conclusions: Our results indicate that in patients on long term stable treatment for ischaemic heart disease and chronic heart failure, progressive RV but not LV dilatation persists. This is most obvious in patients with RV dilatation at baseline.

P774 Cardiac MRI for differential diagnosis of the apical ballooning syndrome

H. Thiele, F. Behrendt, K. Schindler, D. Kivelitz, G. Schuler. *Leipzig, Germany*

Background: The apical ballooning syndrome (ABS) has first been described in Japan and has recently been recognized in western countries. The underlying mechanisms of this clinical entity mimicking acute coronary syndromes (ACS) are still controversially discussed. Coronary spasm, coronary emboli with spontaneous fibrinolysis, regional myocarditis, and stunning as a result of excessive catecholamines are some of the potential mechanisms. Cardiac MRI might be an imaging tool to further elucidate the underlying mechanisms.
Methods: Between January 2005 and December 2006 27 consecutive patients, showing a left ventricular dysfunction with apical ballooning not explainable by the coronary artery status and initially admitted with ACS underwent cardiac MRI using a 1.5 T MRI scanner. Left ventricular function, T2-weighted spin echo sequence for oedema and delayed enhancement images after administration of. Gadoteridol were assessed.
Results: Between January 2005 and December 2006 2889 patients were admitted presenting with ACS with ST-elevation or non-ST-elevation myocardial infarction. Of these 27 (0.9%) patients (25 female, age 68±12 years) were identified with ABS without significant coronary artery disease. Cardiac MRI revealed extensive delayed enhancement in the territory of the LAD in 4 patients and a delayed enhancement pattern suggestive of acute myocarditis in 1. In all other patients neither delayed enhancement nor oedema was detected. In these latter patients cardiac MRI showed impaired left ventricular ejection fraction which normalized at 3 months follow-up (EF baseline: 49.6±11.0%; EF 3 months: 67.9±4.5%; $p<0.001$ versus baseline). Similarly, the enddiastolic volume (EDV) and endsystolic volume (ESV) improved at follow-up (EDV baseline: 131.5±27.2 ml; EDV 3 months: 115.1±22.3 ml; $p<0.001$ vs. baseline; ESV baseline 65.7±21.7 ml; ESV 3 months: 37.3±10.2 ml; $p<0.001$ vs. baseline). There were no differences in patient characteristics between patients with presumed coronary emboli with spontaneous lysis and myocarditis in comparison to those with ABS with the exception that in patients with ABS emotional stress as a trigger could be identified in 14 (64%) versus 0 ($p=0.03$).
Conclusions: The ABS is a phenomenon mimicking ACS which has a prevalence of approximately 1% in our patient series. Cardiac MRI allows differentiating ABS from other rare causes such as myocarditis and coronary emboli with spontaneous lysis. Therefore cardiac MRI should be performed in all patients with suspected ABS for differential diagnosis.

P775 Therapeutic angiogenesis with direct endomyocardial implantation of autologous bone marrow cells in patients with severe coronary artery diseases: insight from cardiac magnetic resonance imaging

W.S. Chan[1], S. Thambar[2], Y.L. Kwong[3], J. Mccrohon[4], P. Thomas[5], J.K.F. Chan[6], G. Lo[2], R.Y. Kwong[7], C.P. Lau[6], H.F. Tse[6]. *[1]Hong Kong, China, People's Republic of; [2]John Hunter Hospital, Cardiovascular Division, Newcastle, Australia; [3]Queen Mary Hospital, Department of Medicine, Hong Kong, Hong Kong SAR, People's Republic of China; [4]St George Hospital, Department of Cardiology, Sydney, Australia; [5]John Hunter Hospital, Cardiovascular Division, Sydney, Australia; [6]Hong Kong Sanatorium & Hospital, eDepartment of Radiology & Radiotherapy, Hong Kong, Hong Kong SAR, People's Republic of China; [7]Brigham and Women's Hospital, Cardiovascular division, Boston, United States of America*

Purpose: This study sought to investigate the changes in myocardial function and perfusion using cardiac magnetic resonance (CMR) imaging in patients with severe coronary artery disease (CAD) following direct endomyocardial bone marrow (BM) implantation.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Methods and Results: validated computer automated threshold-detection algorithm (GE Medical). A total of 12 (M: F = 11:1, mean age 65±10 yrs) patients with severe CAD who failed conventional medical therapy and received catheter-based direct endomyocardial implantation of autologous BM cells (16±6 x 106 cells per patient) into target ischemic zone at border of infarcted area as guided by electromechanical mapping were included. All patients underwent adenosine stress and rest gadolinium-enhanced CMR at baseline and 6-months follow-up to determine left ventricular ejection fraction (LVEF), first-pass myocardial perfusion and delayed contrast enhancement imaging. The results were analyzed using a computer automated threshold-detection algorithm (GE Medical). After 6-months, there was significant decrease in percentage area of peri-infarct regions (-10%, P=0.04) and increase in global LVEF (+5%, P=0.04) compared with baseline, without any change in the percentage area of total infarct (-6%, P= 0.06). Furthermore, the percentage of regional wall thickening (+5.2%, P= 0.04) and myocardial perfusion reserve (MPR) (+0.4, P=0.02) over the target regions, were significantly increased at 6-months compared with baseline.

Serial Changes in MRI Measurements

	Baseline	6 months
% $MDE_{peri\_infarct}$	26±0.1	16±0.1*
Wall thickening (%)	48.2±10.3	53.4±14.9*
LVEF (%)	51±9	56±10*
MPR	1.2±0.3	1.6±0.4*

(*P<0.05 vs. Baseline).

Conclusion: Direct endomyocardial implantation of autologous BM cells significantly improved global LVEF, regional wall thickening and myocardial perfusion reserve, and reduced percentage area of peri-infarct region regions in patients with severe CAD. These findings suggest that the beneficial effects of BM cells implantation are attributed by therapeutic angiogenesis.

YOUNG INVESTIGATORS' AWARD SESSION: BASIC SCIENCE

777 Epiblastic Cited2 function explains pleiotropy and penetrance of cardiac malformation resulting from its deficiency

S.T. Macdonald[1], S.D. Bamforth[1], C.R. Farthing[1], A.J. Franklyn[1], C. Broadbent[1], J. Schneider[1], R.J. Schwartz[2], Y. Saga[3], S. Bhattacharya[3]. *[1]University of Oxford, John Radcliffe Hospital, Cardiovascular Medicine, Oxford, United Kingdom; [2]Baylor College of Medicine, Department of Molecular and Cellular Biology, Houston, United States of America; [3]National Institute of Genetics, Division of Mammilian Development, Mishima, Japan*

Deletion of the transcription factor Cited2 results in highly pleiotropic and penetrant cardiac malformations including septal, outflow tract and aortic arch defects, and also adrenal agenesis and neural crest defects. At lower penetrance, Cited2 deficiency results in abnormal left-right patterning manifested by right atrial and pulmonary isomerism and abnormal ventricular topology. We used a conditional knockout approach to dissect the cardiovascular pleiotropy arising from Cited2 deficiency.

Methods: Conditional Cited2 deletion was achieved by crossing Cre-expressing and Cited2 floxed mouse strains. The Cited2 floxed allele activated lacZ expression following Cre-mediated recombination. Embryos were examined with magnetic resonance imaging and recombination assessed by lacZ staining. Quantitative-RT PCR was performed on 13.5 day post-coitum heart RNA.

Results: Conditional Cited2 deletion using an epiblast expressing Cre (Sox2Cre) completely recapitulated the global knockout phenotype with 10/10 knockout embryos showing cardiac defects and 6/10 showing left-right patterning defects. Neural crest Cited2 deletion using Wnt1Cre resulted in cranial ganglia fusions and exencephaly but no laterality, cardiac or adrenal abnormalities. Deletion in the cardiac mesoderm using Nkx2.5Cre, Mesp1Cre or Isl1Cre resulted in low penetrance of septal defects (4/11, 2/18 and 0/14 respectively) with no outflow tract, aortic arch or laterality defects. LacZ staining revealed recombination efficiencies over 90%. Cited2 expression was reduced 4.7 fold in Cited2-/flox:Nkx2.5Cre hearts in comparison to Cited2+/flox:Nkx2.5Cre hearts (p= $1.1x10^{-5}$) but in keeping with the absence of a left-right patterning defect and low frequency of septal defect, there was no difference in cardiac Pitx2c expression.

Conclusions: The high penetrance and pleiotropy of cardiac malformation in Cited2 deficiency arises from an essential requirement in the epiblast or in germ layers (meso, endo and ectoderm) deriving from it, not a later cell autonomous function in cardiogenic mesoderm or neural crest. As epiblastic Cited2 deletion recapitulates the left-right patterning defects, cardiac malformations such as ASD, VSD, DORV, TGA, and aberrant right-sided aortic arches can arise from a subtle abnormality of a left-right patterning pathway in epiblast derived tissues. Our results explain how diverse cardiac malformations can arise as the consequence of a defect in a single gene and support the idea that left-right patterning genes are candidates for human congenital heart disease, even in the absence of a classical laterality defect such as isomerism.

778 Intramyocardial delivery of protease-resistant Stromal cell derived factor-1 by self-assembling peptide nanofibers

V.F.M. Segers, T. Tokunou, C. Macgillivray, J. Gannon, L.J. Higgins, R.T. Lee. *BWH, Harvard Medical School, Medicine, Cambridge, United States of America*

A useful approach to cardiac regeneration after myocardial infarction could be local intramyocardial delivery of the stem cell chemoattractant Stromal cell derived factor-1 (SDF-1). However, injected SDF-1 rapidly diffuses away from the site of injection. Therefore, we designed fusion proteins of SDF-1 and the sequence of self-assembling peptides, allowing prolonged delivery in the myocardium. Self-assembling peptides are soluble at low pH and ionic strength, but form a stable hydrogel of nanofibers when exposed to physiological pH and ionic strength. In addition to rapid diffusion, SDF-1 delivery is also challenged by inactivation by matrix metalloproteinase-2 (MMP-2), which is expressed after myocardial infarction.

Methods: We designed a mutant SDF-1 resistant to MMP-2. Recombinant SDF-1 proteins were expressed in E coli and purified by a 4 step procedure consisting of affinity chromatography, cation exchange chromatography, oxidative refolding, and reversed phase-chromatography. The mutant SDF-1, called SDF-1(S4V), was resistant to MMP-2 cleavage but remained bioactive in chemotaxis assays. SDF-1-RAD fusion proteins (RAD representing the 16 amino acid sequence of self-assembling peptides) were made and incorporation into self-assembling peptides was measured in vitro by radioactive labeling of SDF-1. SDF-1, SDF-1(S4V), SDF-1-RAD and SDF-1(S4V)-RAD (30nM) were injected with 80μl self-assembling peptides intramyocardially in infarcted myocardium of rats after ligation of the LAD. Left ventricular function was measured 28d after surgery by catheterization.

Results: SDF-1-RAD fusion proteins stably incorporated into self-assembling peptides and were retained even after extensively washing in vitro. Intramyocardial injection of the MMP-2 resistant SDF-1(S4V)-RAD fusion protein with nanofibers increased ejection fraction from 34.0±2.5% (n=21) in the myocardial infarction only group to 49.5±2.9% (n=18, p=0.004). SDF-1, SDF-1(S4V), and SDF-1-RAD did not improve cardiac function. Capillary density increased from 169±42/mm^2 in MI only group to 283±27/mm^2 in SDF-1(S4V)-RAD + self-assembling peptide group (p=0.035). Finally, c-Kit+/Flk-1+ cells (consistent with endothelial progenitor cell phenotype) increased from 46±7 cells/section in MI only to 132±35 cells/section in MI+NF/SDF-1(S4V)-RAD (p=0.002).

Conclusions: By the combined effect of mutating SDF-1 to be resistant to MMP-2 cleavage and prolonged delivery by self-assembling peptides, cardiac function after myocardial infarction is improved. This combined strategy also increased capillary density and endothelial progenitor cell infiltration.

779 Myocyte enhancer binding factor 2 activity disruption induces phenotypic changes and signs of bleeding in atherosclerotic plaques

A.O. Kraaijeveld[1], M.L. Lucerna[1], R. Van Oort[2], T.J.C. Van Berkel[2], J.W. Jukema[3], L.J. De Windt[1], E.A.L. Biessen[2]. *[1]Lacdr, Biopharmaceutics Dept., Leiden, Netherlands; [2]Hubrecht Laboratory, Utrecht, Netherlands; [3]Leiden University Medical Centre, Cardiology, Leiden, Netherlands*

Background: The transcription factor myocyte enhancer factor 2A (MEF2A) was recently found to be expressed in vascular smooth muscle (VSMC) and endothelial cells. Furthermore, MEF2A polymorphisms were identified that imparted an increased risk for coronary artery disease and myocardial infarction, suggestive of a role of MEF2 family members in these disorders. This led us to investigate whether MEF2 does so by modulating atherogenesis and/or angiogenesis.

Methods and Results: Murine VSMC proliferationon Matrigel was 3.1-fold increased after infection with constitutively active MEF2 adenovirus (Ad-caMEF2) compared to Ad-empty (P=0.007). Likewise, MEF2 overexpression markedly enhanced the proliferation of mouse hemangioma endothelial cells (41,700±9,118 vs. 11,400±2,789 DPM/mg for Ad-empty treated cells; P=0.015). These findings were confirmed in vivo in a Matrigel plug assay, while 1 week after s.c. injection of C57/Bl6 mice with Matrigel containing Ad-caMEF2 or Ad-empty, Ad-caMEF2 plugs (N=5) revealed a clear induction of neovessel formation compared to Ad-Empty plugs, as assessed by the number of infiltrating neovessels. Next, we addressed the effect of vascular MEF2 activity modulation on plaque formation in Western type diet (0.25% cholesterol) diet fed apoE-/- mice (n=34) using an model of collar-aided, flow induced carotid artery atherosclerosis. Four weeks after surgery, the resulting plaques were incubated transluminally on the left side-with Ad-caMEF2, Ad-dnMEF2 (dominant negative MEF2) or Ad-empty and sham operated on the right side. After 17 days, mice were sacrificed and carotid artery plaques were analysed morphometrically and histologically. No differences were seen in plaque size, media size and percentage stenosis. Also, plaque morphology and composition remained unaffected as well. Interestingly however, more intraplaque haemorrhages were observed in the dnMEF2 versus sham treated groups (38 vs. 0% Perl's iron positive plaques; P<0.01).

Conclusion: We are the first to show thatMEF2 activation is highly mitogenic and proangiogenic to vascular wall cells in vitro and in vivo. Futhermore, vascular modulation of MEF2 activity leads to significant alterations in atherosclerotic plaque phenotype in vivo.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

780 Atherosclerotic plaque regression and stabilization following short term treatment with ApoAI-Milano

B. Ibanez[1], G. Vilahur[2], G. Cimmino[2], W.S. Speidl[2], A. Pinero[2], M.U. Zafar[2], B.G. Choi[3], I. Sorokin[3], V. Fuster[3], J.J. Badimon[3]. [1]*Mount Sinai School of Medicine, Cardiovascular Institute, New York, United States of America;* [2]*CSIC-ICCC, Cardiovascular Research Center, Barcelona, Spain;* [3]*Mount Sinai Hospital, Cardiovascular Institute, New York, United States of America*

ApoAI-Milano (ApoAI-M) is a mutant form of ApoAI that has shown to regress atherosclerotic (AT) lesions in humans after 5 weeks of treatment. Magnetic Resonance Imaging (MRI) is an accurate non-invasive tool to assess changes of AT plaques. The aim of this study was to investigate the effects of short-term administration of recombinant (r) ApoAI-M on lesion volume, as well as gene and protein expression at the vascular level, in an experimental AT model.

Methods: AT lesions were induced in rabbits (n=40) by a combination of 9-months of atherogenic diet plus 2 aortic balloon denudations. MRI images (T2W and PDW) were acquired using a 1.5T MRI system by scanning 33 consecutive abdominal aorta segments (3 mm thickness, no gap) at the end of AT induction. Animals were randomized into rApoAI-M (ETC-216; Pfizer): 2 injections (75mg/kg) in 4 days, or placebo.

A second MRI was performed 4 days after last dose, followed by animals sacrifice. The 10 most diseased segments were selected to assess the efficacy of treatment (a total of 400 segments were analyzed).

Inflammation was assessed in the aortic wall by Polymerase chain reaction (gene expression), Western-blot (protein expression), and zymography.

Results: At the end of AT induction, both groups showed similar plaque volume: 29.5±0.5 in rApoAI-M vs 29.0±0.6 mm^3 in placebo. Administration of rApoAI-M resulted in a 5.5% regression of plaque volume ($p<0.001$ vs. baseline) compared to 2.7% progression in placebo (p=NS) resulting in a difference of 6.5% (rApo AI-M 27.9±0.5 mm^3 vs. 29.7±0.7 mm^3 in placebo; p=0.02).

rApoAI-M induced a significant decrease in the expression of genes encoding inflammation-related proteins: MCP-1 (p=0.03), COX-2 ($p<0.05$). Western blot revealed that treatment resulted in significant lower antigen levels of tissue factor (p=0.032), MCP-1 (p=0.024), and COX-2 (p=0.04).

Gelatinolytic activity, levels of pro- and active MMP-2 on zymography, was dramatically reduced by rApoAI-M (p=0.01).

In addition we found a significant up-regulation of COX-1, both at the gene(p=0.02), and the protein levels ($p<0.05$).

Conclusions: The administration of rApoAI-M induced a significant (6.5%) regression of established atherosclerotic plaques. Furthermore, gene and protein expression at the wall level revealed signs of plaque stabilization (down-regulation of inflammatory markers at pre-and post-transcriptional levels, along with a recuced gelatinolytic activity).

Our results suggest that interventions raising HDL via increase in ApoAI may have a dual effect by not only regressing established AT lesions but also changing them into a more "stable" phenotype.

YOUNG INVESTIGATORS' AWARD SESSION: CORONARY PATHOPHYSIOLOGY AND MICROCIRCULATION

782 Plasma asymmetrical-dimethyl-arginine (ADMA) regulates nitric oxide bioavailability and vascular superoxide production in human vessels

C. Antoniades[1], C. Shirodaria[2], P. Leeson[1], D. Tousoulis[3], R. Pillai[2], C. Ratnatunga[2], C. Vasiliadou[1], A.S. Antonopoulos[1], C. Stefanadis[1], K.M. Channon[2]. [1]*University of Oxford, Cardiovascular Medicine Dept, Lab 3, Oxford, United Kingdom;* [2]*Oxford, United Kingdom;* [3]*Athens, Greece*

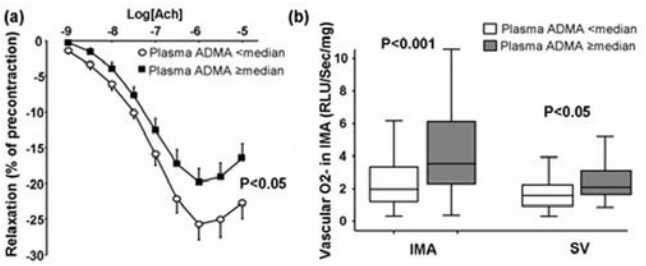
Asymmetrical dimethylarginine (ADMA) is an endogenous inhibitor of endothelial nitric oxide synthase (eNOS). Although its role has been evaluated in-vitro and in animal models, its effects in human vasculature are unknown.

Aim: We examined the effect of plasma ADMA on endothelial NO bioavailability and superoxide radicals (O2-) production in human vessels, from patients with advanced atherosclerosis.

Methods: Paired samples of saphenous veins (SV) and internal mammary arteries (IMA) were collected from 160 patients (aged 65.2±0.64 years old) undergoing CABG. The vasomotor responses to acetylcholine (Ach) were evaluated in SV segments ex-vivo. Vascular O2- (in the presence or absence of eNOS inhibitor LNAME) was measured in paired samples of SV and IMA, by lucigenin-enhanced chemiluminescence.

Results: High plasma ADMA levels were associated with decreased vasorelaxations of SV to Ach (Fig. a). Similarly, ADMA was associated with higher O2- production in both SV and IMA (Fig b), while there was a rather weak association between plasma ADMA and the LNAME-inhibitable O2- production in IMA (r=-0.259, p=0.008) but not in SV (r=-0.173, p=0.074). In multivariate linear regression, plasma ADMA was an independent predictor of vascular O2- (β(SE):3.39(0.416), p=0.0001), along with diabetes mellitus (p=0.042), dyslipidemia (p=0.018) and the angiographic extend of coronary atherosclerosis (p=0.048).

Conclusions: This is the first study demonstrating that ADMA has a direct impact on vascular NO bioavailability and O2- production in human vessels, in patients with coronary artery disease. However, further studies are required to elucidate the exact role of ADMA on eNOS coupling in human vessels.



783 Plasma levels of Tromboxane A2 at admission predict no-reflow after primary percutaneous coronary intervention

G. Niccoli[1], S. Giubilato[1], E. Russo[1], C. Spaziani[1], B. Fusco[1], A. Leo[1], S. Riondino[2], F. Pulcinelli[2], L.M. Biasucci[1], F. Crea[1]. [1]*Catholic University Medical School, Institute of Cardiology, Rome, Italy;* [2]*La Sapienza University Medical School, Institute of Pathology, Rome, Italy*

Purpose: Experimental studies suggest an important pathophysiological role of platelets in coronary no-reflow.A recent report has shown that increased platelet volume in man predicts no-reflow after primary percutaneous coronary intervention (PCI) despite early aspirin administration in patients with ST elevation MI. In this study, we aimed at assessing if pre- PCI platelet hyperactivity as assessed by plasma levels of tromboxane A2 (TXA2) predicts coronary no-reflow.

Methods: we enrolled 47 consecutive patients (age 61±12, male sex 76%) admitted for their first ST elevation myocardial infarction undergoing primary PCI between May and October 2006. All patients were treated with aspirin (300 mg) and clopidogrel (600 mg) on admission in the emergency room. In the catheterization laboratory a venous blood sample was collected at the beginning of the procedure. Plasma was obtained and stored at -80 for planned analysis. TXA2 levels were assessed by ELISA and expressed as pg/ml. All patients were treated with Abciximab during the procedure (after confirmation of coronary TIMI flow 0-1) and thrombus aspiration was performed in 35% of patients. Coronary angiograms were independently reviewed by two expert angiographers. Angiographic no reflow was defined as final TIMI flow ≤2 or final TIMI flow 3 with a MBG <2. Data are presented as median and interquartile interval.

Results: TXA2 levels were higher in patients with TIMI flow ≤2 compared to those with TIMI flow 3 [17 (11.6-29.6) vs 4.9 (0.4-19), p=0.035]. Higher levels of TXA2 were found in patients with final MBG <2 compared to those with final MBG ≥2 [17.7 (8.4-31.5) vs 4 (0.4-10.4), p=0.006]. At multivariate analysis TXA2 levels were independent predictor of no-reflow (Odds ratio (OR) 1.05 95% Confidence interval (CI) 1-1.12, p=0.04). No-reflow also significantly correlated with infarct size as detected by Troponin T peak levels (p=0.025).

Conclusions: Our finding suggests that platelet activity may contribute to reperfusion injury in the setting of primary coronary intervention, opening new perspectives in the understanding and treatment of no-reflow phenomenon.

784 Circulating and graft-infiltrating dendritic cells after human heart transplantation

S. Kofler, Z. Sisic, I. Kazcmarek, B. Meiser, B. Reichart, M. Weis. *University Hospital Grosshadern, cardiology, Munich, Germany*

The pathway of indirect allorecognition, by which donor-MHC-derived peptides are presented to host alloreactive T-cells (TC) by recipient's antigen presenting dendritic cells (DCs), plays a fundamental role in the process of chronic rejection. We characterized circulating (peripheral blood mononuclear cells, PBMCs) and graft-infiltrating DCs in patients after heart transplantation (HTx).

Methods: PBMCs and myocardial DCs were quantified using real-time PCR in 33 consecutive patients during the first two years after HTx (1, 6, 12, 24 months follow-up). DC were characterized using specific primers for CD1a (immature DCs), CD86 (mature DCs), CD123 (plasmacytoid DCs), BDCA1 (myeloid DCs), CD178 (activated TCs) and FOXP3 (regulatory TCs).

Results: CD86, CD123, and BDCA1 gene expression in PBMCs is highly up-regulated in transplant recipients during follow-up (6-24 months versus 1 month after HTx; $p<0.05$). Graft infiltrating DCs are of a plasmacytoid genotype and are mainly expressing markers of immaturity. Gene expression for regulatory TC and DCs is enhanced during longtime follow-up compared to baseline ($p<0.05$). Circulating and graft-infiltrating CD1a gene expression was closely related (r=0.7; $p<0.05$). Patients with ISHLT>1a acute rejection showed a significantly increased myocardial mRNA expression for CD1a, CD86 and activated TCs compared to patients without acute rejection. With regard to the different immunosuppressive regimens there was a significant increase of CD123 expressing PBMCs in tacrolimus (tac)/Mycophenolatmofetil (mmf) vs. sirolimus (sir)/mmf ($p<0.05$) and sir/tac ($p<0.05$) treated patients. Moreover, CD178 gene expression was enhanced in tac/sir patients compared to patients treated with sir/tac (p=0.049).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusions: Circulating and graft infiltrating DCs are time-dependently enhanced after human heart transplantation. Patients with even minor acute rejection episodes have increased myocardial gene expression for immature and mature DCs.

785 Should we use bosentan to treat systemic sclerosis associated pulmonary hypertension in the presence of pulmonary fibrosis?

P. Kabunga[1], C.E. Handler[1], C. Das[1], A. Kotecha[1], C. Denton[1], S. Reddecliffe[1], C. Black[1], C. Smith[2], J.G. Coghlan[1]. [1]*Royal Free Hospital, Cardiology, London, United Kingdom;* [2]*University College Medical School, Primary care and Population Sciences, London, United Kingdom*

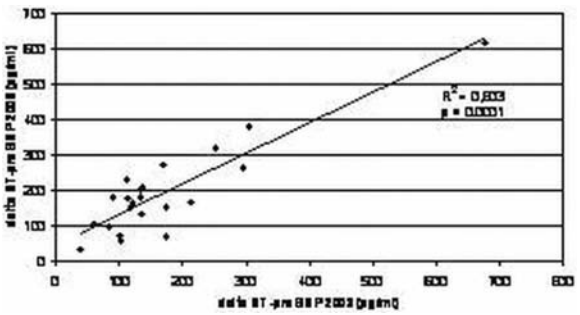
Purpose: To evaluate the impact of bosentan on survival in patients with systemic sclerosis associated pulmonary arterial hypertension (SSc-PAH) and pulmonary fibrosis (PF) before 2002 (pre-bosentan era) and after 2002 (bosentan era).
Background: We have previously reported improved survival in patients with isolated SSc-PAH treated with bosentan. Patients with SSc-PAH may have a "disproportionately" high mean pulmonary arterial pressure (mPAP) despite having only minor PF diagnosed by lung function tests (LFT, FVC < 70%) and high resolution CT scanning (HRCT). Bosentan should theoretically show some benefit irrespective of the presence of PF.
Methods: We have used bosentan as first line treatment for SSc-PAH since 2002. We retrospectively studied 305 consecutive SSc-PAH patients diagnosed by right heart catheterisation between 1996 and 2006. Data in 80 patients with pulmonary fibrosis (PF+) (diagnosed by HRCT and LFT, FVC < 70%) and 225 SSc-PAH patients without pulmonary fibrosis (PF-) were analysed. All patients received therapy, according to local protocols. The mPAP in the PF- and PF + groups were 41 and 38 mmHg respectively. Mean age was 61 years in the PF- and 56 years in the PF+ group [p = 0.0002].
The mPAP in PF- patients before 2002 was 41 mmHg and 40 mmHg after 2002. The mPAP in PF + patients before 2002 was 37mmHg and 39mmHg after 2002. Survival at 3 years (reported as Kaplan–Meier estimates) before and after 2002 was compared in the two groups.
Results: In the whole group of patients, survival at 1 year, in the PF - group was 80% and 76% in the PF+ patients, and at 3 years survival was 55% of PF- and 48% of PF+ patients. After adjusting for age, in a proportional hazards model, the hazard ratio (95% CI, p value) in the PF + group was 1.36 (0.85, 1.94; p = 0.09). In the PF- group, survival at 3 years was 44% in the pre bosentan era and 65% in the bosentan era. [p = 0.005].
In the PF +ve group, survival at 3 yearswas 49% in the pre Bosentan era and 48% in the Bosentan era. [p = 0.85].
Conclusion: Survival was better in PF- patients with SSc-PAH, treated with bosentan but not improved in PF+ patients, despite the younger age and lower mPAP in the PF+ patients. The presence of pulmonary fibrosis may influence the use of bosentan in patients with SSc-PAH.

YOUNG INVESTIGATORS' AWARD SESSION: CLINICAL SCIENCE

787 High reproducibility of cardiac biomarker release in response to endurance exercise

A. Sahlen[1], M. Stahlberg[1], T. Fux[1], A. Rubulis[1], J. Svensson[1], T. Marklund[2], F. Braunschweig[1]. [1]*Karolinska University Hospital, Stockholm, Sweden;* [2]*Roche Diagnostics Scandinavia, Stockholm, Sweden*

Purpose: Long-distance running has been shown to induce transient cardiac dysfunction and release of cardiac injury markers in certain individuals. It is not known if the magnitude of biomarker release is reproducible and characteristic for each individual.
Methods: We studied 22 runners (18 male, mean age 62 years, range 57-72) who participated in a 30 km cross-country race (Lidingöloppet) both 2003 and 2006. Blood samples were taken before and immediately after the race for a panel of blood tests including N-terminal pro-Brain Natriuretic Peptide (NT-proBNP), Troponin T (TnT). NT-proBNP <194 pg/ml and TnT <0.03 μg/l were considered normal.



Results: At both races, all subjects had baseline TnT levels in the normal range. Abnormal TnT was seen in 7 and 10 subjects, after the first and second race, respectively. The delta TnT in the first and second race correlated strongly (0.84, p<0.001). Baseline NT-proBNP in 2003 and 2006 was 84±63 and 80±74 (ns) and increased by 198% and 221% during the races. A strong correlation was seen between the delta NT-proBNP in race 1 and 2 (r=0.9, p=0.001; Fig. 1). Both the mean increase in TnT (0,02 vs 0,03 μg/l, p<0.01) and in NT-proBNP (170 vs 194 pg/ml, p=0.05) were significantly larger in 2006.
Conclusion: Strenuous physical exertion in senior athletes leads to a marked elevation in Troponin T and NT-proBNP, suggestive of myocardial damage. This phenomenon is highly reproducible, which raises concerns that certain runners may be predisposed to exercise-induced cardiac dysfunction. The larger release of biomarkers in the second race may reflect increasing age and/or environmental factors.

788 Coronary artery spatial distribution of thin-cap fibroatheroma: A three-vessel optical coherence tomography study

K. Fujii, M. Masutani, T. Okumura, D. Kawasaki, T. Akagami, S. Morimoto, T. Sakoda, T. Masuyama, M. Ohyanagi. *Hyogo College of Medicine, Division of Cardiovascular Disease, Nishinomiya, Japan*

Purpose: Plaque rupture is the most frequent cause of coronary thrombosis such as acute myocardial infarction (AMI). It has been recognized that thin-cap fibroatheroma (TCFA) is the precursor lesion of plaque rupture. It is clinically important to understand the potential sites of TCFA in order to prevent coronary events. Therefore, we evaluated the coronary spatial distribution of TCFAs using optical coherence tomography (OCT) that is a new high-resolution (approximately 10microm) imaging modality.
Methods: We performed three-vessel OCT examinations in 46 patients; 34 patients with AMI and 12 patients with stable angina pectoris (SAP). OCT criteria for TCFA was lipid-rich plaque with cap thickness <65microm. The distance between each TCFA segment and the respective coronary ostium was measured with motorized OCT transducer pullback. The overall length of the region of interest, subsequently divided into 10mm segments, was 60.2±21.6 mm long (range: 18.9 – 121.1 mm).
Results: The OCT detected 82 TCFAs in 37 patients: 76 were identified in AMI patients and 6 in SAP patients. Of all TCFAs, 24 were located in the left anterior descending artery (LAD), 16 in the left circumflex artery (LCX), and 42 in the right coronary artery (RCA). Most LAD TCFAs were located between 0 and 40mm from the LAD ostium (96%). Similarly, LCX TCFAs were predominantly located between 0 and 40mm from the LCX ostium (69%). Conversely, RCA TCFAs were evenly distributed in the entire coronary trees.

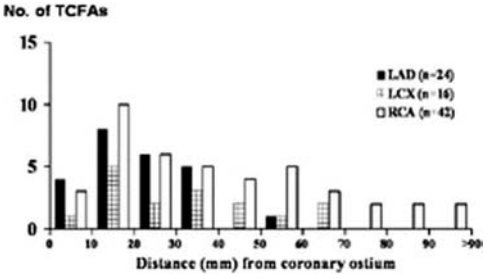


Figure 1

Conclusion: Three-vessel OCT imaging showed that TCFAs tend to cluster in predictable "hot spots" within the proximal segments of the LAD and LCX, and the entire segments of the RCA.

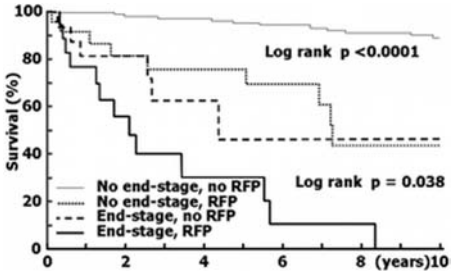
789 Left ventricular restrictive filling pattern in hypertrophic cardiomyopathy: prevalence, incidence, clinical/pathophisiological profile and prognostic implications

E. Biagini, G. Rocchi, C. Lofiego, F. Coccolo, M. Ferlito, F. Pasquale, C. Borghi, S. Rosmini, A. Branzi, C. Rapezzi. *University Hospital S. Orsola-Malpighi, Dept. of Cardiology, Bologna, Italy*

Purpose: Investigate frequency, clinical correlates and prognostic significance of left ventricular (LV) restrictive filling pattern (RFP) in a large cohort of patients with HCM.
Methods: We reviewed echocardiograms of 239 consecutive HCM patients diagnosed from 1987 to 2005 (65% men; age 42±19 yr) submitted to annual clinical, ECG and echocardiographic evaluation. RFP was considered as E-deceleration time ≤130msec and E/A ratio ≥2.
Results: Prevalence of RFP at 1st evaluation was 6% (14/239). Incidence of RFP was 12 per 1000 patient-years (22 new cases during 15±8 years). Pa-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

tients with prevalent/incident RFP more often had family history of sudden death (33% [12/36] vs 15% [30/203], p=0.007) and atrial fibrillation (22% [8/36] vs 10% [20/203], p=0.03); had larger left atrial (51±11 vs 44±9, p<0.001) and LV end-diastolic (47±11 vs 43±8 mm, p=0.005) diameters; and had lower LVEF (53±11% vs 69±14%, p=0.007). Annual incidence of sudden death was higher among patients with RFP (5.0% vs 0.4%, p<0.0001). At multivariable Cox analysis of baseline variables, predictors of cardiac death/heart transplantation were prevalent RFP (OR 7.2, 95%CI 3.3–15.7) and end-stage HCM (OR 33.6, 95%CI 12.5–90.5). The Figure reports time-dependent analysis of freedom from cardiac death/heart transplantation. Stratifying by ongoing end-stage HCM, RFP was associated with poorer survival in both strata (annual event rates, 7% vs 1%, p<0.0001 with end-stage; 32% vs 11%, p=0.038 without end-stage).



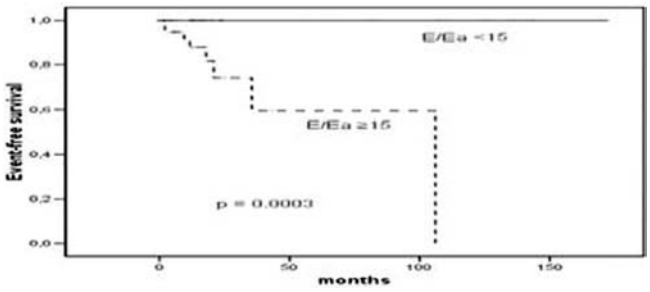
Time-dependent survival analysis

Conclusions: RFP occurs in a relevant minority of HCM patients with/without end-stage evolution, and is associated with increased risk of sudden death and cardiac death/heart transplantation. The different combinations of presence/absence of RFP and end-stage HCM may confer different degrees of prognostic severity.

790 Utility of tissue doppler imaging in predicting outcome in patients with hypertrophic cardiomyopathy

G. Efthimiadis, G. Giannakoulas, D. Parcharidou, H. Karvounis, S. Mochlas, I. Styliadis, C. Papadopoulos, P. Kounatiadis, C. Pliakos, G. Parcharidis. *AHEPA Hospital, First Cardiology Department, Thessaloniki, Greece*

Purpose: Transmitral E/septal Ea ratio ≥15 is an excellent predictor of adverse outcome in cardiac disease. We hypothesized that a transmitral E/septal Ea ≥15 would predict the risk of adverse outcome, including sustained ventricular tachycardia (VT), cardiac arrest, implantable cardioverter defibrillator (ICD)-discharge, or sudden death (SD) in patients with hypertrophic cardiomyopathy (HCM).
Methods: We prospectively studied 96 consecutive patients with HCM and normal sinus rhythm (median age 53 years) who completed all noninvasive tests for risk stratification, i.e., personal and family history, clinical evaluation, 12-lead ECG, echocardiography, 24-h ECG monitoring, and exercise test. Patients were followed for a median of 20.6 months.
Results: The variables predictive of adverse clinical outcomes by stepwise regression analysis were family history of premature SD (p=0.03), syncope (p<0.001), maximum wall thickness ≥3 cm (p=0.02), and septal E/Ea ≥15 (p<0.001). In a stepwise multivariable model the only independent prognostic indicator was a septal E/Ea ≥15 (RR 0.26, 95% CI 0.2 to 0.58, p<0.001). The cumulative event-free survival rate was 78.9% in patients with septal E/Ea ≥15, and 100% in patients with septal E/Ea <15 (p=0.0003, Figure). Patients with septal E/Ea ≥15 had more frequently family history of HCM (p<0.0001), obstructive HCM (p=0.012), NYHA class III/IV (p=0.04), syncope (p=0.01) and maximum wall thickness ≥3 cm (p=0.01).



Figure

Conclusions: Transmitral E/septal Ea ratio ≥15 predicts patients with HCM who are at risk of sustained VT, cardiac arrest, ICD-discharge, or SD. It also provides useful information for patient clinical status.

YOUNG INVESTIGATORS' AWARD SESSION: THROMBOSIS

792 The search for the origin of blood-borne tissue factor using siRNA-mediated gene silencing approach

M. Sovershaev[1], E. Egorina[2], Y. Kiselev[1], H. Devold[1], J.-O. Olsen[1], B. Osterud[1]. *[1]University of Tromsoe, Biochemistry Department, Tromsoe, Norway; [2]University of Tromsoe, Biochemistry Department, Tromsoe, Norway*

Tissue factor (TF) is a major initiator of blood coagulation and its disregulation plays an important role in pathogenesis of thrombosis. Although conflicting studies found monocytes, granulocytes and lymphocytes as being positive for TF, the exact source of blood-borne TF remains unclear. In attempt to obtain a definitive answer to this question, we applied the technique of TF gene silencing by use of nucleofection delivery of siRNA into immunologically purified human peripheral blood monocytes, eosinophils and granulocytes. The purity of cell preparations was assessed by flow cytometrical analysis and was over 96-98%. Assessed by confocal microscopy, siRNA was delivered into over 85% of cells. This resulted in efficient silencing of TF expression judged by immunoblotting and TF activity assay. LPS-stimulation of plated monocytes resulted in a 20-fold increase in TF protein levels and a 10-fold increase in TF activity. Neither the stimulation of plated eosinophils granulocytes with Ca-ionophore or LPS/PMA, respectively, yielded any detectable TF levels and activity. After isolation of cells from LPS-stimulated whole blood, monocytes and granulocytes possessed 39±3 and 5±2 mU/10 mln cells of TF activity. Isolated eosinophils contained no detectable TF activity and antigen levels after stimulation of whole blood with Ca-ionophore. In the separate experiments TF siRNA-nucleofected monocytes, eosinophils or granulocytes were reintroduced to the whole blood depleted for the corresponding cell type and the aforementioned stimuli were applied. A 7-fold reduction of TF activity and similar reduction in TF antigen levels were observed, when comparing samples of mononuclear cell (MNC) fraction from LPS-stimulated whole blood containing reintroduced TF siRNA- and control-siRNA-nucleofected monocytes. No reduction of active TF antigen was observed in MNC faction, when TF-silenced granulocytes were reintroduced to the whole blood. When TF-silenced monocytes were reintroduced, whole blood was LPS-stimulated and granulocytes isolated, the TF activity was reduced to non-detectable levels. Our results, for the first time, demonstrate that monocytes are the only source and blood-borne TF. TF activity in granulocytes isolated from stimulated whole blood reflects the transfer of active TF antigen derived from activated monocytes.

793 Dual P2Y12 and CYP2C19 gene polymorphism as a better marker of clopidogrel resistence

L.A. Malek[1], B. Kisiel[2], M. Spiewak[3], K.J. Filipiak[2], M. Grabowski[2], G. Kostrzewa[2], R. Ploski[2], G. Opolski[2]. *[1]Warsaw, Poland; [2]Military Institute of Medicine, Internal Medicine and Rheumatol, Warsaw, Poland; [3]Medical University of Warsaw, 1st Deptartment of Cardiology, Warsaw, Poland*

Introduction: Variability in response to clopidogrel is a mulifactorial phenomenon with potential genetic risk factors such as polymorhisms in genes responsible for drug metabolism and platelet response to clopidogrel.
Aim: To determine platelet function on clopidogrel in carriers of two common gene polymorphisms in comparison to carriers of single gene polymorphism and wild-type patients.
Materials and methods: Study included 105 patients with acute myocardial infarction undergoing percutaneous coronary intervention with stenting who received dual antiplatelet treatment (aspirin and clopidogrel). Platelet function was measured with means of Platelet Function Analyzer (PFA-100) after minimum 48h of clopidogrel treatment and registered as closure time in test with collagen and adenosine diphosphate (CADP-CT). Screening for i-T744C polymorphisms in the P2Y12 gene and for G681A (*2) polymorphism in the CYP2C19 gene was performed.
Results: Genotyping revealed 7 carriers of both polymorphisms (allele C of P2Y12 gene and allel *2 of CYP2C19 gene - group 1), 17 carriers of allele *2

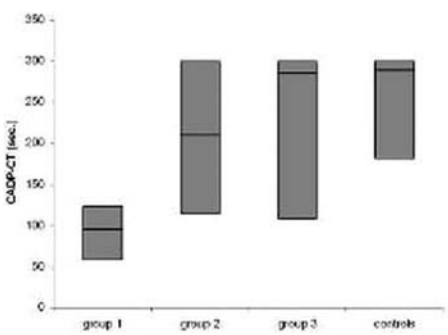


Figure 1

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

of CYP2C19 gene polymorphism (group 2), 14 carriers of allele C of P2Y12 gene polymorphism (group 3) and 67 wild-type patients (controls). Median CADP-CT value was significantly lower in group 1 comparing to groups 2 or 3 ($p<.01$) and controls ($p<.002$) [Fig. 1, median and 95% CI]. There were not any significant differences between groups 2 or 3 and controls.
Conclusions: Our study is the first one to demonstrate that dual polymorphism in genes responsible for clopidogrel activity may be a better marker of clopidogrel resistance then screening for single gene variant.

794 Intraplaque hemorrhage detected by magnetic resonance imaging using a fibrin-targeted contrast agent in-vivo

M. Sirol[1], V. Fuster[2], J.T. Fallon[2], Z.A. Fayad[2]. [1]*Hopital Lariboisiere, Cardiologie Dept., Paris, France;* [2]*Mount Sinai School of Medicine, Cardiology, New York, United States of America*

Purpose: A large body of evidence suggests that intraplaque hemorrhage (IPH) plays an important role in atherosclerotic plaque instability, leading to plaque rupture and therefore to severe clinical manifestation such as stroke or myocardial infarction. The ability to detect IPH in vivo using a non-invasive technique has a significant clinical implication.We sought to evaluate and compare to non contast-enhanced MRI (non CE), the use of a fibrin-targeted peptide for detection of IPH in an animal model of carotid thrombosis.
Methods: Cardotid artery IPH and thrombosis was induced by external injury and stasis in 12 NZW rabbits. T1-weighted MRI was performed before and 30 minutes after injection of a fibrin-targeted contrast agent (EPIX Pharmaceuticals Inc). Sacrifice was performed in order to corralate MRI findings with histopathology. ICPms measurements of gadolinium (Gd) content in the thrombus and in the arterial wall were performed and were corroborated to the MRI enhancement.
Results: Detection of thrombus was achieved in all cases after injection, compare to non-CE MRI (100% vs 43% respectively; $P<0.001$). IPH was induced in 66.7% of the cases (n=8) but was readilly detected by fibrin-targeted contrast agent when compared to non-CE MRI ($P<0.001$). Gd content was high in all injured arteries with IPH as defined by histopathology, in particular when IPH was detected by MRI.
Conclusion: We demonstrated the feasibility of fibrin-targeted MR contrast agent to detect intraplaque hemorrhage in vivo in addition to previously demonstrated thrombosis. This new approach may contribute significantly in better indentification of vulnerable atherosclerotic plaque in vivo.

795 Lack of correlation between different methods assessing ex vivo platelet function in aspirin-treated patients - relevance for the definition of aspirin resistance

G. Renda[1], B. Rocca[1], M. Zurro[1], R. De Cristofaro[2], R. De Caterina[2]. [1]*G. d'Annunzio University, Institute of Cardiology, Chieti, Italy;* [2]*Catholic University School of Medicine, Institute of Internal Medicine, Roma, Italy*

Introduction: Different ex vivo functional assays are often interchangeably used to assess platelet response in different pathophysiological conditions. Aspirin (ASA) response has been investigated by using the whole blood Platelet Function Analyzer (PFA) assay or the turbidimetric aggregation in response to ADP and/or collagen and/or arachidonic acid (AA), often with heterogeneous results.
Methods: We performed an observational study aimed at assessing and comparing the performance of different ex vivo platelet functional assays. We studied 99 consecutive subjects referred to our outpatient clinic for a pre-operative screening of hemostasis: 56 were on low-dose ASA for $\geq$1 month and 43 had no bleeding disorders nor had taken any antiplatelet drug. Each subject answered a questionnaire on current therapies and underwent the following measurements: complete blood cell count, PFA collagen-ADP (CADP)- and collagen-epinephrine (CEPI) Closure Times (CT), turbidimetric aggregometry in response to collagen and ADP. AA-induced aggregation was performed in patients on ASA.
Results: In untreated patients, CADP-CT did not correlate with ADP- or collagen-induced aggregation (r=-0.01 and -0.13, respectively, p=n.s.), while it was inversely affected by platelet count (r=-0.5, $p<0.01$). CEPI-CT also did not correlate with ADP-induced aggregation (r=0.22, p=n.s.), but was inversely correlated with collagen-induced aggregation (r=-0.5, $p<0.01$). In ASA-treated patients, AA-induced platelet aggregation was almost completely suppressed (6$\pm$17% max aggregation); CADP-CT were not different compared with untreated patients (117$\pm$35 vs. 117$\pm$32 seconds), while CEPI-CT, as well as ADP- and collagen-induced aggregation were significantly different from untreated patients (CEPI-CT= 223$\pm$85 vs. 170$\pm$55 seconds, $p<0.01$; ADP-induced aggregation= 44$\pm$13 vs. 52$\pm$10%, $p<0.05$; collagen-induced aggregation= 72$\pm$24 vs. 85$\pm$10%, $p<0.05$). Nevertheless, while only 8% of patient treated with ASA had an aggregation within normal range (>60%), 38% of these patients had a CEPI-CT within normal range (<165 seconds) and CEPI-CT did not correlate with turbidimetric aggregation induced by AA (r=-0.12, p=n.s.) or ADP (r=0.22, p=n.s.) or collagen (r=-0.15, p=n.s.).
Conclusion: PFA-based measurements and turbidimetric assays in response to AA, ADP and collagen are not correlated in ASA-treated subjects and explore different aspects of platelet function. Studies defining "aspirin resistance" with such methods are not comparable with each other, because low-responders with one test are not necessarily the same low-responders with other tests.

YOUNG INVESTIGATORS' AWARD SESSION: POPULATION SCIENCES

797 High density lipoprotein cholesterol is a powerful independent predictor of cardiovascular death, and is strongly related to body mass index

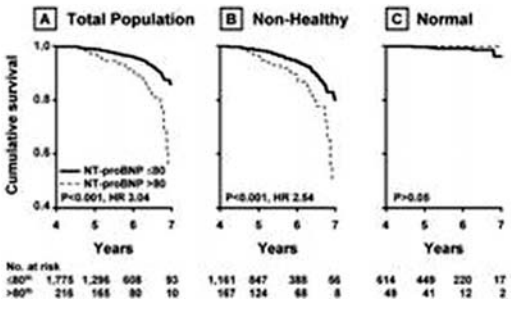
M.T. Cooney, A.L. Dudina, C.M. Mc Gorrian, E.B. Hand, I.M. Graham on behalf of SCORE Investigators. *Adelaide Meath Hospital, Cardiology, Dublin, Ireland*

Purpose: Cardiovascular disease (CVD) remains the most common cause of death in the Europe. US and smaller European studies have demonstrated the deleterious effect of reduced levels of high density lipoprotein cholesterol (HDL-C) on CVD risk. Our primary objective in this study was to examine the effect of HDL-C on cardiovascular risk in the SCORE population. The secondary objective was to examine the relationship between HDL-C and other CVD risk factors. The SCORE (Systematic Coronary Risk Evaluation) dataset makes this the largest study investigating this relationship to date.
Methods: The SCORE data set comprises 205,178 persons, representing 2.7 million years of follow-up, from 12 European cohort studies. Data for HDL-C was available from 9 countries, including 118,528 persons (65.735 men, 52,793 women), representing 1.04 million person-years of follow-up. We analysed the effect of HDL-C on CVD risk by examining the mortality rate in each quartile of HDL-C. The effect of decreasing HDL-C on CVD mortality rate within each quartile of total cholesterol (TC) was also examined. A multivariate analysis of the effect of HDL-C on CVD mortality was performed using Cox regression analysis. Age, TC, smoking status, systolic blood pressure, presence of diabetes, body mass index (BMI) were included as covariates. Those with previous CVD were excluded. The relationship between HDL-C and age, SBP, BMI, TC, smoking and diabetes was also examined.
Results: Both univariate and multivariate analysis showed a strong, graded, inverse relationship between HDL-C and CVD mortality. Rate ratios comparing the lowest to the highest quartile of HDL-C were 1.51 (95%CI: 1.35 to 1.69) and 2.31 (95%CI: 1.84 to 2.95) in men and women respectively. On multivariate analysis, hazard ratios for CVD mortality for each increase of 0.5 mmol/l in HDL-C were protective; 0.76 (95%CI: 0.69 to 0.83) in men and 0.62 (95%CI: 0.54 to 0.73) in women, adjusted for the factors listed above. A strong, graded, inverse relationship between BMI and HDL-C was seen. A decrease in mean HDL-C of 0.26 mmol/l was seen between those with BMI 20 and 30.
Conclusions: This study, the largest investigating this relationship to date, shows that low HDL-C is a strong, independent predictor of cardiovascular death, especially in women. The SCORE dataset provides the power to allow detailed analysis of the relationship between HDL-C and other cardiovascular risk factors. The inverse relationship between BMI and HDL-C was stronger than expected. Incorporation of HDL-C into existing risk estimation functions, such as HeartScore may improve risk estimation.

798 The predictive value of elevated NT-proBNP and BNP for mortality in the absence of cardiovascular risk factors or structural cardiac abnormalities in the general community

P.M. Mckie, R. Rodeheffer, D. Mahoney, A. Cataliotti, S. Jacobsen, M. Redfield, J. Burnett. *Mayo Clinic, Cardiorenal Research Laboratory, Rochester, United States of America*

Purpose: Studies report that plasma NT-proBNP and BNP have prognostic value for mortality in the general population even in the absence of heart failure (HF). It is unclear if NT-proBNP and BNP retain prognostic value in individuals who are free of traditional cardiovascular risk factors (CV RFs) or structural cardiac abnormalities (SCA).
Methods: We identified a community-based cohort of 2,006 subjects in Olmsted Co, Minnesota. We excluded those with HF. The remaining 1,991 subjects underwent echocardiography, NT-proBNP and BNP (Biosite and Shionogi) measurement, and identification of age/gender specific 80th percentile NT-proBNP and BNP levels. Subjects were divided into a normal group without CV RFs or SCA (n=663) and a non-healthy group with 1 or more CV RFs or SCA (n=1,328). CV RFs were diabetes, hypertension, coronary artery disease, any arrhythmia, car-



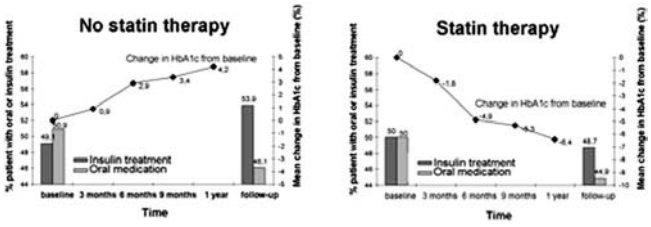
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

diovascular drug use, prior MI, or chronic obstructive pulmonary disease. SCA were left ventricular hypertrophy, atrial enlargement, diastolic dysfunction, systolic dysfunction, and valvular disease. Median follow up for mortality was 5.6 years.
Results: Ninety three deaths were recorded. Figure 1 shows mortality in the general population, non-healthy, and normal subgroups according to NT-proBNP above and below the 80th percentile. There was a higher mortality above the 80th percentile in the total population and non-healthy subgroup. There was no increase in mortality above the 80th percentile in the normal subgroup. BNP by Shionogi and Biosite assay followed a similar pattern.
Conclusion: These findings suggest that the predictive value of NT-proBNP and BNP for future events may be limited to individuals with CV RFs or SCA. These results may have implications in primary and secondary early detection strategies for cardiovascular disease.

799 The effect of lipid lowering treatment on glycemic control and prognosis in diabetic patients with peripheral atherosclerotic disease

H.H.H. Feringa[1], R. Vidakovic[1], S.E. Karagiannis[1], P. Van Der Horst[1], O. Schouten[1], M. Dunkelgrun[1], S. Hoeks[1], J. Klein[1], J.J. Bax[2], D. Poldermans[3]. *[1]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; [2]Leiden University Medical Center, Cardiology, Leiden, Netherlands; [3]Erasmus Medical Center, Anesthesiology, Rotterdam, Netherlands*

Purpose: The effect of statins on insulin sensitivity in diabetic patients are controversial. Some studies showed an improvement in insulin sensitivity with statins, while other studies did not. We hypothesized that statins are associated with improved glycemic control and survival in diabetic patients with peripheral atherosclerotic disease (PAD).
Methods: In a prospective observational cohort study of 425 consecutive diabetic patients with PAD, clinical characteristics were noted and patients were divided according to chronic statin therapy. Glycemic hemoglobin (HbA1c) was measured at baseline and at 3, 6, 9 and 12 months after enrolment. The % change of HbA1c during 12-months follow-up was calculated. During a median follow-up of 7 years, endpoints were all-cause mortality and cardiac death.
Results: HbA1c decreased with 6.4% in patients using statins (n=158) and increased with 4.2% in patients using no statins (n=267) ($p<0.001$) (Figure). The variability in HbA1c values (standard deviation of the serial HbA1c values) was also lower in statin users ($p<0.001$). Daily insulin requirements were reduced among statin users and insulin therapy could be stopped in 7% versus 0.4% among non-statin users ($p<0.001$) (Figure). In multivariate analysis, patients with chronic statins were more likely to have decreasing HbA1c values (adjusted HR: 1.86, 95% CI: 1.27-2.74) and HbA1c values <7% (adjusted HR 2.58, 95% CI: 1.49-4.48). Mortality and cardiac death occurred in 37% and 22%, respectively. Statins were significantly associated with lower mortality (adjusted HR: 0.39, 95% CI: 0.26-0.61) and cardiac death rate (adjusted HR: 0.40, 95% CI: 0.24-0.76).



Conclusion: Statins are associated with improved glycemic control and lower mortality and cardiac death rate in diabetic patients with PAD.

800 Genetic variants within the LPIN1 gene, encoding lipin, are influencing phenotypes of the metabolic syndrome in human

S. Wiedmann[1], M. Fischer[2], M. Koehler[1], K. Neureuther[1], G. Riegger[1], A. Doering[3], H. Schunkert[4], C. Hengstenberg[3], A. Baessler[3]. *[1]Klinikum Der Universitaet Regensburg, Innere Medizin Ii, Kardiologie, Regensburg, Germany; [2]Regensburg, Germany; [3]Muenchen, Germany; [4]Luebeck, Germany*

Background: Lipin, a molecular protein expressed by adipocytes, has marked effects on adipose tissue mass, insulin sensitivity, and glucose homeostasis. We hypothesized that genetic variants within the lipin gene, LPIN1, are associated with traits of the metabolic syndrome (MetS).
Methods: 15 SNPs densely covering the LPIN1 gene region were genotyped in an age- and sex- stratified sample of the general population (German MONICA study Augsburg, n=1,416 DNA and phenotypes). Ten of these SNPs were also genotyped for replication in an independent sample of 1,030 subjects recruited throughout Germany. The MetS was defined via the sum of its core components and additionally by a factor score derived from factor analysis. Permutation based methods were used to test the association between genetic LPIN1 variants and metabolic traits for empirical significance.
Results: Linkage disequilibrium (LD) analysis revealed three LD blocks encompassing LPIN1. We identified three associated three-marker haplotypes: one common haplotype (26.8% frequency) increases the risk for the MetS (OR=1.6, 95% CI[1.2-2.2]), while the other two being less common (5.7% and 4.0%) are strongly associated with lower blood pressure ($p<0.0001$), a lower BMI and waist circumference ($p<0.0001$), lower HbA1c ($p<0.01$) as well as a lower MetS factor score ($p<0.0001$). Furthermore, the frequencies of arterial hypertension ($p<0.0001$), obesity ($p<0.0001$), diabetes ($p<0.05$), and the presence of ≥ 3 MetS components ($p<0.0006$) were significantly lower than in subjects not carrying one of these protective haplotypes. These findings could be largely confirmed in the replication sample.
Discussion: These data confirm that allelic variants of the LPIN1 gene have significant effects in human metabolic traits and highlight the importance of lipin in the pathophysiology of the MetS. Permutation-based low p-values and the consistent findings in several populations across multiple phenotypes of the MetS reflect the robustness of these results.

ATRIAL FIBRILLATION ABLATION: TECHNIQUES AND OUTCOMES

829 Pulmonary Vein Isolation (PVI) alone versus PVI + ablation of Complex Fractionated Atrial Electrograms (CFAE) in paroxysmal atrial fibrillation: results of a controlled randomized study

I. Deisenhofer[1], C. Schmitt[2], H.L. Estner[1], A. Luik[1], J. Schreieck[3], N. Langwieser[1], C. Kolb[1], G. Hessling[1], B. Zrenner[1]. *[1]German Heart Center, Cardiology Dpt., Munich, Germany; [2]Staedt. Klinikum Karlsruhe, II. Medizinische Klinik, Karlsruhe, Germany; [3]Universitaetsklinik Tuebingen, III. Medizinische Klinik, Tuebingen, Germany*

Background: Segmental pulmonary vein isolation (PVI) can cure paroxysmal atrial fibrillation (AF) in 65-75% of patients (pts). Ablation of complex fractionated atrial electrograms (CFAE) is an alternative ablation approach in AF. This prospective randomized study sought to evaluate the additional effect of CFAE ablation in pts with paroxysmal AF after PVI.
Methods: 98 pts with paroxysmal AF (57±10 years, 74 male) were randomly assigned to undergo PVI alone (48 pts) or PVI+CFAE ablation (50 pts). Baseline characteristics showed no significant difference between both groups. After PVI, inducibility of sustained AF by atrial burst pacing was tested in all patients. Additional CFAE ablation was only performed in patients with inducible AF randomized to combined PVI+CFAE ablation. Primary endpoint was freedom of atrial tachyarrhythmia >30 seconds in a 7 days Holter ECG at 3 months after one single procedure (off antiarrhythmic drugs). Secondary endpoint was a combined safety endpoint (pericardiac tamponade, thromboembolic accident and PV stenosis).
Results: In both groups, 98% of targeted pulmonary veins (PV) were isolated (171/175 PV in PVI alone vs. 181/185 PV in PVI+CFAE ablation). Sustained AF was inducible in 31/48 pts (64%) in the PVI alone group and in 30/50 pts (60%) in the PVI+CFAE ablation group (p=ns). an additional CFAE ablation was performed in with inducible AF. In the intention-to-treat analysis, 36/48 (75%) of pts in the PVI alone and 37/50 (73%) of pts in the PVI+CFAE ablation group were in stable sinus rhythm 3 month after a single procedure (p=ns). In subgroup analysis, best success rates were achieved in pts randomized to PVI alone with non-inducibility of AF (82%; 14/17 pts) and in pts actually treated with combined PVI+CFAE ablation (77%; 23/30 pts). Pericardiac tamponade requiring pericardiocentesis occurred in 1 patient (PVI+CFAE group).
Conclusion: In paroxysmal AF, combination of PVI with ablation of CFAE showed in the intention-to-treat analysis no advantage to PVI alone (73% vs. 75% in sinus rhythm). However, pts without AF inducibility after PVI alone and pts undergoing additional CFAE ablation due to inducible AF showed a trend towards a better rhythm outcome.

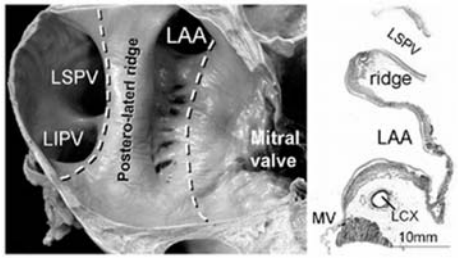
830 The variable dimensions and thickness of the postero-lateral ridge of the left atrium: relevance for endocardial ablation of atrial fibrillation

J.A. Cabrera[1], V. Climent[2], Y. Ho[3], A. Fernandez-Ruiz[2], D. Sanchez-Quintana[1]. *[1]Hospital Quiron Madrid, Cardiology, Madrid, Spain; [2]Facultad de Medicina. UEX, Anatomia Humana, Badajoz, Spain; [3]Royal Brompton Hospital, Cardiac morphology, London, United Kingdom*

Introduction: The postero-lateral ridge between the orifices of the left pulmonary veins (LPVs) and the mouth of the left atrial appendage (LAA) is the most relevant structural prominence of the endocardial left atrium (LA). Detailed anatomic information of this atrial structure may be useful to perform the ablation techniques more efficiently and safely during PVs isolation.
Methods: Thirty-two structurally normal human heart (24 males, 46±18 years) were carefully dissected. We distinguished by gross inspection 3 morphological areas within the postero-lateral wall of the LA (figure): a) the anterior smooth myocardial vestibule or pre-mitral area, b) the postero-lateral ridge and LAA and c) the orifices of the LPVs. We examined by gross inspection and histological sections the dimensions and anatomic relations of the LA ridge with these anatomic structures.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: The LA ridge is a fold of the postero-lateral wall of the LA protruding into the endocardial surface as prominent crest or ridge. The ridge showed a variable extension along the lateral wall of the LA from its antero-superior to the postero-inferior region. The mean length of the ridge was 24.2±5.3 mm (range 14.2 to 32.5 mm). The ridge showed a constant superior insertion at the lateral roof of the LA extending inferiorly to reach the inferior margin of the left inferior PV orifice in 88% of hearts. Histological examination revealed a thicker myocardial wall of the ridge at its superior level with a range between 1.5 to 4.2 mm (mean 2.8± 1.1 mm).



The postero-lateral ridge of the LA

Conclusions: Our anatomic findings showed for the first time the variable myocardial thickness of the postero-lateral ridge. A larger left atrial ridge with a thicker myocardial content are anatomic features of clinical relevance during ablation around the orifices of the PVs.

831 Catheter ablation achieving termination of chronic AF is associated with a better clinical outcome

M.D. O' Neill, P. Jais, Y. Takahashi, M. Hocini, A. Jonsson, K.T. Lim, S. Matsuo, L. Arantes, F. Sacher, M. Haissaguerre. *Hopital Cardiologique du Haut-Leveque, Bordeaux, France*

Introduction: Termination of long lasting persistent AF (CAF) can be performed by catheter ablation targeting thoracic veins and multiple left atrial sites. This study describes the clinical outcome and subsequent arrhythmia recurrence depending on the achievement of acute AF termination in a cohort of consecutive patients.
Methods: 178 consecutive patients, 147 (83%) men and 31 (17%) women, mean age (56±10 yrs) underwent ablation of CAF (25±42months) using a sequential catheter ablation approach involving isolation of pulmonary veins, ablation of coronary sinus and all left atrial areas showing rapid/heterogeneous activity, and linear lesions at the roof and mitral isthmus. Activation mapping was performed after conversion to atrial tachycardias (AT) until restoration of sinus rhythm. At 1, 3, 6 and 12 months after ablation, patients underwent clinical review and 24-hour ambulatory ECG monitoring to identify asymptomatic arrhythmia. Repeat mapping and ablation was performed in patients with persistent arrhythmia.
Results: AF was terminated in 149 patients (84%), directly to sinus rhythm in 23 or via ablation of intermediate AT in 126 pts. AF could not be terminated without DC or pharmacological cardioversion in 29 patients (No Term 16%). The amount of delivered RF energy did not differ between groups (Term 86±27 vs 96±28min; p=0.08). Following the index ablation, sustained arrhythmia recurrence was documented in 79 pts with a lower incidence in Term (64 pts, 44%) compared to No Term groups (15 pts, 50%, p=0.4). Most importantly, AT was the dominant mode of recurrence in Term pts (56/64) whereas AF was the most common arrhythmia observed in No Term pts (8/15; p=0.0015). Re-ablation of recurrent arrhythmia was limited in the former and extensive in the latter group. Among the total cohort after repeat ablation, sinus rhythm was maintained in 95% (Term) vs 57% (no Term) of patients during a follow-up of 10.5±6 months.
Conclusions: Acute CAF termination during catheter ablation is predictive of subsequent maintenance of sinus rhythm. However, repeat procedures are commonly required for arrhythmia recurrence which takes the form of AT in Term pts and of AF in no term pts.

832 Prospective identification of anomalous veno-atrial connections complicating pulmonary vein isolation

N. Perez Castellano, J. Perez-Villacastin, J. Moreno Planas, J. Salinas Arce, M. Vega Olvera, S. Garraza, M. Doblado, E. Ruiz, R. Isa Param, C. Macaya. *San Carlos University Hospital, Arrhythmia Unit, Cardiovascular Institute, Madrid, Spain*

Some reports have described the existence of electrical connections between contiguous pulmonary veins (PVs) in patients undergoing atrial fibrillation (AF) ablation. Our objective was to prospectively determine the prevalence and clinical impact of these PV connections.
Methods: This study was performed in 25 consecutive patients with drug-refractory AF scheduled for ostial isolation of the 4 PVs. Two mapping catheters were introduced into the left atrium. A vein to vein (V-V) connection was considered if PV pacing resulted in ipsilateral PV activation preceding atrial activation, requiring the ablation of both PV ostia to isolate either PV.
Results: V-V connections (4 left and 2 right) were observed in 6 patients (24%). In 3 of these 6 patients, we also identified connections between PVs and left atrium resistant to ostial PV ablation, probably due to an epicardial course. Two of them were ablated at 15 and 22 mm from the PV ostium, and the other connected the left superior PV with the coronary sinus, probably through the vein of Marshall, and could not be ablated. All anomalous connections appeared in men (38% vs 0%; P=0.05). There were no other clinical variables associated with V-V connections. The existence of V-V connections was associated with a higher number of radiofrequency (RF) applications per procedure (53±21) and a higher cumulated RF time (40±12 min) than patients without them (33±14 applications and 28±11 min; P values 0.01 and 0.03, respectively). Patients with V-V connections showed a higher rate of AF recurrence after ablation (33% vs 5%; P=0.1).
Conclusions: The prevalence of electrical connections between ipsilateral PVs is high in patients with AF. It is important to detect them to achieve complete PV isolation and avoid unnecessary applications. The higher rate of AF recurrences in patients with PV connections induces to speculate about their role in the origin and/or maintenance of AF.

833 Circumferential left atrial PV ablation - is it possible to predict long term success?

C. Piorkowski[1], H. Kottkamp[2], P. Sommer[2], C. Henker[2], A. Arya[2], J.H. Gerds-Li[2], G. Hindricks[2]. *[1]University Leipzig, Heart Center, Electrophysiology, Leipzig, Germany; [2]Heart Center Hirslanden, Zurich, Switzerland*

Background: Current concepts of AF catheter ablation use long circumferential left atrial ablation lines around the funnel of the pulmonary veins (PV). Discontinuous ablation lines due to a lack of catheter stability and left atrial wall contact are one of the major limitations. Additionally, the phenomenon of early recurrences and only delayed cure after substrate modification has been described. The present study analysed the predictive value of different patient and rhythm characteristics for long term success.
Methods: 180 consecutive patients with highly symptomatic AF (56±10 years, 75% male, 81% paroxysmal AF, duration of AF history 53 (12,124) months, 15% previous AF ablations, 56% lone AF) received a circumferential left atrial PV ablation. Follow-up was performed with serial 7-day-holter before ablation, after ablation, after 3, 6 and 12 months. The following patient and rhythm characteristics were studied in relation to long term success: paroxysmal vs persistent AF, duration of AF history, presence of structural heart disease, complete postinterventional PV isolation, termination of AF during ablation, ablation time, appearance of early postinterventional recurrences.
Results: Prior to ablation 75% of the patients showed AF during the 7-day-holter. After ablation, after 3, 6 and 12 months that number declined to 58%, 31%, 27% and 30% respectively. Among the studied parameters only the lack of early postinterventional AF recurrences showed a highly positive predictive value for long term success. After 6 and 12 months patients without early recurrences showed freedom from AF in 92% and 86% of the cases. For patients with early recurrences the success rate reduced to 59% and 45% (p=0.001, p=0.005). Interestingly the success rate was not different in patients with paroxysmal versus persistent AF [freedom fro AF after 6 months 64% vs 72% (p=0.27); after 12 months 75% vs 69% (p=0.52)]. Also the presence of complete PV isolation was not predictive for long term success [freedom from AF after 6 months 77% vs 73% (p=0.39); after 12 months 78% vs 75% (p=0.57)].
Conclusions: The occurrence of early postinterventional AF relapses was the only predictive parameter for long term success. Especially patients with paroxysmal or persistent AF and patients with or without complete PV isolation did not show a significantly different ablation result.

834 Catheter ablation for permanent atrial fibrillation: are outcomes improved by ablation restoring sinus rhythm without electrical cardioversion?

K. Rajappan, P. Kistler, M. Kalla, S. Kalra, L. Richmond, M.J. Earley, S. Harris, D. Gupta, S.C. Sporton, R.J. Schilling. *St Bartholomew's Hosp/Queen Mary University, Deaprtment of Cardiology, London, United Kingdom*

Introduction: Catheter ablation (CA) is successful in restoring sinus rhythm (SR) in patients with long standing persistent atrial fibrillation (AF). However whether AF which terminates as a direct result of CA translates to an improved clinical outcome is yet to be determined. The aim of the study was to determine if clinical outcomes were improved in patients where SR was restored in response to CA.
Methods & Results: 71 consecutive patients (60±10 years, 55M) with chronic AF underwent first-time CA guided by electroanatomic mapping and CT integration. Following double trans-septal puncture wide encirclement of pulmonary vein (PV) pairs was performed with the endpoint of electrical isolation. If AF persisted linear ablation was performed at the left atrial (LA) roof (55 patients), inferior LA and coronary sinus (CS) (37 patients) and cavotricuspid isthmus (34 patients). Complex fractionated LA electrical activity was targeted in 46 patients. If AF persisted following the standard lesion set DCCV was performed (DCCV group; n=48). CA restored SR in 23 patients (ABL group). During CA if SR was restored (n=9) the lesion set was not completed. If AF organised activation mapping was performed (14 patients). All patients were in SR at the end of the procedure and on the 1st

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

day afterwards. Based on absence of symptoms and freedom from AF on 7day Holter monitor, success after a single procedure off antiarrhythmic drugs was achieved in 20/48 patients (42%) in the DCCV group vs. 12/23 patients (52%) in the ABL group (chi-squared=0.69; p=ns) at a median follow up of 16±12 weeks. Recurrent arrhythmias (n=39) were AF (19 DCCV vs. 8 ABL) and atrial tachycardia (AT) (9 DCCV vs. 3 ABL) (chi-squared=0.09 for AF vs. AT in each group; p=ns). These results were not affected by ablation within the CS.
Conclusions: Permanent AF which terminates as a direct result of CA was not associated with an improvement in clinical outcomes at medium term follow up in this group of patients. Whether this result is reproduced in a larger group of patients with longer term follow up remains to be seen. Following completion of a standardised lesion set, DCCV was successful in restoring sinus rhythm.

PHARMACOLOGICAL TREATMENT IN ATRIAL FIBRILLATION

835 The role of Candesartan in maintaining sinus rhytm and reducing the relapses of atrial fibrillation. Four years follow up results

M.L. Cavarra[1], C. Romeo[2], G. Chiaranda[3], I.P. Monte[3]. [1]*Cardiology Policlinic, Catania, Italy;* [2]*Cardiology Garibaldi Hospital, Catania, Italy;* [3]*Cardiology Muscatello Hospital, Augusta (Sr), Italy*

In 2002 we have begun a prospective study to verify the efficacy of Candesartan (Ca) prophylactic treatment in atrial fibrillation (AF) relapses after electrical (ECV) or pharmacological cardioversion (PCV). We have based our research on the rational Angiotensin II antagonists role in the prevention of atrium electrical remodelling. Aim of study is to evaluate the efficacy of therapy with Ca in reducing AF relapses in a four years follow up. 149 pts with AF ≥48 hours where enroled, treated with ECV or PCV, randomized in group A, 79 pts treated with antiarrhythmics (AA) in optimal dosages, and group B, 66 pts treated with AA and Ca 8-16 mg. All pts were anticoagulated and subjected to ECV or PCV. The two groups were not statistical different for clinical characteristics, but the first results at three and six months showed AF relapses reduction in group B. Among the 149 pts of the initial study, 106 were followed for four year: 46 in A group, 60 in B group; the clinical characteristics of the two groups were not different. The pts were subjected to an ECG Holter every 6 months and an echocardiogram every 12 months; a continuous telephone contact has also been maintained. We have evaluated the results at 4 years (V4) by comparing them with those of 2002 (V0). In V4 the EF was 49±12% in A group respect to V0 where it was 63%, in B group it was 58±23% respect to 65% in V0. Left atrium diameter (LAD) was 47±26 mm in A group, substantially unchanged respect to V0 echocardiogram which showed LAD 47 mm and 42±21 mm in B group which was 42.8 mm in V0; LVDT was 52 mm in A group in V0 and 43±17 mm in V4, 49 mm in V0 and 48±25 mm in V4 in B group. Analysing again the data, in the 60% of B group pts there was a LVDT reduction while in the 40% it remained unvaried or increased. In A group the 29% of pts has shown a LVDT increase while in the 70% it remained unvaried. Left atrium diameter and the EF variations have shown no significance among the two groups and no influences it seems be determined by Ca use. Moreover in A group the 50% of pts had 2-3 AF episodes in the year and in the 26% of pts the AF became permanent. In B group only the 20% of pts had 1-2 AF episodes and in the 10% of pts it became chronic. In conclusions, the 4 years follow-up in pts subjected to AA and Ca prophylactic therapy has confirmed the first data obtained from the 12 months study about Ca efficacy in prevention and reducing AF relapses in comparison with only AA therapy and has confirmed once again Angiotensin II antagonists efficacy on ventricular remodelling, whereas no incidence on atrium dimensions has been still shown.

836 The effect of intensive cholesterol-lowering therapy with atorvastatin and ezetimibe on neurocognitive deficits, depression and white matter lesions in elderly patients with atrial fibrillation

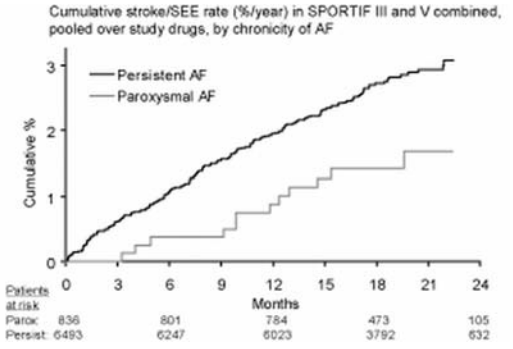
E. Wezenberg, M. Dartel Van, M. Zwiers, J. Kuilenburg Van, G. Pop, M. Pop-Purceleanu. *Radboud University Nijmegen Medical Center, Psychiatry Department (961), Nijmegen, Netherlands*

Purpose: to investigate the effect of atorvastatin (40 mg) in combination with ezetimibe (10 mg) on neurocognitive decline, depression and cerebral white matter lesions (WML) in elderly patients with atrial fibrillation (AF), who are under adequate oral anticoagulation (INR 2.0-3.0).
Methods: 32 elderly patients (mean age: 74 years) with AF (mean duration: 14.41 years) and adequate oral anticoagulation, completed a one year prospective pilot study with a double-blind placebo-controlled design. The intervention group received a combination of atorvastatin (40mg) and ezetimibe (10mg). Patients were examined on an extended neuropsychological battery (testing memory, language, speed of information processing and executive functioning), the Montgomery-Asberg Depression Rating Scale (MADRS) and by MRI, at baseline and one year follow-up. Cholesterol levels and hs CRP were assessed at 0, 1, 3, 6, 9 and 12 months.
Results: Patients were asymptomatic in daily functioning and had a general cognitive screening (MMSE) without impairments at baseline and endpoint. However, in more specific neurocognitive tests, patients showed significant slowing in speed of information processing at baseline. There was a significant improvement in the intervention group on speed of information processing (p = .003), memory (p = .028), and executive functioning (p = .015). No clinically relevant depression was found at baseline or endpoint. Nevertheless, there was an improvement in mood symptoms in the intervention group (p = .021). At baseline, memory performance correlated with WML volumetrics: subcortical and periventricular lesions. Over a year a decrease in WM volume was found in the control group which was not found in the intervention group. WML and higher hs CRP values were found to be correlated at baseline (p = .068). A significant decrease in hs CRP was found over a year (p = .003), which correlated with improvement in speed of information processing (p = .021).
Conclusions: The data show that elderly AF patients despite adequate oral anticoagulation therapy have worse cognitive functioning than healthy elderly. Significant improvement is found in speed of information processing, memory and executive function after one year of additional, intensive cholesterol-lowering treatment with a combination of atorvastatin (40mg) and ezetimibe (10mg). These results encourage further study of the evaluation of this intervention strategy for elderly AF patients.

837 Stroke and thromboembolism in anticoagulated patients with paroxysmal vs. persistent atrial fibrillation

G. Lip[1], L. Frison[2], M. Grind[3] on behalf of SPORTIF Investigators. [1]*City Hospital, Department of Medicine, Birmingham, United Kingdom;* [2]*AstraZeneca R&D, Molndal, Sweden;* [3]*AstraZeneca R&D, Molndal, Sweden*

Purpose: To test the hypothesis that stroke and systemic embolic events (SEE) were different between patients (pts) with paroxysmal and persistent/permanent atrial fibrillation (AF) in the SPORTIF (SP) III and V trials.
Methods: A cross-sectional, longitudinal analysis was conducted, using data from the SP III and V trials (n=7329): 836 pts (11.4%) with paroxysmal AF, classified at study entry, (mean age 70.1 years [SD 9.5]) were compared to 6493 pts with persistent AF (mean age 70.0 years [SD 8.8]) for this ancillary study.
Results: Annual event rates (AERs) for stroke/SEE were 1.73% for persistent AF, and 0.93% for paroxysmal AF. In a multivariate analysis, after adjusting for stroke risk factors, gender and aspirin usage, the differences remained statistically significant, with a higher hazard ratio (HR) for stroke/SEE in persistent AF (vs. paroxysmal AF, HR 1.87; 95% CI 1.04–3.36; p=0.037) (Figure). In 'high risk' pts with ≥2 stroke risk factors AERs for stroke/SEE were 2.08% for persistent, and 1.27% for paroxysmal AF (HR 1.62; p=0.12 in a univariate, and HR 1.68; p=0.098 in a multivariate analysis). Elderly pts (age≥75, n=3804) had AERs for stroke/SEE of 2.38% for persistent AF, and 1.13% for paroxysmal AF (adjusted HR 2.27; p=0.075).



Conclusion: In this large cohort of anticoagulated AF pts, those with paroxysmal AF had stroke rates which were lower than pts with persistent AF, although both groups had broadly similar stroke risk factors. Subjects with paroxysmal AF at 'high risk' had stroke/SEE rates that were not significantly different to persistent AF subjects, consistent with the recommendation that such subjects should not be denied anticoagulation therapy.

838 Antiarrhythmic therapy in atrial fibrillation in Denmark: a shift towards beta-blockers

M.L. Hansen[1], N. Gadsboll[2], G. Gislason[3], F. Folke[4], T.K. Schramm[1], J. Friberg[5], S.Z. Abildstrom[3], M. Madsen[6], L. Kober[5], C. Torp-Pedersen[1]. [1]*Bispebjerg University Hospital, Dept of Cardiovascular Medicine, Copenhagen, Denmark;* [2]*Sygehus Oest Koge, Department of Medicine, Koge, Denmark;* [3]*Gentofte University Hospital, Department of Cardiology, Copenhagen, Denmark;* [4]*Bispebjerg University Hospital, Department of Cardiovascular Medicine, Copenhagen, Denmark;* [5]*Rigshospitalet, Department of Cardiology, Copenhagen, Denmark;* [6]*National Institute of Public Health, Copenhagen, Denmark*

Background: Beta-blockers, nondihydropyridine calcium channel blockers

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(CCB's), digoxin, amiodarone, sotalol and class 1C – antiarrhythmics are recommended drugs for treatment of atrial fibrillation (AF). Recent trials have questioned the efficacy of drug used for rhythm control but how daily clinical practice is influenced by the results of these studies remains unknown. We studied temporal trends in antiarrhythmic treatment in patients following a first-time admission for AF in Denmark from 1995-2004.
Methods: Patients discharged with a diagnosis of AF who subsequently claimed a prescription of an antiarrhythmic drug within 90 days were identified by the Danish National Patient Registry and The Danish Registry of Medicinal Product Statistics. Multiple logistic regression analyses were used to identify variables associated with antiarrhythmic treatment.
Results: A total of 108, 791 patients were included into the study. During the study period use of beta-blockers and amiodarone increased considerable, whereas the use of digoxin, CCB's, sotalol and class 1C antiarrhytmics decreased (figure 1). Male gender was associated with significantly more use of amiodarone (adjusted odds-ratio (OR) = 1.39 (95% confidence interval 1.31-1.49)), but less use of beta-blockers (OR = 0.87 (0.85-0.90)), CCB's (OR = 0.84 (0.81-0.87)) and digoxin (OR = 0.86 (0.83-0.89)), than female gender (reference). Finally, increasing age was positively associated with digoxin treatment, but negatively associated with treatment with any other antiarrhythmics.

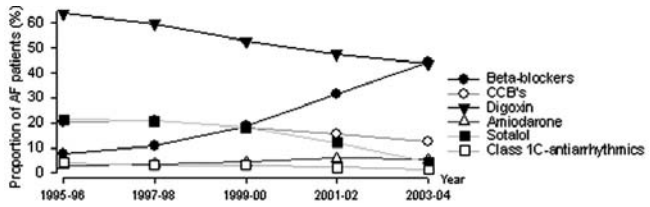


Fig1. Antiarrhythmic treatment in AF.

Conclusion: Treatment of AF has shifted towards the use of primarily beta-blockers and amiodarone, but less use of other traditional antiarrhythmics. Although the use of digoxin generally declined, it is still widely used particularly in women and elderly patients.

839 Antithrombotic guideline adherence in atrial fibrillation patients admitted with stroke. Do we use our safety-belt?

R. Pisters, I. Knottnerus, H.J. Crijns, J. Lodder, A. Boreas, R. Van Oostenbrugge, M.H. Prins, R.G. Tieleman. *University Hospital Maastricht, Cardiology, Maastricht, Netherlands*

Purpose: Despite the knowledge that atrial fibrillation (AF) increases the risk of stroke and that oral anticoagulation (OAC) significantly reduces this chance in high risk patients, each year some 4,000 patients with ischemic stroke and AF are admitted in the Netherlands. The aim of the present study was to investigate whether this implicates that we need better therapies, or that we should improved implementation of the current guidelines?
Methods: We retrospectively examined all patients admitted with ischemic strokes to our hospital during 2003-2006 in which the diagnosis AF was either known or established during hospital stay and classified patients with known AF using the CHADS2 scheme. Subsequently, we studied if their antithrombotic therapy (ATT) was in accordance with the 2001 ACC/AHA/ESC AF guidelines and calculated the number of strokes due to inadequate therapy. Furthermore, we looked at the ATT guideline adherence of all surviving patients at discharge.
Results: Of the 1120 patients admitted with CT or MRI proven stroke 163 (15%) had a diagnosis of AF. Within this group (mean age 80±8years), 89 patients (55%) had an electrocardiographically proven history of AF and in 77 (45%) patients AF was diagnosed during hospital stay. The average CHADS2 score before index stroke was 2,34. At admission only 44 out of the 89 (49%) patients with known AF received guideline adherent ATT, whereas 47% of these patients were undertreated and 4% were overtreated. Assuming that OAC gives a stroke risk reduction of 61% versus placebo and 42% versus aspirin we calculated that 100% guideline adherence would have led to prevention of 25 out of the 89 strokes, but also to an increase of intracranial haemorrhage (ICH) of 5. Therefore the overall benefit/risk ratio is 5. Extrapolation to the Dutch situation would mean that per year 550 strokes could have been prevented at the cost of 112 extra cases of ICH (overall reduction >1 stroke/day). Of the 138 (85%) surviving patients, still 15% were not treated with OAC and therefore insufficiently protected against TEC.
Conclusions: In order to reduce the number of strokes occurring in patients with AF we first need to improve the use of our antithombotic safety-belt, i.e. OAC, by improving the implementation of the guidelines, e.g. by increasing (public) awareness of the CHADS2 score. Adequate guideline adherence would save a considerable amount of strokes per year, thereby saving lives as well as reducing health care costs. ATT at discharge is still disappointing, leaving patients at an unacceptably high stroke risk.

840 Analysis of patients with atrial fibrillation and low CHADS score (CHADS 0-1) at index admission who suffer from nonfatal stroke during a 5-year follow-up period

T. Kleemann, T. Becker, M. Vater, K. Doenges, S. Schneider, J. Senges, K. Seidl. *Herzzentrum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany*

Background: The CHADS score is a clinical classification scheme for predicting stroke in nonvalvular atrial fibrillation (AF). CHADS is an acronym for congestive heart failure, hypertension, age>75 years, diabetes, and prior stroke. Patients (Pts) with a CHADS score of 0 or 1 are classified as being at low risk for stroke. Aim of the study was to analyse Pts with AF at low risk for stroke who suffered from nonfatal stroke during a follow-up period of 5 years.
Methods: 556 consecutive Pts with AF and a CHADS-score of 0 or 1 from the prospective single center registry ANTIK who were admitted for cardioversion of AF were analysed. The median follow-up was 5 years. Two groups of Pts were compared: Pts suffering from nonfatal stroke during the follow-up and Pts without nonfatal stroke during follow-up.
Results: 3,8% of Pts with AF at low risk for stroke at index admission suffered from nonfatal stroke during the follow-up of 5 years.

Table 1. Clinical characteristics of Pts with AF and CHADS 0-1 at index admission

	Stroke n = 21	No stroke n = 535	p-value
Age (years)	62 (58-70)	61 (54-67)	n.s.
Male	76%	75%	n.s.
Coronary artery disease	38%	22%	0,1
Left atrial thrombus	0%	2,7%	n.a.
Moderate/severe left atrial spontaneous echo contrast	0%	22%	n.a.
Oral anticoagulation at discharge	81%	86%	n.s.
Cardioversion performed	100%	87%	n.s.
Atherosclerotic aortic debris	44%	18%	< 0,05
PCI during follow-up	14%	2%	< 0,01

Conclusions: 1. 3,8% of Pts with AF at low risk for stroke according to the CHADS score suffered from nonfatal stroke during a follow-up of 5 years. 2. Pts with nonfatal stroke had no left atrial thrombus or severe sponaneous echo contrast at index admission. 3. However, these patients had a higher prevalence of atherosclerosis at index admission (atherosclerotic aortic debris and coronary artery disease) and percutaneous coronary interventions during follow-up.

IMPLANTABLE DEFIBRILLATORS: LARGE POPULATION TRIALS

911 Survival after myocardial infarction in the Post-MADIT-Era: results from the PreSCD-registry with 10,654 patients in clinical practice

H. Voeller[1], M. Block[2], H. Klein[3], R. Reibis[1], W. Kamke[4], T. Fetsch[5], K. Wegscheider[6] on behalf of PreSCD study group. *[1]Klinik Am See, Cardiology Dpt., Rudersdorf, Germany; [2]Klinikum Augustinum, Muenchen, Germany; [3]Uniklinik Magdeburg, Magdeburg, Germany; [4]Spreewaldklinik, Burg, Germany; [5]IKKF, Muenchen, Germany; [6]University Hamburg, Hamburg, Germany*

Introduction: Implantable cardioverter-defibrillators (ICD) have shown to reduce mortality in patients (pts) with impaired left ventricular ejection fraction (LVEF) < 35% after myocardial infarction (MI). Insufficient data exist about the effectiveness of this therapy in clinical practice. Therefore the aim of the Prevention of Sudden Cardiac Death II Registry (PreSCD II) is to describe the chosen therapy in patients at high risk for Sudden Cardiac Death (SCD) and their prognosis in relation to their initial LVEF as the primary risk marker.
Methods: Between Dec 2002 and Apr 2005, 10,654 consecutive pts > 1 month post MI were included in 22 centres for cardiac rehabilitation in Germany (75.5% male, 61±12 yrs). 75% of pts had their last MI 4 to 8 weeks prior to inclusion, for 90% it was their first MI. 90% of the pts had revascularization before inclusion, mainly PCI (74.8%) and/or CABG (24.7%). Additional diseases as hypertension (73.3%), diabetes (24.2%) or renal insufficiency (5.3%) were documented. 3.0% had atrial fibrillation, 3.4% had left bundle branch block. Medication at discharge from rehabilitation consisted of beta-blockers (95%), ACE-inhibitors (90.2%), statins (95.7%) and antiplatelet agents (95.7%). Mean LVEF of all pts was 55.5±11%. Pts were classified in 3 groups according to their LVEF at inclusion in the registry: Group 1 were 277 pts with LVEF ≤ 30% (mean 26.3%), group 2 were 761 pts with 30% < LVEF ≤ 40% (mean 37.1%), 1140 pts with initially preserved LVEF > 40% (mean 57.9%) formed the control group 3 (= 2,186 pts all together). Overall mortality, cardiac and non-cardiac death, SCD, and device implantation were documented at regular follow-ups 4, 8, 12, 24 and 36 months after inclusion for these 3 groups.
Results: After a mean follow-up time of 478.2±239.3 days data from 1811 pts (84%) could be collected. The relative number of ICD implantations for primary prevention during the first 180 days of follow-up was 23.7% in group 1, 2.5% in group 2 and 0.3% in group 3. Estimated overall mortality according to Kaplan-Meier after 24 months was significantly higher in group 1 and 2 vs. group 3

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(11.5%, 9% vs. 1.9%, p < 0.0001). Both groups 1 and 2 showed significantly higher rate of SCD as compared to group 3 (3.9%, 3.4%, 0.9%; group 1 vs. 3, p = 0.004; group 2 vs. 3, p = 0. 03, resp.).
Conclusion: Patients with reduced LVEF ≤ 40% today still have a poor prognosis despite the option for primary prevention of SCD, possibly due to sustained low rates of ICD implantation in clinical practice.

912 Sudden cardiac death and heart failure death in patients with implantable cardiac defibrillator. Analysis of predictive factors in a french cohort study

E. Marijon[1], L. Trinquart[1], H. Le Marec[2], B. Chevalier[3], X. Waintraub[1], A. Otmani[1], G. Chatellier[1], J.Y. Le Heuzey[1]. *[1]European Georges Pompidou Hospital, Cardiology, Paris, France; [2]University Nantes Hospital, Cardiology, Nantes, France; [3]University Lyon Hospital, Cardiology, Lyon, France*

Background: There is very little available data that identify baseline predictive factors for both heart failure and sudden cardiac death in patients with implantable cardiac defibrillator (ICD).
Methods: Causes of death were analysed in 2396 patients who had required an ICD, and were enrolled in EVADEF, a prospective and multicentric french cohort study (60.4±15 years, 86.1% men, New York Heart Association (NYHA) functional class I 33.%, II 50.5%, III 14.7%, IV 1.5%, coronary artery disease 57.3%, mean left ventricular ejection fraction (LVEF) 38±16%, mean QRS duration 120±30 ms, secondary prevention 81.1%). Data concerning sex, age (>68 or ≤68 years), primary or secondary prevention, NYHA functional class, LVEF (≤35%), QRS duration (≥120 ms, <120 ms), and heart disease were studied.
Results: Within 2 years after the implantation, there were 274 deaths, i.e. a mortality rate of 13.0% (95%CI: 12.3-13.7). Circumstances of death were sudden in 29 patients (10.6%), and secondary to heart failure in 146 patients (53.3%). Only low LVEF (<35%) was found to be predictive of sudden cardiac death (OR: 2.6; 95%CI: 1.2–6.4, p<0.01). Sex, age, primary or secondary prevention, high NYHA functional class, QRS duration and heart disease were not found to be significantly predictive of sudden cardiac death. On the other hand, age (OR: 2.1; 95%CI: 1.5–2.9, p<0.0001), low LVEF (OR: 5.8; 95%CI: 3.8–9.3, p<0.0001), QRS duration (OR: 2.8; 95%CI: 1.9–4.2, p<0.0001), NYHA functional class (III vs I, OR: 43.5.; 95%CI: 16.2–164.8, p<0.0001), and dilated cardiomyopathy versus the other causes (OR: 2.1; 95%CI: 1.8-3.2, p<0.001) were predictive of cardiac failure death.
Conclusion: Age, low LVEF, enlarged QRS, high NYHA functionnal class, and dilated cardiomyopathy are all predictive of fatal cardiac failure. On the opposite, in these patients with ICD, sudden cardiac death risk was only associated with lower LVEF.

913 Use of cardioverter-defibrillator in inherited arrhythmogenic diseases/cardiomyopathies. Data from Italian ICD registry during the years 2001-2005

A. Proclemer[1], M. Ghidina[2], M. Gasparini[3], D. Corrado[4], D. Facchin[2], L. Rebellato[2], P.M. Fioretti[2] on behalf of Italian Association of Arrhythmology and Cardiac Pacing. *[1]Az. Ospedaliero-Universitaria, U.O Cardiologia, Udine, Italy; [2]Fondazione IRCAB, Udine, Italy; [3]Clinica Humanitas, Rozzano, Italy; [4]Az. Osp. Univ., Padova, Italy*

Background: Previous studies demonstrated the life saving role of implantable cardioverter-defibrillator (ICD) in high risk patients with genetic arrhythmogenic diseases/cardiomyopathies.
Aim: We report the main clinical data of patients with hypertrophic cardiomyopathy (HCM), right ventricular cardiomyopathy (ARVC), Long QT syndrome (LQT), idiopathic ventricular arrhythmias (IDIO) including Brugada syndrome (BS) and Short QT syndrome (SQT), enrolled in the Italian ICD Registry in the years 2001–2005.
Methods: The survey collected prospectively 90% of national ICD implantation activity on the basis of European ICD form, including the relevant clinical data of the enrolled patients and the technical characteristics of first ICD implants.
Results: The number of patients treated by ICD was 731 in HCM group, 285 in ARVC group, 133 in LQT group, 304 in IDIO plus BS and SQT group. Main clinical data and ICD type are reported in Table 1.

Table 1

	HCM	ARVC	IDIO + BS + SQT	LQT
Implant rate (% of total ICDs)	3,3	1,3	1,4	0,6
Mean age (std)	56,1 (16,9)	49,7 (17,3)	57,2 (15,9)	43,6 (23,7)
Male (%)	528 (72,9)	208 (73,8)	234 (77,7)	54 (41,2)
Primary prevention (%)	197 (27,6)	40 (14,2)	49 (16,3)	19 (14,3)
Secondary prevention (%)	517 (72,4)	241 (85,8)	252 (83,7)	114 (85,7)
VT (%)	309 (45,3)	194 (71,3)	141 (47,8)	23 (18,1)
VF (%)	117 (17,1)	39 (14,3)	95 (32,2)	66 (52)
Syncope (%)	179 (24,5)	69 (24,2)	66 (21,7)	36 (27,1)
AA drugs (%)	472 (64,5)	177 (62,1)	161 (53,0)	69 (51,9)
Single chamber ICD (%)	317 (43,4)	161 (56,5)	163 (53,6)	72 (54,5)

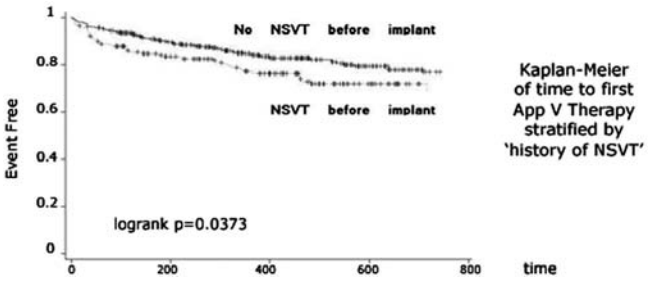
HCM: hypertophyc cardyomyopathy, ARVC: arrhythmogenic right ventricular cardiomyopathy, IDIO: idiopathic ventricular arrhythmias, BS: Brugada syndrome, SQT: Short QT syndrome, LQT: Long QT syndrome, AA: Antiarrhythmic drugs, VT: Ventricular tachycardia, VF: Ventricular fibrillation.

Conclusion: The ICD use in patients with inherited arrhythmogenic diseases/cardiomyopathies regarded in Italy a low number of cases with respect to the other main clinical indications. The mean age appeared lower in comparison with general ICD population (68 yrs). Secondary prevention is the main indication and the majority of patients are on antiarrhythmic drug therapy at the moment of ICD implant.

914 Implementation of MADIT II in "real world" clinical practice: data from a multicenter international registry

G. Boriani[1], B. Shmidt[2], M. Lunati[3], G. Botto[4], A. Proclemer[5], A. Erdogan[6], W. Rahue[7], M. Russo[8], M. Santini[5] on behalf of The Search-MI investigators. *[1]Institute of Cardiology, Univ. of Bologna, Cardiology Dept., Bologna, Italy; [2]Universitatsklinikum, Freiburg, Germany; [3]Niguarda Ca Grande Hospital, Cardiology, Milano, Italy; [4]S. Anna Hospital, Cardiology, Como, Italy; [5]S. M. della Misericordia Hospital, Cardiology, Udine, Italy; [6]Klinikum der Justus-Liebig-Universitat, Cardiology, Giessen, Germany; [7]S. Maurizio Hospital, Cardiology, Bolzano, Italy; [8]S. Filippo Neri Hospital, Cardiology, Roma, Italy*

MADIT II (MII) trial showed that post-infarction pts with LVEF≤30% had a significant survival benefit, when assigned to defibrillator (ICD) therapy. Search-MI is a European observational registry, monitoring current implant practices in the "real world" according to MADIT II inclusion criteria. The objective is to prospectively stratify the incidence of ICD interventions and to identify potential predictors of appropriate ICD therapy.
Methods and population: Between 11/2002 and 12/2005, 824 pts (89% male, mean age 66) were enrolled after implant of various types of ICDs (single-ch in 50%, dual-ch in 25%, biventricular in 25%). Mean LVEF was 26±6% (MII 23±6%), and NYHA class distribution was: I 9%, II 46%, III 43% and IV 2% (MII 35%, 35%, 25% and 5%).
Results: 787 pts were evaluated at an interim mean follow-up of 17 months. Overall, the incidence of first appropriate ICD therapy was 20%. At one year and two years, 18% and 26% of pts received at least an appropriate treatment for ventricular tachyarrhytmia (17% and 27% respectively in MII study). The presence of non sustained ventricular tachycardia (NSVT) documented by Holter or ECG before implant was associated with an higher chance of first appropriate ICD therapy and the Kaplan-Meier curves according to presence/absence of NSVT before implant separated early (Log-Rank p=0.037)(Figure). QRS at baseline did not predict appropriate ICD therapy.



Appropriate ICD therapy and NSVT

Conclusion: MADIT II-like patients implanted in the "real world" have a worse baseline clinical profile in comparison to original trial patients. Following implant with various types of ICDs (25% biventricular) NSVT identifies subjects with an higher incidence of appropriate ICD therapy. This observation may be clinically useful for selecting pts at higher arrhythmic risk.

915 QRS width is a predicting factor for implantable cardioverter-defibrillator shocks in patients with coronary artery disease

J.M. Rubio, A. Pinero, P.P. Perez, A. Garrido, P. Ramirez, M. Orejas, J. Benezet, J. Farre. *Fundacion Jimenez Diaz, Cardiology, Madrid, Spain*

Introduction: The incidence of implantable cardioverter-defibrillator (ICD) shocks in patients (Pts) with coronary artery disease (CAD) is variable and may depend on factors such as the left ventricular ejection fraction (LVEF). We also know that a QRS complex of ≥ 120 ms is considered an independent predictor of total mortality and sudden death in Pts with impaired LVEF.
Methods: In 189 CAD Pts (65±10 years; 89% male) with an ICD because of previous documented ventricular arrhythmias, we have analyzed the relation between the QRS width (QRSw) and LVEF before the implantation and the incidence of shocks in the follow-up.
Results: Mean QRSw before implantation was 104±27 ms, and mean LVEF was 32±11%. In 77 Pts (41%) a bundle branch block (BBB, QRS ≥ 120 ms) was present. After a mean follow-up of 82±53 months, 87 Pts (47%) had ICD shocks (87% of them appropriate). Pts with ICD shocks had a significantly wider QRS complex than Pts without shocks (115±27 ms vs. 95±22 ms; p <0.001), and a

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

higher incidence of BBB (57% vs. 27%; p<0.001). LVEF was significantly lower in Pts with ICD shocks than in Pts without shocks (30±12 vs. 34±12; p<0.05), but there were no differences in age (63±10 vs. 66±9 years; p=NS). In Pts with a baseline QRS≥120ms, the incidence of ICD shocks was significantly higher than in Pts with a QRS<120ms (64% vs. 34%, p <0.001). Moreover, the wider the QRS complex, the higher the incidence of ICD shocks (QRS 120-140 ms, 59%; QRS 140-160 ms, 64%; QRS > 160 ms, 89%; p<0.001). In a multivariate analysis, a QRS≥120 ms (OR 3.4 [1.8-6.3] CI 95%; p< 0.001) and a LVEF <25% (OR 1.9 [1.0-3.6] CI 95%; p<0.05) were independent predictors for ICD shocks.
Conclusions: Baseline QRS is significantly wider and LVEF significantly lower in Pts with ICD shocks during follow-up. A QRS ≥ 120 ms and a LVEF < 25% are independent predictors of the presence of ICD shocks. Moreover, the wider the QRS complex, the higher the incidence of ICD shocks.

916 ICD reduces mortality in CRT population: a seven years experience of a single centre

E. Baracca, F. Zanon, S. Aggio, G. Pastore, E. Bacchiega, L. Conte, M. Carraro, G. Braggion, A. Badin, P. Zonzin. *General Hospital, Division of Cardiology, Rovigo, Italy*

Cardiac resynchronization therapy (CRT) has become one of the main therapeutic alternatives for advanced congestive heart failure (CHF), but the long term effects on morbidity and mortality are still unclear. Aim of the study was to analyze hospitalization rate and mortality - total mortality (TM), cardiac mortality (CM) and sudden death (SD) – in a wide patient population implanted in our institution in the last six years.
Methods: Since 1999, 356 pts (261 male) underwent CRT for severe CHF (EF 27±8.2%). In 166 pts backup ICD therapy was selected. The mean age was 71.3±10 years (range 36 - 92); 187 pts (53%) had ischemic heart disease (IHD) while 169 were non ischemic (NIHD); 67 pts were in atrial fibrillation at the time of implant; 79 pts were previously paced via the right ventricular apex; 18 pts were candidates for heart transplantation. All pts were evaluated in our clinic and follow-up was scheduled every three months for the first year and then twice per year.
Results: The implant success rate was 99%. The mean follow-up was 37±25 months (range 1 – 93 months). Compared to the year before CRT, a significant decrease in hospitalization rate was observed during the first year of follow-up (2.55±1.6 vs. 0.81±0.7, p<.001). TM was 11.0%, CM was 8.2%. The "ICD group" compared to the "CRT-only group" shows a reduction of TM: 11.4% vs.15.3%; CM: 7,2% vs.11,5%; SD:1,1% vs. 5,5%.
TM was also evaluated at implant (0.23%), at 6 months and steps of 1 year as reported in the table.
In the group of IHD vs: NIHD, TM was 11.7% % vs. 9.5%, CM was 10.8% vs. 4.6%, SD 7% vs. 1,1% respectively. The main causes of death in IHD were heart failure and sudden death (6 pts). In NIHD 4 pts died from cancer and 1 due to acute abdomen.

6 months	1 year	2 years	3 years	4 years	5 years	6 years	7 years
3.3%	6.1%	11.1%	16.7%	21.7%	33.3%	38%	41.2%

Conclusions: 1) the benefit of CRT is similar in IHD and NIHD; 2) IHD seems to have a worse prognosis than NIHD in term of TM, CM and SD; 3) CRT decreases the hospitalization rate and increases survival; 4) the addition of a back-up ICD strongly reduces SD, CM and TM in this population.

CONTRAST NEPHROPATHY; RISK FACTORS, TREATMENT AND PROGNOSIS

917 Contrast-induced nephropathy after primary percutaneous coronary intervention; diabetes mellitus affects development of contrast-induced nephropathy

M. Nanasato, M. Matsumoto, T. Yamamoto, Y. Aoyama, Y. Ogura, H. Suzuki, T. Muramatsu, Y. Tatematsu, Y. Yoshida, H. Hirayama. *Nagoya Daini Red Cross Hospital, Cardiovascular Center, Nagoya, Japan*

Purpose: It has been well established that contrast-induced nephropathy (CIN) is one of the most serious complications on percutaneous coronary intervention (PCI). However, there is little information on CIN in patients treated with primary PCI for acute myocardial infarction. The aim of this study was to assess clinical predictors of CIN in patients treated with primary PCI.
Methods: In 166 consecutive patients undergoing primary PCI for acute myocardial infarction, serum creatinine concentration was measured at emergency room and each day for the following three days. CIN was defined as a rise in Cr more than 25% to the one at emergency room. Creatinine clearance rate was calculated by Cockcroft-Gault formula.
Results: Of 166 patients (125 men, 41 women, mean age 60.3±9.4 years), 38 patients (22.3%) developed CIN. Patients with diabetes mellitus (33% vs. 10%; p<0.03), calculated creatinine clearance less than 60 ml/min (32% vs. 13%; p<0.03), higher Killip classification (II, III and IV vs. I) (10% vs. 45%; p<0.05) more frequently developed CIN after the admission. Patients develping CIN had significantly lower base excess (-5.8±7.4 vs. -1.5±7.1; p <0.05), higher blood sugar (247±110 g/dl vs. 157±49 g/dl; p <0.01) at emergency room, significantly higher HbA1c (7.1±2.1% vs. 5.7±1.0%; p <0.01) at admission and higher creatine phosphokinase at maximum (4191±3698 IU vs. 2385±2274 IU; p <0.01). In multivariate analysis, Killip classification (II, III and IV vs. I) (odds ratio 1.77), creatinine clearance less than 60 ml/min (odds ratio 1.34) and HbA1c (odds ratio 2.01) were independent predictors of CIN. Patients developing CIN had significantly higher in-hospital mortality rate (18.4% vs. 3.1%; p<0.01). At discharge, patients with CIN had significantly higher serum creatinine (1.71±1.8 mg/dl vs. 1.06±1.17 mg/dl; p <0.05), B-type natriuretic peptide (491±673 pg/ml vs. 164± 152 pg/ml; p <0.05) and fasting blood sugar (147±71 g/dl vs. 103 ±19 g/dl; p <0.01).
Conclusions: CIN frequently complicates primary PCI, resulting in higher unfavorable clinical outcome. Diabetes mellitus as well as impaired renal function and hemodynamics affect development of CIN in patients treated with primary PCI. Diabetic patients should be carefully treated with primary PCI to prevent CIN, especially diabetic patients with poor control of blood sugar.

918 NGAL(Neutrophil Gelatinase-Associated Lipocalin) and cystatin C could predict contrast nephropathy after percutaneous coronary interventions in patients with stable angina and normal serum creatinine

H. Bachorzewska-Gajewska, J. Malyszko, E. Sitniewska, J.S. Malyszko, P. Kralisz, B. Poniatowski, S. Dobrzycki. *Bialystok, Poland*

The value of NGAL was highlighted as a novel biomarker of detection of acute renal failure in children after cardiac surgery. Interventional cardiologists are being asked more frequently to perform percutaneous coronary intervention-PCI and contrast nephropathy-CIN is its potentially serious complication. We tested the hypothesis whether NGAL could represent an early biomarker of CIN in 100 patients with normal serum creatinine. In addition, we assessed serum and urinary NGAL in relation to cystatin C, eGFR serum and urinary creatinine in these patients. We measured urinary and serum NGAL before, 2, 4,8, 24 and 48 hours after PCI. We found a significant rise in serum NGAL after 2, 4 and 8 hours, and in urinary NGAL after 4, 8 and 24 hours after PCI. Cystatin C rose significantly 24 hours after the procedure. When contrast nephropathy was defined as an increase in serum creatinine by >25% of the baseline level 48 hours after PCI, the prevalence of CIN was 11%. Patients with CIN received significantly more contrast agent (p<0.01, all received low-osmolal contrast), but duration of PCI was similar. NGAL levels were significantly higher in patients with CIN starting 2 hours after PCI (serum NGAL) or 4 hours (urinary NGAL). Cystatin C were higher only 8&24 hours after PCI in patients with CIN. In multivariate analysis, only serum creatinine was the predictor of serum NGAL before PCI. Serum NGAL before PCI was significantly higher in diabetics than in non-diabetics (p<0.05). Moreover, serum NGAL was significantly higher in diabetics 2, 4, 8 and 24 hours after PCI relative to non-diabetics. Normotensives had significantly lower NGAL 2 and 4 hours after PCI than hypertensives. NGAL may represent a sensitive early biomarkers of renal impairment after PCI. Our findings may have important implications for the clinical management of patients undergoing PCI. The "window of opportunity" is narrow in contrast nephropathy and time is limited to introduce proper treatment after initiating insult, particularly when patients are discharged within 24 – 48 hours after the procedure. Therefore, NGAL needs to be investigated as a potential early marker for nephrotoxicity, especially in the upcoming setting of short-time hospitalizations for coronary angiographies and interventions. Thus, further studies in patients with renal failure undergoing radiocontrast application are warranted to assess the usefulness of NGAL in respect of an earlier detection of radiocontrast nephrotoxicity.

919 Evaluation of contrast nephropathy in high risk patients undergoing either PCI or diagnostic angiography

A.E. Moreyra[1], M. Natarajan[2], S. Doucet[3], S.K. Sharma[4], C. Staniloae[5], R.E. Katholi[6], R.J. Solomon[7] on behalf of The CARE Study Group. *[1]Robert Wood Johnson Medical Center, Cardiology, New Brunswick, New Jersey, United States of America; [2]Hamilton Health Sciences, Cardiology, Hamilton, Ontario, Canada; [3]Montreal Cardiac Institute, Cardiology, Montreal, Quebec, Canada; [4]Mt Sinai Medical Center, Catheterization laboratory, New York, New York, United States of America; [5]St Vincents Manhattan Medical Center, Cardiology, New York, New York, United States of America; [6]Southern Illinois University, Medicine, Springfield, Illinois, United States of America; [7]University of Vermont, Renal Services, Burlington, Vermont, United States of America*

Purpose: We compared the rate of contrast-induced nephropathy (CIN) in high risk patients undergoing either diagnostic cardiac angiography or percutaneous coronary interventions (PCI) receiving either the nonionic dimer iodixanol-320 or the nonionic monomer iopamidol-370.
Methods: Patients with chronic kidney disease (eGFR 20-59 mL/min) enrolled in the CARE (Cardiac Angiography in REnally Impaired Patients) study were randomized to receive either iodixanol (n=210) or iopamidol (n=204) for their cardiac procedure. Serum creatinine (SCr) levels were assessed at baseline and 2-5 days postdose. Fisher's exact test was used to evaluate differences in CIN incidence, prospectively defined as a postdose SCr increase of ≥ 0.5 mg/dL. Increases in SCr ≥ 25% and decreases in eGFR ≥ 25% were also evaluated.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: No significant differences in baseline characteristics (age, gender, SCr, eGFR, % diabetes) were seen patients undergoing cardiac angiography (n=251) or PCI (n=163). Baseline SCr values were 1.46±0.36 mg/dL in the PCI group and 1.44±0.41 mg/dL in the cardiac angiography (non-PCI) group (p=0.64). IV hydration volume was similar in the two groups, however, patients in the PCI group received a higher mean contrast dose than those in the non-PCI group (178.4 mL vs 106.9 mL, p<0.0001). The CIN rate was similar in the PCI (8/163, 4.9%) and non-PCI groups (15/251, 6.0%) [p=0.64]. CIN rates were also similar after iopamidol or iodixanol, both in the overall population (9/204, 4.4% vs. 14/210, 6.7%, p=0.39), in the subset of patients undergoing diagnostic angiography, (7/123, 5.7% vs. 8/128, 6.3%, p=1.0), and in the PCI subset (2/81, 2.5% vs. 6/82, 7.3%, p=0.28). Similar results were observed for increase in SCr ≥ 25% and decrease in eGFR ≥ 25%.
Conclusions: CIN rates were similar in patients undergoing angiography vs. PCI, despite significantly increased contrast media exposure in patients undergoing PCI. Differences in the rate of CIN between iopamidol-370 and iodixanol-320 were not statistically significant, either in patients undergoing diagnostic angiography or in patients undergoing cardiac interventions.

920 Contrast-induced nephropathy after primary percutaneous intervention for ST elevation myocardial infarction

N. Jepkes-Bruin, I. Andrade Ferreira, J.C.A. Hoorntje, A.W.J. Van 'T Hof. *Isala Klinieken, cardiology, Zwolle, Netherlands*

Purpose: Nephropathy after STEMI is related to poor outcome. Measures that may prevent contrast induced nephropathy (CIN) are not common in patients undergoing primary percutaneous intervention (PCI) for STEMI. The goal of this study is to (i) assess the incidence of CIN in a large STEMI population, and (ii) whether CIN is related to poor outcome, (iii) and to identify persons at risk of developing CIN.
Methods: A retrospective analysis was conducted of 1407 consecutive patients undergoing primary PCI for STEMI in a large PCI centre from 1991 to 2004. Creatinine values at admission (baseline) and maximum values within 72 hours were evaluated. CIN was defined as an increase in serum creatinine of 25% or more as reported earlier (Marenzi et al, NEJM 2006, 354: 2773).
Results: At baseline mean creatinine was 91.77±25.48 μmol/L. After primary PCI, creatinine increased to a maximal creatinine of 105.62±35.12 μmol/L (15.59±20.57%, P<0.001). Overall, 21.0% of our study population developed CIN. The development of CIN was related to an increased mortality risk (both in-hospital, after 30 days and one year (P<0.05), recurrent myocardial infarction (MI) within 30 days of admission (P<0.04), and coronary bypass surgery after 30 days and one year (P<0.05). Multivariate analysis showed that an age above 60 years, hypertension, a prolonged ischemic time of more than 5h and a Killip class score greater than 1 were independent predictors for developing CIN (P<0.005). Furthermore, baseline creatinine, CIN and an age above 60 years were predictors for in-hospital death (P<0.03). Although being predictors for renovascular disease, the presence of diabetes mellitus or smoking was not related to CIN in our study population.
Conclusions: Overall renal function is impaired in STEMI patients undergoing primary PCI. A large subgroup of patients develops CIN, which is related to an increased risk of mortality and recurrent MI within 30 days. Additional measures before or during PCI to help prevent CIN might be necessary to improve final outcome.

921 Statin therapy reduces contrast induced impairment of renal function in patients undergoing elective coronary angiography

S. Acikel, H. Muderrisoglu, A. Yildirir, A. Aydinalp, E. Sade, K. Demirtas, U. Bal, G. Kaynar, Y. Gursoy, B. Ozin. *Baskent University Faculty of Medicine, Cardiology, Ankara, Turkey*

Background: A decline in kidney function after contrast exposure is associated with higher in morbidity and mortality both the hospitalization period and in the long term. It has been demonstrated in a few clinical trials that statin therapy might prevent contrast nephropathy in patients undergoing coronary angiography (CAG). In this prospective study, we aimed to asses the effects of two different statin therapy regimens on renal function after contrast administration in patients undergoing elective CAG.
Methods: Two hundred and forty patients undergoing elective CAG were included in 3 groups (Group 1: Control, Group 2: Chronic statin therapy, Group 3: Atorvastatin 40 mg/day). The study drug in Group 3 was started 3 days before CAG. The patients who had severe co-morbidities, those with serum creatinine≥1.5 mg/dL and using antioxidant, nephrotoxic agent or other lipid lowering therapies were not included study. All patients had standard oral and intravenous hydration and exposed to same low-osmolar contrast agent. The serum creatinine and glomerular filtration rate (GFR) were measured before and after 48 hours of CAG. Cockcroft-Gault formula was used to determine GFR.
Results: The mean age of the patients was 59.8±9.7 years, 152 (63%) were men, 151 (63%) were hypertensive, 166 (69%) were dyslipidemic and 69 (28%) were diabetic. The incidence of dyslipidemia, history of myocardial infarction and coronary revascularization were higher in Group 2 compared to Group 1 and 3 (p<0.001, p=0.005, p<0.001, respectively). The amounts of hydration and contrast agent used in CAG did not differ between groups (p>0.05). Baseline serum creatinine and GFR values were also similar. After CAG, serum creatinine and GFR values were statistically better in statin users compared to controls (Table).

Renal function parameters between groups

	Group 1 n=80	Group 2 n=80	Group 3 n=80	P
Baseline creatinine, mg/dL	0.85±0.16	0.87±0.16	0.84±0.14	0.502
48.hour creatinine, mg/dL	1.00±0.18	0.92±0.18	0.91±0.15	0.003
Baseline GFR, ml/min	97.0±28.1	95.9±25.6	97.7±23.3	0.903
48.hour GFR, ml/min	82.4±25.3	91.1±24.8	90.5±22.0	0.041

Conclusion: Short or long term use of statin therapy may have a protective role for the impairment of renal function in patients undergoing elective CAG.

922 Contrast induced nephropathy is related to long term mortality in elderly patients treated with primary angioplasty

T. Pawlowski[1], T. Kulawik[2], J. Rzezak[1], K. Stepien[3], B. Kaluza[2], T. Niemirka[2], S. Golebiewski[2], H. Rdzanek[2], R.J. Gil[2]. *[1]Klinika Kardiologii Inwazyjnej, Csk Mswia (Central Hospital), Warsaw, Poland; [2]Klinika Kardiologii Inwazyjnej, Warsaw, Poland; [3]Zaklad Diagnostyki Labolatoryjnej, Warsaw, Poland*

Background: Primary angioplasty is the treatment of choice for acute myocardial infarction (AMI), especially in elderly patients. The aim of the study was to evaluated the long term outcome of elderly patients with contrast induced nephropathy (CIN).
Methods: Single, interventional cardiology center registry consists of 3436 patients with AMI. Out of the population, 358 patients over 75 years old were selected. Based on the following criteria-creatinine increase more then 0.5 mg% or more then 25% of baseline value of creatinine - the CIN was diagnosed. This criteria was fulfilled in 78 patients (21.7%). The registry population was divided into groups according to the presence of CIN: Group 1 – 78 patients (mean age: 79±14 y.) with CIN and Group 2 – 280 patients (mean age: 78±13y.) without CIN. The prevention regimen was left to the discretion of cardiologist. Clinical follow-up was assessed by taking major adverse cardio-cerebral events as death, stroke and infarction at 7 and 30 days, 1 year and 3 years after coronary angioplasty.
Results: There were no differences across demographic, angiographic characteristics. Long term mortality and MACCE is presented in Table 1, although there were no differences in terms of stroke and infarction. There was a significant trend to higher mortality rate in Group 1 then in Group 2, increasing with follow-up time.

Table 1

	7 day death	30 days death	1 year death	1 year MACCE	3 years death
Group 1 (%)	19.2	28.2	37.1	57.6	48.7
Group 2 (%)	12.5	13.2*	16.7*	32.1*	20.7*

p<0.05.

Conclusions: Contrast induced nephropathy in elderly population with AMI is related to worse long term outcome. Effective prevention regimen should be developed for this population.

TRIALS AND REGISTRIES IN PERCUTANEOUS CORONARY INTERVENTION

923 Safety of drug eluting stents compared to bare stents in patients with acute coronary syndromes undergoing percutaneous coronary intervention: the ACUITY trial

R. Mehran[1], J.W. Moses[1], G. Dangas[1], S.V. Manoukian[2], H.D. White[3], E.M. Ohman[4], S.J. Pocock[5], F. Feit[6], A. Colombo[7], G.W. Stone[2]. *[1]Cardiovascular Research Foundation, New York, United States of America; [2]Crawford Long Hospital, Atlanta, United States of America; [3]Auckland City Hospital, Auckland, New Zealand; [4]Duke University Medical Center, Durham, United States of America; [5]London School of Hygiene and Tropical Medicin, London, United Kingdom; [6]New York University School of Medicine, New York, United States of America; [7]Ospedale San Raphael, Milan, Italy*

Background: Drug-eluting stents (DES) are the dominant therapy in patients undergoing percutaneous coronary intervention (PCI). However the safety of DES in pts with acute coronary syndromes (ACS) undergoing PCI has not been established.
Methods: In the ACUITY trial, 13,819 pts with moderate and high risk ACS were randomized to heparin (unfractionated or enoxaparin) + glycoprotein IIb/IIIa inhibitor (GPI), bivalirudin + GPI or bivalirudin monotherapy. Following angiography, pts were treated with PCI (56%, n= 7789), bypass surgery (11%) or medical therapy (33%). In patients undergoing PCI, 60% received DES, 37% received bare metal stents (BMS), and 4% were treated with non-stent PCI. Composite ischemia (death, myocardial infarction (MI), unplanned revascularization) and acute/subacute stent thrombosis were adjudicated by an independent clinical events committee.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: Among the 7,789 patients undergoing PCI, 4415 received DES (Cypher, n=1897 or TAXUS, n=2309, both, n=219), 2420 received BMS. DES patients had more diabetes (29.5% v. 27%, p<0.001) and multivessel stenting (21.5% v. 13.4%, p<0.0001). Pharmacologic treatment assignment was well matched between groups. The 30 day results are shown in the Table. In patients receiving only Cypher or Taxus stents, 30 day stent thrombosis occurred in 1.5% vs. 1.2%, p=0.38.

Events at 30 days

	DES (N=4415)	BMS (N=2420)	P value
Composite ischemia	8.8%	7.7%	0.12
– Death	0.8%	1.3%	0.53
– MI	6.6%	5.7%	0.19
– Unplanned revasc.	3.4%	2.5%	0.03
– Stent thrombosis	1.3%	1.6%	0.35

Conclusions: Among moderate and high risk pts with ACS undergoing PCI, DES and BMS result in similar rates of adverse ischemic events and stent thrombosis. Cypher and Taxus also had a similar early safety profile in this unadjusted analysis. Follow-up to 1 year is complet and the late safety and efficacy of DES compared with BMS in high risk ACS patients will be presented.

924 Real-world results with TAXUS Liberte: One-year results from the TAXUS OLYMPIA global post-approval registry with emphasis on diabetic patients

M. Thomas[1], W. Ahmed[2], O. Mendiz[3], S. Mascioli[4] on behalf of The TAXUS OLYMPIA Investigators. *[1]King's College Hospital, Department of Cardiology, London, United Kingdom; [2]Armed Forces Hospital, Jeddah, Saudi Arabia; [3]Fundacion Favaloro, Department of Interventional Cardiology, Buenos Aires, Argentina; [4]Boston Scientific Corporation, Marlborough, Ma, United States of America*

Purpose: TAXUS OLYMPIA is a global, multicenter, prospective, web-based registry capturing clinical outcomes in up to 28,000 patients receiving the next-generation TAXUS Liberté-SR paclitaxel-eluting stent in routine clinical practice.
Methods: TAXUS OLYMPIA Phase I included 529 patients in 7 countries in the Middle East, South and Central America, and Asia Pacific, and has completed 12-month follow-up. Phase II is currently enrolling up to 10,000 patients in up to 40 countries outside the US, Europe, and Japan while Phase III is enrolling up to 14,000 patients in up to 20 European countries. Clinical follow-up occurs at 6 and 12 months post procedure, including source data verification for all patients with reported cardiac events. The primary endpoint is the rate of TAXUS Liberté-related cardiac events (cardiac death, MI, and re-intervention of the target vessel) at 12 months post-procedure adjudicated by an independent medical reviewer. TAXUS Liberté is a second-generation drug-eluting stent designed to enhance lesion access in challenging anatomies.
Results: In the 529 Phase I patients (50% diabetic), the 12-month TAXUS Liberté-related cardiac event rate was 3.7%. Preliminary data from the first 2,066 patients (2,602 lesions, 3,008 stents) in Phase III show that the TAXUS Liberté stent continues to be used in a wide variety of complex patient and lesion types. Patient baseline demographics included 59% multivessel disease, 32% diabetes and 19% acute MI. Lesion characteristics included 24% long lesions (> 20 mm), and 39% small vessel diameter (≤ 2.75 mm). Approximately 65% of the initial Phase III patients had baseline demographic or lesion characteristics that would have excluded them from the primary randomized, controlled clinical trial of the TAXUS Liberté stent. In this group the TAXUS Liberté-related cardiac event rate was 3.0% at 6 months, including a 1.8% re-intervention rate, total mortality of 1.3% (0.9% cardiac death, 0.4% non-cardiac death) and a 0.9% rate of MI. Additionally, 0.5% of patients experienced angiographically-confirmed stent thrombosis. The 6-month TAXUS Liberté-related cardiac event rate in diabetics was 4.0%. One-year outcome data for approximately 7,000 patients, including high-risk subsets, will be available at the time of presentation.
Conclusions: One-year outcomes in the real-world TAXUS OLYMPIA registry confirm the clinical benefit of the TAXUS Liberté stent seen in the randomized, controlled studies. Stent thrombosis is low and outcomes in diabetics appear particularly encouraging.

925 Long-term safety and efficacy of paclitaxel-eluting stents in chronic total coronary occlusions: 3 year follow-up from the Paclitaxel in chronic total occlusion (PACTO) study

G.S. Werner[1], M. Ferrari[2], M. Fritzenwanger[1], S. Betge[1], H.R. Figulla[1]. *[1]Klinikum Darmstadt, Medizinische Klinik I, Darmstadt, Germany; [2]Friedrich-Schiller-University, Jena, Germany*

Background: Drug-eluting stents (DES) provide a new therapeutic approach to improve the high recurrence rate after percutaneous coronary intervention (PCI) in chronic total coronary occlusions (CTO). In view of the unknown risk of late catch-up and late stent thrombosis, the long-term benefit of DES remains to be established.
This study addresses these issues with a long-term follow-up over 3 years after treatment of CTOs with a paclitaxel-eluting stent (Taxus).
Methods: In 95 consecutive patients Taxus stents were implanted after recanalization of a CTO. Patients underwent angiographic follow-up at 6 months and clinical follow-up for 3 years. Patients with restenosis underwent repeat PCI and another follow-up angiography. The Taxus group was compared to a group of 95 matched patients treated with BMS. Major adverse cardiac events (MACE) and long-term angiographic patency were assessed.
Results: The 1-year event-free survival was 14.7% in the Taxus group, and 52.6% in the BMS group (p<0.001) due to a reduced need for repeat revascularization. There was only 1 reocclusion at angiographic follow-up with Taxus (1.1%) as compared to 22.2% with BMS (p<0.005). All non-occlusive restenosis in the Taxus group were focal and treated successfully with an additional short Taxus stent leading to a secondary patency of 99%. During subsequent follow-up 20% of all patients underwent additional angiographies, demonstrating a stable situation at the treatment site without late progression. Three patients in the Taxus group with excellent 6 months angiographic result, however, presented with unstable angina during subsequent follow-up, and angiography showed late stent thrombosis 10-32 months after PCI. Still, the MACE rate remained lower in the Taxus group after 3 years (18.9%) as compared to the BMS group (55.8%; p<0.001). The incidence of late stent thrombosis was 3 confirmed and 2 possible cases (sudden death) in the Taxus group, and 2 possible cases (sudden death) in the BMS group. Cardiovascular mortality was slightly lower in the Taxus group (2.2%) as compared to the BMS group (8.4%; p<0.05).
Conclusions: The treatment of CTOs with a paclitaxel-eluting stent lead to a drastically reduced MACE rate after 1 year, which persisted after 3 years. The incidence of confirmed or possible late stent thrombosis in the Taxus group was 5.3% within 3 years, which requires further attention and continuous follow-up. Still, the overall benefit of the DES remained unchanged by these events, and did not increase mortality.

926 Gender differences in the application and outcome of PCI, Euro Heart Survey PCI

C. Daly[1], C. Di Mario[1], F. Weidinger[2], W. Wijns[3], R. Seabra Gomez[4], P. Serruys[5], S. Silber[6], A. Vahanian[7], J. Marco[8], A. Gitt[9] on behalf of Euro Heart Survey PCI. *[1]Royal Brompton Hospital, Cardiology Dept., London, United Kingdom; [2]Innsbruck, Austria; [3]Louvain, Belgium; [4]Carnaxide, Portugal; [5]Rotterdam, Netherlands; [6]Munich, Germany; [7]Paris, France; [8]Clinique Pasteur, Interventional Cardiology Unit, Toulouse, France; [9]Ludwigshafen Heart Centre, Ludwigshafen, Germany*

The aim of this study was to assess gender differences in the application of PCI and in procedural and clinical outcomes across a range of clinical settings.
The Euro Heart Survey PCI included 13,152 consecutive patients undergoing PCI across Europe in 2005. One third had PCI in the setting of ACS with ongoing instability, 24% had stabilised ACS and 42% were elective. Overall 25% were female, but with a higher proportion of women (29%) in the non-ST elevation ACS setting. Women were older (68 vs 62 yrs, p<0.0001), with a higher prevalence of diabetes (33% vs 23%, p< 0.0001). More women were in cardiogenic shock at presentation (12% of women with STEMI vs 8% of men, p=0.001). Shorter stent lengths, and smaller diameter balloons/stents were used in women. However the use of stents and drug eluting stents was similar, except in the setting of STEMI, where fewer women had stent implantation (89% vs 94%, p=0.004). Adjuvant drug therapies and medications on discharge were not substantially different between genders. Women had more frequent arterial complications (false aneurysm 1.4% vs 0.6%, p<0.001), more significant bleeding complications (0.8% vs 0.3%, p= 0.008) and overall had a two fold greater in-hospital mortality rate (2.2% vs 1.2%, p<0.0001) than men. The increased mortality rate in women was greatest in patients with ST elevation MI (7.7% v 4.1%, OR 1.95 [1.34-2.85] p=0.004), but was not apparent after adjustment for age, OR 1.27 [0.85-1.89]; p=0.25. Although the absolute numbers were considerably lower, there was also excess mortality in women undergoing elective PCI (0.5% v 0.2%, OR 2.77 [1.0-7.65] p=0.04), but again this was no longer significant when adjusted for age, OR 2.43 (0.85-6.89); p=0.096
Despite similar application of stent technology and adjuvant therapy women have a small but significant excess risk of procedural complications, and a significantly higher in-hospital mortality post PCI compared to men. This is most obvious, but not only restricted to patients in the setting of STEMI, and the differences between genders are not statistically significant after adjustment for age.

927 Complete vs. two-stage revascularization in patients with ST elevation myocardial infarction and multivessel coronary disease: final results of the prospective, randomized, multicentre trial

A. Ochala[1], W. Wojakowski[2], G. Smolka[1], R. Wyderka[1], Z. Krolikowski[3], D. Dudek[4], J.S. Dubiel[2], M. Tendera[3]. *[1]Silesian School of Medicine, III Division of Cardiology, Katowice, Poland; [2]Silesian School of Medicine, 3Rd Division of Cardiology, Katowice, Poland; [3]Hospital Bytom, Cardiology Ward, Bytom, Poland; [4]Medical College Jagiellonian University, Haemodynamics and Angiocardiography, Krakow, Poland*

Recanalization of the infarct-related artery is the main goal of primary angioplasty in STEMI. With the exception of cardiogenic shock, staged procedures are performed in patients with STEMI and multivessel disease. We tested the hypothesis

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

that complete one-stage revascularization procedures are safe and associated with favorable recovery of the left ventricular contractility.
Patients and methods: 156 patients with STEMI and multivessel disease (both culprit lesion and 1 to 3 critical lesions in main epicardial vessels suitable for stenting) were randomized to: group A – one stage complete revascularization (80 pts), group B (n=76) primary angioplasty in infarct-related artery and staged complete revascularization procedure in 30 days. 12 months follow-up (f-u) was done post final revascularization (clinical, treadmill test, echocardiography, angiography in 102 cases). Primary end-point: left ventricular ejection fraction (LVEF) increase $\geq$ 5%. Secondary: (1) composite end point: death, reinfarction and any repeat revascularization in 12-month f-u, (2) total 12 month in-hospital cost.
Results: Both groups were comparable in terms of clinical characteristics, number of disease vessels, angiopraphic characteristics of the culprit vessel, use of stents and IIb/IIIa blockers. In group A 2,29±0,68 lesions/pts were treated using 1,14±0,35 stents and in group B 2,30±0,69 lesions/pts and 1,13±0,34 stents. The amount of contrast agent used in group A was 270±50 ml vs 490±140 ml in group B ($p<0,001$) and fluoroscopy time was significantly shorter 28±6 min vs 48±7 min ($p<0,001$) to achive complete revascularization. LVEF increased after 30 days in group A from 41±4,5% to 47±3,8%, $p<0,001$ vs 42±4,1% to 44±4,6%, p=0,002 in group B, the difference between group A and B was significant ($p<0,001$). However after 12 month f-u the final results of LVEF were similar in both groups 48±4,3% vs 46±4,3%, p=0,13. TIMI myocardial blush grade (TMBG) and ST segment resolution were comparable in group A and B, although there was a trend towards better improvement in group A (p=0,057). Low incidence of MACE was similar in both groups during all f-u (p=0,09). 12-months in-hospital costs were higher in group B (2610±655 vs 3309±599 EUR, $p<0,001$).
Conclusions: One-stage multivessel, complete revascularization during primary PCI is safe and feasible. The number of MACE was low and comparable in both groups. In one-stage group LVEF improved faster, and was significantly higher after 30 days. The in-hospital costs of the one-stage procedure were significantly lower in comparison to two-stage revascularization.

928 Long term predictors of death in patients treated by drug-eluting stents for unprotected lef main lesions: Insights from the French Left Main Taxus Registry

B. Vaquerizo[1], T. Lefevre[1], P. Garot[1], M. Silvestri[2], Y. Louvard[2], H. Routledge[2], F. De Marco[2], O. Darremont[3], M.C. Morice[3].
[1]ICPS, Massy, France; [2]Clinique du Parc Rambot, Cardiologie Interventionnelle,Angio/Icps, Aix En Provence, France; [3]Clinique St Augustin, Cardiologie Interventionnelle,Angio/Icps, Bordeau, France

Background: Although drug-eluting stents (DES) have emerged as an alternative to surgery (CABG) in patients with unprotected left main (LM) lesions, the predictors of death remain unknown.
Methods: In order to assess the long term predictors of death after LM stenting, univariate and multivariate analysis were performed in the French LM Taxus Registry database.
Results: In this real world study 291 patients were included, age 69±11 years, 77% male, 29% diabetic, 5% renal failure, 17% previous or recent MI, 38% acute coronary syndrome, 25% 3-vessel disease, 78% distal LM and Euroscore 4.8±3.4 (CABG predicted in-hospital mortality 6.3±10.4%). Other lesions were treated during the same stage in 77% of cases. Angiographic success was obtained in 99.7%. Follow-up at 22±3 months was obtained in 93% of cases. Total death rate was 5.6% (cardiac death 3.3%). Univariate predictors of death are summarized in the table. By multivariate analysis, Euroscore (OR 1.65; 95% CI 1.15-2.37; p=0.006) and terminal renal failure with dialysis therapy (OR 0.02; 95% CI 0.001-0.48; p=0.016) were the only independent predictors of death.

	Death (N=15)	Survival (N=255)	P value
Ejection fraction (%)	58±10	61±13	NS
3-vessel disease (%)	33.3	23.5	NS
Distal left main stenting (%)	93.3	78.8	0.08
Femoral access (%)	66.6	39.9	<0.05
Age (year)	74±11	68±11	<0.05
Stent side branch in distal LM (%)	53.3	22.7	0.01
Diabetes (%)	60.0	25.8	0.008
Creatinine (µmol/l)	268±234	92±22	<0.001
Dialysis therapy (%)	33.3	0.8	<0.001
T shape bifurcation (%)	84.6	35.9	<0.001
PCI success (%)	93.3	100	<0.001
Euroscore	6.4±2.4	4.0±3.1	<0.0001

Conclusion: Elective stenting using paclitaxel eluting stent for the treatment of LM lesion is associated with a 2-years total death rate of 5.6%. This compares favorably to the "predicted" in-hospital mortality of 6.3%. Euroscore and chronic renal failure on dialysis were the only independent predictors of death.

DIAGNOSTIC CHALLENGES IN CARDIOMYOPATHIES

997 Comparative investigation in the clinical value of endomyocardial catheter biopsy (EMCB) in patients with hypertrophic (HNCM) and dilated (DCM) cardiomyopathy

G. Beer, T. Lawrenz, C. Stellbrink, H. Kuhn. *Bielefeld, Germany*

In pts with HNCM and DCM (regarding the diagnosis of myocarditis (M)) there is debate about the clinical value of EMCB.
Methods: We investigated 100 consecutive pts with HNCM (male/female: 62/38 pts; mean age 56 years) and DCM and/or clinical suspicion of M (male/female: 68/32 pts; mean age 50 years) by right ventricular EMCB. Additionally we investigated in a blinded prospective study a group of 100 consecutive symptomatic pts with 7 different cardiac disorders by EMCB which were used as controls. In these 100 pts the pathologist performed a "blinded evaluation" (i.e. written report without any clinical information) of the EMCB. In all pts EMCB (4 to 5 EMCB per pt) was performed during the routine diagnostic coronary angiogram and ventricular angiogram. All EMCB were evaluated by electron and light microscopy (LM). The morphologic diagnosis of M was based on the Dallas Criteria. The results of EMCB were correlated to clinical, echocardiographic and invasive data.
Results: LM alterations in the 100 pts with HNCM showed the unspecific findings of interstitial fibrosis and myocyte hypertrophy without any difference regarding frequency and extent from the 100 pts of the "blinded" controls. In 10/100 pts (10%) with HNCM, EMCB revealed the surprising result of concealed cardiac storage disease (Amyloid heart disease: 3/100 pts, 3%; cardiac Fabry disease: 7/100 pts, 7%) with diagnostic and therapeutic consequences. In 45/100 pts with DCM, EMCB revealed an interstitial inflammatory infiltrate; this unspecific finding was similar to controls (38/100 pts). Only in 1 pt with DCM (1%) EMCB revealed M with pronounced myocyte necrosis which resulted in therapeutic consequences. In 20/100 pts of the "blinded study", the pathologist stated a diagnosis of HCM or DCM, because he suspected the morphological alterations to be characteristic. However only in 2/20 pts (10%) this diagnosis was correct.
Conclusion: In pts with HNCM, EMCB revealed in 10% of consecutive pts concealed cardiac storage resulting in specific therapeutic (enzyme replacement therapy, chemotherapy) and pronounced prognostic consequences. In a subgroup of pts with the clinical features of HNCM, a causal therapy is initiated on the basis of EMCB. This diagnosis could only be made by EMCB. Therefore the clinical value of EMCB in routine evaluation of symptomatic pts with HNCM seems to be high (10%), in contrast to pts with DCM (1%). In highly symptomatic pts with HNCM additional EMCB should be performed during necessary invasive investigation. EMCB should be used reluctantly in clinical routine evaluation in DCM.

998 Electroanatomic and histologic findings in patients with clinical and instrumental diagnosis of arrhythmogenic right ventricular cardiomyopathy

M. Pieroni, F. Marzo, A. Dello Russo, M. Casella, G. Pelargonio, M.L. Narducci, R. Biddau, M.B. Giannico, F. Bellocci, F. Crea. *Catholic University, Cardiology Department, Rome, Italy*

Purpose: Electroanatomic mapping (EAM) has been proposed as a new tool to distinguish arrhythmogenic right ventricular cardiomyopathy (ARVC) from other right ventricular (RV) disorders. We compared EAM and myocardial biopsy findings in patients with clinical and instrumental diagnosis of ARVC.
Methods: We studied 23 consecutive patients (10M/13F, 41±16 yrs) with a diagnosis of ARVC according to recent criteria. All patients underwent 3D-EAM, cardiac magnetic resonance (CMR) and cardiac catheterization with multiple RV biopsies obtained from RV regions with abnormal electrograms. The EAM color display ranged from red, (scar tissue, amplitude <0.5 mV), to purple (normal tissue amplitude 1.5 mV).
Results: Clinical presentation included sustained ventricular tachycardia (n= 4), non-sustained ventricular tachycardia (n=13) and frequent ventricular ectopic beats (n=6). All patients showed RV wall motion abnormalities and/or enlargement at angiography and CMR. Twenty patients (87%) had an abnormal EAM and in all cases low-voltage areas corresponded to wall motion abnormalities. Myocardial biopsy confirmed the diagnosis of ARVC in 9 cases (39%), while showed the presence of active myocarditis in the absence of fibrofatty replacement in the remaining 14 cases (61%) (Figure 1), including the 3 patients with normal EAM. Abnormal voltages in the RV outflow tract were observed in all ARVC patients but only in 5 pts (36%) with myocarditis; in the latter septal, lateral and apical RVwall were most frequently involved.

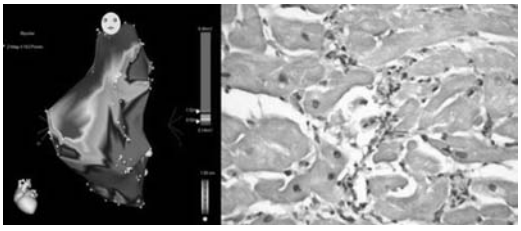


Figure 1

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusions: Myocarditis of the RV may produce electroanatomic abnormalities causing ventricular arrhythmias and mimicking ARVC. EAM may guide endomyocardial biopsy improving its diagnostic sensitivity and contributing to distinguish the pathological substrate of ventricular arrhythmias.

999 Diagnostic implications of Right Ventricular Systolic Dysfunction in patients with Dilated Cardiomyopathy

M.F. Elnoamany. *Shebin Elkom, Egypt*

Background: Unlike left ventricular (LV) function, right ventricular (RV) function has not been widely studied in ischemic patients. The role of RV function is emerging in patients with heart failure of different etiologies.
Objectives: To investigate the diagnostic role of RV systolic dysfunction (RVSD) in idiopathic dilated cardiomyopathy (IDC) & ischemic cardiomyopathy (ICM).
Methods: A series of 102 patients with dilated cardiomyopathy, either non ischemic (n=49, IDC group) or ischemic (n= 53, ICM group) & 20 healthy volunteers as a control group were included in this study. RVS function was assessed by pulsed - wave Doppler tissue imaging (PWDTI) of tricuspid annular systolic (TAS) motion. Ejection Fraction (EF) of both RV & LV were estimated by Simpson's rule. Coronary angiography was performed to rule in or out coronary artery disease. RVD was defined as a RV EF $<$ 35% or TAS velocity (TASV) $<$ 12 cm/s & ventricular concordance (VC) was defined as a $<$10% difference between RV and LV EF.
Results: Patients with IDC and ICM had comparable LV EF (36.7% $\pm$7.2% vs. 39% $\pm$6.6%, $p < 0.1$) and pulmonary artery systolic pressures (38.1$\pm$5.7 mm Hg. Vs. 35.8$\pm$7.5 mm Hg., $p < 0.08$). TASV & RV EF were significantly lower in IDC compared to ICM (10.6$\pm$ 1.2 cm/s vs. 12.7$\pm$1.4 cm/s, $p < 0.001$) & (34.1% $\pm$4.1% vs. 47.6% $\pm$7.5%, $p < 0.001$) respectively. The prevalence of RVD & VC was significantly higher in the IDC compared with ICM (67.4% vs. 17%, $p < 0.001$) & (85.7% vs. 15.1%, $p < 0.001$) respectively. Reduced RV EF, low TASV & VC were powerful independent predictors of IDC compared with ICM (OR for each = 0.78, 0.21, 0.63 respectively & 95% CI [0.72-0.85], [0.12 – 0.38] & [0.54-0.73] respectively, $p < 0.001$ for each). Reduced TASV had a positive predictive value (PV) of 88% & a negative PV of 90% to diagnose IDC, for reduced RV EF these values were 79% & 73%, & for VC, 85% & 87% respectively. The correlation between TASV & RV EF was stronger in IDC compared with ICM ($r = 0.87$, $p < 0.001$ in IDC while $r= 0.69$, $p < 0.001$ in ICM) respectively.
Conclusions: PWDTI has a high predictive power for RVSD & in the presence of LVD, the combination of low TASV, VC & reduced RV EF is a powerful marker for IDC compared with ICM, independent of pulmonary hypertension & LV EF. These findings support the concept that IDC is frequently characterized by a biventricular affection & that the presence of RVD represents a distinguishing feature of this disease.

1000 Relative utility of genotyping, diagnostic criteria, and cardiovascular magnetic resonance in the clinical diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy

S. Sen-Chowdhry[1], P. Syrris[1], A. Asimaki[1], G.C. Smith[2], R. Wage[1], N. Keenan[1], W.J. Mckenna[2]. *[1]The Heart Hospital, Cardiology In The Young, London, United Kingdom; [2]National Heart & Lung Institute, Cardiovascular Magnetic Resonance Unit, London, United Kingdom*

Purpose: Timely diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) is difficult as early findings may be subtle and non-specific. The 1994 Task Force (TF) criteria appear highly specific but lack sensitivity for early disease. Modified criteria have been proposed for familial ARVC.
The role of cardiovascular magnetic resonance (CMR) in the evaluation of ARVC is controversial owing to absence of a standardized protocol, insufficient experience with the modality, and inherent difficulties imaging the right ventricle. We sought to compare the diagnostic accuracy of CMR, TF and modified criteria in a genotyped sample.
Method: The protocol included 12-lead and signal-averaged ECG, 2D-echocardiography, exercise testing, ambulatory ECG monitoring, CMR with late-enhancement imaging and mutation screening of 5 desmosomal genes (plakoglobin, desmoplakin, desmoglein-2, plakophilin-2, desmocollin-2). CMR readers were blinded to genetic and clinical data.
Results: Of 66 genotyped patients, 39 were gene-positive and 27 were gene-negative. Employing gene-carrier status as a gold standard, the TF criteria (independent of CMR data) had a sensitivity of 36% and a specificity of 89%; incorporating the proposed modifications for familial disease increased the sensitivity to 64% but reduced the specificity to 63%. The area under the ROC curve was 0.65 for the TF criteria as an ordinal rating scale.
In contrast, CMR had 95% sensitivity and 48% specificity in relation to genotype, with an area under the ROC curve of 0.83. Fourteen gene-negative subjects from 3 different families had suspicious CMR scans, of whom 10 (71%) prospectively fulfilled TF or modified criteria owing to unequivocal arrhythmic, ECG, or echocardiographic abnormalities. Retrospective review suggested that clinical and genetic data might be best reconciled by postulating a second, hitherto unidentified gene in these 3 families. Exclusion of these families would have resulted in: 33% sensitivity and 100% specificity for the TF criteria; 61% sensitivity and 100% specificity for the modified criteria; 94% sensitivity and 100% specificity for CMR, with an area under the ROC curve of 0.98.
Conclusions: In a genotyped population of ARVC patients, the TF criteria had low sensitivity and excellent specificity. The proposed modifications for familial ARVC substantially enhanced sensitivity. CMR has high diagnostic accuracy when performed with a dedicated protocol and analysed by experienced reviewers. Clinical evaluation of a proportion of genotyped ARVC families strongly suggests digenicity.

1001 Early detection of myocardial fibrosis in asymptomatic scleroderma patients

F. Breuckmann[1], K. Nassenstein[1], A. Kreuter[2], P. Altmeyer[1], J. Barkhausen[2], R. Erbel[2]. *[1]University Duisburg-Essen, West German Heart Center, Cardiology, Essen, Germany; [2]Ruhr-University Bochum, Department of Dermatology, Bochum, Germany*

Purpose: Cardiac manifestations of progressive systemic sclerosis (PSS) may result in pericardial disease, vavular diseases, conduction system abnormalities and arrhythmias. Early myocardial involvement is characterized by interstitial inflammatory alterations leading to patchy areas of fibrosis. Our current study aimed to assess the potential of contrast enhanced MRI for early detection of cardiac involvement in patients with systemic sclerosis.
Methods: The open study included 36 patients (31 female, 5 male, mean age of 53$\pm$14 years) suffering from severe PSS. Patients with known coronary artery disease (CAD) or a history of myocardial infarction were excluded from the study. The MRI protocol (1.5T MR scanner) included steady State Free Precession (SSFP, TR 3ms, TE 1.5ms, FA 60°) cine sequences, fat-suppressed T2-weighted turbo spin echo (TR 2 heart beats, TE 49ms, FA 180°) sequences and inversion recovery fast low angle shot (IR-turboFLASH: TR 8.0ms, TE 4.0ms, TI 180-240ms, FA 20°) sequences.
Results: Cardiac pathologies were detected in 51% of our patients. Evaluation of the left ventricular function revealed a mean ejection fraction (EF) of 60$\pm$10%. A reduced EF was observed in 23% (8 of 35). 7 of 35 patients (20%) showed a pericardial effusion. Mitral valve prolaps was observed in 9, low grade aortic valve insufficiency in 3 and tricuspidal valve insufficiency in 1 patient. No patient showed a myocardial edema on T2 images. The analysis of the contrast enhanced images showed either a slight diffuse or a spotted, well defined focal delayed-enhancement of less than 25% of the myocardial mass in 5 patients (15%).
Conclusions: LE occurs in myocardial areas of inflammation, edema, as well as fibrosis. Contrast enhanced MRI must be considered as imaging modality of first choice for the detection of small areas of myocardial fibrosis in vivo. Our data show that late enhancement as a marker of myocardial fibrosis can be detected in 15% of PSS patients with no clinical evidence of myocardial involvement. Therefore, contrast enhanced MRI seems to be well suited for screening of myocardial fibrosis, monitoring the progression and possibly evaluating therapeutic effects. However, long-term follow-up studies are mandatory to investigate the impact of late enhancement on patients' prognosis.

1002 Cardiodepressant effect and autoantigens of anti myocardial autoantibody

A. Baba, M. Shimada, M. Takahashi, M. Akaishi. *The Kitasato Institute Hospital, Cardiology Dept., Tokyo, Japan*

Not only acute homodynamic but also chronic prognosis improvements were reported at the immunoadsorption in some patients with dilated cardiomyopathy. Moreover, cardiodepressant autoantibodies, as defined as a decrease of both calcium transient and cell shortening in adult rat ventricular myocytes, were the predictor of improved cardiac function by immunoadsorption. However, autoantigens of these autoantibodies were not determined. The objective of this study was to identify the cardiodepressant autoantibodies which could directly influence left ventricular ejection fraction in patients with dilated cardiomyopathy, as well as to establish simple screening method of these autoantibodies. Various autoantibodies determined by immunohistochemistry, immunoblotting, and ELISA ($\geq$ β1-adrenergic receptors, muscarinic M2-acetylcholine receptors, Troponin I, or Na-K-ATPase) were measured in 104 patients with dilated cardiomyopathy. Cardiodepressant autoantibodies were also determined by echocardiography of 18th days chick embryos adding patients purified IgG, and compared with clinical features as follows: age, gender, NYHA class, left ventricular ejection fraction, neurohumoral factors, arrhythmias, and other autoantibodies. We also checked in vitro immunoadsorption effect against these cardiodepressant autoantibodies. Cardiodepressant autoantibodies were found in 63% of 104 patients with dilated cardiomyopathy, and had no relation to other clinical parameters except for some autoantibodies such as anti β1-adrenergic receptors autoantibodies (81% vs. 52%, $p<0.01$), anti M2-acetylcholine receptor autoantibodies (83% vs. 48%, $p<0.01$), or anti Na-K-ATPase autoantibodies (85% vs. 55%, $p<0.01$). However, cardiodepressant autoantibodies were similarly found in patients between with and without autoantibodies against Troponin I (56% vs. 64%). Left ventricular ejection fraction of chick embryos measured by echocardiography in the presence of patients serum was improved after in vitro immunoadsorption. By multivariate analysis, autoantibodies against β1-adrenergic or M2-acetylcholine receptor was a predictor of these autoantibodies. In conclusion, we established a new simple screening method of cardiodepressant autoantibodies by recording echocardiography of chick embryo adding patients' purified IgG. Some G-protein coupled receptors seemed to be autoantigens of cardiodepressant autoantibodies.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

PULMONARY EMBOLISM-CAN WE DO BETTER?

1003 Diagnostic discrepancy between clinical and autopsy diagnoses: pulmonary embolism still ranks first

A.T. Yamada[1], R. Saad[2], P.S. Gutierrez[1], A.J. Mansur[1]. [1]*Heart Institute (Incor), Uni.Sao Paulo, Sao Paulo, Brazil;* [2]*Sao Paulo, Brazil*

Diagnostic accuracy is a cornerstone of medical practice and may be also evaluated by the comparison between clinical and autopsy diagnoses.
Methods: 406 consecutive autopsy cases during 2 years were studied in a hospital devoted to the care of patients with heart diseases. Patients aged 47.4 + 28.4 years; 236 (58.1%) were men and 170 (41.9%) women. The comparison of diagnoses was categorized in classes I to V (class I: a discrepant major diagnosis with potential adverse impact on survival; class II: a discrepant major diagnosis with equivocal impact on survival; class III: a discrepant minor diagnosable disease that was not directly related to the cause of death but either should have been treated or would have eventually affected prognosis; class IV: a discrepant non-diagnosable minor disease of possible genetical or epidemiological importance; class V: diagnostic concordance). Each case was scored based on the highest degree of discrepancy. Statistical analysis was performed with Chi2 test and stepwise logistic regression. P values < 0.05 were considered significant.
Results: The distribution of the diagnoses in the classes of diagnostic comparison was: class I in 41 (1.4%) diagnoses, class II in 96 (3.3%), class III in 198 (6.9%), class IV in 642 (22.3%) and class V in 1907 (66.1%) diagnoses. Diseases of the circulatory system with higher discrepancy rate were pulmonary embolism (57/88, 64.8%), infective endocarditis (7/26, 26.9%) and aortic dissection (4/16, 25%). In the 41 diagnoses categorized in class I (a discrepant major diagnosis with potential adverse impact on survival), 13 (31.7%) were pulmonary embolism. Increasing age and hospital ward where the patient died were associated with the higher frequency of patients in classes I and II in comparison to frequency of patients in classes III, IV and V. Each age increase of 10 years, added 15.2% to the risk of the patient to be categorized in classes I and II. The admission in intensive care units decreased in 53% the risk of categorization in classes I and II. Sex, length of hospitalization and surgery (previous or during the admission in which death occurred) had no influence in the diagnostic concordance. Each age increase of 10 years reduced in 15% the risk of diagnostic discrepancy in the 109 autopsy diagnoses of acute myocardial infarction. In conclusion,the most frequent diagnostic discrepancy of cardiovascular disease was observed in pulmonary embolism. Factors related to the patients (age) and related to care (hospital ward) had influence in the comparison between clinical and autopsy diagnoses.

1004 Comparison of clinical, hemodynamic and angiographic findings in patients with submassive pulmonary embolism and right ventricular dysfunction as related to a positive or negative troponin T test

V. Kurowski[1], E. Giannitsis[2], D.P. Killermann[2], C. Paetzold[2], M. Muller-Bardorff[2], H. Schunkert[2], P.W. Radke[2]. [1]*University Hospital, Luebeck, Germany;* [2]*University Hospital, Heidelberg, Germany*

Background: A positive ($>$0.1 ng/ml) troponin T (TnT) test in patients with acute pulmonary embolism (PE) is significantly correlated with concomitant right ventricular dysfunction (RVD) and predicts an adverse outcome. Variables associated with TnT elevation in patients with acute PE who present with RVD are not yet defined.
Methods: We studied 96 consecutive patients with angiographically proven PE. All patients revealed an acute onset of symptoms (chest pain and/or dyspnea and/or syncope) and echocardiographic signs of RVD. TnT tests were performed serially within the initial 72 hours of hospital stay.
Results: A positive TnT test was obtained in 55 patients, 41 patients remained TnT-negative. No significant differences in heart rate (104 vs 106 bpm), mean arterial blood pressure (89 vs 93 mm Hg), mean pulmonary pressure (34 vs 35 mm Hg), right ventricular diameter (39 vs 36 mm), paO2/FiO2-ratio (231 vs 246), and the extend of pulmonary artery obstruction (Miller-Score 25 vs 26) were found between TnT-positive vs TnT-negative patients. In TnT-positive patients chest pain and syncope as the presenting symptoms were significantly more prevalent (80% vs 19,5%, $p<0.01$, and 34,5% vs 12,2%, $p<0,05$, respectively). A history of former deep venous thrombosis (DVT) and/or former PE correlated significantly with a negative TnT-test (65,9% vs 14,5% in TnT-positive patients, $p<0.001$).
Six patients died within 21 days after the index event, all of them were TnT-positive. Coronary angiography within 3 months before or after PE was performed in 46 patients. Significant coronary artery disease was present in 9 of TnT-positive and in 6 of TnT-negative patients, respectivly.
In a multivariate regression analysis (including age, gender, presenting sympptom, history of PE and/or DVT, Miller-Score, paO2/FiO2-ratio, mean pulmonary arterial pressure, and right ventricular diameter) we identified a history of former PE and/or DVT as an independent predictor of a negative TnT-test, whereas chest pain on admission was significantly correlated with a positive TnT-test.
Conclusions: In submassive PE with concomitant RVD, hemodynamic and angiographic parameters are not different between TnT-positive and TnT-negative patients. Factors associated with TnT-elevation are chest pain (possibly due to RV distension) and a negative history of former DVT and/or PE (possibly no "preconditioning" of the right ventricle).

1005 Heart-type fatty acid-binding protein correlates better than troponin with in hospital mortality and right ventricular dysfunction in patients with pulmonary embolism

A. Boscheri, C. Wunderlich, D. Stolte, T.P. Rauwolf, J. Fuhrmann, A. Schmeisser, R.H. Strasser. *Medical clinic, Technical University Dresden, Cardiology, Dresden, Germany*

Purpose: Accumulating evidence indicates that elevated serum troponin levels are a reliable indicator of right ventricular myocardial injury in patients with acute pulmonary artery embolism (PE) that additionally correlates with in hospital mortality in affected individuals. Recent studies have demonstrated that heart-type fatty acid-binding protein (H-FABP) also enables early and precise diagnosis and risk assessment of acute coronary syndrome as compared with other biomarkers. There are only few data about the diagnostic and prognostic value of H-FABP in PE. Thus the aim of the present study was to determine the role of H-FABP in PE and to correlate it to troponin and echocardiographic parameter.
Methods: Consecutive patients (n=70) with confirmed PE were included in the study. Besides serial measurements of cardiac troponin I (cTnI), D- dimer and creatine kinase (CK), a qualitative H-FABP-test (CardioDetect®med, rennesens, Berlin) was performed on arrival at the intensive care unit. The positive cut-off for this H-FABP-test was 7ng/ml. Echocardiography was performed in all patients with specific focus on the right ventricular performance.
Results: Of the included 70 patients, 14 had positive H-FABP-tests (20%). Right ventricular function was severely deteriorated in 10 patients (71%) of the H-FABP-positive group and in 1 patient (2%) of the negative group ($p<0.005$). 13/14 patients (93%) of the positive group needed inotropic support, 12 of these severely compromised patients (86%) died in hospital in the course of the disease. Only one out of 56 patients with a negative test needed vasoactive drugs, and none of these patients died ($p<0.005$). H-FABP had a significantly higher correlation with in-hospital mortality than troponin I ($p<0.005$).
Conclusion: Our data show that H-FABP significantly predicts in hospital and 30-day mortality. It is furthermore significantly associated with impaired right ventricular function and showed better correlation with in-hospital mortality than Troponin I in patients with acute PE. It may thus become an easily available, novel tool for optimizing the management strategy in patients with acute PE.

1006 Platelet activation correlates with poor prognosis in patients with acute pulmonary embolism

C. Dellas, M. Puls, M. Lankeit, K. Schaefer, G. Hasenfuss, S. Konstantinides. *Herzzentrum der Universitaet Goettingen, Cardiology&Pneumology, Goettingen, Germany*

Purpose: Risk stratification in patients with acute pulmonary embolism (PE) is currently based on the assessment of right ventricular function by echocardiography and the measurement of cardiac biomarkers. However, the role of platelets in the pathophysiology of thromboembolic events has often been neglected despite the fact that platelets accumulate early in venous thrombi and their activation leads to the secretion of vasoactive substances. Retrospective studies have shown a reduced rate of deep venous thrombosis (DVT) in patients with antiplatelet therapy. The aim of our study was to investigate a correlation between platelet activation and prognosis in patients with PE. Circulating soluble CD40 ligand (sCD40L) originates to more than 95% from platelets and high sCD40L-levels correlate with an increased thrombotic risk in patients with ACS.
Methods and Results: We measured plasma sCD40L by ELISA in 119 consecutive patients with acute PE (47 men/72 women, mean age 63$\pm$16 years). On hospital admission, sCD40L levels ranged between 51 to 2272 pg/mL (mean 346$\pm$307) and were independent of sex (p=0.2111), BMI (p=0.2326), age (p=0.7805), CRP (p=0.4283) and leukocytes (p=0.051), but correlated with number of platelets (r=0.2175, p=0.0201). Soluble CD40L correlated significantly with other biomarkers, namely H-FABP (r=0.37, P=0.0003) und NT-proBNP (r=0.27, P=0.007), but not with troponin T (p=0.422), indicating that sCD40L is an early marker in PE. Importantly, sCD40L levels were significantly higher in patients reaching the primary endpoint (PE-related death, resuscitation, intubation, use of catecholamines; n=14) compared to patients with an uncomplicated in-hospital course (511$\pm$165 pg/mL vs. 324$\pm$23 pg/mL, p=0.032) and in patients dying during the hospital stay (secondary endpoint, n=12; 562$\pm$190 vs. 322$\pm$23; p=0.0096). However, platelet number itself did not correlate with intrahospital course. Patients with echocardiographic signs of right ventricular (RV) dysfunction (n=41) had significantly higher levels of sCD40L than PE-patients without RV-dysfunction (435$\pm$69 pg/mL vs. 288$\pm$24 pg/mL; p=0.0188). There was no correlation (p=0.5762) between sCD40L levels and risk factors for PE (history of DVT/PE, tumor, immobilisation).
Conclusion: These data suggest that sCD40L is an early prognostic marker for acute PE and indicate that platelets and their activation are important pathogenetic factors for this disease probably leading to new diagnostic and therapeutic strategies regarding antiplatelet therapy.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

1007 Recanalization of pulmonary circulation after an episode of acute pulmonary embolism and noninvasive diagnostic methods that allow to suspect presence of residual thrombi

A. Kaczynska, G. Styczynski, M. Szulc, M. Kostrubiec, A. Kuch-Wocial, R. Pacho, J. Kunikowska, P. Pruszczyk. *Medical University of Warsaw, Dept. of Internal Medicine and Cardiology, Warsaw, Poland*

Background: Despite long-term anticoagulation in some patients after acute pulmonary embolism (APE) pulmonary artery clots are not completely resolved. Incomplete recanalization may lead to chronic thromboembolic pulmonary hypertension. We assessed the incidence of incomplete recanalization of pulmonary artery thrombi and its influence on right ventricle (RV) function at echocardiography and on physical capability.
Methods: 55 patients aged 54,7±18,6 years were observed. In acute phase 4 patients (7,2%) received thrombolysis. For 6 months patients were anticoagulated (74,5% -acenocumarol and 25,5% - low molecular weight heparin). Then spiral computed tomography (sCT), lung perfusion scintigraphy, 6-minute walk test and NTproBNP assessment were performed.
Results: Incomplete recanalisation of pulmonary circulation was detected in 38 (69,1%) patients - thrombi at sCT and/or $\geq$ 1 wedge-shaped perfusion defect at scintigraphy. Age, sex, rate of unprovoked APE, thrombophilia, malignancies, thrombolysis in the acute phase and type of long term anticoagulation were similar in patients without and with complete recanalization. Patients with incomplete recanalization had shorter distance at 6-minute walk test (417 (120-672) vs 570 (264-750) m, p = 0,03), but the distance depended on patient's age and comorbidities. No difference in NTproBNP concentration, as a potential indicator of RV overload, was observed in patients with complete and incomplete recanalization of pulmonary circulation. Tricuspid valve peak systolic gradient $\geq$ 30 mmHg (range 30-39 mmHg) was observed in 6 (10,9%) patients; all of them with incomplete recanalization, however, it did not reach statistical significance. Patients with incomplete recanalization had shorter acceleration time of pulmonary ejection (Act) then patients with complete recanalization (100 (80-140) vs 123 (80-150) ms, p = 0,02). In multivariate analysis only Act allowed to predict incomplete recanalization (OR 0,92 (95% CI 0,85-0,98), p = 0,002).
Conclusion: Incomplete thrombi resolution occurs frequently despite 6-month anticoagulation after the first episode of APE and impaired pulmonary ejection at echocardiography is useful in the identification of these patients.

1008 Duration of oral anticoagulant treatment after unprovoked pulmonary embolism: role of D-dimer testing

V. Pengo[1], B. Cosmi[2], C. Legnani[1], F. Marzot[2], A. Tosetto[3], S. Testa[4], A. Ghirarduzzi[5], G. Palareti[1] on behalf of FCSA, Italian Federation of Anticoagulation Clinics. *[1]Padova, Italy; [2]Bologna, Italy; [3]Vicenza, Italy; [4]Cremona, Italy; [5]Reggio Emilia, Italy*

Introduction: Abnormal D-dimer 1 month after suspension of oral anticoagulant treatment is associated with a significant increase in recurrent venous thromboembolism (VTE) after a first episode of unprovoked VTE. Treatment resumption is beneficial in these patients. Whether this general observation is valid for the subgroup of patients with pulmonary embolism (PE) is unknown.
Methods: At the end of treatment period, oral anticoagulation was stopped and D-dimer assay was performed after 1 month. Patients with normal D-dimer test did not continue anticoagulation, whereas those with abnormal D-dimer were randomized to either stop or resume anticoagulation. Follow up was 18 months. Principal end points were recurrent VTE and major bleeding.
Results: 227 patients of Prolong study had unprovoked PE. Of these, 83 with abnormal D-dimer were randomized either to be untreated (n=47) or to resume VKA treatment (n=36) while the remaining 144 with normal D-dimer remained untreated during follow up. Among the 191 patients who permanently discontinued anticoagulation 13 had recurrent VTE, 8 (12.1 per 100 patient/years) with abnormal and 5 (2.4 per 100 patients/years) with normal D-dimer levels (HR 3.7;. 95% C I, 1.2-12.3; p=0,03). In most patients (8 of 13, 61%) recurrent VTE was PE and the association between initial event and type of recurrence was statistically significant ($p<0.01$). No recurrence and a single major bleeding episode occurred in patients with abnormal D-dimer level treated with VKA. Principal end points in randomized group with abnormal D-dimer occurred more frequently when previous VKA treatment was 6 months or less (HR=13.7; 95% CI 1.3 to 149.1, p=0.03).
Conclusions: Abnormal D-dimer levels one month after treatment suspension can identify patients with unprovoked PE at risk of subsequent VTE (in most cases a fresh PE). VKA treatment apparently eliminates recurrent VTE which is more frequent when previous anticoagulation lasted 6 months or less.

TREATMENT OF PULMONARY ARTERIAL HYPERTENSION. WHERE ARE WE, WHICH WAY TO GO?

1009 A meta-analysis of trials of pulmonary hypertension: a clinical condition looking for drugs and research methodology

A. Macchia[1], R. Marchioli[1], G. Levantesi[1], R.M. Marfisi[1], M. Scarano[1], L. Tavazzi[2], G. Tognoni[1]. *[1]Consorzio Mario Negri Sud, Clinical Pharmacology And Epidemiology, Santa Maria Imbaro, Italy; [2]IRCCS Policlinico San Matteo, Pavia, Italy*

Background: Various innovative pharmacological strategies for the treatment of patients with pulmonary hypertension have been tested in recent years. Neither their comparative efficacy on surrogate end-points, nor the overall impact on mortality have been formally reviewed.
Methods: Systematic overview of all randomized trials on the therapeutic yield of prostacyclin and analogues, endothelin receptor antagonists and phosphodiesterase type 5 inhibitors in patients with pulmonary hypertension searched in EMBASE, MEDLINE, and CINAHL databases from January 1985 up to December 2005.
Results: Sixteen trials involving 1,962 patients met the inclusion criteria. Up to 80% of the patients were in functional class III/IV with a median walking distance at baseline of 330 meters. Overall, experimental treatments were associated with 1) a non significant reduction in all-cause mortality (relative risk [RR], 0.70 [95% CI, 0.41 to 1.22); 2) a minor but statistically significant improvement in exercise capacity of 42.8 meters [95% CI 27.8 – 57.8], and 3) an improved dyspnea status by at least one functional class (RR 1.83, [95% CI, 1.26-2.66]). Changes in exercise capacity were not found to be predictive of a survival benefit.
Conclusions: While confirming the limited benefits in clinical end points documented by each trial, the overview fails to support a significant survival advantage and does not support the predictive power of surrogates end points.

1010 Initial results of the united kingdom audit of pulmonary arterial hypertension associated with connective tissue disease (CTD-PAH)

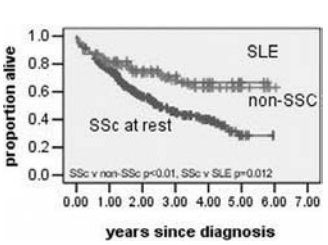
R. Condliffe[1], D.G. Kiely[2], A. Peacock[3], P.A. Corris[4], J.S.R. Gibbs[5], J. Pepke-Zaba[3], J.G. Coghlan[6]. *[1]Papworth Hospital, Pulmonary Vascular Disease Unit, Cambridge, United Kingdom; [2]Royal Hallamshire Hospital, Pulmonary Vascular Disease Unit, Sheffield, United Kingdom; [3]Western Infirmary, Scottish Pulmonary Vascular Unit, Glasgow, United Kingdom; [4]Freeman Hospital, Department of Respiratory Medicine, Newcastle-Upon-Tyne, United Kingdom; [5]Hammersmith Hospital, Department of Cardiology, London, United Kingdom; [6]Royal Free Hospital, Department of Cardiology, London, United Kingdom*

Purpose: To define the characteristics and survival of all patients with CTD-PAH within the UK.
Methods: Diagnostic and follow-up data was collected retrospectively for all 531 patients diagnosed with CTD-PAH at the six adult UK PAH centres between January 2001 and June 2006.
Results: Mean follow up was 749±534 days. 76% had systemic sclerosis (SSc), 8% SLE, 7% mixed connective tissue disease, 3% polymyosistis/dermatomyositis and 3% rheumatoid arthritis. 1 to 5 year combined survival was 80%, 65%, 57%, 50% and 43%. Median survival for SSc-PAH at rest was 2.4 and 4.6 years for mPAP above and below 40mmHg, 1.8 and 4.3 years for PVR above and below 800dyn.s.cm5 and 2.3 and 6.1 years for NYHA classes I/II and III/IV respectively (p all <0.01). Further baseline and survival data is shown below.

Baseline data for main subgroups

	n	Age (years)	mPAP (mmHg)	PVR (dyn·s·cm^5)	NYHA III (%)	NYHA IV (%)	SMWT (metres)	KCO (%)
SSc at rest	342	62.5±11	42.4±12	742±445	65	20	204±122	57±19.4
non-SSc	136	52.4±13	42.7±14	674±434	68	17	253±136	68±19.7
p value		<0.001	0.8	0.16			0.006	<0.001

mPAP, mean pulmonary artery pressure; PVR, pulmonary vascular resistance; SMWT, six minute walk test.



Conclusion: The current era prognosis for SSc has improved from a 50% 1 year survival seen in historical series to around a 50% 3 year survival. PAH in non-SSc CTD patients has a significantly better prognosis; although baseline walk tests and gas transfer were better than in SSc patients there was no significant

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

difference in haemodynamics or functional class suggesting a real difference in natural history.

1011 Bosentan improves hemodynamics and delays time to clinical worsening in patients with mildly symptomatic Pulmonary Arterial Hypertension (PAH): results of the EARLY study

N. Galie[1], L.J. Rubin[2], M.M. Hoeper[3], P. Jansa[4], A. Kusic-Pajic[5], G. Simonneau[6]. *[1]Universita di Bologna, Bologna, Italy; [2]University of California San Diego, La Jolla, United States of America; [3]University of Hannover Medical School, Hannover, Germany; [4]Charles University, Prague, Czech Republic; [5]Actelion Pharmaceuticals Ltd, Allschwil, Switzerland; [6]Hopital Antoine-Beclere, Clamart, France*

Purpose: While late stage PAH has been well characterised, limited data are available on the natural history and response to therapy of mildly symptomatic (WHO Class II) PAH. The EARLY study was designed to provide insights into the characteristics of mildly symptomatic PAH and to assess the effects of treatment in this population with bosentan (BOS), a dual endothelin receptor antagonist.
Methods: Patients (pts) $\geq$ 12 years with PAH (idiopathic or related to HIV, congenital heart disease or connective tissue disease) were included; WHO Class II, 6-minute walk distance (6MWD) $<$ 80% normal, or $<$ 500 m associated with a Borg dyspnoea index of $\geq$ 2 points. Pts were randomised 1:1 to receive placebo (PLC) or BOS (62.5 mg bid for 4 weeks and 125 mg bid thereafter) for a double-blind period of 6 months (end-of-study; EOS). The primary endpoints were pulmonary vascular resistance (PVR) at rest at EOS, expressed as percent of baseline, and change from baseline to EOS in absolute 6MWD. The main secondary endpoint was time to clinical worsening (TTCW). Safety and tolerability were also evaluated.
Results: 185 pts were enrolled (BOS, n=93; PLC, n=92). Mean ($\pm$SD) baseline PVR was 851$\pm$535 and 802$\pm$365 dyne.s.cm-5 in the BOS and PLC groups, respectively. At EOS, the PVR (geometric mean, 95% CI) in the BOS and PLC groups, respectively, was 83% (74, 94) and 107% (98, 118) of baseline value, representing a treatment effect (TE) of 23% ($p<0.0001$) in favour of BOS. Mean ($\pm$SD) baseline 6MWD was 443$\pm$83 and 431$\pm$92 m in the BOS and PLC groups, respectively. The mean (95% CI) change from baseline in 6MWD at EOS in the BOS and PLC groups was +11 m (-5, 27) and -8 m (-24, 9), respectively, representing a TE of 19 m (p=0.0758). TTCW was significantly delayed in BOS-treated patients: Kaplan-Meier estimates of worsening (95% CI) at week 24: 3% (0, 7) versus 11% (5, 17), indicating a 77% reduction in hazard (p(log-rank)=0.0114). The safety and tolerability profile was consistent with that observed in previous PLC-controlled trials: 13% of BOS pts developed aminotransferase levels $>$3xULN, compared with 2% of PLC pts.
Conclusions: The significant reduction in PVR and delay in TTCW, along with a trend towards improved exercise capacity, in WHO Class II PAH pts treated with BOS suggest that early treatment of PAH may result in delay of disease progression.

1012 Acute administration of sildenafil in patients with pulmonary arterial hypertension (PAH) treated with bosentan produced a significant hemodynamic response: results of the COMPASS-1 study

E. Gruenig[1], E. Michelakis[2], J.-L. Vachiery[3], C.D. Vizza[4], F.J. Meyer[2], N. Galie[5]. *[1]University Hospital, Heidelberg, Germany; [2]University of Alberta Hospital, Alberta, Canada; [3]ULB-Erasme University Hospital, Brussels, Belgium; [4]University of Rome, Rome, Italy; [5]Universita di Bologna, Bologna, Italy*

Rationale: Bosentan, a dual endothelin receptor antagonist, and sildenafil, a phosphodiesterase type 5 inhibitor, are both approved for the treatment of PAH. Preliminary data suggest that the combination of bosentan and sildenafil is well tolerated. However, a mutual pharmacokinetic interaction has been reported, with a decrease in sildenafil blood levels by about 60% in the presence of bosentan. An increase in sildenafil metabolism through P450 induction by bosentan and/or in the volume of distribution of sildenafil by bosentan may contribute to these pharmacokinetic findings. Therefore, pharmacodynamic data are needed to evaluate whether sildenafil remains effective when added to chronic bosentan treatment. COMPASS-1 investigated the acute hemodynamic effects of sildenafil in PAH patients receiving bosentan therapy.
Methods: Patients ($\geq$18 years) with PAH (idiopathic, familial, associated with corrected congenital systemic-to-pulmonary shunts or with drugs and toxins) were included in this open-label, non-comparative, prospective study. PAH had been diagnosed by right heart catheterization (RHC), and all patients had been on bosentan therapy for at least 12 weeks. Patients received a single oral dose of sildenafil (25 mg) in combination with bosentan therapy during RHC. The primary endpoint was percent reduction in pulmonary vascular resistance (PVR) from baseline to 60 min post-sildenafil administration. Similarly, percent reduction in total pulmonary resistance (TPR) was evaluated as the main secondary endpoint.
Results: Forty-five patients were enrolled. All values presented here are from the per-protocol (n=40) analysis and are given as mean (95% confidence interval; p-value): PVR decreased by 15.2% (-20.8, -9.6; $<$0.0001) and TPR by 13.3% (-17.0, -9.6; $<$0.0001) 60 min after administration of sildenafil. These changes were based on a reduction in mean pulmonary arterial pressure (mPAP) of 9.1% (-12.2, -6.0; $<$0.0001) and an increase in cardiac output of 5.8% (2.1, 9.4; 0.0026). There were no serious adverse events.
Conclusions: Acute oral administration of sildenafil to PAH patients treated with bosentan produced significant reductions of PVR and TPR. This suggests that the pharmacokinetic interaction between sildenafil and bosentan may have no relevance to the acute pharmacodynamic effects of sildenafil when used in combination with bosentan.

1013 BAY 63-2521, an oral soluble guanylate cyclase stimulator, has a favourable safety profile, improves cardiopulmonary haemodynamics and has therapeutic potential in pulmonary hypertension

H.A. Ghofrani[1], G. Weimann[2], R. Frey[1], R. Voswinckel[2], D. Boelkow[2], N. Weissmann[2], W. Mueck[1], S. Unger[1], R.T. Schermuly[2], F. Grimminger[2]. *[1]University Hospital Giessen and Marburg, Department of Internal Medicine Ii/V, Giessen, Germany; [2]Bayer Schering Pharma AG, Wuppertal, Germany*

Purpose: This proof-of-concept study evaluated BAY 63-2521, a soluble nitric-oxide (NO)-independent guanylate cyclase stimulator, in patients with moderate-to-severe pulmonary hypertension (PH) (pulmonary vascular resistance [PVR] $>$ 300 dyn s cm6-5).
Methods: This non-randomized, non-blinded, single-site study assessed safety, tolerability, cardiopulmonary haemodynamics, gas exchange and ventilation–perfusion mismatch (VQM). Initially, BAY 63-2521 was evaluated in 4 patients given hourly incremental doses orally (0.5 + 1 + 1 mg = 2.5 mg; 1 + 2 + 2 mg = 5 mg). Further evaluation of 1 mg and 2.5 mg doses was performed in 15 patients using Swan–Ganz catheterization, multiple inert gas elimination technique and blood gas measurements. Results were compared with peak intervention values for inhaled NO (iNO) (8–20 ppm) and post-NO-intervention baseline values. Adverse events (AEs), vital signs, ECGs and laboratory values were monitored.
Results: Baseline measures (2.5mg group) were: mean pulmonary arterial pressure (mPAP), 42.1$\pm$11.3 mmHg; PVR, 566$\pm$209 dyn$\cdot$s$\cdot$cm^{-5}; systolic blood pressure (SBP), 133$\pm$20 mmHg; cardiac index (CI), 2.74 $\pm$0.82 l/min/m^2. BAY 63-2521 was well tolerated up to 2.5 mg while 5.0 mg caused asymptomatic hypotension in 1 patient. Six mild AEs (three of which were attributed to BAY 63-2521) occurred in 4 of 19 patients, all resolving by study completion. No serious AEs occurred. BAY 63-2521 had no clinically relevant effects on vital signs, ECGs or laboratory values. No major changes were noted in blood gases or VQM. BAY 63-2521 dose dependently (1 mg and 2.5 mg, $p < 0.0001$ each) reduced mPAP, PVR, SBP, SVR, and increased CI (table), while maintaining SBP above 110 mmHg. These effects were greater than those of iNO for SBP, SVR, PVR and CI, and approached significance for mPAP. Effects correlated closely with plasma concentrations.

Haemodynamic effects of BAY 63-2521, 2.5

	SBP	p	SVR	p	mPAP	p	PVR	p	CI	p
vs baseline	–28.6	<0.0001	–545.9	<0.0001	–5.1	0.0001	–168.1	0.0046	0.95	<0.0001
vs iNO	–25.7	<0.0001	–541.5	<0.0001	–3.1	0.0546	–132.9	0.0220	0.89	<0.0001

SBP (mmHg), SVR (dyn$\cdot$s$\cdot$cm^{-5}), mPAP (mmHg), PVR (dyn$\cdot$s$\cdot$cm^{-5}), CI (L/min/m^2).

Conclusions: BAY 63-2521 has a favourable safety profile and does not alter gas exchange or VQM at single doses up to 2.5 mg in PH patients. Pulmonary haemodynamics were improved dose-dependently and to a greater extent than with iNO. BAY 63-2521 has therapeutic potential. Further studies are warranted.

1014 Mesenchymal stem cell-based prostacyclin synthase gene therapy for monocrotaline-induced pulmonary hypertension

K. Takemiya, H. Kai, N. Takayama, N. Tahara, T. Imaizumi. *Kurume University School of Medicine, Department of Cardiovascular Medicine, Kurume City, Japan*

Purpose: Mesenchymal stem cells (MSCs) are known to accumulate in various cardiovascular lesions. We assessed the hypotheses that MSCs accumulate selectively in the pulmonary circulation with pulmonary hypertension (PH) and that MSC-based prostacyclin synthase (PGIS) gene therapy ameliorates monocrotaline-induced PH in rats.
Methods: MSCs were obtained by culturing bone marrow mononuclear cells of Lewis rats. In Lewis rats, PH was induced by injecting monocrotaline at 7 weeks old. Experiment 1: 111Indium oxine-labeled MSCs (5x10^5 cells/rat) were transplanted intravenously 2 weeks after monocrotaline treatment (n=5/group). The radioactivities in the lung, liver, and other organs were measured 1 and 14 days after MSC transplantation. Experiment 2: PGIS- or GFP- gene was transfected to MSCs using a retrovirus vector. PGIS- or GFP- MSCs (5x10^5 cells/rat) were transplanted intravenously 2 weeks after injection of monocrotaline (PH-PGIS group and PH-GFP group, respectively, n=5/group). Control PH rats received PBS injection (PH group). Pressure measurement and morphological study were performed at 14days after MSCs transplantation. Experiment 3: Another 48 rats were divided into PH-PGIS group, PH-GFP group and PH group (each n=16). Their prognoses were evaluated at 49 days after monocrotaline injection.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: Experiment 1: In the intact rats, the lungs contained 2.6±0.3% and 0.7±0.3% of transplanted MSCs at 1 and 14 days after transplantation, respectively. In PH rats, accumulated MSCs in the lungs increased to 8.5±2.5% and 4.0±1.1% at 1 and 14 days, respectively. Monocrotaline did not affect MSCs accumulation in other organs. Experiment 2: In PH group, RV pressure increased to 66±4 mmHg. RV pressure was decreased to 42±4 mmHg in PH-PGIS group ($p<0.05$), whereas it was not changed in PH-GFP group (62±6 mmHg). Aortic pressure did not differ among the three groups. In morphological study, wall thickening of pulmonary arterioles was significantly attenuated in PH-PGIS group, compared with PH-GFP and control groups (%wall thickness, 22±5 vs. 34±4 and 36±8% respectively, [$p<0.05$]). Experiment 3: At 49 days after monocrotaline injection, the prognosis of PH-PGIS was significantly improved compared with another 2 groups. The survival rates of PH-PGIS, PH-GFP and PH groups were 100%, 43.8% and 37.5%, respectively.
Conclusions: MSCs preferentially accumulated in the lung of PH rats, suggesting that MSCs are suitable vector for gene therapy targeting PH. MSC-based PGIS gene therapy may be a new treatment strategy for PH.

BIOMARKERS IN HEART FAILURE: NEW ONES AND NOVEL APPLICATIONS

1033 Circulating levels of tumor necrosis factor-alpha, brain natriuretic peptide and cardiac troponin I upon admission and 180-day mortality in patients with acutely decompensated low output chronic heart

J. Papadopoulos, M. Zairis, M. Prodromiti, O. Ampartzidou, D. Mytas, C. Papoulis, D. Beldekos, K. Katsaros, E. Adamopoulou, S. Foussas. *Tzanio Hospital, Cardiology, Piraeus, Greece*

Purpose: Elevated circulating levels of tumor necrosis factor alpha (TNF-α), brain natriuretic peptide (BNP) and cardiac troponin I (cTnI) have been connected with adverse prognosis in pts with chronic heart failure (CHF). However there are scant data about the predictive value of these biomarkers in combination.
Methods: A total of 577 consecutive pts (mean age:73±9 yrs), who were hospitalized for acute decompensation of NYHA class III/IV(65.3% of ischemic etiology) low-output (mean LVEF:22±5) CHF, were studied. Biochemical markers were measured upon admission. The incidence of 180-day death was the prespecified primary endpoint.
Results: The incidence of the primary endpoint was 23.1%. By multivariate Cox analysis, including baseline characteristics and the study biomarkers, elevated circulating levels of TNF-α (RR=2.2; $p<0.001$), BNP (RR=3.4; $p<0.001$ and cTnI (RR=3.2; $p<0.001$ were independently associated with the primary endpoint. When the pts were divided according to the number of positive biomarkers (estimated by ROC analysis) there was a significant gradual increase in the rate of the primary endpoint with increasing of the number of the positive biomarkers (6.1%, 12.4%, 33.3% and 61.6% for the pts with 0, 1, 2 and 3 positive biomarkers respectively) (Figure 1).

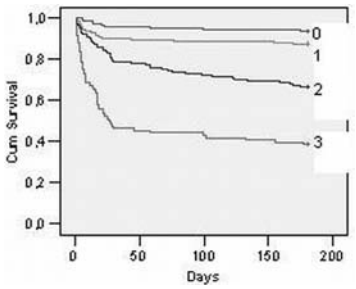


Figure 1

Conclusions: The present results suggest in patients who hospitalized due to acutely decompensated severe low-output chronic heart failure, serum levels of TNF-α, BNP and cTnI can be used in combination for enhanced early risk stratification.

1034 New cardiac biomarkers in monitoring of cardiotoxicity during hematopoietic cell transplantation in hematooncology

J.M. Horacek[1], M. Tichy[1], R. Pudil[2], L. Jebavy[2], V. Palicka[1], L. Slovacek[2], J. Vavrova[1], M. Ulrychova[1]. *[1]Faculty of Military Health Sciences, Internal Medicine, Hradec Kralove, Czech Republic; [2]Charles University Hospital, Hradec Kralove, Czech Republic*

Purpose: Monitoring of cardiotoxicity during preparative regimen (PR) and hematopoietic cell transplantation (HCT) with cardiac biomarkers – N-terminal pro brain natriuretic peptide (NT-proBNP), creatine kinase MB (CK-MB mass), cardiac troponin T (cTnT), cardiac troponin I (cTnI), fatty acid binding protein (FABP), glycogen phosphorylase BB (GPBB).
Methods: 23 patients (pts) treated with anthracyclines for acute leukemia (mean age 44.5±10.6 years, 15 males) were studied. PR consisted of Cyclophosphamide (HD-C) and Busulphan in 17 pts, HD-C and total body irradiation (TBI) in 6 pts followed by HCT. Cardiac biomarkers were measured the day before PR, the day after PR, the day after HCT and at the time of bone marrow recovery (after circa 14 days).
Results: The results are summarized in the Table.

Cardiac biomarkers during PR and HCT

cardiac biomarkers	before PR	after PR	after HCT	14 days after HCT
NT-proBNP above 100/150 ng/l	4 (17.4%)	14 (60.9%)	16 (69.6%)	16 (69.6%)
NT-proBNP above 500 ng/l	0	6 (26.1%)	9 (39.1%)	7 (30.4%)
CK-MB mass above 4.8 μg/l	0	0	0	0
cTnT above 0.01 μg/l	0	0	0	0
cTnI above 0.40 μg/l	0	0	0	0
FABP above 4.5 μg/l	0	0	0	1 (4.3%)
GPBB above 7.3 μg/l	0	5 (21.7%)	5 (21.7%)	2 (8.7%)

Conclusions: Our results suggest that administration of PR and HCT is in most acute leukemia pts associated with acute neurohumoral activation (significant rise in NT-proBNP). In our study, NT-proBNP remained markedly elevated in 7 (30.4%) pts at the time of bone marrow recovery. These persistent NT-proBNP elevations indicate subclinical cardiotoxicity (risk for development of heart failure) and require further follow-up.
From markers of myocardial ischemia and necrosis, only GPBB became elevated after PR and HCT. These changes could be considered a sign of subclinical cardiotoxicity. CK-MB mass, cTnT, cTnI, FABP does not seem to be of value in detection of cardiotoxicity in peritransplant period. These findings need to be confirmed in larger studies with longer follow-up.

1035 Relationship between galectin-3 and NT pro-BNP and outcome in patients with chronic congestive heart failure

D.J.A. Lok[1], P. Van Der Meer[1], P. Bruggink-Andre De La Porte[1], E. Lipsic[1], J. Van Wijngaarden[1], D.J. Van Veldhuisen[2], Y. Pinto[3]. *[1]Deventer hospital, cardiology, Deventer, Netherlands; [2]University Hospital, cardiology, Groningen, Netherlands; [3]University Hospital, cardiology, Maastricht, Netherlands*

Background: Galectin-3 (gal-3) is produced by activated cardiac macrophages and marks prognosis in hypertrophied rat hearts as well as in patients with acute heart failure. However, no data are yet available regarding the relationship between gal-3, a marker for inflammation, with B-type natriuretic peptide (NT-proBNP) and outcome in Chronic Heart Failure.
Methods and results: We included 240 patients with stable treated CHF, NYHA class III-IV, mean left ventricular ejection fraction 31% ±1, mean age 71±0.6 years, 73% male. The mean follow up was 3.8 years. The primary endpoint was all cause mortality (N=94, 39%). Gal-3 and NT-proBNP levels were both strongly related to outcome (log rank: p= 0.003 and p=0.0003). The ROC analysis for mortality showed an area under the curve for gal-3 of 0.61 (p = 0.005) and for NT-proBNP of 0.62 (p = 0.002). Multivariate analysis revealed that low levels of Gal-3 in combination with low levels of NT-proBNP were related to the best prognosis (HR:0.45 [95% CI 0.23-0.89], p=0.017). High levels of Gal-3, NT-proBNP or both were similar related to an impaired outcome (figure 1). Remarkably, a low level of NT-proBNP in the presence of elevated gal-3 still carried a poor prognosis.

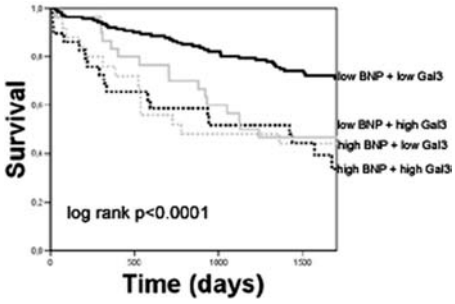


Figure 1

Discussion: Gal-3, a marker of activated macrophages, predicts mortality in stable CHF patients as accurately as NT-proBNP. Low levels of NT-proBNP in combination with low levels of gal-3 clearly herald the best prognosis. Interestingly, Gal-3 added prognostic information to that provided by NT-proBNP alone, as prognosis was poor even in patients with low NT-proBNP yet with elevated gal-3. Measuring only NT-proBNP could underestimate a poor prognosis, which can be detected by elevated Gal-3 levels. This suggests that for prognostication a multimarker strategy is needed in patients with CHF.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

1036 Effects of anti-depressive medication on tumor necrosis factor alpha and C-reactive protein in patients with congestive heart failure

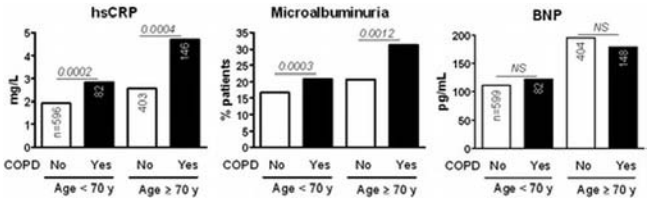
A. Drollias, D. Tousoulis, C. Antoniades, C. Tentolouris, C. Vasiliadou, G. Latsios, E. Stefanadi, C. Stefanadis. *Athens, Greece*

Major depression is common in patients with heart failure (HF), and has been associated with higher tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), affecting the prognosis in these patients.
Aim: We compared the effect of anti-depressive medication with tricyclic antidepressants (TA), serotonin and norepinephrine reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitors (SSRIs) on endothelial function and inflammatory process in patients with congestive HF.
Methods: A population of 250 patients with HF(154 of which suffering from major depression) were recruited. Patients with major depression were under selective serotonine reuptake inhibitors (SSRIs, n=120) or tricyclic antidepressants (TCA) and/or serotonin/norepinephrine reuptake inhibitors (SNRIs) (n=34). Forearm blood flow was measured by venous occlusion strain-gauge plethysmography.
Results: Levels of TNF-α and CRP were not significantly different between HF patients with depression under treatment (4.70±0.17pg/ml and 15.13±1.75mg/dl) and those without depression (5.02±1.99pg/ml and 19.5±3.1mg/dl, p=NS for all). There was no difference in EDD and EID between patients under SNRIs (44.7±1.6% and 63.2±1.1%), SSRIs (45.1±3.1% and 58.2±1.2%) and non depressive patients (43.0±2.1% and 63.2±2.2%), p=NS for all. However, TNF-α and CRP were significantly lower in patients receiving TCA/SNRI (4.3±0.4pg/ml and 7.3±1.1mg/dL) compared to patients under SSRIs (4.8±0.2pg/ml and 17.4±2.2mg/dl $p<0.05$ for both) or those without depression (5.01±3.2pg/ml and 19.5±3.2mg/dl, $p<0.05$ for both). Similarly, TCA/SNRI had lower heart rate (70.7±0.53bpm) compared to SSRIs (74.5±1.3bpm, $p<0.05$) or those without depression (74.2±6.3bpm, $p<0.05$). Treatment with SNRI/TCA was an independent predictor for TNF-α (β=0.036(SE:0.016) and CRP (β=0.099(SE:0.048), p=0.041).
Conclusions: Patients with HF and depression receiving NSSRIs have lower TNF-α and CRP compared to those receiving SSRIs or those receiving no antidepressives. These findings suggest that the type of anti-depressive medication may affect inflammatory process in patients with heart failure.

1037 Circulating biomarkers in patients with chronic obstructive pulmonary disease and symptomatic heart failure. Data from the GISSI-HF trial

R. Latini[1], S. Masson[1], S. Ciricugno[2], A. Mezzani[3], M. Buccolieri[4], J. Norman[5], L. Angelici[3], L. Staszewsky[3], G. Tognoni[6], L. Tavazzi[7] on behalf of GISSI-HF Investigators. *[1]Milan, Italy; [2]Casarano, Italy; [3]Veruno, Italy; [4]Gubbio, Italy; [5]Seregno, Italy; [6]S. Maria Imbaro, Chieti, Italy; [7]Pavia, Italy*

Purpose: Chronic obstructive pulmonary disease (COPD) and heart failure (HF) are major causes of death and disability. Since little information is available on patients with both syndromes, we assessed their clinical and biohumoral profiles.
Methods: A group of 1237 patients with chronic HF enrolled in the ongoing trial GISSI-HF, had plasma BNP (IRMA), CRP (immunoturbidimetry) and microalbuminuria (MA) measured at study entry. They were divided according to the presence (n=231) or absence of COPD (n=1006), and stratified by age. Association between COPD and biomarkers was tested by stepwise logistic multivariable analysis.
Results: Prevalence of COPD was 18.6%, higher in patients ≥70 y (26.9%) than in those below (12.0%). Patients with COPD and HF had higher CRP and more frequently MA compared to HF alone, irrespective of age (Figure). Though patients with COPD were more symptomatic, BNP was not higher. The independent variables more closely associated to COPD were older age, smoking, higher BMI, leukocyte count, prescription of diuretics (yes) and beta-blockers (no).



Figure

Conclusions: Patients with COPD and HF have marked systemic inflammation and renal/endothelial dysfunction compared to those with HF alone, independent of age. This observation may have pathophysiological and therapeutic implications.

1038 NT-proBNP is a marker of right ventricular dysfunction in thalassemia major

A. Pepe[1], C. Prontera[1], L. Zyw[1], A. Agazio[1], F. Fabrizio[1], B. Scattini[1], A. Ramazzotti[1], M.E. Lai[2], L. Lombardi[1], M. Emdin[1]. *[1]Institute of Clinical Physiology, CNR, MRI Lab, Pisa, Italy; [2]University of Cagliari, Cagliari, Italy*

Purpose: Ventricular dysfunction secondary to myocardial iron overload is a main cause of morbidity and mortality in thalassemia major (TM). In particular, thalassemic cardiomiopathy include forms with right involvement difficult to diagnose by usual clinical and instrumental findings. Early diagnosis of myocardial involvement in TM patients could permit early treatment and improvement in prognosis. Plasma N-terminal fragment of proBNP (NT-proBNP) concentration is altered even in asymptomatic subjects with left and/or right ventricular structural impairment and has significant diagnostic and prognostic value in various forms of heart disease. Nevertheless, its usefulness in the management of thalassemia patients has not been fully investigated. Aim of our study was to assess the diagnostic role of NT-proBNP assay in a large prospective cohort of TM patients, evaluated by cardiovascular magnetic resonance (CMR).
Methods: Seventy consecutive TM patients (age 31±8 years; 29 male) underwent CMR (1.5 T, GE) and blood sampling for plasma assay of NT-proBNP. Myocardial iron overload was assessed using a multislice multiecho T2* approach. Cine sequences were obtained to quantify atrial areas and biventricular morphological and functional parameters. Myocardial fibrosis was evaluated by late gadolinium-enhanced acquisitions.
Results: NT-proBNP was positively related with right ventricular (RV) end diastolic volumes (EDV) ($r = 0.3$, $P = 0.008$) and RV end systolic volumes ($r = 0.4$, $P = 0.002$). We found an inverse correlation between NT-proBNP and RV ejection fraction (EF) ($r = - 0.4$, $P = 0.003$). By ROC curve analysis, TM patients with NT-proBNP levels > 208 pg/mL showed chance of having RV dysfunction (EF < 49%) with a sensitivity of 100%, and specificity of 84%. We did not find significant correlations between NT-proBNP level and myocardial iron overload, myocardial fibrosis, atrial areas and left morphological and functional parameters.
Conclusions: In TM patients NT-proBNP concentration were significantly related positively to RV EDV and RV ESV and inversely to RV EF. NT-proBNP assay showed a high degree of diagnostic accuracy for identifying RV dysfunction in this population, suggesting a possible routinary use in the anaemic TM population.

NOVEL NON PHARMACOLOGICAL THERAPIES IN HEART FAILURE

1043 Impact of a 3 months exercise training program on the regulation of the catabolic ubiquitin-proteasome system in patients with end-stage chronic heart failure

S. Erbs[1], R. Hoellriegel[1], A. Linke[1], V. Adams[1], E.B. Beck[1], S. Gielen[1], S. Moebius-Winkler[1], R. Hambrecht[2], G. Schuler[2]. *[1]University of Leipzig - Heart Center, Department of Cardiology, Leipzig, Germany; [2]Klinikum Links der Weser, Department of Cardiology, Bremen, Germany*

The severe limitation of exercise capacity - the key symptom in patients with end-stage chronic heart failure - is not only a result of central hemodynamic alterations, but also caused by a progressive peripheral muscle wasting and muscle atrophy. The so-called cardiac cachexia has been recently linked to an upregulation of E3 ligases MuRF1 and MAFbx, which activate the ubiquitin-proteasome pathway and thereby contribute to muscle proteolysis. Aim of the present study was to determine, whether an individually tailored exercise training program in patients with end-stage chronic heart failure (NYHA IIIb) impacts on the activation of the ubiqitin-proteasom-system and thereby positively influences skeletal muscle degradation.
Methods: Thirty-seven patients with terminal CHF (due to ischemic heart disease (n=20) or dilative cardiomyopathy (n=17); LV-EF 24±1%, LV-EDD 68±1 mm, peak VO2 15.3±0.6 mL/min/kg) were randomized to either 3 months of exercise training (50-60% of peak VO2, 30 min/d on a bicycle ergometer) or sedentary lifestyle (control group, C). At begin and after 3 months percutaneous biopsies of the vastus lateralis muscle were obtained, and mRNA expression of the E3 ligases MuRF1 and MAFbx were quantified by PCR. Protein expression of MuRF1 was determined by Western blot. Additionally, CT scans were recorded from lower limb at mid-femur level to analyze skeletal muscle cross sectional area (CSA).
Results: Three months of exercise training resulted in a reduction of MAFbx mRNA expression in skeletal muscle by –29% (from 280±70 to 200±37 rel. units, $p<0.05$ vs. begin and C) and of MuRF1 mRNA expression by –39% (from 14.3±2.0 to 8.7±1.4 rel. units, $p<0.05$ vs. begin and C). Protein expression of MuRF1 decreased by –43% from 3.5±1.2 to 2.0±0.6 arbitrary units ($p<0.05$ vs. begin and C). This was associated with a significant increase in muscle CSA by +6% (from 141±5 to 149±5 cm^2, $p<0.05$ vs. begin and C for change). There is a close, inverse correlation between the reduction of MuRF1 expression and the increase in skeletal muscle size ($r=0.66$, $p<0.05$). All of the above mentioned parameters remained unchanged in C.
Conclusion: Regular exercise training in patients with CHF reduces the expression of the E3 ligases MuRF1 and MAFbx in the peripheral skeletal muscle. The blunted activation of the catabolic ubiquitin-proteasome system might contribute

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

to the training-induced gain in muscle mass in patients with end-stage chronic heart failure.

1044 Structured exercise training early after hospitalization for congestive heart failure: a quality of life and cost-effectiveness analysis

M.P. Kossovsky[1], M. Louis Simonet[1], M. Rabaeus[1], M. Bettoni[2], P. Sigaud[1], T.V. Perneger[1], J.M. Gaspoz[1]. [1]*Geneva University Hospitals, Department of Community Medicine, Geneva, Switzerland;* [2]*Hopital de la Tour, Meyrin, Switzerland*

Background: Exercise training (ET) in patients with congestive heart failure (CHF) reduces hospital readmissions for heart failure, improves quality of life and reduces all-cause mortality. Prior studies only enrolled patients in stable condition. We sought to determine if a structured exercise training program performed early after a hospital stay was safe, beneficial and cost-effective.
Methods: Design: randomized clinical trial. Eligibility: patients admitted for CHF with a left ventricular ejection fraction (LVEF) <45% and able to perform a moderate exercise. Intervention: random allocation to usual care or to a structured 7-month ambulatory exercise program consisting in at least 3 sessions/week during the first month, followed by 2 sessions/week for 6 months. Outcomes: time to readmission for any cause or CHF related during the year after inclusion, survival, quality of life, exercise tolerance and direct medical costs. For readmissions, patients' individual costs were extracted from the hospital accounting system; ambulatory costs were built from patients' report of their medication, the number of visits to their primary care physicians and the number of rehabilitation sessions. Due to skewness, analyses were performed on log transformed costs.
Results: From Jan. 2002 to Feb. 2005, 130 patients were allocated to the control group (63) or to the ET group (67). Groups were similar in terms of age (Mean age: 69±12 years), gender, CHF severity, comorbidity and medications. ET was started 20±15 days after hospital discharge. The proportion of patients readmitted for any cause was not statistically different between groups [18/67 (27%) in the ET group vs. 19/63 (30%); p=0.68)] That held also true when only readmissions for CHF were considered [10/67 (15%) in the ET group vs. 10/63 (16%) in the control group; p= 0.88]. Direct medical costs were significantly lower in the ET group (15,349±20,250 Swiss Francs) as compared with the control group (24,579±35,129; p<0.01). Patients in the ET group having completed the program improved significantly more than patients in the control group for 2 of the 7 health domains explored by the Kansas City Cardiomyopathy Questionnaire (symptom change over time and quality of life). Improvement in exercise tolerance (6 minute walk) was much higher among them than in the control group (test + 97m±105 vs. + 33m±73; p=0.008).
Conclusions: Early exercise training among unselected, aged and polymorbid patients discharged from general internal medicine wards for systolic CHF is secure, beneficial in terms of exercise tolerance and quality of life and cost-effective.

1045 Electrical reverse remodeling during left ventricular assist device support

S. Drakos[1], M. Anastasiou-Nana[1], E. Charitos[1], A. Ntalianis[1], J. Terrovitis[1], E. Tsagalou[1], E. Kaldara[1], S. Theodoropoulos[2], M. Yacoub[3], J. Nanas[3]. [1]*University of Athens, Department of Clinical Therapeutics, Athens, Greece;* [2]*Iaso General Hospital, Athens, Greece;* [3]*Harefield Heart Science Center, Harefield, United Kingdom*

Introduction: Ventricular unloading during chronic left ventricular assist device (LVAD) has been shown to cause structural and functional "reverse remodeling" of the failing heart. Our aim was to investigate the effect of LVAD support on specific electrocardiograhic (ECG) parameters in patients with end-stage idiopathic dilated cardiomyopathy (IDC).
Methods: Eight patients, age 47±13 years, with end-stage IDC underwent LVAD implantation (Heartmate XVE). The impact of LVAD support on the frequency of ventricular arrhythmias and specific ECG parameters [QRS, QT and QT corrected (QTc)] were evaluated after analyzing a total of 149 electrocardiograms and 39 24-hour ambulatory ECG monitorings performed both before and after LVAD implantation.
Results: These observations were performed from day 7th to day 180th during a follow-up
period of 892 patient days. QTc decreased from 575±65 ms pre-LVAD implantation to 446±53 ms after the completion of the first week of LVAD support (23% decrease, p=0.001). The QTc continued to decrease during LVAD support and by the completion of the sixth LVAD support month was QTc 387±66 ms (p=0.007). The pre-implant QRS duration decreased from 153±50 to 128±31 ms after the first week of LVAD support (16% decrease, p=0.024) and continued to decrease until the fourth month of support. The frequency of ventricular arrhythmias compared to the pre-implant values significantly decreased after the completion of 2 months of LVAD support (premature ventricular contractions from 3044±2904/24h to 137±94/24h, p=0.068, ventricular couplets from 49±24/24h to 7.7±8.3/24h, p=0.037, ventricular runs from 12±7/24h to 1.5±1.7/24h, p=0.035). No incidence of symptomatic arrhythmias or sudden death was observed during the follow-up period.
Conclusion: LVAD support induced early and continuous decrease of QTc and QRS duration suggesting a form of electrical reverse remodeling of the failing heart which was accompanied by a more delayed decrease in the frequency of ventricular arrhythmias.

1046 Long term vagal stimulation in patients with advanced heart failure. First human experience

G.M. De Ferrari, N. Ajmone-Marsan, M. Revera, M. Landolina, R. Rordorf, A. Sanzo, C. Campana, A. Odero, L. Tavazzi, P.J. Schwartz. *Fondazione IRCCS Policlinico San Matteo, Dept. of Cardiology, Pavia, Italy*

Increased sympathetic and reduced vagal activity are associated with increased mortality in post-infarction or heart failure (HF) patients. Animal studies suggested that vagal stimulation (VS) is protective both during acute ischemia and in chronic HF. In the latter condition, chronic VS, markedly improves left ventricular function and has anti-inflammatory effects.
We are currently assessing feasibility, safety, and possible efficacy of chronic VS in NYHA class III patients. We use CardioFit (BioControl Medical), a VS implantable system delivering through a tri-polar cuff electrode pulses synchronous with the heart beat adjustable to patients' heart rate by an imbedded microprocessor. VS is started 2-4 weeks after implant, slowly raising intensity to achieve the appropriate HR effect. Of the 7 patients enrolled, the first 4 (age 30-64 yrs, all with markers of severe prognosis) have completed a 6-month follow up. All procedures have been successful: as sole side-effect, one patient had transient voice alteration. VS is well tolerated, with only mild side-effects (cough and sensation of electrical stimulation), that have all subsided within the first two weeks.
The main findings, shown in the table, suggest a significant improvement in the first 3 months (when all pts were in NYHA class II) with a trend toward regression to baseline thereafter, likely due to the severity and unstoppable progression of the underlying disease.

Variable	Baseline	1 month	3 months	6 month	ANOVA p
LVEDV (ml)	326±72	283±29	288±39	272±65	0.059
LVESV (ml)	250±68	203±53	213±69	213±73	0.003
LV EF (%)	24±7	29±14	27±16	23±10	0.35
NYHA 1/2/3/4	0/0/4/0	0/3/1/0	0/4/0/0	0/1/3/0	
SMWT (m)	397±45		449±147	428±107	0.43
Minnesota QoL	58±14		22±9	35±31	0.002
IL 6 (pg/ml)	27±8	18±8	7±0.6	26±9	0.007

LV=left ventricle; EDV=end-diastolic volume; ESV=end-systolic volume; SMWT=six-minute walk test; QoL=quality of life.

This novel approach to the treatment of patients with HF is feasible, safe, and warrants further evaluation. Accordingly, a multicentre clinical trial has been designed and is currently ongoing.

1047 Percutaneous renal artery angioplasty for renal artery stenosis reduces the incidences of flash pulmonary edema and hospitalizations rate for acute heart failure

M. Hammoud[1], D. Sharif[2], U. Rosenschein[1]. [1]*Bnei-Zion Medical Center, Cardiology Dept., Haifa, Israel;* [2]*Bnai-Zion Medical Center, Cardiology, Haifa, Israel*

Background: Renal artery stenosis may cause uncontrolled hypertension, renal azotemia, episodes of acute heart failure and flash pulmonary edema. Aim: to evaluate the clinical benefit of renal artery angioplasty with stenting for the control of recurrent, refractory congestive heart failure.
Methods: Renal artery angiography was performed in 470 patients having coronary angiography according to pre-selected criteria, 98 patients from these cohort (21%) had a recurrent episodes of flash pulmonary edema requiring hospitalization and treatment.
Results: Significant renal artery stenosis (luminal narrowing > 70%) was found in 46 patients, 21 patients (46%) of them had recurrent episodes of flash pulmonary edema before performing the procedure. The rate of hospitalizations for acute heart failure after performing renal artery angioplasty was reduced significantly from 2.31+ 1.25 hospitalizations per year to 0.5+0.5 per year after the procedure,(p=0.002), a reduction that was not observed in the remaining group of patients not having a significant renal artery stenosis. The reduction of hospitalizations was observed not only among those with preserved left ventricular ejection fraction (LVEF), but also among patients with moderate and moderate to severe reduced LVEF.
Conclusions and implications: Renal artery angioplasty for significant renal artery stenosis reduces hospitalizations for flash pulmonary edema and events of congestive heart failure exacerbation independently of the LVEF rate. Screening, diagnosis and treatment of significant renal artery stenosis is an important factor for reduction of morbidity and mortality among patients suffering from recurrent episodes of heart failure.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

1048 Long-term improvement of left ventricular function after percutaneous recanalisation of chronic total coronary occlusions: 3 years follow-up

S.W.M. Kirschbaum, T. Baks, M. Van Den Ent, G. Sianos, G. Krestin, P.W. Serruys, P.J. De Feyter, R.J.M. Van Geuns. *Erasmus Medical Center, Cardiology, Rotterdam, Netherlands*

Background: The long-term effect of percutaneous recanalisation of a CTO on LV function and volumes is currently unknown. Therefore we investigated the early and late effects of percutaneous revascularization for chronic total coronary occlusion (CTO) on left ventricular (LV) function and volumes.
Methods: MRI was performed in 21 patients before, at 5 months, and at 3 years after recanalisation of CTO. Global LV function and volumes and segmental wall thickening (SWT) were quantified on cine-images. Two viability indexes were used; the transmural extent of infarction (TEI) on delayed contrast enhancement images and end-diastolic wall thickness at baseline (EDWT).
Results: A significant decrease in mean end-diastolic volume index (86 ±14 ml/m^2 to 78±15 ml/m^2; p=0.02) and mean end-systolic volume index (35±13 ml/m^2 to 30±13ml/m^2; p=0.03) was observed three years after recanalisation. Mean ejection fraction tended to improve (60 ±9% to 63±11%; p=0.11). SWT increased significantly at 5 month follow-up (p<0.001) and an additional improvement was found at 3 years (p=0.04) follow-up in segments with TEI of <25%. In segments with TEI between 25% and 75%, SWT remained unchanged at 5-month follow-up (p=0.89), but improved after 5 months (p=0.04). SWT remained unchanged in segments with transmural scars. TEI was a better predictor for segmental functional recovery than EDWT (odds ratio 5.6, CI: 1.5-21.1; p=0.01 versus 2.5, CI: 0.7-8.3; p=0.14).

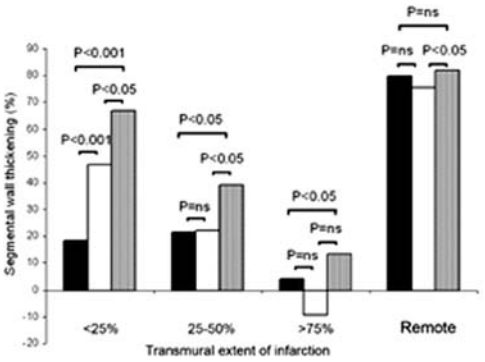


Figure 1

Conclusion: The beneficial effect of recanalisation of a CTO is observed at 5 months with even further improvement at 3 years follow-up.The time course of recovery can be predicted by pre treatment MRI analysis.

HEART FAILURE WITH PRESERVED EJECTION FRACTION: WE KEEP LEARNING

1049 Heart-rate dependent regulation of intrinsic contractility and hemodynamics in patients with diastolic heart failure

R. Wachter[1], S. Schmidt-Schweda[1], D. Westermann[2], C. Tschoepe[1], H. Post[2], B. Pieske[2] on behalf of German Competence Network Heart Failure Study Group. [1]*University of Goettingen, Cardiology and Pneumology Department, Goettingen, Germany;* [2]*Charite, Campus Benjamin Franklin, Cardiology and Pneumology, Berlin, Germany*

Background: In systolic heart failure (SHF), the positive force-frequency relationship is blunted, and this contributes to exertional dyspnea in these patients. However, there is little information on heart-rate dependent regulation of contractility and hemodynamics in patients with diastolic heart failure (i.e., heart failure with normal ejection fraction, HFNEF). We tested intrinsic contractility and hemodynamic consequences of increasing heart rates in patients with HFNEF.
Methods: 9 patients (7 female; age 64±3 years, no coronary artery disease) fulfilling recent criteria for HFNEF as proposed by the Working Group on Heart Failure of the ESC were invasively evaluated. Pressure-volume-loops were obtained by conductance catheter technique at baseline and during atrial pacing to 80, 100, and 120 beats/min (bpm). At each heart rate, preload reduction was performed by transient vena cava inferior occlusion.
Results: At an average baseline heart rate of 62±2 bpm, stroke volume, cardiac output and measures of intrinsic contractility (maximum rate of systolic left ventricular pressure rise (dP/dtmax); endsystolic elastance as a relatively preload-independent measure of left ventricular contractility) were normal, but left ventricular end-diastolic pressure (LVEDP) was increased. With increasing heart rates, contractility parameters continuously increased suggesting a preserved force-frequency relationship. In contrast, stroke volume declined at higher heart rates. In consequence, cardiac output was maximum at 100 bpm and even declined with further increases in heart rate.

Table 1. Hemodynamic findings

	Baseline	80 bpm	100 bpm	120 bpm
Cardiac output (ml/min)	5129.7±339.7	5911.3±397.0	6955.8±654.4*	5998.4±377.7
Stroke volume (ml)	83.313±5.838	74.724±5.907	69.428±6.805	49.545±3.175$
LVEDP (mmHg)	19.0±1.9	16.4±2.4	15.7±3.6	14.8±3.6
dP/dtmax (mmHg/s)	1434.8±94.4	1570.0±103.0	1734.5±127.9	1841.1±140.4*
Endsystolic elastance, Ees (mmHg/ml)	1.971±0.551	2.312±0.723	3.090±0.840	4.379±1.830

*p < 0.05 vs. baseline; $p < 0.001 vs. baseline. All values Mean ± S.E.M.

Conclusion: Patients with HFNEF show a preserved force-frequency relation, but a pronounced reduction in stroke volume at higher pacing rates. These unique hemodynamic properties in diastolic heart failure are distinctive from SHF.

1050 Heart failure with preserved ejection fraction. A severe disease

D. Rusinaru, H. Mahjoub, F. Levy, L. Kesri, C. Durier, M. Peltier, C. Tribouilloy. *CHU Amiens Sud, INSERM, ERI 12, Cardiology, Amiens, France*

Background: Heart failure (HF) represents a major health concern with a severe outcome despite modern therapies. In more than 50% of cases left ventricular (LV) systolic function is preserved. The prognosis of HF with preserved left ventricular ejection fraction (HFPEF) has been largely debated. Few data are available on patients hospitalized for a first episode of HF. Objective: We followed prospectively a large cohort of consecutive patients (pts) hospitalized for a first episode of HF. Our purpose was to identify the prevalence, characteristics and prognosis of HFPEF.
Method: All consecutive pts (n=799) hospitalized for a first episode of HF during the year 2000 in the Somme district (France) were recruited. Information on the LV systolic function was available in 622 pts (83%) which represented the study population.
Results: LVEF was preserved in more than half of the study population (55.6%). Pts with HFPEF were significantly older (75.8 vs. 71 years; p<0.001), had a higher prevalence of women (53% vs. 38%; p<0.001) and more comorbidities (p=0.01). A hypertensive (53% vs. 10%; p<0.001) or valvular (13% vs. 7.8%; p=0.032) etiology of HF was more frequent in the HFPEF group. Ischemic heart disease was less prevalent in pts with HFPEF (28% vs. 49%; p<0.001). During the 5-year follow-up, 370 pts (56%) died. 3-year and 5-year survival rates were not significantly different in pts with HFPEF and pts with systolic dysfunction (58% vs. 57%, p=0.48; 43% vs. 45%; p=0.95). Both groups had similar relative 5-year survival rates as compared to the age- and sex-matched general population (60% vs. 62%). In univariate analysis, predictors of 5-year mortality in pts with HFPEF were: older age (p<0.001), low body mass index (p=0.005), comorbidities (diabetes, p=0.01; stroke, p=0.001; peripheral artery disease, p=0.016), atrial fibrillation on admission (p=0.04), elevated serum creatinine (p=0.001) and hyponatremia (p<0.001). In multivariate analysis, older age (p<0.001), stroke (p=0.001), chronic obstructive lung disease (p=0.001), diabetes (p=0.003), elevated serum creatinine (p<0.001) and hyponatremia (p=0.008) were identified as independent predictors of 5-year mortality in patients with HFPEF.
Conclusion: Prognosis of HFPEF is severe, with a 5-year survival rate after a first episode of HF of 43%. HFPEF and HF with systolic dysfunction have comparable prognosis, with similar 5-year relative survival rates as compared to the general population. Further research is needed to establish a reliable diagnosis and identify beneficial therapies for HFPEF.

1051 Inhibition of Interleukin-1 activity by anankinra improves left ventricular function: a randomized cross-over, placebo-controlled, trial

I. Ikonomidis, M. Nikolaou, I. Paraskevaidis, J. Lekakis, G. Skarantavos, T. Kaplanoglou, P. Katsibri, P. Soucacos, D.T. Kremastinos. *University of Athens, Attikon Hospital, Athens, Greece*

Background: Interleukin-1 mediates atherogenesis and coronary vasoreactivity. Anakinra, a human recombinant inerleukin-1a receptor antagonist, is used for the treatment of rheumatoid arthritis. We investigated the effects of anakinra on left ventricular (LV) function.
Methods: 23 patients with rheumatoid arthritis were randomized to receive a single injection of anakinra (150mg s.c.) or placebo and after 48 hours the alternative treatment in a double-blind trial and 23 age and sex matched subjects with similar risk factors served as controls. At baseline and 3 hours after the single injection we assessed LV function using echocardiography. Myocardial velocities were recorded by using colour tissue Doppler (TDI). The mean value of the systolic (Sm), early diastolic (Em) and late diastolic velocity (Am) at all 6 sites of the mitral annulus was used in the analysis. The ratio of E wave of the mitral inflow measured by pulsed wave Doppler to the mean Em was calculated as an index of LV diastolic filling pressures. Patients were reassessed after 30 days of anakinra treatment. All patients had no clinical history for CAD and a negative for ischaemia treadmill exercise test.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: Patients had impaired baseline Sm, Em/Am and E/Em compared to controls (table, $p<0.05$). There was an increase in the systolic (Sm) velocity and the Em/Am of mitral annulus, along with a decrease in the E/Em 3 hours after the injection of anakinra and after 30 days of treatment (F = 6.2, p=0.001 and F=4.2, p=0.04 respectively) compared to baseline. No change was observed in the Sm, Em/Am or E/Em after treatment with placebo compared to baseline (p=0.87, p=0.33, p=0.4 respectively). Despite the improvement in Em/Am and E/Em after treatment with anakinra, patients had lower Em/Am and higher E/Em than controls at 3h and 30 days ($p<0.05$).

	Baseline	3h-post placebo	3h-post anakinra	Post month	F	p	Controls	p
Sm (cm/s)	8.4±2.1	8.3±1.5	9.5±2.4	9.4±2.4	6.2	0.001	9.3±1.6	0.028
Em/Am	0.83±0.4	0.85±0.5	0.88±0.4	0.99±0.4	4.3	0.04	1.6±0.6	<0.01
E/Em	10.2±4.0	9.85±3.8	8.9±3.6	8.1±2.0	5.7	<0.01	6±1.1	<0.01

Conclusion: Treatment with anakinra improves systolic and diastolic markers of LV function by inhibiting the detrimental action of IL-1 on myocardium.

1052 Tissue Doppler indices of diastolic function correlate with collagen content of endomyocardial biopsies in patients with heart failure and normal EF

M. Kasner[1], D. Westermann[1], A. Kawellis-Opara[2], R. Gaub[2], D. Sinning[2], H.P. Schultheiss[2], M. Pauschinger[2], C. Tschoepe[2]. *[1]Charite Campus Benjamin Franklin, Kardiologie Dept., Berlin, Germany; [2]Berlin, Germany*

Background: The accuracy of conventional Doppler echocardiography and Tissue Doppler analysing differs in the diagnostic of LV diastolic function. Here we correlated morphological changes known to be crucial in LV compliance by endomyocardial biopsies (EMBs) and correlated them with different echocardiographic techniques in patients with HFNEF.
Method: We investigated 24 patients (51±10 years) with normal EF (65±8) and heart failure symptoms, whose endomyocardial biopsies (EMBs) were previously taken. Patients with coronary artery disease, valvular disease or atrial fibrillation were excluded. Total collagen content was determined using Sirius red staining. Collagen subtypes I and III, matrix metalloproteinases: MMP-1, MMP-3, MMP-9, tissue inhibitor of MMP (TIMP) were determined by standard immunohistochemistry methods. Assessment of diastolic function was performed by conventional Doppler (E/A, DT, IVRT), tissue Doppler measurements (E'/A') and LV filling index E/E'.
Results: Tissue Doppler parameters E'/A' and E/E' correlated strong with collagen content (r=-0.52, p=0.028 and r=0.50, p=0.040 respectively) and with collagen subtype I (r=-0.68, p=0.015 and r=0.66, p=0.018), whereas E/A (r= -0.34, p=0.078 and r=-0.28, p=0.268) and DT (r=0.22, p=0.093 and r=0.21, p=0.211) did not reach a statistical significance. Relaxation index IVRT correlated with collagen subtype I (r=0.62, p=0.014). Only LV filling index E/E' correlated with MMP-1 (r=0.45, p=0.033).
Conclusion: Of all parameters tissue Doppler and LV filling index E/E' correlated best with increased collagen content of endomyocardial biopsies in patients with heart failure and normal EF indicating induced cardiac remodelling process in those patients.

1053 K201 (JTV-519) improves norepinephrine-induced diastolic dysfunction with preservation of the ejection fraction

R. Matsuda[1], N. Otani[2], T. Nakajima[1], S. Abe[1], M. Shinozaki[1], H. Hasumi[1], M. Kikuchi[1], N. Kaneko[1]. *[1]Dokkyo Medical University School of Medicine, Dept. of Cardiology & Pneumology, Tochigi, Japan; [2]Dokkyo Medical University School of Medicine, Cardiology & Pneumology, Tochigi, Japan*

Purpose: A high plasma norepinephrine (NE) concentration is associated with severe heart failure and poor prognosis. An increase in the diastolic intracellular Ca^{2+} level has also been shown in heart failure. Recently, we showed that NE under Ca^{2+} loading induces severe diastolic dysfunction without significant change in the left ventricular ejection fraction (LV-EF). The goal of the study was to elucidate the relationship between high NE levels and diastolic dysfunction, and to determine if K201 (JTV519), a 1,4-benzothiazepine derivative, improves diastolic dysfunction, compared with diltiazem.
Methods: Adult Wistar Rats were administered NE (30 μg/kg/min for 25 min) with calcium loading (12 mg/kg/min for 45 min), and K201 or diltiazem at 100 μg/kg/min for the first 3 min and at 10 μg/kg/min for 27 min was infused from 5 min before administration of NE.
Results: In the Ca^{2+}–NE group, significantly increased left ventricular end-diastolic pressure (LVEDP) using a micromanometer-tipped pressure catheter and decreased E and Ea waves and deceleration time (DCT) using Doppler echocardiography were found, but LV function was preserved. NE-induced diastolic contraction (NEIDC) with aortic valve opening occurred in diastole and pulmonary hemorrhage was observed. These changes did not occur after calcium loading only or with administration of NE alone. K201 significantly reduced LVEDP, improved diastolic dysfunction and decreased NEIDC, but diltiazem did not do so. The mortality in the diltiazem group was 57%, compared to 0% in the K201 group.
Conclusions: The results indicate that NE may be an important factor in development of diastolic heart failure. Dual actions of K201 in inhibiting Ca^{2+} leakage from the sarcoplasmic reticulum in diastole and blocking the alpha1-adrenoceptor may be related to improvement of diastolic dysfunction.

1054 Baseline plasma NT-proBNP concentrations in relation to clinical characteristics: results from the irbesartan in heart failure with preserved systolic function trial

R.S. Mckelvie[1], M. Komajda[2], J. Mcmurray[3], M. Zile[4], A. Ptaszynska[5], A. Bhaumik[3], P. Carson[6], B. Massie[7] on behalf of I-PRESERVE Investigators. *[1]Hamilton Health Sciences, General Site, Hamilton, Canada; [2]Pitie-Salpetriere Hospital, Paris, France; [3]University of Glasglow, Glasgow, United Kingdom; [4]Medical Univ. of S. Carolina/RHJ Dept of VAMC, Charleston, United States of America; [5]Pharmaceutical Research Institute, Bristol-Myers Squibb, Princeton, New Jersey, United States of America; [6]VAMC, Washington, District of Columbia, United States of America; [7]University of California & San Francisco VAMC, San Francisco, California, United States of America*

Purpose: Plasma N terminal B type natriuretic factor (NT-proBNP) is elevated in heart failure (HF) patients with reduced systolic function and is a useful "rule out test" for that diagnosis. Little is known about NT-proBNP in HF with preserved systolic function patients (HFPSF). We measured NT-proBNP in 3485 patients with HFPSF, randomized in the Irbesartan in Heart Failure with Preserved Systolic Function Trial (I-PRESERVE).
Methods: Patients with symptoms/signs of HF, ejection fraction (EF) ≥ 45%, age ≥ 60 years, and either NYHA II-IV with HF hospitalization (HF Hosp) within 6 months or NYHA III-IV with corroborative ECG, X-ray pulmonary congestion or echocardiographic evidence of LVH or LA enlargement were recruited. The NT-proBNP was measured in a central laboratory using the Elecsys proBNP assay (Roche) and reported as the mean ±SE pg/ml.
Results: Baseline characteristics included mean age 72±7 years, 60% women, 43% prior HF Hosp; medications: diuretics 83%, β-blocker 59%, ACE inhibitor 25% (limited by protocol to 1/3 patients), and spironolactone 15%. The mean NT-proBNP was 349±8 pg/ml. NT-proBNP increased with advancing age and was higher in men vs women (mean 387±15 pg/ml vs 326±10 pg/ml, p=0.0003). In multivariate analysis the baseline characteristics most strongly associated with higher NT-proBNP levels were AF on ECG, lower creatinine clearance (CrCl), lower hemoglobin levels (Hgb), lower EF, and prior HF Hosp.

NT-proBNP Related to Clinical Findings

	Yes		No		p
	Mean (SE)	n	Mean (SE)	n	p
≥ median creatinine	450 (13)	2191	225 (8)	1270	<0.0001
AF on ECG	807 (28)	1105	237 (6)	2380	<0.0001
HF Hosp	494 (18)	1509	268 (8)	1976	<0.0001
Anemia (<11.5 g/dl)	695 (82)	130	339 (8)	3289	<0.0001
< median EF (59%)	440 (15)	1683	281 (9)	1802	<0.0001
Pulm congestion	462 (18)	1357	289 (8)	2009	<0.0001

Conclusion: Patients with clinical findings commonly associated with worse outcomes, such as prior HF Hosp, lower CrCl, lower Hgb, lower EF, and AF on ECG, had higher NT-proBNP levels. NT-proBNP is elevated in HFPSF patients, particularly in those with findings suggestive of a poorer prognosis, thus potentially representing a marker of increased risk.

DO WE NEED BOB GELDOF? SOCIOECONOMIC STATUS AND CARDIOVASCULAR DISEASE

1073 Secular trends and gender differences in cardiovascular mortality in the Greek population during the past five decades

T. Chimonas[1], I. Fanouraki[2], E. Chimonas[3], D.V. Cokkinos[2]. *[1]Onassis Cardiac Surgery Center, Athens, Greece; [2]Perama Health Center, Rethimno, Greece; [3]Athens, Greece*

Purpose: To study trends and gender differences in mortality rates for cardiovascular disease (CVD), stroke and coronary heart disease (CHD), as well as in all-cause mortality in the Greek population during the period from 1956 to 2005.
Methods: Mortality data and intercensal yearly population estimates were obtained from the vital statistics tables published by the National Statistical Service of Greece. Age-standardization was performed by the direct method, using the population of 1961 as standard. Trends over time were determined using linear regression models.
Results: In 1956, age-adjusted all-cause mortality (per 100,000 population aged 45-74 years old) was 1455 in men and 1005 in women. Since 1970, it has declined steadily in both sexes, reaching 930 (-36%) in men and 443 (-56%) in women by 2005. Age-adjusted CVD was 420 in men and 355 in women. It increased initially, until the late '80s; since then it has decreased to 353 (-16%) in men and 146 (-59%) in women. Age-adjusted mortality from stroke was 148 in men and 160 in women. An initial increase, until 1976, was followed by a decline, to 82 (-45%) in men and 53 (-67%) in women. Age-adjusted mortality from CHD was 136 in men and 90 in women. After increasing initially, since 1989 it has decreased. However,

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

only in women has it returned below 1956 levels: in 2005, it was 196 in men (higher by 44%) and 49 in women (-45%). Sex ratios (men/women) in 1956 were 1.4 for all-cause, 1.2 for CVD, 0.9 for stroke and 1.5 for CHD mortality. Mortality in women has decreased to a significantly greater degree, resulting in sex ratios of 2.1 for all-cause, 2.4 for CVD, 1.5 for stroke and 4 for CHD mortality, an increase of 45%, 104%, 67% and 165% respectively. The ratio of stroke mortality/CHD mortality in 1956 was 1.1 in men and 1.8 in women. By 2005 it had become 0.4 in men and 1.1 in women.

Conclusions: During the past five decades, Greece has seen dramatic progress in economic growth, living standards and quality of healthcare. This is reflected on the steady decline in all-cause mortality rates. However, this was accompanied by an increase in the prevalence of cardiovascular risk factors, which led to an increase in CVD, CHD and stroke mortality rates for several decades. Their more recent, mostly therapy-driven, decline has brought them below their 1956 levels in women. However, these gains have been smaller in men, especially regarding CHD. These gender differences show that there is still room for improvement in the prevention and treatment of CHD and other CVDs in men, with the aim of returning the sex ratio to at least its former levels.

1074 Socioeconomic development and stroke mortality-an ecological study among 23 populations

S.H. Wu[1], X.-H. Zhang[2], J. Woo[1]. [1]*Chinese University of Hong Kong, School of Public Health, Hong Kong, Sar, China, People's Republic of;* [2]*Chinese University of Hong Kong, Community and Family Medicine, Hong Kong, Hong Kong SAR, People's Republic of China*

Purpose: Studies from developed countries demonstrated that socioeconomic status (SES) relates to the risk of stroke at individual level: children who were brought up in families at low SES indicated higher risk of stroke in their later life than those who were from high SES families; adults living in low SES also had higher risk of stroke than those living at high SES. We aimed to explore the association between stroke mortality (SM) with socioeconomic development among countries/territories with emerging or established market economies.

Methods: SM in the age group of 45-54y for men and women in the latest available 3 years were averaged using data from the World Health Organization, while the Human Development Index (HDI), a composite of longevity, education, and standard of living, defined by the United Nations, was used as an indicator of socioeconomic development. The association of SM with current HDI (adulthood SES) and in 1960 (childhood SES) for the cohorts was examined with regression analysis. Mortality from infectious disease and the prevalence of hypertension were controlled as major confounders.

Results: Only 23 countries/territories with death registry covered >90% population, ≥50 stroke deaths in the age-sex-specific group occurred yearly and HDI available were included. The countries are from Europe, America, Australasia and Asia. T he lowest SM rate was observed in Switzerland (7.7 per 100,000 in men and 7.5 in women) and the highest in Hungary (66.7 and 29.1 respectively). The highest HDI in 1960 and 1999 was in Canada (0.865, and 0.936) and the lowest HDI in 1960 was in Portugal (0.468) and in 1999 was in Venezuela (0.765). Childhood SES accounted for 32% of variance of SM among countries in men, and 34% in women ($p<0.05$); while adulthood SES explained 38% in men and 50% in women ($p<0.01$). The countries at top tertile of HDI in both 1960 and 1999 had much lower SM than those at the bottom tertile (12.6 per 100,000 per year (95%CI: 8.3-16.8) vs 36.8 (19.3-54.3) in men, 10.4 (6.6-14.3) vs 23.6 (15.4-31.7) in women).

Conclusions: The level of SM is significantly influenced by socioeconomic development at population level. The results support the findings from studies with individual subjects. Socioeconomic development may reduce the vulnerability to stroke through better nutrition for children, health education and health care services through life.

1075 Effect of including social deprivation and family history into the new ASSIGN cardiovascular risk score for use in Scotland

H. Tunstall-Pedoe, M. Woodward on behalf of SIGN group on risk estimation. *University of Dundee, Cardiovascular Epidemiology Unit, Dundee, United Kingdom*

Purpose: Excess cardiovascular risk in socially deprived and certain ethnic population groups is inadequately explained by classic risk factors. The standard Framingham cardiovascular risk score therefore assigns less preventive treatment to these groups than they merit compared to others – unacceptable to population-based health services championing equity. We explored adding social deprivation and family history into the new ASSIGN cardiovascular risk score for use in Scotland, to try making it fairer than the Framingham score in this respect.

Methods: 6540 men and 6757 women aged 30-74 from the Scottish Heart Health Extended Cohort (SHHEC), had an initial cardiovascular assessment and were followed-up for 11-21 years with 1604 cardiovascular events (coronary or cerebrovascular disease) in men and 1015 in women. A new cardiovascular risk score for each sex, generally similar to Framingham was derived from all risk factors found to be independently predictive in both sexes at $p<0.05$. Like Framingham these were found to include age, systolic blood pressure, total cholesterol, HDL-cholesterol, cigarette smoking and diabetes, but unlike Framingham we added in numbers of cigarettes, family history of coronary disease or stroke below age 60, and social deprivation. The latter was assessed by the Scottish Index of Social Deprivation, an index ranging from 0.54 (least) to 87.6 (most deprived), derived from multiple social indicators and linked to postcode of residence, a powerful continuous risk factor when tested both alone and after correction for all others.

Results: Tested against Framingham in the SHHEC population the new ASSIGN score discriminated significantly better (but not greatly so) overall. There was a high correlation between these scores so those identified as high risk were 80% the same, but the other 20% resulted in greater identification of events by the ASSIGN score among those with a positive family history and/or social deprivation. This abolished a social gradient in false negative cases found with the Framingham score. ASSIGN scores were generally lower than the Framingham equivalent but exceeded them in the socially deprived, in those with a positive family history, and in heavy smokers.

Conclusions: The ASSIGN score addresses the Scottish problem of social deprivation and social equity and there are plans to adopt it nationwide. It warrants consideration elsewhere, particularly in populations of heterogeneous ethnic composition, where we expect positive family history to act as a surrogate, and to compensate, for ethnic susceptibility to cardiovascular disease.

1076 The effects of socio-economic status on the prevalence of cardiovascular risk factors in healthy individuals in western and eastern parts of Slovakia

G. Kamensky[1], M. Avdicova[2], Z. Gerova[3], A. Egnerova[4], J. Krak[5], J. Murin[6], R. Sidlo[7]. [1]*University Hospital Bratislava Ruzinov, Dpt. Noninvasive Cardiovascular Diagnostics, Bratislava, Slovak Republic;* [2]*Regional Public Health Authority, Regional Public Health Authority,, Banska Bystrica, Slovak Republic;* [3]*Regional Public Health Authority, Regional Public Health Authority,, Bratislava, Slovak Republic;* [4]*Slovak Health University, Faculty of Public Health, Bratislava, Slovak Republic;* [5]*Regional Public Health Authority, Poprad, Slovak Republic;* [6]*University Hospital, Bratislava, 1st Internal Clinic, Bratislava, Slovak Republic;* [7]*Economic University, Faculty of statistics, Bratislava, Slovak Republic*

Background: Socioeconomical status has been related with the prevalence and incidence of cardiovascular (CV) disease. However, there is still controversy regarding inverse association between socioeconomic status and obesity indices, which has been confirmed in most univariate analyses, but not after udjusting for other covariates in multivariant analyses.

Objective: The goal of the study was to compare the socio-economic status with prevalence of CV risk factors in healthy persons in two Slovakian counties: Bratislava county with the highest GDP and the lowest unemployment rate and Presov county, with one of the lowest GDP and highest unemployment rates in Slovakia.

Methods: During the period of 1995 – 2005, 27 797 healthy volunteers from Bratislava and Presov counties were examined in Counselling centers. For the purposes of statistical comparison all examined persons from both counties were matched by age, gender and the year of examination. Finally, 12 024 persons (mean age 46.9±12.7 yrs, 3458 men, 8566 women) were entered into the retrospective analysis. Trends in established and emerging cardiovascular risk factors were examined accross the participants'socio-economic status.

Results: Persons from Presov county had significantly higher systolic blood pressure, heart rate, BMI, waist circumference, total and LDL cholesterol, triglycerides (all $p < 0.0001$) and lower HDL cholesterol ($p < 0.0001$) compared to volunteers from Bratislava county in univariate analysis. The lower the social class the higher the proportion of obesity, which was more prominent in women. Simultaneously they were significantly more physically inactive, they preferred less healthy food and were much less educated regarding their risk factors (all $p < 0.01$). Using stepwise adjusted multivariate logistic regression analysis, age (OR 1.061, 95% CI 1.047-1.075, $P < 0.0001$), socio-economic status (manual versus nonmanual work: OR 2.09, CI 1.52-2.86, $P < 0.0001$), low leisure time physical activity (OR 1.90, CI 1.44-2.52, $P < 0.0001$), and unhealthy food (OR 1.91, CI 1.44-2.54, $P < 0.0001$), all were independent predictors of obesity in this cohort.

Conclusions: Lifestyle factors including low socio-economical class, were strongly associated with obesity and other conventional cardiovascular risk factors. Socioeconomic disparities have persisted and in former eastern European countries have even widened in some populations, which underlines the need to improve preventive care among the lower socioeconomic groups.

1077 Risk of first major coronary events or ischemic stroke among occupational and educational social classes. 12-year follow-up of the MONICA Brianza and PAMELA male cohorts

M. Ferrario[1], G. Veronesi[1], L.E. Chambless[2], G. Corrao[3], R. Sega[4], R. Borchini[5], G.C. Cesana[1]. [1]*Universita' Degli Studi Dell'insubria, Scienze Cliniche E Biologiche, Varese, Italy;* [2]*University of North Carolina at Chapel Hill, Biostatistics, Chapel Hill (Nc), United States of America;* [3]*Universita' di Milano - Bicocca, Statistica, Milano, Italy;* [4]*Centro Studi Patologie Cronico-Degenerative, Monza, Italy;* [5]*Ospedale di Circolo - Fondazione Macchi, Varese, Italy*

Purpose: The aim is to assess occupational (OC) and educational (ED) class

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

differences in incidence of major coronary or ischemic stroke events in northern Italian cohorts.
Methods: In a prospective cohort study, 2,989 25-74 year old ever-employed men, CVD-free at baseline were recruited from four population-based cohorts (MONICA Brianza surveys and the PAMELA Study) from 1986 to 1994, and followed-up until the end of 2002 to ascertain first major cardiovascular (CVD) events: acute MI or ischemic stroke, fatal or non fatal (MONICA validated), or coronary revascularisation (bypass or PTCA) or carotid endarterectomies. At baseline, systolic blood pressure, cigarette smoking, total and HDL cholesterol, triglycerides and diabetes mellitus were investigated according to the standardised MONICA protocol. Four OC classes were derived from the Erikson, Golthorpe and Portocarero scheme, using information on the current or last job position. ED classes were obtained from age-specific quartiles of years of schooling. Age-adjusted and multi-factor-adjusted hazard ratios (HRs) and 95% confidence intervals (CI) were calculated from Cox proportional hazards models, with non-manual workers and the highest ED category as reference levels.
Results: In 12-year median follow-up, 220 first CVD events occurred (incidence rate 6.3 per 1000 person-years). Lower ED and OC classes were characterized by higher prevalence of current cigarette smoking and diabetes mellitus. ED classes showed an inverse linear association with CVD risk (chi-square for trend test, p-value = 0.017). Differences in CVD risk were also observed among OC classes (chi-square for heterogeneity test p-value = 0.038). Risk excesses were found among non manual (HR=1.79; CI: 1.20-2.66) and self-employed (HR=1.65; CI: 1.05-2.59). Administrators and professionals had a non significant 50% higher risk than non-manual workers. A separate end-point analysis revealed a higher risk among administrators and professionals for CHD alone. The contribution of CVD risk factors in explaining the risk excess was evident for the lower social classes only.
Conclusions: In this northern Italian cohorts, higher risk of first coronary or ischemic stroke event among lower OC and ED classes is confirmed, but an higher risk was also detected, in particular for CHD, in the higher OC class. Further investigation are needed to confirm these partially unusual findings.

1078 Local access to hospital technology and not socioeconomic status determines resource use in myocardial infarction care

M.G. Cohen, G.M. Holmes, S.B. Greene, K.A. Selzman, S.C. Smith, T.S. Carey, C. Patterson. *University of North Carolina At Chapel Hill, Division of Cardiology, Chapel Hill, United States of America*

Background: Process of care and resource use in myocardial infarction (MI) is influenced by patient socioeconomic status (SES). It is unknown whether these differences persist in patients of different SES treated at hospitals with equal availability of advanced technologies. We sought to investigate the effect of SES on access to medical technology and process of care for MI.
Methods: A retrospective analysis of 205,917 MI patients admitted to non-federal hospitals in North Carolina (USA) between 1997 and 2003 was done. Census data on the household income for the residential postal code of each individual patient were used as a proxy for SES. We analyzed the difference in mortality, use of invasive procedures (diagnostic catheterization, percutaneous coronary intervention [PCI], and coronary artery bypass graft [CABG]) controlling for Charlson comorbidity index, insurance status, hospital volume, number of beds, hospital resources, urban location, government management, and teaching status.
Results: Low SES patients were more likely to die during hospitalization and less likely to receive diagnostic catheterization, PCI and CABG compared to high SES patients. After controlling for differences in hospital techonologies and other factors, these disparities were eliminated for diagnostic catheterization and CABG and attenuated for PCI.(Table).

	Unadjusted OR (95%CI)	Adjusted OR (95% CI)
Hospital mortality	1.21 (1.15, 1.26)	1.07 (1.02, 1.12)
Diagnostic catheterization	0.74 (0.72, 0.76)	1.08 (1.04, 1.12)
PCI	0.67 (0.65, 0.69)	0.94 (0.91, 0.98)
CABG	0.89 (0.85, 0.93)	1.12 (1.07, 1.18)

Conclusions: Low SES MI patients experience a less invasive process of care primarily due to geographic barriers in accessing hospitals with extensive cardiac technology. High and low SES patients admitted to hospitals with similar availability of resources experience similar use of invasive cardiac procedures. Policymakers should ensure geographic access to high technology hospitals to all patients regardless of socioeconomic status.

RISK ASSESSMENT: WHAT ARE WE LOOKING FOR?

1079 Is self report of diabetes mellitus a coronary heart disease risk equivalent for fatal cardiovascular events? Experience from the SCORE project

C. Mc Gorrian[1], A.P. Fitzgerald[2], T. Leong[3], R. Conroy[4], S. Sans[5], I.M. Graham[6] on behalf of The SCORE investigators. *[1]Mc Master University, Hamilton, Ontario, Canada; [2]University College Cork, Cork, Ireland; [3]Our Lady's Hospital, Navan, Ireland; [4]Royal College of Surgeons in Ireland, Dublin, Ireland; [5]Institute of Health Studies, Barcelona, Spain; [6]The Adelaide and Meath Hospitals, Dublin, Ireland*

Background: Diabetes mellitus in an established risk factor for cardiovascular diseases (CVD). Previous studies have found that the CVD risk conferred by diabetes is not different to that conferred by prior coronary heart disease (CHD). We examined the relative effects of self reported diabetes and previous CHD on CVD risk within the SCORE project.
Methods: SCORE (Systematic COronary Risk Evaluation) pooled 12 European cohorts that had information on risk factors for CVD. This analysis included cohorts that had data on self-reported diabetes. We defined previous CHD as self reported or ECG evidence of a previous MI. We used Cox proportional hazards models with age as the time variable, stratified by cohort. We examined two outcomes: CHD death and total CVD death. Dummy variables were used to model the risks of diabetes compared with previous MI.
Results: Data on 145,403 participants were included. 2462 (1.7%) of the participants had established diabetes on entry to the study, and 2047 (1.4%) of the subjects had a previous MI. Mean follow up time was 15.15 years (SD 5.15). Table 1 presents hazard ratios (HRs) for diabetes and for previous CHD for the two endpoints. Interaction modelling revealed a significant antagonistic interaction between diabetes and previous CHD (p=0.009). The HR for the risk conferred by prior CHD compared with diabetes was 1.70 (95% CI 1.46, 1.97) for CHD death and 1.52 (95% CI 1.33, 1.73) for CVD death, in a multivariable model.

Table 1

Risk factor	Hazard ratios for CHD death (95% CI)	Hazard ratios for CVD death (95% CI)
Diabetes*	3.24 (2.90, 3.62)	3.17 (2.89, 3.48)
Diabetes in subjects with previous CHD†	1.96 (1.45, 2.63)	2.12 (1.64, 2.74)
Diabetes in subjects without previous CHD†	3.19 (2.83, 3.60)	3.06 (2.76, 3.38)
Previous CHD*	5.63 (5.12, 6.19)	4.72 (4.34, 5.14)
Previous CHD in subjects with diabetes†	3.32 (2.45, 4.50)	3.21 (2.47, 4.17)
Previous CHD in subjects without diabetes†	5.42 (4.91, 5.99)	4.63 (4.23, 5.07)

*Model 1: With age as time variable, adjusted for sex & stratified by cohort†Model 2: As Model 1, also adjusted for smoking, cholesterol, SBP, diabetes, previous CHD & an interaction term for diabetes & previous CHD.

Conclusions: A history of previous CHD conveys a higher risk of both CHD and CVD death than does self reported diabetes. Nevertheless, diabetes is an important risk factor, and one which is a vital focus for preventive cardiology.

1080 Three quarters of coronary heart disease is attributable to conventional modifiable cardiovascular risk factors in a French Cohort of 7161 men

V. Bongard[1], J.B. Ruidavets[1], D. Arveiler[2], P. Amouyel[3], P. Ducimetiere[4], L. Vo[1], J. Ferrieres[5] on behalf of The Prime Study Group. *[1]INSERM U558, University School of Medicine, Department of Epidemiology, Toulouse, France; [2]University School of Medicine, Department of Epidemiology and Public Health, Strasbourg, France; [3]INSERM U744, Institut Pasteur, Lille, France; [4]INSERM U780, Villejuif, France; [5]CHU Rangueil, INSERM U558, Department of Cardiology B, Toulouse, France*

Purpose: From a public health point of view, it is important to assess the impact of modifiable cardiovascular risk factors on the population burden of coronary heart disease (CHD), in order to evaluate the proportion of cases that could be avoided. We aimed at estimating the population attributable risks (PARs) for CHD associated with the main cardiovascular risk factors.
Methods: The French PRIME study is a prospective population-based cohort of men recruited in 1991-93, aged 50-59 at baseline and followed over 10 years. Health status was obtained by annual follow-up and an international medical committee validated all new cases of CHD according to standardised clinical, biological and electrocardiographic criteria. Independent predictors of hard CHD (myocardial infarction or coronary death) were assessed using multivariate Cox models and PARs were calculated.
Results: The cohort comprised 7161 men (mean age 54.9 years, standard deviation (SD) 2.9), free of CHD at baseline. After 10 years, the incident rate of hard CHD was 2.7 per 1000 person-years. In multivariate analysis, independent predictors of incident hard CHD were age (hazard ratio (HR)=1.06 for each increment in 1 SD, p=0.03), a previous history of hypertension (HR=1.71, $p<0.01$), baseline blood pressure above 140-90 mm Hg (HR=1.60, $p<0.01$), LDL-cholesterol above 4.1 mmol/l (HR=1.78, $p<0.001$), HDL-cholesterol below 1 mmol/l (HR=1.47, p=0.02), diabetes (HR=2.23, $p<0.01$), current smoking (HR=1.59, $p<0.01$), obesity (HR=1.43 for subjects with body mass index over 30 $kg.m^2$, p=0.04) and no alcohol consumption (HR=1.75 for teetotallers, p=0.01). After adjustment for age

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

and centre, high baseline blood pressure (above 140-90 mm Hg) accounted for 29% of the PAR for hard CHD, high LDL-cholesterol (above 4.1 mmol/l) for 15%, low HDL-cholesterol (below 1 mmol/l) for 14%, current smoking for 12%, obesity for 11% and diabetes for 5%. After full adjustment for age, centre, alcohol use and antihypertensive or hypo-cholesterolemic drugs, the five main modifiable cardiovascular risk factors (high blood pressure, high LDL-cholesterol, low HDL-cholesterol, diabetes and current smoking) were responsible for 74% (95% confidence interval [73-76]) of all incident cases of hard CHD. Adding obesity did not significantly rise this proportion.
Conclusion: Major modifiable cardiovascular risk factors account for three quarters of CHD in this large population-based cohort. This finding confirms that most cases of premature CHD are highly preventable.

1081 PROCAM vs. SCORE in detecting subclinical atherosclerosis

S.I. Dumitrescu[1], I. Tintoiu[1], C. Manole[2], R. Orosan[2], M. Vicol[2], V. Greere[1], I. Raduta[1], I. Moscaliuc[1], G. Neagoe[1], V. Voicu[3]. *[1]Center for Cardiovascular Disease of Army, Cardiology, Bucharest, Romania; [2]STS Medical Center, Cardiology, Bucharest, Romania; [3]Romanian Academy, Bucharest, Romania*

Purpose: To compare SCORE and PROCAM risk scores and their correlation with markers of subclinical cardiovascular impairment: brachial artery Flow Mediated Dilatation (FMD), carotid artery Intima Media Thickness (IMT), left ventricular mass indexed to BSA (LVMI), E wave deceleration time (EDT), isovolumetric relaxation time (IVRT) and myocardial performance index (Tei).
Methods: Through a cardiovascular primary prevention program we screened 141 subjects (age 45.5±8.8, 47.5% males) recording history, BMI 27.1±4.9 kg/m^2, waist circumference 94.3±4.6 cm, blood pressure 130.2±20.6/81.1±11.7 mmHg, blood glucose 94.9±31.7 mg/dl, total cholesterol 212.5±42.7 mg/dl, LDL 135.3±37.1 mg/dl, HDL 46.6±12.1 mg/dl, triglycerides 158.6±127.4 mg/dl. The echographic evaluation included IMT 0.66±0.17 mm, FMD 7.08±3.56%, LVMI 95.5±28.8 g/m^2, EDT 178.2±31.9 ms, IVRT 85.0±14.2 ms, Tei 0.50±0.07. After calculation of 10 years risk of coronary heart disease operating with SCORE HIGH and PROCAM standards, we performed the statistical analysis.
Results: There are significant disparities between SCORE and PROCAM data (Wilcoxon Signed Ranks test z = -8.43, p<0.001, sign-test z = -9.141, p<0.001, K-S test D = 0.5439, p<0.001). Moreover, after setting apart the study group in low risk (PROCAM <10%, SCORE<3%), medium risk (PROCAM 10 – 20%, SCORE 3 – 5%) and high risk (PROCAM > 20%, SCORE > 5%), the agreement between risk ranks was 'fair' for low (k=0.388; CI 95% 0.208-0.564) and high risk (k=0.3; CI 95% 0.070-0.531) and 'slight' for medium risk (k= -0.051; CI 95% -0.184-0.083). The relationship of subclinical atherosclerosis with the risk scores is reported in table. The analysis between risk groups yielded only 2 significant correlations: an abnormal FMD is more frequent in the medium risk PROCAM group (p=0.0038) and an abnormal LVMI is less frequent in low risk SCORE group (p=0.046).

Correlation with markers

	FMD	IMT	LVMI	EDT	IVRT	Tei
rho(PROCAM)	-0.362	0.625	0.581	0.294	0.493	0.380
rho(SCORE)	-0.340	0.612	0.614	0.206	0.526	0.368

All correlation (Spearman's rho) achieved significance (2-tailed) p<0.001, except for rho(SCORE) with EDT (p=0.014).

Conclusions: Evaluation by both scores seems reasonable considering their modest accordance in risk classification and the need to discriminate the presence of subclinical atherosclerosis.

1082 Dietary pattern and the risks of mortality, major coronary events and diabetes in the Whitehall II study over 13 years of follow-up

E. Brunner[1], A. Mosdol[1], M. Shipley[1], D. Witte[1], P. Martikainen[2], M. Marmot[1] on behalf of Whitehall II study. *[1]University College London, Department of Epidemiology And Public Health, London, United Kingdom; [2]University of Helsinki, Helsinki Collegium for Advanced Studies, Helsinki, Finland*

Purpose: To examine the health effects of dietary patterns in a middle-aged cohort using verified major coronary events.
Methods: Prospective study with 13 years of follow-up (time at risk=93,295 person-years) among 5385 men and 2346 women, mean age 50 years at dietary assessment (1991-93). Outcome measures are all-cause and cancer mortality, coronary death/non-fatal myocardial infarction and incident diabetes verified by record tracing and oral glucose tolerance tests.
Results: Cluster analysis identified four dietary patterns at baseline. The patterns were 'Unhealthy' (white bread, processed meat, chips, full cream milk, n=2665), 'Sweet British' (white bread, biscuits, cakes, processed meat, high fat dairy products, n=1042), 'Continental' (fruit, vegetables, rice, pasta, wine, n=1361) and 'Healthy' (fruit, vegetables, wholemeal bread, low fat dairy, little alcohol, n=2663). Compared to the 'Unhealthy' pattern, the 'Healthy' pattern reduced the risk of coronary death/non-fatal myocardial infarction and diabetes, hazard ratios (95%CI) 0.71 (0.51-0.98) and 0.72 (0.56-0.93) after adjustment for age, sex, ethnicity, dietary energy misreporting, social position, smoking status and leisure-time physical activity. Mortality did not differ by dietary pattern in this relatively young cohort.
Conclusions: Healthy eating patterns observed in British adults reduced risks of diabetes and major coronary events. This eating pattern offers considerable health benefits to individuals and contributes to public health.

1083 Is the association between atherosclerosis and inflammation obligatory, or conditional upon an unhealthy lifestyle?

E.R. Rietzschel[1], M.L. De Buyzere[1], D. De Bacquer[2], S. Bekaert[1], M. Langlois[3], P. Segers[4], L. Cooman[5], P. Verdonck[3], G.G. De Backer[2], T.C. Gillebert[5] on behalf of the ASKLEPIOS investigators. *[1]University Hospital Ghent, Department of Cardiovascular Diseases, Ghent, Belgium; [2]Ghent University, Department of Public Health, Ghent, Belgium; [3]AZ St-Jan AV Hospital, Department of Clinical Chemistry, Bruges, Belgium; [4]IBITECH, Ghent University, Cardiovascular Dynamics and Biofluid Dynamics, Ghent, Belgium; [5]Primary Care Physicians Asklepios VOF, Nieuwerkerken-Aalst, Belgium*

Purpose: Inflammation is a key feature in the pathogenesis of atherosclerosis. High-sensitive C-reactive protein (hs-CRP) is a marker of inflammation, identifying individuals at increased cardiovascular risk. The widespread hypothesis that a major stimulus for hs-CRP arises from the inflammatory burden from atherosclerosis is attractive but still unproven. Specifically, it is unknown whether the relation between atherosclerosis and hs-CRP is obligatory or significantly modulated by co-factors such as lifestyle?
Methods: The Asklepios study is a blinded sample of 2498 M/F volunteers, representative of the Belgian population between 35-55 years, free from overt cardiovascular disease. Vascular echography (carotid, femoral) was systematically performed. Atherosclerosis was defined as carotid or femoral plaque or intima-media thickness ≥0.9mm. hs-CRP was assayed by particle-enhanced immunoturbidimetry on fasting subjects, free from clinical inflammation.
Results: Results adjusted for age, gender, BMI, season, blood pressure, cholesterol, diabetes and drug use. Echographically detectable atherosclerosis is independently and uniformly associated with a moderate 7% higher hs-CRP level throughout ranges of blood pressure, cholesterol levels, educational class, weight and glycemia. The exceptions are lifestyle variables: physical activity, fruit and vegetable intake and smoking, for which the increase in hs-CRP associated with atherosclerosis was not uniform (p for interaction <0.05). The "best" categories (active lifestyle, sufficient fruit and vegetable intake) are uniquely associated with the loss of extra inflammation associated with presence of atherosclerosis. In the "worst" categories (active smoking, inactivity, insufficient fruit and vegetable intake), atherosclerosis is associated with significant rises in hs-CRP. In case of sufficient fruit & vegetable intake, regular physical activity and avoidance of smoking ("healthy lifestyle"), no atherosclerosis-associated rise in hs-CRP was detectable.
Conclusions: Generally, at the population level atherosclerosis is associated with a moderate increase in hs-CRP, which is prerequisite upon an "unhealthy lifestyle". In subjects with an "unhealthy lifestyle", presence of atherosclerosis is clearly associated with an increase in hs-CRP. In subjects with a "healthy lifestyle", atherosclerosis was not associated with an increase in CRP. It is alarming that less than 1 in 20 of 35-55 year-olds in our population sample achieved straightforward public health recommendations for a healthy lifestyle, a target which must be continually re-emphasized to all.

1084 Favorable cardiovascular risk profile and 10-year cardiovascular disease incidence in women and men: results from the CUORE Project

L. Palmieri[1], J. Stamler[2], C. Donfrancesco[1], S. Panico[3], D. Vanuzzo[4], L. Pilotto[1], G. Cesana[5], M. Ferrario[6], R. Sega[5], S. Giampaoli[2]. *[1]Istituto Superiore di Sanita', Centro Nazionale di Epidemiologia, Rome, Italy; [2]Northwestern University, Feinberg School of Medicine, Chicago, United States of America; [3]Universita' Federico II, Dip. di Medicina Clinica e Sperimentale, Naples, Italy; [4]Agenzia Regionale della Sanita', Centro per la Prevenzione Cardiovascolare, Udine, Italy; [5]Universita' degli Studi Milano-Bicocca, Centro Ricerche Pat. Cronico-degenerativ, Monza, Italy; [6]Universita' degli Studi dell'Insubria, Dipartimento di Scienze Cliniche e Biologiche, Monza, Italy*

Purpose: Cardiovascular risk factor research has recently broadened its focus based on new data demonstrating benefits of low risk, i.e., favorable levels of all major risk factors. Aims are to assess relation of LRi to cardiovascular disease (CVD) risk of men and women, and implications for prevention.
Methods: Prospective population-based Italian study, 7,438 men and 13,009 women ages 35-69 years without previous cardiovascular disease, mean follow-up 10.3 years, validated first coronary and stroke events. Baseline CVD risk was classified in three categories: low risk (LRi); unfavorable but not high risk (U-NHRi); high risk (HRi). To analyze relation of these risk profiles to CVD incidence, age-adjusted CVD incidence was calculated, stratified as baseline LRi, U-NHRi, or HRi. To assess independent relationship of individual risk factors to CVD incidence, multivariate proportional hazards models were computed for combinations of risk factors.
Results: Only 1.4% of men and 3.4% of women met LRi criteria; 85.0% and 79.3% were high risk (HRi). No CVD events occurred in LRi men, only 2 in LRi

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

women. Age-adjusted CVD incidence rates for men and women not high risk were 31.8/10,000 persons-years and 16.9/10,000 persons-years - 63% and 49% lower respectively than for HRi participants. Blood pressure, need for antihypertensive medication, smoking, hyperglycemia, diabetes, total and HDL-cholesterol were independently related to CVD risk.
Conclusions: Low risk is a rare condition; favorable levels of all risk factors assure low rates of cardiovascular disease. To make cardiovascular disease become endemic, not epidemic, preventive action strategy should aim to increase the proportion of low risk people in the general population.

THE SMALLER THE PATIENT, THE BIGGER THE PROBLEM – NEW QUESTIONS IN PEDIATRIC CARDIOLOGY

1085 Fetal left heart obstructions- diagnosis, development and outcome during the first year of life

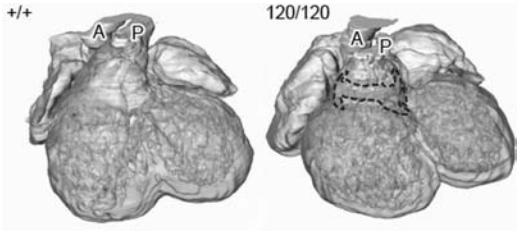
R.M. Oberhoffer, A. Zimmermann, K.T.M. Schneider, G. Czettritz, J. Hess. *University of Technology, Pediatrics, Munich, Germany*

Fetal heart disease may progress during intrauterine life. Our objective was to examine the cardiac characteristics, intrauterine development and first year outcome in fetuses with left heart obstructive lesions (LHO).
Therefore, we retrospectively evaluated complete datasets and video documentations of 55 fetuses which had been referred to our center between 1999 and 2006 because of suspected LHO. In 33 of them, hypoplastic left heart syndrome (HLHS) was diagnosed at a median gestational age of 22.5 weeks, in 12 of them critical aortic stenosis (AS, median age 25.5.weeks), and in 10 coarctation (CoA, median age 27 weeks).
Termination of pregnancy was performed in 7/33 cases with HLHS, intrauterine death occurred in one, and neonatal death due to denied surgery in seven. The remaining 18 patients underwent Norwood procedure with 3 deaths postoperatively due to restrictive foramen ovale or acute shunt thrombosis. Prenatal prediction of a restrictive foramen ovale was correct in 2 cases and false positive in 4.
Out of the 12 fetuses with AS, 10 had concomitant endocardial fibroelastosis. 3 of them developed HLHS within 7 to 10 weeks and underwent Norwood operation postnatally; 1 of them died. In the remaining 9, ballon dilatation was performed post partum. It resulted in severe aortic insufficiency in 2 and death in 1, and ended up in an univentricular approach in 3 of them (1 death).
Of the 10 patients with CoA, 6 had an hypoplastic aortic arch initially, 2 during later examinations. Surgery was necessary in 9/10, and all patients survived.
In summary, survival rate of fetuses with HLHS was 45.5%, of fetuses with AS 75%, and with CoA 100%. 25% of fetuses with AS ended up in HLHS before 30 weeks of gestation, and 25% in a Norwood procedure despite successful valvuloplasty postnatally. Thus, for optimal perinatal management, follow up intervals should be at least 4 weeks, and councelling should include developmental patterns.

1086 Development of cardiac outflow tract malformations in a mouse model with Tetralogy of Fallot

N.M.S. Van Den Akker[1], D.G.M. Molin[2], P.P.W. Peters[2], S. Maas[1], L.J. Wisse[1], C.J. Van Munsteren[1], M.M. Bartelings[1], R.E. Poelmann[1], P. Carmeliet[3], A.C. Gittenberger-De Groot[1]. *[1]Leiden University Medical Center, Anatomy And Embryology, Leiden, Netherlands; [2]Maastricht University, Physiology, CARIM, Maastricht, Netherlands; [3]University Leuven, Center for Transgene Technology &Gene Therapy, Leuven, Belgium*

Purpose: In this research we explored developmental processes that lead to outflow tract abnormalities by making use of Vegf120/120 mouse embryos, which have earlier been described to be susceptible to the development of cardiac malformations1. Although genetic heterogeneity and mutations of genes involved in VEGF-signalling in both humans and mouse models relate to a high susceptibility to develop outflow tract malformations such as Tetralogy of Fallot and peripheral pulmonary stenosis, the pathomorphogenesis is unknown.
Methods: We used immunohistochemistry, in situ hybridisation, RT-qPCR and 3D-reconstruction techniques on embryonic hearts, to compare Vegf120/120 embryos ranging in age from E10.5 to E19.5 with wild type littermates.
Results: We have shown spatiotemporal increase and abnormal patterning of Vegf/VEGF/(phosphorylated) VEGFR-2, (cleaved) Notch1 and Jagged2 in the outflow tract of Vegf120/120 mouse embryos. These alterations in expression patterns coincide with hyperplasia of specifically the outflow tract cushions and a high degree of subpulmonary myocardial apoptosis (dotted area in right figure) that, in later stages, manifest as pulmonary stenosis and ventricular septal defects.
Conclusions: We postulate that increase of VEGF- and Notch-signalling during right ventricular outflow tract development can lead to abnormal development of both cushion and myocardial structures. Defective right ventricular outflow tract development as presented provides new insight in the etiology of Tetralogy of Fallot.
Reference: 1. Stalmans,I. et al. VEGF: a modifier of the del22q11 (DiGeorge) syndrome? Nat. Med. 9, 173-182 (2003).



Apoptotic myocardium at E12.5

1087 A study of humoral immunity in children with cyanotic congenital heart disease

O.A. Elmasry, S.R. Youssef. *Ain Shams University Faculty of Medicine, Pediatric, Cairo, Egypt*

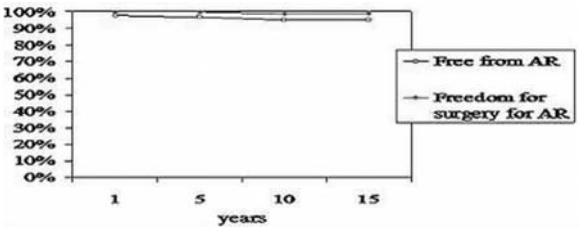
Children with congenital heart disease (CHD) are susceptible to serious infections and demonstrate high morbidity and mortality from respiratory tract infections.
We aimed to assess CD19 lymphocyte subpopulations and immunoglobulin G (IgG) levels, and their relationship to T-cell receptor αβ positive (TcRαβ+ve) lymphocyte subpopulations and oxygen saturation, in these children.
Methods: 25 children with cyanotic CHD and 10 healthy age- and sex-matched children underwent clinical assessment, echocardiographic examination and measurement of oxygen saturation by pulse oximetry (SpO2). CD19 and TcRαβ+ve lymphocyte subpopulations were enumerated by flow cytometry and serum IgG concentrations were measured by immunoturbidimetry.
Results: Patients had significantly lower percent of lymphocytes [(41.8±13.76%) vs.(58.7±23.66%) ($p<0.05$)], absolute lymphocyte counts [(4360±2399.7 cells/μL) vs. (7195±2648.8 cells/μL) ($p<0.01$)], absolute CD19 lymphocyte counts [(515±688.41 cell/μL) vs. (1096±588.95 cell/μL) ($p<0.01$)] and absolute TcRαβ+ve lymphocyte counts [(1721±1405.44 cells/μL) vs. (3666±2160.99 cells/μL) ($p<0.01$)] than controls. IgG levels were not significantly decreased in patients. There was no significant correlation between SpO_2 and any of the lymphocyte parameters or the IgG level. A highly significant positive correlation was found between the absolute TcRαβ+ve lymphocyte count and the absolute CD19 lymphocyte count in the patient group($p<0.01$). Patients with decreased absolute CD19 lymphocyte count for age had significantly lower absolute lymphocyte counts [(3374±1866.17 cells/μL) vs. (5270±2540.64 cells/μL) ($p<0.05$)], percent of TcRαβ+ve lymphocytes[(19.6±18.88%) vs. (50.9±12.96%) ($p<0.001$)], absolute TcRαβ+ve lymphocyte counts [(770±954.48 cells/μL) vs. (2599±1173.1 cells/μL) ($p<0.001$)], and IgG levels [(777.5±493.52 mg/dl) vs. (1303.7±627.07 mg/dl) ($p<0.05$)] than those with normal CD19 lymphocyte count. The only predictive variable for decreased absolute CD19 lymphocyte count was the absolute count of TcRαβ+ve lymphocytes (beta: 0.845; p=0.013).
Conclusion: Children with cyanotic CHD demonstrate decreased humoral immunity that is not related to the degree of desaturation, is not manifest as an IgG deficiency, and probably reflects an underlying cellular immune defect. They can be classified immunologically according to the adequacy of their absolute CD19 lymphocyte count for age. Immunological evaluation of children with cyanotic CHD is recommended as several immune defects are now amenable to treatment.

1088 Prevalence and predictors of neoaortic regurgitation following Arterial Switch Operation

Q. Ferrer Menduina[1], F.G. Gran[2], B.M. Manso[1], G.G. Giralt[1], J.C. Casaldaliga[1], P.B. Betrian[1], J.M.G. Gil-Jaurena[1], L.M. Miro[1], A.G. Gonzalves[1], J.G.C. Girona[1]. *[1]Hospital Universitari Vall D'hebron, Pediatric Cardiology Unit, Barcelona, Spain; [2]Barcelona, Spain*

Purpose: Concerns regarding neoaortic regurgitation (AR) following arterial switch operation (ASO) have been raised. The objective of this study is to determine the prevalence of AR after ASO for Transposition of the Great Arteries (TGA) at long-term follow-up and to identify risk factors for late AR.
Methods: Between 1991 and 2006, 198 patients underwent ASO for TGA with intact ventricular septum or ventricular septal defect (VSD) including Double-outlet right ventricle (DORV). We retrospectively reviewed the files of all hospital survivors (174). We analyzed: weight at surgery (3505g ± 1143); associated malformations: VSD (33%), aortic coarctation (7%), DORV (6%) and subpulmonary stenosis (2%); previous pulmonary artery banding and/or Blalock-Taussig shunt (7%); surgery for associated lesions at the time of ASO (39%); anatomical features: bicuspid pulmonary (neoaortic) valve (7%), pulmonary/aortic ratio>1.5 (30%) and complex coronary pattern (12%).
Results: After a median follow-up of 9.4 years (one to 15 years) actuarial survival was 99%, 99%, 99% and 99% at 1,5,10 and 15 years respectively. Significant AR free survival was 98%,97%, 95% and 95% and freedom from surgery for AR and/or root dilation was 100%, 100%, 99% and 99% at 1, 5,10 and 15 years respectively. Univariate analysis identified pulmonary/aortic ratio>1,5, previous banding, complex coronay pattern and presence of VSD as risk factors for AR (62% patients with VSD had a pulmonary/aortic ratio>1,5 p1,5 (p 0.029) and previous banding (p 0.04) remain significative at the multivariate analysis.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020



Free of AR and free of surgery for AR

Conclusions: The prevalence of late AR after ASO is 5%. Aortic-Pulmonary mismatch and previous banding are strong predictors for AR. VSD is highly associated with pulmonary/aortic ratio>1,5 but it's not an independent risk factor.

1089 Management of children without preexcitation syndrome, but complaining of tachycardia

B. Brembilla-Perrot[1], O. Huttin[2], O. Yangni N'da[1], C. Tatar[1], F. Chometon[1], F. Duhoux[1], N. Zhang[1], J. Cedano[1], P. Admant[1], F. Marcon[1]. [1]*Chu De Brabois, Departement De Cardiologie, Vandoeuvre Les Nancy, France;* [2]*Vandoeuvre Les Nancy, France*

The purpose of study was to report the results of transesophageal electrophysiological study in children complaining of tachycardia, but with normal non-invasive studies. Symptoms are often difficult to interpret in children. In those complaining of tachycardias with abrupt beginning, non-invasive studies are frequently negative and the management of these children is debatable.
Methods: 62 children and teenagers aged 7 to 19 years (mean 15±3), 29 boys, 33 girls were consecutively recruited for possible paroxysmal junctional tachycardia (PJT). Tachycardias were not documented. The ECG was normal and a Wolff-Parkinson-White syndrome was excluded. Holter monitoring and exercise testing were negative and echocardiogram was normal; 18 children had dizziness or syncope associated with tachycardias. Transesophageal electrophysiological study (EPS) was performed in the non sedated state during a consultation and consisted of atrial pacing up to 2nd d AV block, programmed atrial stimulation with 1 and 2 extrastimuli in control state and after isoproterenol.
Results: EPS was performed in all children but one with syncope. The mean time of study was 19±5 min. Radiation was not used. EPS remained negative in 17 children, 6 boys, 11 girls aged 7 to 19 years (mean 15±3); 7 of them have syncope. AV nodal re-entrant tachycardia (AVNRT) was induced in 36 children; 10 of them had syncope. A re-entrant tachycardia in a concealed accessory pathway was induced in 7 children without syncope. Verapamil-sensitive ventricular tachycardia was induced in one 16 year-old boy. Age, sex or presence or syncope were not significant predictors of the induction of a tachycardia. During a mean follow-up of 3±1 years, none child with a negative study developed documented tachycardia. Catheter ablation of slow pathway or accessory pathway was required in 10 children with inducible PJT. Remaining children are free of tachycardia, but 10 of them had beta-blockers or antiarrhythmic drugs.
Conclusion: Transesophageal EPS was a rapid and low-cost method to prove the nature of paroxysmal tachycardia in children and teenagers with a normal ECG. A tachycardia was induced in 72% of them. AVNRT was the most frequent tachycardia. There was no significant clinical predictor of the induction of a tachycardia. When the study was negative, a paroxysmal junctional tachycardia can be excluded.

1090 Pharmacokinetics and safety profile of a novel formulation of bosentan in children with pulmonary arterial hypertension (PAH): FUTURE-1 study

M. Beghetti[1], S.G. Haworth[2], R.J. Barst[3], X. Jais[4], P. Acar[5], A. Fraisse[6], D. Ivy[7], I. Schulze-Neick[8], D. Bonnet[9], R.M.F. Berger[10]. [1]*Geneva, Switzerland;* [2]*London, United Kingdom;* [3]*New York, United States of America;* [4]*Clamart, France;* [5]*Toulouse, France;* [6]*Marseille, France;* [7]*Denver, United States of America;* [8]*Berlin, Germany;* [9]*Paris, France;* [10]*Groningen, Netherlands*

Purpose: 2 non-controlled paediatric studies suggest that bosentan (BOS) is effective for treatment of PAH in children. FUTURE-1 was designed to evaluate the pharmacokinetics (PK) of a new paediatric oral formulation of BOS in children with PAH and to compare it to that of adult PAH patients (pts) from a previous study. Paediatric data are reported.
Methods: Children with idiopathic PAH (IPAH) or familial PAH (FPAH), 2-12 years were enrolled in this open-label, multicentre study. Pts were treated with the new BOS oral, dispersible, quadrisected, paediatric formulation: 2 mg/kg BID x 4 weeks (wks), then 4 mg/kg BID until wk 12. Primary endpoint: exposure (AUCtau) to BOS at wk 12. Secondary endpoints: Cmax and tmax. In 11 pts the PK of BOS were evaluated after 2 and 4 mg/kg. Safety and tolerability were assessed.
Results: 36 pts were enrolled: 31 IPAH/5 FPAH; 21 male; mean age 6.8 years; mean weight 22.3 kg; functional class II/III: 64%/36%. 14 pts changed from the adult formulation to the paediatric formulation. No pts were down-titrated. 1 pt was excluded due to protocol violation. PK parameters are shown in Table 1.

Table 1: Bosentan PK at 12 weeks

	n	AUCtau (ng·h/mL) geomean (%CV)	Cmax (ng/mL) geomean (%CV)	tmax (h) median (range)
Bosentan (BOS)				
4 mg/kg BOS	35	4383 (78)	895 (82)	3.0 (0.0-8.5)
4 mg/kg BOS	11	3371 (58)	649 (61)	3.0 (0.0-7.5)
2 mg/kg BOS	11	3577 (74)	583 (86)	3.0 (1.0-7.5)

Preliminary data suggest that the covariates gender, WHO class, epoprostenol, and prior BOS treatment had no effect on BOS PK. Safety was similar to that reported previously. Most frequently reported adverse events were respiratory tract infections (n=10) and gastrointestinal disorders (n=9). There were no elevated liver aminotransferases >3xULN. 1 pt discontinued (withdrawal of consent). 1 death occurred (unrelated to study drug).
Conclusions: In this first PK characterisation of a novel oral paediatric formulation of BOS in children with PAH exposure was similar after dosing with 2 and 4 mg/kg indicating non-linear PK. BOS was well tolerated. The long-term safety will be further studied in the FUTURE-2 extension study.

HOT TOPICS IN ADULT CONGENITAL HEART DISEASE

1091 Maternal outcome in women with heart disease - a UK single centre experience at University College London Hospitals NHS Trust

R. Brooks[1], P. O'brien[2], S. Abdin[1], D. Peebles[1], R. Bell[1], F. Walker[2] on behalf of The high-risk cardiac pregnancy service, UCLH. [1]*The Heart Hospital, The Guch Department, London, United Kingdom;* [2]*Elizabeth Garret Anderson Hospital, Department of Obstetrics & Gynaecology, London, United Kingdom*

Purpose: With improved survival of those born with congenital and inherited heart disease, the prevalence and complexity of maternal heart disease is increasing. Congenital heart disorders (CHD) are now more common in pregnancy than acquired heart diseases (Incidence 0.8% v's 0.1%), which means pregnancy care for these women requires specialist cardiology input. It is likely that the numbers requring such specialist antenatal care (ANC) are going to increase further in the next decade, with an estimated 166,000 adults with CHD in the UK by 2010, 15000 of whom will have complex lesions.
Aim: To review experience of an ANC service for women with complex heart disease and report maternal complication and outcome.
Methods: The Obstetric Cardiac Database (OCDB) at the Heart Hospital, UCLH, was analysed. Patients who had completed pregnancy between Sept 1st 2003 - Sept 1st 2006 were identified. Demographics, including New York Heart Association (NYHA) functional class, cardiac lesion complexity (as per the European Society of Cardiology [ESC] definitions), maternal cardiac events and overall outcome were recorded.
Results: There were 208 completed pregnancies in 191 women (age range 17.9 yrs - 39.9 yrs). Lesion complexity; Simple n=78 (41%), moderately complex n=77 (40%) and highly complex n=36 (19%). NYHA functional class pre-pregnancy, I (92, 47%), II (97, 51%), III (1, 1%), IV (1, 1%). Maternal cardiac events were defined as new onset of heart failure (HF) n=23 (12%), arrhythmias (ARR) n=2 (1%), thromboembolic event (TE) n=1 (0.5%), or death n=2 (1%). HF, was gradual in onset in 21, and had been prior predicted during pre-conceptual work-up. It was detected early and successfully medically treated in all cases. Two patients presented in acute pulmonary oedema, one secondary to mechanical mitral valve thrombosis and the other referred at 36 weeks gestation with undiagnosed severe mitral stenosis. There were 2 maternal deaths, one direct obstetric death and the other secondary to aortic dissection in a patient with Marfan syndrome and normal root measurements.
Conclusion: The majority of women having ANC at UCLH have moderate or highly complex heart disease, however the maternal cardiac event rate is low especially if subdivided into predicted events (n=23) (12%) and non-predicted events (n=3) (2%). Maternal mortality is also low at 1%. A good maternal outcome without complications was achieved in the majority (88%) thanks to prior planning and specialist multi-disciplinary ANC.

1092 Predictors of pregnancy-related cardiac, obstetric and neonatal complications in women with congenital heart disease

W. Drenthen[1], J.W. Roos-Hesselink[2], K. Van Der Tuuk[2], B.J.M. Mulder[3], A.P.J. Van Dijk[4], H.W. Vliegen[5], S.C. Yap[2], P. Moons[6], P.G. Pieper[6], D.J. Van Veldhuisen[6] on behalf of ZAHARA investigators. [1]*University Medical Center Groningen, Cardiology Dept., Groningen, Netherlands;* [2]*ErasmusMC, Rotterdam, Netherlands;* [3]*AMC, Amsterdam, Netherlands;* [4]*St RadboudMC, Nijmegen, Netherlands;* [5]*LUMC, Leiden, Netherlands;* [6]*University Hospitals Leuven, Leuven, Belgium*

Background: Pregnancy in women with congenital heart disease (CHD) is associated with significant cardiac, obstetric and neonatal complications. The available risk score (Siu 2001) identifying patients at higher risk has its limitations due to the incorporation of patients with acquired and primarily electrical heart disease.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Purpose: To identify predictors of pregnancy-related complications in CHD patients and modify the available risk score.
Patients and Methods: Using two registries, 1802 (82%) of 2196 identified adult female CHD patients provided consent and reported 1302 completed (>20 weeks) gestations. Per composite endpoint (cardiac, obstetric and neonatal complications) separately, independent predictors were identified using multivariable logistic regression (GEE) analysis.
Results: A history of arrhythmia (p=0.0011), cyanotic heart disease (p<0.0001) or mechanical valve replacement (p=0.0014), NYHA functional class prior to pregnancy (p=0.03), left ventricular outflow tract obstruction (p<0.0001), systemic (p=0.04) or pulmonary atrio-ventricular valve regurgitation (p=0.03) and the use of cardiac medication (p<0.0001) independently predicted maternal cardiac complications. No predictors of obstetric complications were identified. A history of arrhythmia (p=0.05), cyanotic heart disease (p=0.0003) or mechanical valve replacement (p=0.03), maternal smoking during pregnancy (p=0.007), the presence of a multiple gestation (p=0.0014) and the use of cardiac medication (p=0.0009) proved to be independent predictors of neonatal outcome. A modified risk score of cardiac and neonatal events incorporating these (new) predictors was validated.
Conclusion: In this large CHD cohort, predictors of adverse cardiac and neonatal pregnancy outcome were identified. These (new) predictors were incorporated into a modified risk score identifying patients at higher risk for adverse outcome.

1093 Heart transplantation in adolescent and adult patients with congenital heart disease: a case-control study

M. Greutmann[1], R. Pretre[2], U. Bauersfeld[3], M. Turina[2], M. Genoni[2], G. Noll[1], P. Trigo Trindade[1]. [1]*Cardiology, University Hospital, Internal Medicine, Zurich, Switzerland;* [2]*Cardiovascular Surgery, University Hospital, Cardiovascular Surgery, Zurich, Switzerland;* [3]*Pediatric Cardiology, University Children's Hospital, Zurich, Switzerland*

Background: Orthotopic heart transplantation (HTPL) is an accepted and successful treatment for patients (pts) with end-stage heart failure. The majority of adult pts undergoing HTPL suffer from dilated or ischemic cardiomyopathy. However, the number of adolescent and adult pts with congenital heart disease (CHD) undergoing HTPL is increasing. The outcome of this last group of pts has not been well defined.
Methods: We performed a case-control-study in 13 pts undergoing HTPL due to CHD comparing their outcome with a control group of 18 pts with dilated cardiomyopathy (DCM). Pts were matched for age, gender and the year of transplantation (±1 year).
Patient and procedural characteristics: Thirteen pts (mean age 27.5 yrs; range 13.7-52 yrs) with CHD underwent HTPL since the beginning of the HTPL program at our institution in 1985. Nine pts had transposition complexes, 2 pts tricuspid atresia, 1 pt mitral atresia and 1 pt a single ventricle.Ten pts (77%) had previous open-heart surgery and in 8 pts two or even more open-heart surgeries had been performed. At the time of transplantation 8 pts presented with single-ventricle-physiology and 4 pts required major reconstructive surgery. The pt group with CHD was compared with 18 matched pts (mean age 28.1 yrs; range11.3-57.9 yrs) with DCM.
Results: The short-term survival in the 2 groups was 85% and 94% respectively at 30 days. In the CHD group 2 pts died in the first 30 days, one due to acute rejection and the other of right ventricular failure. A third pt died after 10.6 yrs because of metastatic spinocellular carcinoma. The mean survival in the CHD group was 11.5 yrs, whereas in the DCM group the mean survival was only 9.5 yrs. The causes for death in the DCM group were acute rejection (1pt), graft failure (1pt), severe graft atherosclerosis (1pt), liver failure (1pt) and malignancies (4pts). The cumulative rate of graft atherosclerosis amounted to 38% in the CHD group and 33% in the DCM group.
Conclusion: HTPL is a good therapeutic option in adolescent and adult patients born with CHD and in end-stage heart failure. Although a higher perioperative morbidity and mortality is anticipated in pts with CHD due to previous open-heart surgery short term survival is satisfactory. Furthermore, in our experience long-term survival of CHD patients after HTPL compares favourably with long-term survival of transplanted patients with DCM.

1094 Is coarctation of the aorta an independent risk factor for ascending aorta complications in patients with bicuspid aortic valve?

P. Gallego Garcia De Vinuesa[1], R. Alonso Gonzalez[2], A. Gonzalez Garcia[2], C. Iborra[2], A. Sanchez-Recalde[2], A. Aroca[2], J.M. Oliver[2]. [1]*Sevilla, Spain;* [2]*Adult Congenital Heart Disease Hosp. La Paz, Madrid, Spain*

Background: Association of bicuspid aortic valve (BAV) and ascending aortic complications has been known and confirmed in many reports. Recent studies have also shown a higher incidence of aortic complications in BAV with coexistent coarctation of the aorta (CA). However, whether CA is an independent risk factor for ascending aortic complications has not been well defined yet.
Methods: An ascending aorta complication was diagnosed when one of the following criteria were present: aortic dilatation of a diameter > 55 mm; dissection; acute rupture resulting in sudden death or rupture of a sinus of Valsalva aneurysm. 652 patients with a BAV (mean age 38 + 18; 69% male) were analysed. A coexistent CA was present in 143 (22%). 363 out of the 652 (118 with a CA) were followed-up for a period superior to one year [median 8 years, 25th and 75th percentiles 4.1 and 12.5 years respectively]. Incidence of aortic complications in the whole group and over the follow-up period in patients with and without a coexistent CA were analysed.
Results: A total of twenty-seven aortic complications were found among 652 BAV (4.1%): an ascending aortic aneurysm of a diameter > 55 mm, 19; aortic dissection, 6; ruptured sinus of Valsalva aneurysm, 1; aortic rupture resulting in sudden death, 1. Eleven out of the 27 patients with an aortic complication had a coexistent CA (7.7%) vs. 16 without CA (3.1%) p<0.02. 13 patients had an aortic complication at first examination and 14 patients had a complication at follow-up: 8 with CA (6.8%) and 6 without CA (2.4%, p<0.05).
Conclusions: In patients with a bicuspid aortic valve there is a higher incidence of ascending aortic complications when a coarctation of the aorta coexists. In many cases, an aortic complications is the clinical presentation. However, the incidence of aortic complications at follow-up in patients with a BAV without a coexistent CA is very low.

1095 The impact of cusps fusion orientation in patients with bicuspid aortic valve on ascending aortic wall mechanics. A Tissue Doppler Imaging study

M. Kalinowski[1], M. Szulik[1], T. Niklewski[1], B. Dziobek[1], W. Streb[1], J. Nowak[1], M. Kukla[2], Z. Kalarus[2], T. Kukulski[2]. [1]*Silesian Center for Heart Disease, Zabrze, Poland;* [2]*Silesian Academy of Medicine, Department of Physiology, Zabrze, Poland*

The hemodynamic consequences of bicuspid aortic valve (BAV) could be related to the type of cusps fusion orientation, which influence the progression of ascending aorta dilatation and subsequent fatal complications.
Aim Of The Study: To determine the differences in mechanical properties of both anterior and posterior wall of ascending aorta (AA) in BAV patients (pts) with various types of cusps fusion orientation using tissue doppler imaging (TDI).
Methods: The study group consisted of 30 pts with BAV and 28 healthy pts with tricuspid aortic valve (normals). BAV group was divided into gr I (N+R, n=16) with noncoronary (NCC) and right coronary cusps (RCC) fused and gr II (L+R, n=14) with left coronary (LCC) and RCC fused. The groups I and II were sex and age matched with comparable LV outflow tract diameter: 23,5±8,8 vs 25,7±4,9 mm (p=ns), aortic valve maximal gradient: 14±4,6 vs 18±7,4 mmHg (p=ns). Velocity profiles were derived from colour tissue doppler data set collected in long axis parasternal view that were suitable for both anterior (ant) and posterior (post) AA wall analysis. The evaluated parameters were: peak systolic velocity [m/s] (VEL) and systolic velocity acceleration [m/s2] (ACC).
Results: L+R cusps fusion type compared with N+R and normal group is associated with higher VEL and ACC of aortic walls. Results are presented in table I.

Table I. Cusps fusion and TDI of aorta

	ACC ant [m/s2]	ACC post [m/s2]	VEL ant [m/s]	VEL post [m/s]
gr I	1,02±0,27	0,69±0,3	0,044±0,012	0,033±0,012
gr II	1,59±0,9	1,37±0,7	0,064±0,029	0,05±0,02
Normals	1,13±0,41	1,01±0,4	0,042±0,01	0,035±0,013
p gr I vs gr II	<0,05	<0,05	0,053 - ns	<0,05
p gr II vs normals	<0,05	0,07 - ns	<0,05	<0,05

N+R - noncoronary and right coronary cusp fusion, L+R - left coronary and right coronary cusp fusion, ACC - acceleration of aortic wall movement, VEL - peak velocity of aortic wall movement, ant - anterior wall, post - posterior wall.

Conclusion: The BAV cuspidal fusion orientation results in different blood flow distribution in the asccending aorta. The fusion of RCC and LCC unfavourably affects the mechanical properties of AA during ejection. AA wall velocity measurement by TDI is a feasible method to monitor disease progression in BAV patients.

1096 Microvolt T-wave alternans is related to ventricular tachycardia in adults with repaired tetralogy of fallot

O. Goktekin[1], Z. Kucukdurmaz[2], S. Babu-Narayan[2], T. Wong[2], M.G. Kaya[2], M.A. Vatankulu[2], Y.Y. Lam[2], P. Kilner[2], R. Sutton[2], M.A. Gatzoulis[2]. [1]*Osmangasi University, Faculty of Medicine, Dept of Cardiology, Eskisehir, Turkey;* [2]*Royal Bromton Hospital, Cardiology Department, London, United Kingdom*

Purpose: Microvolt T-wave alternans (MTWA) is a novel non-invasive method to identify patients at increased risk of cardiac arrest and sudden cardiac death from ventricular arrhythmias in ischemic heart disease and cardiomyopathies. Ventricular arrhythmia and sudden death are leading causes of morbidity and mortality late after repair of tetralogy of Fallot. We hypothesised that MTWA may related to the ventricular tachycardia (VT).
Method: Fifty-five patients with repaired ToF and freepulmonary regurgitation and 11 patients with ToF and documented VT were included study. Microvolt TWA was measured during submaximal treadmill exercise in all patients. Eight patients were excluded from the study because of poor electrocardiogram recordings with noise or frequent ectopic beats (n=4) and indeterminate result (n=4). As a result 58 patients (36 male, mean age, 35.3±12.2)including 9 patients with history of VT were evaluated for further analysis.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: MTWA was positive in 18 patients (31%) and negative in 40 patients (69%). Patients with VT were older than those without VT (45.14±13.4 versus 33.9±11.5 years, p=0.02). Age at first intervention (7.7±4.2 versus 4.4±5.3 years, p=0.2), age of repair (7±3.7 versus 5.7±5.6 years, p=0.1) or follow-up duration (34.5±2.7 years 28.2±8.2 versus p=0.09) were not significantly different between patients with and without VT. The sensitivity, specificity and negative predictive value of MTWA for VT were 66.6%, 75.5% and 92.5%, respectively. Patients with VT had more positive MTWA results than the ones without VT (6/9 (66%) versus 12/49 (24%) p=0.01). Patients with positive MTWA test had 6.1 times risk for having ventricular tachycardia (odds ratio 6.1, 95% CI 1.3 to 28.2). No significant relationship was found between presence of VT, maximal V_{alt} and onset heart rate in patients with positive TWA (7.4±2.8 versus 6.7±2.1 mV, p=0.6 and 104.4±6.1 versus 102.5±5.7 bpm, p=0.5, respectively)Conclusion: MTWA was relatively common and relate to a history of documented VT in adult patients with repaired tetralogy of Fallot. Therefore MTWA may emerge as a useful non-invasive tool to identify Fallot patients at risk for malignant arrhythmia. Further prospective studies are needed to evaluate the prognostic value of this test.

POSTER SESSION 2

MODERATED POSTERS 1: VALVE DISEASE: INTERVENTION AND SURGERY

P1118 Elective aortic valve repair for pure regurgitation: a tailored surgical approach to the individual pathology

L.L.A. De Kerchove, D. Glineur, A. Poncelet, R. Verhelst, J. Rubay, M. Van Dyck, J.L. Vanoverschelde, P.H. Noirhomme, G. El Khoury. *universite catholique de louvain, Cardiothoracic Surgery Dept., Brussel, Belgium*

Purpose: Pure aortic valve regurgitation has a variety of mechanisms related to leaflets and/or root pathology. Accurate recognition of the underlying mecanism(s) has allowed us to use a systematic and tailored patient-to-patient surgical approach for valve reconstruction.
Method: Between January 1996 and Jully 2006, 259 patients underwent aortic valve repair and/or sparing procedures at our Institution. Aortic annulus, root or ascending aorta dilatations were managed by following techniques: subcommissural annuloplasty, sinotubular junction plication, ascending aorta replacement, root remodelling or valve reimplantation into a graft. Cusp prolapses were corrected by plication, triangular resection or free margin shortening with PTFE (Goretex 7/0). Cusps perforation were closed with autologous pericardial patches.
Results: Hospital mortality was 1.5% (4 patients). Five (2%) patients needed early aortic valve reoperation, 2 of them were re-repaired. Follow-up is 94% complete and reach a mean of 45±32 months. During this period, 14 late deaths occurred, 10 cardiac related. Eleven patients needed late aortic valve reoperation, 2 of them were re-repaired. At 3 and 6 year, overall survival, freedom from aortic valve reoperation and freedom from aortic valve regurgitation >2 were 96±2% and 91±6%, 95±3% and 94±4%, 93±4% and 86±7% respectively. Thromboembolic events occurred in 6 (2.3%) patients during the follow-up and no aortic valve endocarditis were recorded.
Conclusion: In patients with pure aortic regurgitation, systematic and individually tailored approach may allow cardiac surgeon to achieve a safe and durable aortic valve repair with low valve related morbidity and mortality.

P1119 Are there gender differences in clinical presentation and surgical outcome of aortic stenosis?

C. Fuchs, R. Rosenhek, J. Mascherbauer, F. Rader, U. Klaar, C. Scholten, M. Heger, G. Maurer, H. Baumgartner. *Medical University of Vienna, Departement of Cardiology, Vienna, Austria*

Background: Aortic stenosis (AS) has become the most frequent valve disease and has extensively been studied in recent years. Although gender differences have gained increasing attention in cardiolgy, little is known about gender differences in presentation and surgical outcome of AS so far.
Methods: In 408 consecutive patients referred to surgery because of symptomatic AS baseline clinical and echocardiographic data as well as outcome data were analyzed with regard to potential gender differences.
Results: Patients were almost equally distributed between men (n=193) and women (n=215). At presentation, female patients were significantly older (73.7±9.3 vs. 66.5±11.5 years; p<0,00001) and more symptomatic (NYHA class 2.3±0.7 vs. 2.0±0.7; p<0.0001). They also had smaller valve areas and after adjusting for body surface area this difference still remained statistically significant (0.32±0.09 vs. 0.34±0.08 cm^2/m^2; p=0.03). Nevertheless, mean gradients were significantly higher in females (67.2±19.1 versus 62.1±20.2 mmHg, p=0.02). Despite the higher risk profile, there was a trend towards better survival in women (hospital mortality 7.3% vs. 8.6%; p=0.7 and long term mortality 14.4% vs. 15.6%; p= 0.2). Overall survival as estimated by Kaplan Meier analysis tended to be slightly better in women (89.1%, 86.6%, 76.3% versus 92.8%, 89.8%, 81.4% at 1-, 2- and 5 years) but this difference did not reach statistical significance (p= 0.3). Despite improvement in both groups after surgery, women remained more symptomatic than men (NYHA class 1.3±0.5 vs. 1.1 ±0.4 (p=0.00002).
Conclusion: Although women with AS are older and more symptomatic than men when referred to surgery, operative and longterm mortality are not different. However, women remain more symptomatic. Further research must address whether differences in baseline characteristics are due to differences in disease onset and progression or whether female patients get delayed medical attention for some reasons.

P1120 Lack of significant deleterious effects of patient-prosthesis mismatch after aortic valve replacement in a consecutive series

J. Radojevic, H. Petit-Eisenmann, M. Kindo, B. Eisenmann. *University Hospital, Bas-Rhin, Strasbourg, France*

Objectives: To determine whether aortic patient-prosthesis mismatch (PPM) has any significant impact on survival, functional recovery and left ventricular remodeling at mid-term follow up.
Methods: 130 consecutive patients operated during 2001-2002 for severe isolated aortic stenosis were included;mean age 73,1±8,3 years.A mechanical prosthesis was implanted in 51 patients,a biological stented prosthesis in 79.The mean preoperative left ventricular ejection fraction (LVEF) was 63,6±13 p.cent;the mean left ventricular mass index (LVMI) was 132±40,7 g/m^2.The follow up was 44,3±13 months.Early and late mortality and NYHA functional class were recorded.Mean and maximal transprosthetic gradients,effective orifice area (EOA),LVMI and LVEF were measured by echocardiography.The early postoperative PPM was determined by using reference normal values of EOA;during follow up the EOA was calculated by the continuity equation from echocardiographic data.An indexed EOAi<0,85cm^2/m^2 was considered as the threshold for PPM; PPM was defined as severe if EOAi was < 0,65 cm^2/m^2 and as moderate for EOAi between those values.
Results: The overall in-hospital mortality was 0,9 p.cent (1/130 patients).There were 24 late deaths (19,2 p.cent).Four patients (3,1 p.cent) were lost from follow up.The prevalence of early PPM was 54,6 p.cent (71/130 patients); 45,3 p.cent moderate and 9,2 p.cent severe. The prevalence of late PPM was 66,6 p.cent (52/78 patients);26,9 p.cent moderate and 39,7 p.cent severe.
Survival at 1 and 4 years (respectively 96 and 74 p.cent) were similar in both groups. No difference was found in NYHA functional class (p=0,23).In multivariate analysis PPM was not an independent predictor for in-hospital or late mortality, for persistence of symptoms or non-regression of left ventricular hypertrophy.

Echocardiographic follow-up data

	Group A = Severe PPM (n=31)	Group B = Moderate PPM (n=21)	GroupC = No PPM (n=26)	p A vs C	p B vs C
Gm (mmHg)	21.15 (±7.49)	15.50 (±4.54)	11.12 (±4.92)	<0.001**	<0.001**
LVMI (g/m^2)	121.64 (±32.61)	114.33 (±34.88)	104.61 (±37.62)	0.076	0.104
LVEF (%)	70.48 (±7.16)	68.47 (±10.51)	66.68 (±10.85)	0.102	0.536

Gm: mean transprosthetic gradient; LVEF: left ventricular ejection fraction; LVMI: left ventricular mass index.

Conclusions: In this study even severe PPM had no impact on mortality,functional status and left ventricular remodeling after aortic valve replacement in the older population at mid-terme follow up.

P1121 Prognostic factors of prosthetic valve endocarditis that requires urgent surgery

A. Revilla Orodea[1], J. Lopez Diaz[1], I. Vilacosta[2], C. Sarria[3], E. Villacorta Arguelles[2], I. Gomez Salvador[2], M.C. Manzano[1], S. Florez[2], M.J. Rollan[4], J.A. San Roman Calvar[2]. *[1]Hospital Clinico Universitario, Cardiology, Valladolid, Spain; [2]Hospital Clinico San Carlos, Cardiology, Madrid, Spain; [3]Hospital La Princesa, Internal Medicine, Madrid, Spain; [4]Hospital Rio Hortega, Cardiology, Valladolid, Spain*

Purpose: Despite major advances in cardiovascular surgical techniques and routine use of prophylactic antimicrobial agents, prosthetic valve endocarditis continues to complicate the course of a small percentage of patients after cardiac valve replacement. The prognosis of these patients is poor, and urgent surgery is needed in many cases because of the development of cardiac and extracardiac complications. Our aims are to describe the clinical, microbiological, echocardiographic and evolutive profile of patients with prosthetic valve endocarditis who need urgent surgery and to determine the risk factors of in-hospital mortality.
Methods: Among 195 episodes of prosthetic valve endocarditis consecutively diagnosed at 3 tertiary centres between 1996 and 2005, 48 (25%) needed urgent surgery and made up our study group. We have described their main characteristics and performed a logistic regression model to determine the prognostic factors of this entity.
Results: Mean age was 60±12 and 59% were male. Clinical manifestations on admission were fever (72%), heart failure (46%), stroke (15%), renal failure (9%) and septic shock (2%). Infection affected mechanical prosthesis in 86% (mitral 48%, aortic 38%) and mitral bioprosthesis in 14%. Endocarditis was multivalvular in 8 patients. The most frequent causal microorganisms were coagulase-negative Staphylococci (28%) and Staphylococcus aureus (20%). A high proportion of patients (22%) had negative blood cultures. In most patients (80%), vegetations were observed on transoesophageal echocardiogram. Perivalvular com-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

plications (58%) and moderate or severe valvular insufficiency (56%) were common echocardiographic findings. The most frequent reasons for urgent surgery were heart failure (50%), persistent infection (32%) and perivalvular complications (13%). In-hospital mortality was 41%. By univariate analysis, factors associated with higher mortality were fever on admission (p=0.004), positive blood cultures (p=0.002), persistent positive blood cultures after 48 hours of antibiotic treatment (p=0.022), vegetations on transoesophageal echocardiography (p=0.006) and persistent infection (p=0.001). Heart failure on admission or developed during hospitalization was a "protective" factor (p=0.014). By multivariate analysis, only persistent infection was associated with poor prognosis (OR 6.6, IC 95% 1.5-29).
Conclusions: Prosthetic valve endocarditis is a devastating disease which frequently needs urgent surgery. It bears a very high mortality, especially in patients with persistent infection. By contrast, heart failure is not associated with a higher mortality.

P1122 Late functional results after percutaneous mitral commissurotomy: does commissural opening matter?

J. Blanc[1], D. Messika-Zeitoun[2], B. Iung[1], E. Brochet[1], B. Cormier[1], D. Himbert[1], A. Vahanian[1]. *[1]AP-HP, Bichat Hospital, Paris, France; [2]AP-HP, Hopital Bichat, Cardiology, Paris, France*

Background: Commissural opening is the main mechanism by which mitral valve area (MVA) increases after percutaneous mitral commissurotomy (PMC) but its specific prognostic impact on long term functional results has never been evaluated.
Methods: We evaluated the outcome of 875 patients (48±13 years, 83% female) with mitral stenosis and good immediate results of PMC (mitral valve area ≥1.5 cm^2 and no regurgitation >2/4). Good functional result was defined as survival without need for mitral surgery or repeat dilatation and NYHA functional class I or II at most recent follow-up. The 875 patients were divided into three groups: group 1 (N=189) if both commissures were neither split or only partially opened, group 2 (N=459) if only one commissure was completely split and group 3 (N=227) if both commissures were completely split. The prognostic impact of commissural opening was evaluated using a multivariate Cox model including 7 previously identified predictive factors of poor functional results: old age, high NYHA functional class, unfavorable mitral valve anatomy, atrial fibrillation, low post-procedure MVA, high post-procedure mean gradient, and grade 2 post-procedure mitral regurgitation.
Results: Immediately after PMC, there were significant differences between the three groups as regards to mean gradient (5.1±2.1 mmHg in group 1, 4.5±1.7 mmHg in group 2 and 4.0±1.6 mmHg in group 3, p<0.0001) and valve area (1.8±0.2 cm^2 in group 1, 1.9±0.2 cm^2 in group 2 and 2.1±0.3 cm^2 in group 3; p<0.0001). Mean follow-up was 55±28 months. Ten-year rates of good functional results were significantly different between the three groups: 39±8% in group 1, 57±11% in group 2 and 76±5% in group 3 (p<0.0001). However, in multivariate analysis, commissural opening did not emerge as an independent predictive factor of good functional results (p=0.76). Nevertheless, when MVA was excluded from the multivariate analysis commissural opening was a significant predictor of good functional results (p<0.05).
Conclusions: Complete commissural opening is associated with larger MVA and smaller mean gradients and functional improvement. However, it does not provide an additional prognostic value in addition to MVA and mean gradient.

P1123 Late results of percutaneous balloon mitral commissurotomy (PBMC) in patients with restenosis after previous surgical commissurotomy

Z. Chmielak, M. Kruk, M. Demkow, M. Karcz, M. Klopotowski, M. Konka, L. Chojnowska, P. Hoffman, W. Ruzyllo. *National Institute of Cardiology, Warsaw, Poland*

Objectives: The aim of this study was to determine long-term results of patients (P) who underwent PBMC after previous surgical commissurotomy and to compare these P with those who were treated with PBMC as an initial procedure.
Methods and results: Between September 1998 and December 2005, 1380 P underwent PBMC in our institution: 198(14.3%) P (mean age 51.5±9.2 years, 88.4% female) with restenosis after surgical commissurotomy (group 1) and 1182(85.7%) P (mean age 49.2±9.5, 86.0% female) with "de novo" mitral stenosis (group 2). Baseline characteristics were similar for both groups.
Initial results: Good immediate results defined as mitral valve area (MVA) ≥1.5 cm^2 without mitral regurgitation >2/4 were obtained in 161(81.3%) P in group 1 and in 988(83.6%) P in group 2 (p ns). Complications: No deaths or technical failures were observed during PBMC.
Mean duration of follow-up was 8.2±6.4(0.5-18) years. The ten years event-free survival rate was 67.3% for group 1 versus 76.9% for group 2 (log-rank p=0.015). Cox regression analysis identified NYHA class (HR 1.4, p=0.005), age (HR 1.02, p=0.04), echocardiographic score (HR 1.3, p<0.0001), MVA after PBMC (HR 0.4, p<0.0001), gradient after PBMC (HR 1.05, p<0.0001), pulmonary artery systolic pressure after PBMC (HR 1.04, p<0.0001), mitral regurgitation after PBMC (1.4, p<0.0001), as independent predictors of event-free survival.
Conclusions: PBMC in patients with restenosis after surgery results in good immediate outcome. Long term results are inferior compared with "de novo" mitral stenosis but are satisfactory.

P1124 Predictors of postoperative improvement in the symptom status after mitral valve repair in patients with impaired left ventricular function

A. Chrustowicz, G. Simonis, T. Rauwolf, R.H. Strasser. *University of Technology, Cardiology, Dresden, Germany*

Aims: To assess the relation between postoperative improvement in heart failure symptoms and preoperative parameters in patients with depressed left ventricular function and severe mitral regurgitation
Methods: The association between preoperative characteristics and postoperative symptom status was analyzed in 60 patients with depressed left ventricular contractility that underwent isolated mitral valve surgery from 2002 to 2006. Mean age±SD was 67,8±7,6 years, 57% were men, preoperative NYHA class was 2,7±0,4, LVEF was 32,2±5,9%, left ventricular end diastolic diameter index (LVEDDi) 33±4,4 mm/m^2 and serum creatinin level 112±34 μmol/l. Preoperative rhythm was atrial fibrillation in 48% of the patients; 28% of the patients had ischemic cardiomyopathy and 38% had a previous admission for decompensation of heart failure. Concomitant tricuspid valve repair was performed in 67% of the patients. Postoperative mitral valve gradient was 3,6±1,1 mm.
Results: Postoperative improvement of the heart failure symptoms was documented in 63% of the patients while the symptom status remained stable in 31,6% during the first year following the operation. Postoperative progression of the heart failure symptoms occurred in 3 patients (5%). By logistic regression analysis, independently from all baseline characteristics, the probability for postoperative clinical improvement was significantly higher in patients with more advanced heart failure symptoms, ischemic cardiomyopathy, lower degree of left ventricular dilatation and lower serum creatinin level (table).

	B	S.E	Wald	p	Odds Ratio	95% CI for OR
NYHA	4,7	1,37	11,7	,001	111,2	7,5-1639
ICM	2,8	1,03	7,5	,006	17	2,2-128,3
LVEDDi	-,31	,10	9,1	,003	,73	,59-,89
Creatinin	-0,3	,01	4,9	,027	,97	,94-99
Constant	-1,3	3,38	,16	,681	,25	

Conclusions: In patients with severe mitral regurgitation and heart failure, surgical correction of the mitral insufficiency offer improvement in the quality of life. Preoperative NYHA class, ischemic cardiomyopathy, left ventricular dilatation and serum creatinin level are significantly associated with the postoperative symptom status.

P1125 Accuracy of real-time 3D echocardiography in assessing the anatomy of the mitral valve in patients undergoing surgery for severe degenerative mitral regurgitation

L.P. Badano, N. Pezzutto, D. Pavoni, M. Cinello, R. Marinigh, P. Gianfagna, P.M. Fioretti. *Az. Osp. Univ. S. Maria della Misericordia, Cardiopulmonary Sciences, Udine, Italy*

Background: Accurate preoperative assessment of mitral valve (MV) morphology and function is essential to predict the likelihood of surgical repair and to plan the most appropriate surgical approach (sternotomy vs miniinvasive). 2D transthoracic (2DE) and transesophageal echo require mental integration of all data about morphology of MV leaflets and have certain spatial limitations that may be overcome by real-time 3D echo (RT3DE).
Method: We compared 2DE and RT3DE reconstruction of MV anatomy with surgical findings in 61 consecutive pts (69±10 yrs, 57% males) undergoing surgery for severe degenerative mitral regurgitation. 3D volume rendered en-face views of the MV from the atrium and the ventricle were reconstructed offline unaware of 2DE and surgical findings. Surgical findings: involved MV leaflet (63% single posterior leaflet, and 11% single anterior leaflet), individual scallop involvement (48% isolated P2 and 11% isolated A2), chordal rupture (72%), and presence of flail leaflet (28%).
Results: 25 pts were excluded: 17 with atrial fibrillation and 8 with poor quality of volume rendered reconstruction (Feasibility= 59%). Diagnostic accuracy of 2DE and RT3DE in the remaining 36 pts is shown in the Table.

	2DE	RT3DE	p Value
Culprit leaflet	78%	96%	0.021
Involved Scallop	63%	93%	0.016
Flail leaflet	82%	85%	NS
Ruptured chordae	80%	67%	NS

Agreement with gross anatomy at surgical inspection.

2DE incorrectly classified 7 leaflets and 12 individual scallop involvements. 3DE incorrectly classified 2 leaflets and 3 individual scallop involvements. Accuracy of the 2 techniques was similar in the identification of lesions limited to a single leaflet and particularly when the involved scallop was P2. 3DE was more accurate in more complex MV lesions.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusions: RT3DE using a rendered en face atrial and ventricular views of the MV showed excellent concordance with surgical inspection in identifying the culprit leaflet and the involved scallops. Limited spatial resolution of RT3DE may explain the limited accuracy of the technique in identifying ruptured chordae. In addition, RT3DE provides easily interpretable images that facilitate communication with cardiac surgeons and non-echocardiographers.

MODERATED POSTERS 2: BASIC ASPECTS OF ATRIAL FIBRILLATION

P1127 Impact of MMP-2 levels on long-term results following pharmacological or electrical cardioversion in patients with atrial fibrillation

K. Kato[1], T. Yoshida[1], K. Yajima[1], T. Hibino[1], M. Oguri[1], S. Murai[1], K. Yokoi[1], T. Murohara[2]. *[1]Gifu Pref Govt Tajimi Hospital, Department of Cardiovascular Medicine, Tajimi, Japan; [2]Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan*

The issue on recurrence and persistence of atrial fibrillation (AF) after electrical or pharmacological cardioversion is still challenging to rhythm-control strategy. Identification of risk factors for refractory AF after cardioversion has a clinical importance to achieve more effective strategy. Matrix metalloproteinase-2 (MMP-2) is proposed as a key factor of structural remodeling in atria involving in the development of AF; however, the relationship of MMP-2 with persistence and recurrence of AF after electrical or pharmacological cardioversion is not fully understood. OBJECTIVE: We have performed a prospective study to determine the predicting factor and the relationship with MMP-2 for the long-term maintenance of sinus rhythm after cardioversion in patients with AF.
Methods: The study population comprised 61 (51men, aged 62.8±10.7) patients with persistent AF. Pharmacological cardioversion was administered for at least 3-mo period with class I anti-arrhythmic drug. Those who failed pharmacological treatments underwent electrical cardioversion (n= 20). Blood samples for MMP-2 and echocardiographic data were obtained before the treatment.
Results: Out of 61 patients, 26 patients (42.6%) were restored to normal sinus rhythm by pharmacological (n= 9) and electrical (n= 17) cardioversion and maintained it during observation period (SR group, 27.7±14.4 mo). The remaining 35 patients were classified to the refractory AF (RAF) group including relapse after electrical caridoversion (n= 14) and unsuccessful electrical or pharmacological cardioversion (n= 21) patients. Duration of AF and the prevalence of hypertension were significantly different between SR and RAF groups. Left atrial diameter and serum MMP-2 (884±233 versus 750±199 ng/ml, $P < 0.05$) in RAF group were significantly higher than those in SR group. The area under the receiver-operating characteristic curve for MMP-2 was 0.701 and the optimal cut-off value determined by analysis was 737 ng/ml with sensitivity of 74.2% and specificity of 69.6%. Multivariable logistic regression analyses and stepwise forward selection procedures after adjusting for clinical, echocardiographic, and laboratory data, revealed that MMP-2 levels above optimal cutt-off value were significantly associated with refractory AF as an independent risk factor.
Conclusions: Our study found that higher level of MMP-2 might be an independent risk factor for difficulty in maintaining sinus rhythm after electrical or pharmacological cardioversion. Stratification of subjects on the basis of MMP-2 may therefore be important to achieve effective management of AF.

P1128 Relation of atrial fibrillation to inflammation status, brain and N-terminal pro-brain natriuretic peptids levels, co-morbidity of diabetes mellitus and prognosis in chronic heart failure patients

A.B. Nargizyan, L.R. Tumasyan, K.G. Adamyan. *Institute of Cardiology, Department of Heart Failure, Yerevan, Armenia*

The aim of study was to assess relation of atrial fibrillation (AF) to levels of interleukin-6 (IL-6), high sensitivity C-reactive protein (hsCRP), brain natriuretic (BNP) and N-terminal pro-brain natriuretic peptides (NT-pro-BNP) and prognosis in pts with CHF of ischemic origin with and without type II diabetes mellitus (DM).
Methods: 26 pts with type II DM and 24 non-diabetic pts in sinus rhythm (SR), 22 pts with type II DM and 23 non-diabetic pts in AF with NYHA III-IV FC CHF were prospectively studied for an average 36±1.1 months. Serum levels of IL-6 (pg/ml) and hsCRP (ng/ml) were determined by ELISA. BNP and NT-pro-BNP levels (pg/ml) were assessed simultaneously.
Results: DM was significantly associated with higher 3-year mortality (50% vs. 39.1% and 42.3% vs. 33.3%) and hospitalization rate (86.4% vs. 69.6% and 80.8% vs. 58.3%) in pts with AF and SR, respectively ($p<0.05$ for all). In pts with AF the levels of IL-6 were at 63.7% ($p<0.01$) and 41.5% ($p<0.05$), hsCRP - at 71.6% ($p<0.01$) and 47.7% ($p<0.05$), BNP at 80.1% ($p<0.001$) and 50.2% ($p<0.01$) and NT-pro-BNP at 86.1% ($p<0.001$) and 51.6% ($p<0.01$) higher compared to pts in SR with and without DM, respectively. In a logistic regression analysis presence of DM with odd ratio (OR) of 3.3, levels of IL-6 (OR 2.5), hsCRP (OR 3.5), BNP (OR 5.4) and NT-pro-BNP (OR 5.2) were the significant predictors of AF. In AF pts with and without DM plasma BNP (adjusted HR 6.5 and 4.6, $p<0.01$), NT-pro-BNP (adjusted HR 6.9 and 4.8, $p<0.01$), serum IL-6 (adjusted HR 4.1 and 3.6, $p<0.05$) and hsCRP (adjusted HR 5.2 and 3.9, $p<0.05$) were independent determinants of cardiovascular morbidity and mortality.
In conclusions: 1) DM, markers of inflammation and BNP and NT-pro-BNP levels are strong independent risk factors for the presence of AF. 2) DM worsens the prognosis of CHF pts with both AF and SR. 3) Worst prognosis of pts with ischemic CHF with type II DM and AF seems to be related to more impaired inflammation status and neurohormonal imbalance compared to their non-diabetic counterparts.

P1129 Changes in numbers of proliferating cardiomyocytes and resident cardiac stem cells due to atrial fibrillation and ACE inhibitor therapy: immunohistological observations in human atrial myocardium

M.B. Arnold[1], A. Schuetz[1], V. Kufer[1], T. Fischlein[1], B. Reiter[2], H. Reichenspurner[1], A. Renz[2], W.G. Daniel[2], C.D. Garlichs[2]. *[1]University Hospital, Cardiology, Erlangen, Germany; [2]University Heart Center, Cardiovascular Surgery, Hamburg, Germany*

Background: Electrical und structural remodeling is part of the pathophysiology of atrial fibrillation (AF). ACE inhibitor therapy is said to have a beneficial effect on these alterations and therefore prevents atrial fibrillation. The purpose of our study was to investigate if atrial fibrillation leads to an increase in proliferative activity in atrial myocardium and to changes of resident cardiac stem cell (c-kit+CD34-CD45-) numbers in patients with or without ACE inhibitor therapy.
Methods: Atrial myocardium of 73 patients was examined by lightmicroscopy after immunohistochemical staining. Proliferating cardiomyocytes were indentified by their morphology and presence of Ki67 (a nuclear protein which is only expressed in cells actively undergoing the cell cycle). C-kit+CD34-CD45- cells were counted as resident cardiac progenitor cells. Cell numbers per area of examined myocardium of patients with or without atrial fibrillation and with or without ACE inhibitor therapy were compared.
Results: In patients with atrial fibrillation a significantly higher number of Ki67 positive cells was found (AF overall: $5,3\pm2,6*10^{-6}/\mu m^2$; AF and ACE-inhibitor: $6.9\pm3,0\ *10^{-6}/\mu m^2$; AF without ACE inhibitor: $4,8\pm2,1*10^{-6}/\mu m^2$) as compared to patients without atrial fibrillation (no AF: $3,6\pm1,9*10^{-6}/\mu m^2$; no AF with ACE inhibitor: $3,8\pm2,0*10^{-6}/\mu m^2$; no AF without ACE inhibitor $3,2\pm1,6*10^{-6}/\mu m^2$) (p=0,0097, p=0,0028, p=0,039). There was no difference in patients without atrial fibrillation with regard to ACE inhibitor therapy ($4,3\pm2,4*10^{-6}/\mu m^2$ vs. $3,6\pm2,0*10^{-6}/\mu m^2$). The number of c-kit+CD34-CD45- cells was significantly lower than the overall number of proliferating myocyctes independently from atrial fibrillation or ACE inhibitor therapy.
Summary: Atrial fibrillation is related to a higher proliferative activity of atrial cardiomyocytes. ACE inhibitors seem not to affect this process in our study. There are no changes in numbers of C-kit+CD34-CD45- cardiac progenitor cells.

P1130 Association of Rac1 GTPase activity with atrial fibrosis

O. Adam, G. Frost, H.J. Schaefers, M. Boehm, U. Laufs. *Universitaetsklinikum des Saarlandes, Kardiologie, Angiologie und int. Intensivmedi, Homburg/Saar, Germany*

Introduction: Patients with atrial fibrillation (AF) are characterized by increased atrial fibrosis. The underlying signal transduction is incompletely understood. We hypothesized that activation of Rac1 GTPase contributes to increased fibrosis and atrial fibrillation via activation of NADPH oxidase and production of reactive oxygen species.
Methods and Results: Samples of the left atrial appendage were analyzed in 8 patients with AF undergoing mitral valve surgery and 7 patients with sinus rhythm (SR) matched for atrial diameter and medication. Despite same size of the atria, collagen content was significantly higher in AF compared to SR (14.9±2.1% vs. 8.5±1.3%). Atria of patients with AF showed significant upregulation of Rac1 total protein expression (Western blot), Rac1 activity (PAK pull-down assays) and a 20-fold upregulation of NADPH oxidase activity compared to SR (2225±500%).
In order to test whether Rac1 plays a causal role in the pathogenesis in AF, transgenic mice with cardiac overexpression (α MHC promoter) o f Rac1 (RacET) were compared to wildtype (WT) and WT undergoing transaortic constriction (TAC, 360 m m). After 16 months, echocardiography showed similar left ventricular hypertrophy in RacET and TAC. RacET but not TAC exhibited atrial enlargement; 75% of RacET but no WT or TAC showed AF. Interstitial collagen content quantitated by sirius red staining was significantly increased in the atria of RacET (44±1% of area) compared to WT (19±5%). In contrast, interstitial fibrosis in TAC atria did not significantly differ from WT(31±6%). In the left ventricle, both RacET and TAC mice showed an elevated collagen content compared to the control group (WT 9±2%, RacET 29±3%; TAC 24±4%). In all mice, atrial collagen content exceeded ventricular collagen. All effects are significant with $p<0.05$.
Conclusion: Left atria of patients with AF are characterized by upregulation of Rac1, increased NADPH oxidase activity and interstitial fibrosis. Cardiac-specific overexpression of Rac1 in mice results atrial fibrosis and fibrillation independent of left ventricular hypertrophy. Rac1-GTPase mediated activation of left atrial NADPH-oxidase may represent a novel target for the prevention of atrial fibrillation.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1131 Inhibition of angiotensin II type I receptors affects atrial fibrillation susceptibility and myocardial interstitial fibrosis in goats

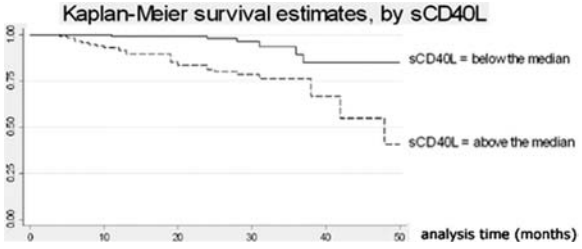
I.K. Karalis, S.I. Chrysostomakis, E.N. Simantirakis, A. Koutsopoulos, H.E. Mavrakis, P.E. Vardas. *Heraklion University Hospital, Cardiology Department, Heraklion, Greece*

Purpose: Structural and electrical remodeling of atrial myocardium, induced in the setting of sustained atrial fibrillation (AF), have been associated with the increased stability of the arrhythmia. Tachy-cardiomyopathy is another problem in cases the ventricular rates are high. Angiotensin II receptor blockers have been found to possess anti-arrhythmic properties in AF, and reduce atrial fibrosis. We used the goat animal model and candesartan to test the hypothesis that angiotensin-II inhibition would have a beneficial effect on the vulnerability to AF induction and fibrosis of the atrial and ventricular myocardium.
Methods: We studied 5 sets of 12 months old triplet goats divided (one from each triplet) in three groups for a 6month period. Group A and B were implanted with a pacemaker capable of maintaining AF with burst pacing and group A goats were treated with candesartan. Group C animals served as controls. The animals were studied for AF induction the first day the burst-pacing was activated, on the following day, and on the 1st, 3rd and 6th month thereafter by calculating the "vulnerability Index" (VI), defined as the ratio of total AF time to the number of bursts per session. At the end of the study, tissue samples were examined from all four heart chambers and fibrosis was quantified.
Results: All A and B group goats (AF goats) developed cardiomegaly after the 6 months observation period due to tachycardiomyopathy. In group B goats the VI was a significantly increasing over time (from 30.3 to 170.8, p=0.045), while in the goats taking candesartan (group A) it did not (from 28.8 to 284.7, p=0.23). Histology showed that in AF goats a significant increase in fibrous tissue was observed compared to controls (groups A and B vs. group C) in all four chambers that were examined and that the degree of fibrosis was significantly lower in those animals taking candesartan.
Conclusions: Our study shows that candesartan reduces the vulnerability to the burst-induced AF in goats. It also confirmed the strong association of AF with atrial fibrosis, as well as the favorable effect of candesartan on atrial structural remodeling and established the beneficial role of the drug in tachyarrhythmia-induced ventricular fibrosis.

P1132 Enhanced soluble CD40L as predictor of vascular events in patients with non-valvular atrial fibrillation: results of a prospective study

D. Ferro, L. Loffredo, F. Fimognari, L. Polimeni, P. Villari, P. Pignatelli, F. Violi. *University of Rome La Sapienza, Department of Experimental Medicine, Rome, Italy*

Purpose: Atrial fibrillation (AF) is associated with an high incidence of vascular disease that may be related to a prothrombotic and inflammatory state. Soluble CD40 ligand (sCD40L), that stems essentially from platelet activation, possess inflammatory and prothrombotic properties. Aim of the study was to assess if sCD40L is a predictor of stroke and/or myocardial infarction(MI) in patients with non-valvular AF.
Methods: Plasma levels of sCD40L were measured in 231 patients [177 (77%) had permanent or persistent AF, and 54 (23%) had paroxysmal AF]. Patients were followed for a mean period of 27.8±8.8 months and cardiovascular events such as fatal and non fatal stroke and MI were recorded.
Results: AF population was divided in two groups patients according to sCD40L level above or below the median (4.76 m g/l). The two patients' groups had similar distribution of cardiovascular risk factors, age, gender, medications or serum PCR levels. During the follow-up period, vascular events occurred in 6 (2 non-fatal MI and 4 non-fatal ischemic strokes) out of 116 patients with low levels of sCD40L (5.1%) and in 29 (11 fatal and 3 non-fatal MI; 3 fatal and 12 non-fatal ischemic strokes) out of 115 patients with high levels (25.2%) (log-rank test: $p<0.001$; Figure). Using the COX proportional Hazards model, patients with sCD40L above the median were 4.63 times more likely to experience a vascular event (95% C.I.: 1.92-11.20).



Figure

Conclusions: This study shows that enhanced soluble CD40L level is predictor of vascular events in patients with non-valvular AF so suggesting that enhanced platelet activation may play an important role in its pathophisiology.

P1133 Heterogeneous atrial sympathetic innervation and altered calcium handling in a rabbit model of left ventricular hypertrophy: implications for atrial fibrillation

T. Liu[1], T.G. Huang[1], K.Y. Chen[1], X. Zhou[2], Y.J. Li[3], W. Cai[1], J.R. Cai[3], P. Korantzopoulos[4], G. Li[4], Y.M. Li[2]. *[1]Second Hospital of Tianjin Medical University, Department of Cardiology, Tianjin, China, People's Republic of; [2]Medical College of Armed Police Forces, Institute of Cardiovascular Disease, Tianjin, China, People's Republic of; [3]Nankai Hospital, Department of Cardiology, Tianjin, China, People's Republic of; [4]'G.Hatzikosta' General Hospital of Ioannina, Institute of Cardiovascular Disease, Ioannina, Greece*

Purpose: To examine the atrial sympathetic neural remodeling and calcium handling protein alterations as well as their potential role in the development of atrial fibrillation (AF), using a rabbit model of left ventricular hypertrophy (LVH).
Methods: Thirty rabbits were randomly divided into 2 groups: LVH (induced by abdominal aortic constriction) (n=16), and Sham-operated group (n=14). Echocardiographic and hemodynamic assessment was performed at baseline, and 2 months after the operation. Isolated Langendorff perfused rabbit hearts were used to evaluate atrial electrophysiological parameters and vulnerability to AF which examined by burst pacing. The distribution and density of sympathetic innervation in the left atrium was examined by immunohistochemical staining for tyrosine hydroxylase (TH). Moreover, the levels of sarcoplasmic reticulum calcium handling proteins were determined by Western blot analysis.
Results: Two months after the operation, left atrial diameter and interventricular septum diastolic thickness were significantly higher in the LVH compared to the Sham group ($P<0.01$), while no significant differences in LV ejection fraction were apparent. Moreover, systolic blood pressure, diastolic blood pressure, LV +dp/dt max, and -dp/dt max were significantly increased in the LVH group. Electrophysiological studies showed that the left atrial effective refractory period (AERP) was shortened in the LVH group while AERP dispersion was increased ($P<0.01$). An increased vulnerability to AF was also evident in the LVH group ($P<0.05$). Left atrial TH density was greater and more heterogeneous in the LVH compared to the Sham group (3753.11±3316.27 vs 2578.00±1658.21$\mu m^2/mm^2$, $P<0.05$). Results of the Western-blot analysis were as follows: 1) FK-506 binding protein12.6 (FKBP12.6), Ryanodine receptor 2 (RyR2)-5029, RyR2-2809P protein levels, and RyR2 relative phosphorylation were significantly increased in the LVH group ($P<0.05$); 2) L-type calcium channel (LTCCs), phospholamban (PLB), PLBp-Ser16 protein levels, and PLB relative phosphorylation were lower in the LVH compared to the Sham group ($P<0.05$); and 3) No significant difference in the sarcoplasmic reticulum Ca^{2+}ATPase$_{2a}$ (SERCA$_{2a}$) protein levels was observed between the 2 groups.
Conclusions: Long-term left atrial pressure overload due to LVH causes left atrial heterogeneous sympathetic innervation, alterations in calcium handling proteins, and changes in the electrophysiologic properties, creating a substrate for AF.

P1134 Atrial fibrillation additionally impairs both myocardial perfusion and perfusion reserve in underlying cardiomyopathy raising coronary resistance

F. Range, M. Schaefers, T. Acil, K.P. Schaefers, M. Paul, G. Breithardt, O. Schober, C. Vahlhaus, T. Wichter. *University Hospital of Muenster, Cardiology and Angiology, Muenster, Germany*

Purpose: Atrial fibrillation is the most common sustained arrhythmia in humans and has proven to inflict the perfusion in otherwise healthy hearts. Yet in a major fraction of cases, atrial fibrillation occurs on the basis of an underlying structural heart disease such as dilatative cardiomyopathy thus in already hampered perfusion conditions. It is unknown whether the additional arrhythmia can further impair myocardial perfusion independently.
Methods: Myocardial perfusion was non-invasively quantified by H_2 15O-Positron-Emission-Tomography in three different groups of male patients. 25 patients with lone chronic atrial fibrillation without underlying structural heart disease (age 59±12 years) were compared to 18 patients with dilatative cardiomyopathy (age 43±15 years) in sinus rhythm and to 12 patients who developed atrial fibrillation on top of a dilatative cardiomyopathy (age 55±12 years). 22 male volunteers served as controls (age 47±13 years). In all subjects, a coronary heart disease was excluded.
Perfusion was measured at rest, under adenosine infusion, provoking the endothelium-independent perfusion reserve and under cold pressor testing to achieve the endothelium-dependent perfusion response. Additionally, the coronary vascular resistance was calculated.
Results: As expected, myocardial perfusion and perfusion reserve proved impaired and coronary resistance raised in lone atrial fibrillation as well as in dilatative cardiomyopathy compared to controls. Interestingly, the patients who suffered from dilatative cardiomyopathy and additional atrial fibrillation showed lowest myocardial perfusion combined with highest coronary resistance of all groups. Compared to the patients with "lone" dilatative cardiomyopathy (DCM), the patients with additional atrial fibrillation (DCM/AF) showed significantly lower perfusion at rest (1,11±0,30 vs. 0,86±0,28 mL/min/mL;P=0.002) as well as under adenosine infusion (2,64±1,45 vs. 1,31±0,93 mL/min/mL;P=0.018) with higher coronary resistance at both conditions (CVR-Base 108±25 vs. 140±35 mmHg*mL-1*min*mL;P=0.009; CVR-ADO: 51±60 vs. 96±45 mmHg*mL-1*min*mL;P=0.065)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusions: Atrial fibrillation reduces myocardial perfusion and perfusion reserve and elevates coronary vascular resistance independently even on the basis of an underlying structural heart disease already impairing these parameters. The results from this study support a rhythm control strategy especially for cases of atrial fibrillation occurring in already critical myocardial perfusion conditions.

ABLATION OF SUPRAVENTRICULAR AND VENTRICULAR ARRHYTHMIAS

P1136 Novel ECG criteria for discrimination of left- and right-sided inferoseptal accessory pathways

N. Dagres[1], K. Wasmer[1], G. Moennig[1], A. Ohlenburger[1], E. Tsougos[2], D.T. Kremastinos[1], M. Borggrefe[3], G. Breithardt[3], L. Eckardt[3]. *[1]University of Muenster, Muenster, Germany; [2]University of Athens, Athens, Greece; [3]University Hospital of Mannheim, Mannheim, Germany*

Purpose: Discrimination of left- and right-sided inferoseptal pathways by ECG algorithms is unsatisfactory. This distinction has great clinical importance because of the different approach (arterial vs venous access). Aim of the study was the definition of easily applicable ECG criteria for this purpose.
Methods: We reviewed the 12-lead ECGs of 113 consecutive patients, undergoing successful radiofrequency ablation of a manifest inferoseptal pathway.
Results: Pathways were left-sided in 45 cases (40%) and right-sided in 68 (60%). Among patients with right-sided pathways, 40% were male compared with 73% in left-sided pathways ($p<0.001$). QRS and delta wave were more often negative in inferior leads II, III, aVF and in V1 and positive in aVL in patients with right-sided pathways. The most useful ECG criteria for prediction of a right-sided location were a) a negative QRS polarity in all three inferior leads and in V1 (positive predictive value (PPV) 0.90, negative predictive value (NPV) 0.51) and b) a negative QRS polarity in at least 2 inferior leads and in V1 (PPV 0.80, NPV 0.56). A positive QRS polarity in at least 1 inferior lead predicted a left-sided location (PPV 0.54, NPV 0.80). Based on the QRS polarity in the inferior leads and V1 and on gender, we defined a new algorithm which had an accuracy of 76%.
Conclusion: Correct prediction of left- or right-sided inferoseptal pathway location based on the 12-lead ECG is challenging. Criteria combining the QRS polarity in the inferior leads and V1 and the gender enable a more correct localization.

P1137 Impact of ablation in slow pathway area on vagal modulation to atria

X. Yin, S. Zhang, L. Gao, Y. Dong, H. Zhao, Y. Xia, Y. Yang. *Dalian Medical University, Department of Cardiology, Dlian, China, People's Republic of*

Little is known about the impact of slow pathway ablation on local vagal innervation to atria. This study aimed to investigate the impact of ablation in slow pathway area on vagal modulation to atria based on changes of atrial effective refractory period (ERP), vulnerability window (VW) of atrial fibrillation (AF).
Methods: Eleven adult mongrel dogs were involved in this study. Bilateral cervical sympathovagal trunks were decentralized. Metoprolol was given to block sympathetic effects. Multipolar catheters were placed into the right atrium and coronary sinus. Linear lesion was performed from coronary sinus ostium to the middle area of Koch triangle. ERP and VW of AF, and sinus rhythm cycle length (SCL) were measured at high right atrium(HRA), lower right atrium(LRA), distal coronary sinus(CSd) and proximal coronary sinus(CSp) at baseline (without vagal stimulation) and during vagal stimulation before and after ablation. The underlying tissue were excised from ablative sites and the same sites without ablation as control specimens. Serial sections were taken and stained with hematoxylin and eosin for microscopic examination.
Results: (1) SCL shortening during vagal stimulation remained unchanged before and after abaltion(107 ± 19 vs 108 ± 8 beats per minute,$P>0.05$). (2) After ablation, ERP shortening during vagal stimulation remained unchanged at HRA (55 ± 34 vs 69 ± 37ms, $P>0.05$), decreased slightly at CSd (42 ± 32 vs 55 ± 30ms, $P=0.08$), decreased significantly at LRA(19 ± 21 vs 66 ± 24ms, $P<0.001$) and CSp (7 ± 18 vs 46 ± 24ms, $P<0.001$).(3) AF was difficult induced at baseline before and after ablation in all sites (VW close to 0). VW of atrial fibrillation to vagal stimulation significantly decreased after ablation at LRA (1 ± 3 vs 49 ± 36ms, $P<0.005$) and CSp (10 ± 12 vs 45 ± 34ms, $P<0.05$), decreased slightly at CSd (35 ± 37 vs 57 ± 28ms, $P=0.07$), and remained unchanged at HRA (63 ± 31 vs 63 ± 25ms, $P>0.05$). (4) The architecture of individual ganglia was significantly altered after ablation.
Conclusions: The decreased ERP shortening to vagal stimulation in coronary sinus and lower right atrium after ablation in the slow pathway area indicates that ablation in the slow pathway area may result in the partly or remarkable vagal dennervation in lower right atrium and coronary sinus, thereby attenuating the susceptibility to vagal mediated atrial fibrillation induced by premature beat originated from these sites. Unchanged SCL, ERP shortening and VW to vagal stimulation in sinus node area and high right atrium indicate that ablation in the slow pathway area could not modify the vagal innervation to these sites.

P1138 Two years follow-up after cavotricuspid isthmus cryoablation for the treatment of common atrial flutter

W. Moreira, C. Timmermans, Y. Mizusawa, S. Philippens, L.M. Rodriguez. *Maastricht, Netherlands*

Background: Cryoablation has been previously validated as an important tool to treat cardiac arrhythmias. It offers particular advantages when compared to radiofrequency ablation (less thrombogenicity, deeper lesions, painless, etc ...). We report the late follow-up of patients (pts) submitted to cavotricuspid isthmus (CTI) ablation using cryothermy for common atrial flutter (AFL).
Methods: Pts with common type AFL referred for CTI ablation were recruited prospectively from July 2001 to July 2006. In all pts a duodecapolar catheter was used to assess conduction along the lateral wall of the right atrium and a decapolar catheter in the coronary sinus evaluated the activation of the left atrium. A 10 F sheath was used for the cryoablation catheter with different electrodes tips (6.5/10 and 15 mm). The duration of a cryoapplication decreased during the study period from 5 to one minute. CTI block was reassessed 30 min after the last application during isoproterenol infusion. Early and late recurrences were evaluated by Holter monitoring at every clinic visit (1/3/6 months after the procedure and yearly thereafter) or if symptoms developed.
Results: The 180 enrolled pts had the following characteristics: 39 women (22%), no structural heart disease in 80 pts (44%), mean LA diameter 44 ± 7 mm and mean LVEF 57 ± 7%. Acute success was achieved in 95% (171) of the pts. There were no complications. The mean follow up was 27 ± 17 months. The late success rate was 91% (156 pts). A prior history of atrial fibrillation (AF) was present in 123 pts (69%). Of these pts, 70% (85 pts) remained having AF on long term follow-up (controlled by antiarrhythmic drugs, pulmonary vein isolation or AV nodal ablation with pacemaker implantation). Among the 57 patients without a history of AF prior to CTI, 20 (35%) developed AF.
Conclusions: This prospective study showed: A) a 91% chronic success rate (2 years follow-up) for cryoablation of the CTI in pts with common AFL. B) a frequent association of AF (69%) with AFL, the former being the main cause of burden in this group of pts. These results are similar to those obtained with radiofrequency energy.

P1139 Adverse effects of Wolff-Parkinson-White syndrome with right septal or paraseptal accessory pathways on cardiac function

M. Tomaske[1], J. Janousek[2], V. Razek[2], G. Hindricks[2], R.A. Gebauer[3], V. Tomek[2], W. Knirsch[1], U. Bauersfeld[1]. *[1]University Children's Hospital, Paediatric Cardiology, Zurich, Switzerland; [2]University of Leipzig, Heartcentre, Leipzig, Germany; [3]University Hospital Motol, Kardiocentrum and Cardiovascular Research Ce, Prague, Czech Republic*

Introduction: Wolff-Parkinson-White syndrome with right septal or paraseptal accessory pathways causes excentric septal mechanical activation and may provoke left ventricular (LV) dyssynchrony and dysfunction. Aim of this study was to evaluate the effect of radiofrequency catheter ablation (RFA) of the accessory pathways on LV function.
Patients and Methods: Retrospectively, transthoracic echocardiography and ECG recordings were analyzed in 40 patients (age: 14.1 ± 2.8 years) with right septal or paraseptal accessory pathways before and after RFA. Fractional shortening and ejection fraction were calculated as a measure of global LV function. Furthermore, septal to posterior wall motion delay (SPWMD) and interventricular mechanical delay (IVMD) was determined as a measure of intra- and interventricular dyssynchrony where feasible. QRS duration was assessed as a measure of dyssynchrony of electrical activation. A p value < 0.05 was considered significant.
Results: Successful RFA was performed in 36/40 (90%) patients. QRS duration was normalized after RFA. Global LV function improved and LV dyssynchrony (SPWMD) decreased. However, interventricular dyssynchrony (IVMD) did not differ from pre RFA findings (Table).

Pre (n=40) and post RFA (n=36) findings

	Pre RFA	Post RFA	p value
QRS duration (ms)	127 ± 19	92 ± 12	< 0.001
Fractional shortening (%)	32 ± 8	38 ± 5	< 0.001
Ejection fraction (%)	49 ± 11	57 ± 9	< 0.001
IVMD (ms)	22 ± 26	22 ± 18	ns
SPWMD (ms)	114 ± 96	57 ± 57	0.009

Data are given as mean $\pm$ SD; ns= not significant.

Conclusions: Wolff-Parkinson-White syndrome with right septal or paraseptal accessory pathways cause LV dyssynchrony and jeopardize global LV function. RFA resulted in normalized QRS duration, mechanical resynchronisation and improved LV function. Even in the absence of arrhythmias RFA of right septal or paraseptal pathways may be considered in patients with decreased LV function.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1140 Utility of the spectral analysis of ventricular fibrillation electrograms for differentiating between normal and radiofrequency ablated myocardium

F.J. Chorro-Gasco[1], L. Such-Miquel[2], I. Trapero[2], F. Pelechano[2], J. Canoves[1], L. Mainar[1], J. Sanchis[1], V. Bodi[1], A. Alberola[2], J. Guerrero[2] on behalf of REDINSCOR. *[1]Clinic University Hospital, Cardiology Service, Valencia, Spain; [2]University of Valencia, Physiotherapy, Valencia, Spain*

Purpose: On the hypothesis that frequency-domain parameters obtained from the spectral analysis of ventricular fibrillation electrograms would allow assessment of lesion creation, we used an experimental model to analyze the changes in spectral characteristics of ventricular fibrillation electrograms after radiofrequency ablation.
Methods: In 11 Langendorff perfused rabbit hearts, ventricular fibrillation recordings were obtained with a multiple epicardial electrode before and after the creation of transmural lesions with radiofrequency currents. Frequency-domain and time-domain parameters were obtained from normal and ablated zones, and logistic regression analysis was performed to determine the parameters that indicate the ablated zones.
Results: In the ablated zones, a significant decrease was observed in the spectral amplitude of the dominant (0.168±0.113 vs 0.025±0.018 mV2/Hz, $p<0.001$) and mean frequencies (0.053±0.057 vs 0.012±0.016 mV2/Hz, $p<0.001$), the power spectrum amplitude (0.860±0.570 vs 0.128±0.091 mV2/Hz, $p<0.001$), and the standard deviation of the power spectrum (0.031±0.020 vs 0.004±0.001 mV2/Hz, $p<0.001$). In the univariate analysis to establish whether the recordings correspond to the radiofrequency-damaged zone, the area under the ROC curve was seen to be greater than 0.8 on using each parameter – with the exception of the dominant frequency (area = 0.53) and the mean frequency (area = 0.56). The parameters entered in the multivariate model to predict the ablated zone were the standard deviation of the power spectrum (odds ratio = 0.021, 95% confidence interval = 0.006-0.070) and the spectral amplitude of the mean frequency (odds ratio = 0.322, 95% confidence interval = 0.127-0.814).
Conclusions: The frequency-domain parameters obtained from the VF electrograms, as well as the time-frequency parameters, show significant modifications in the radiofrequency-damaged zones, and can be used to differentiate between ablated and non-ablated fibrillating myocardium.

P1141 What practical instructions are hidden in electrophysiological characteristics of dual atrioventricular node pathways?

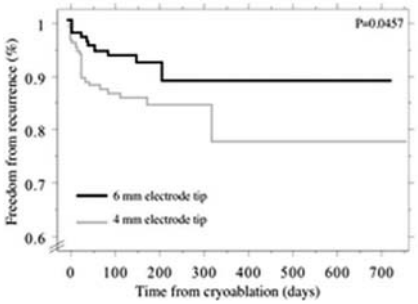
K. Makowski[1], D. Michalkiewicz[2], K. Jacewicz[1], M. Cholewa[1]. *[1]Military Institute of Health Services, Internal Medicine And Cardiology Department, Warsaw, Poland; [2]Military Institute of Health Services, Internal Medicine and Cardiology, Warsaw, Poland*

Aim: 1) to reveal factors related to AVNRT occurrence by comparing AV node properties in patients (pts) with dual anterograde pathways and typical AVNRT with: a) characteristics of pts with dual AV node physiology but without spontaneous/inducible reentrant arrhythmia, and also with b) AV node features observed in pts after the effective RF slow pathway (SP) modification, and 2) to determine differences in baseline AV node characteristics between pts with subsequent complete RF SP ablation and those with only SP modification.
Methods: 60 pts with AH jump and AVNRT referred to hospital for RF ablation (complete SP ablation performed in 36 pts, and SP modification in 24 pts), and 45 age-matched pts with AH jump without history of/without inducible AVNRT, were enrolled. EP study was performed to assess: Wenckebach block cycle length (WCL), effective refractory period of the fast (ERPfast) and slow (ERPslow) pathways, AH interval jump, SPAH, presence of V-A conduction, and cycle length of pacing-induced ventriculo-atrial block (VABCL).
Results: Pts with AVNRT had better anterograde AVN conduction ($p=0.04$), shorter ERPslow, greater difference between ERPfast and ERPslow, and more frequently maintained and qualitatively better retrograde V-A conduction (all variables, $p<0.001$) in comparison with pts with dual AVN pathways without AVNRT. Analysis of the entire population (n=105 pts) revealed conditions necessary for AVNRT: 1) presence of retrograde conduction and ERPslow$\leq$ 220ms or 2) if ERPslow$>$ 220ms, the additional requirement- VABCL$<$ 416 ms (sensitivity 89%, specificity 78%, kappa=0.87). The effective SP modification (24 pts, no recurrence of arrhythmia during 37.62±19.4 month follow-up) resulted in the increase in: -WCL ($p=0.04$), -ERPslow ($p=0.006$), and in SPAH ($p=0.03$), without significant change in retrograde conduction. The absence of AVNRT after SP modification was correctly determined by the formula with simultaneous: ERPslow$>$270 ms, and difference between ERPfast and ERPslow $\leq$ 90 ms, and SPAH$>$254 ms. Comparison of baseline AV nodal characteristics between pts with subsequent complete SP ablation (n=36) and those with only SP modification (n=24) revealed significant difference in ERP window between the fast and slow pathways (79±42 vs. 109±48 ms, respectively, $p=0.01$).
Conclusions: The precise assessment of each reentry circuit component allows of AVNRT prediction, also in pts after SP modification. The baseline difference between ERPslow and ERPfast is related to the-end point of the subsequent SP ablation. The greater the window, the more probable the incomplete SP ablation.

P1142 Acute and long-term cryoablation outcomes for atrioventricular nodal reentrant tachycardia comparing 4 mm and 6 mm electrode tip catheters

L. Rivard, M. Dubuc, P.G. Guerra, P. Novak, D. Roy, L. Macle, B. Thibault, M. Talajic, P. Khairy. *Montreal Heart Institute, Electrophysiology Service, Montreal, Canada*

Background: Transcatheter cryoablation is increasingly utilized for slow pathway modification in patients with AVNRT.
Methods: We compared acute and long-term success rates with 4 versus 6 mm electrode-tip cryocatheters.
Results: At the Montreal Heart Institute, 289 patients had cryoablation as a first-time procedure for AVNRT between January 1999 and February 2006. With the exception of older age (48.9±16.1 versus 42.3±15.2 years) and higher proportion of hypertension (16.8% versus 7.9%, P=0.0240), baseline characteristics were comparable in patients with 6 mm (N=137) versus 4 mm (N=152) cryocatheters. Acute procedural success was achieved in 90.7%, with no significant difference between the two electrode-tip sizes. In interventions using the 6 mm tip cryocatheter, a shorter fluoroscopy time (16.1±11.3 versus 20.3±14.9 minutes, P=0.0096) and trend towards briefer procedural duration (166.6±49.1 versus 173.5±53.0 minutes, P=NS) were noted. No patient in either group developed permanent AV block or required a pacemaker. Over a median follow-up of 155 days, recurrences were less common with 6 mm cryoablation (P=0.0457). Actuarial event-free survival rates at 1, 3, 6, and 12 months with 6 mm versus 4 mm cryoablation were 96.7%, 93.4%, 91.9%, and 88.5% versus 89.9%, 87.0%, 84.1%, and 77.1%, respectively, with no recurrence thereafter. In stepwise multivariate Cox regression analyses adjusting for baseline imbalances and medical therapy post ablation, cryoablation with a 4 mm tip catheter incurred a 2.5 fold increased risk of recurrence [HR 2.50, 95% CI (1.03, 6.05), P=0.0420].



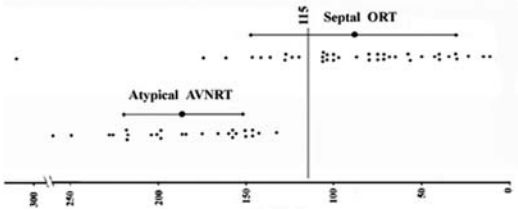
Freedom from recurrence

Conclusion: In patients with AVNRT, slow pathway modification using a 6 mm tip cryocatheter is safe and is associated with a shorter fluoroscopy time and fewer recurrences compared to a 4 mm tip cryocatheter.

P1143 Correction of the postpacing interval to account for decremental AV nodal conduction improves its ability to discriminate atypical AV nodal reentry from septal orthodromic reentrant tachycardia

E. Gonzalez Torrecilla, J. Almendral, A. Arenal, F. Atienza, T. Datino, L. Franco, L. Castilla, A. Estevez, F. Fernandez-Aviles. *Hospital General Gregorio Maranon, Cardiology Department, Madrid, Spain*

The difference between the first postpacing interval (PPI) after tachycardia entrainment from the right ventricular (RV) apex and the tachycardia cycle length (TCL) has been proposed as an interval to differentiate atypical AV nodal reentrant tachycardias (AVNRT) and orthodromic reciprocating tachycardias (ORT) using a septal accessory pathway. However, the expected AV nodal delay induced by the entrainment could alter that interval as an index of proximity to the circuit.
Methods: We included 64 consecutive patients with atypical AVNRT (VA interval $>$100 ms in high right atrium during tachycardia) (25 patients) and with ORT using a concealed septal accessory pathway (39 patients). Tachycardia entrainment was attempted through trains of 5-15 RV apex pacing pulses. The PPI-TCL difference was calculated with and without the subtraction of the increment in AV nodal conduction time (AH increment= AH interval in the first PPI – AH interval in tachycardia).
Results: A difference in PPI-TCL $>$115 ms with the subtraction of AV nodal delay



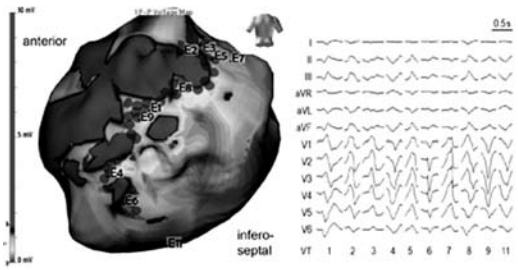
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

correctly identified all the patients with atypical AVNRT with a sensitivity and a specificity of 100%. However, a significant overlap of individual values was observed when comparing PPI-TCL intervals without the subtraction of AH increment, leading to lower specificity of that cut-off value (74.4%) (Figure; values in ms).
Conclusion: The difference in PPI-TCL needs the correction to account for decremental AV nodal conduction in the first PPI to accurately discriminate atypical AVNRT from ORT through a septal AV bypass.

P1144 Catheter ablation of multiple ventricular tachycardias after myocardial infarction guided by combined contact and noncontact mapping

H.U. Klemm, R. Ventura, D. Steven, C. Johnsen, T. Rostock, B. Lutomsky, T. Meinertz, S. Willems. *University Heart Center Hamburg, Cardiology, Hamburg, Germany*

Purpose: This study sought to unify noncontact activation mapping and contact scar mapping for an individualized approach to the patient with multiple ischemic venticular tachycardias (VT) irrespective of cycle length (CL).
Methods: For 12 consecutive patients with chronic myocardial infarction and recurrent VT bipolar contact maps were acquired during sinus or paced rhythm. Additional activation noncontact maps were obtained during 48 induced VTs (CL 192-579 ms). Endocardial exit sites were superimposed on contact maps. Radiofrequency lesions were extended for critical borders defined by multiple neighboring exits and followed the isovoltage contour line of contact maps. Solitary exits were targeted by short ablation lines perpendicular to isthmus conduction.
Results: Nine critical borders were identified in 8 patients and constituted the substrate for 31 VTs. The voltage at exit sites was 1.05±0.6 mV. Noncontact maps revealed 23±18% of isthmus conduction. Pace-mapping reproduced the QRS morphology of 81% of VTs and was associated with successful ablation ($p<0.01$). Thirty-seven (77%) of all and 83% of clinically documented VTs were rendered noninducible irrespective CL by applying 28±11 radiofrequency lesions. Spontaneous transitions between distinct VTs along critical borders were demonstrated in 4 patients. The endpoint of complete non-inducibility of any sustained VT was reached for 8 (67%) patients. These showed a favorable 14±6 months follow-up with 1 of 4 total recurrences of any VT (p=0.03). VT-CL was not predictive for acute or long-term success.



VT exits superimposed on contact map

Conclusions: The combined approach of contact and noncontact mapping effectively defines critical borders as the substrate of multiple VTs with an individualized voltage scar definition and is not limited to fast VTs.

P1145 Epicardial ablation with cooled tip catheter close to the coronary arteries is effective and

M. Kawamura[1], Y. Kobayashi[2], K. Tanno[1]. *[1]Showa University of Medicine, Third Department of Internal Medicine, Tokyo, Japan; [2]Tokyo, Japan*

Introduction: Transthoracic epicardial ablation can be an alternative to conventional therapy for critical pathways of VT located in the epicardium or subepicardium. However the usefulness and safety of epicardial ablation close to coronary arteries (CA) is not clear. The purpose of this study was to analyze the efficacy and safety of epicardial radiofrequency (RF) ablation in the vicinity of CA.
Methods and Results: Fourteen healthy pigs, weighing 29 to 40 kg were used. RF-ablation was performed with cooling, during saline circulation at 0.6 mL/m, with RF power set at 30 W for 60 seconds. RF ablation was performed without cooling at a temperature of 60° for 60 seconds. Ablation was performed for 60 seconds, unless catheter dislodgement, impedance rise or VT occurred sooner. Before RF ablation, coronary angiography was performed to assess the anatomic relationships between the ablation catheter and CA. The amplitudes of ventricular potentials recorded at the ablation catheter and basket catheter were measured before and after RF energy application to analyze the relationship between lesion volume and ventricular potential. Using RF ablation with cooling, 36 of 43 lesions (83%) were created and using RF ablation without cooling, 14 of 25 lesions (56%) were created in the LV-epi. In the LV-epi, ablation with cooling was effective significantly more often than ablation without cooling ($P<0.05$). Of the LV-epi sites, 35 lesions (20 with cooling and 15 without cooling) were close to CA (LAD≦15 mm) and 33 lesions (23 with cooling and 10 without cooling) were further from CA. For sites close to CA, epicardial ablation was effective in 77% (15/20) with cooling and in 40% (6/15) without cooling. There was a significant difference of effective ablation -between with cooling and without cooling ($P<0.05$). For sites further from CA, epicardial ablation was effective in 88% (21/23) with cooling and in 80% (8/10) without cooling. There was no significant difference between with cooling and without cooling. With cooling, epicardial lesion size could be predicted by the change of endocardial ventricular potential using a basket catheter. The ablated lesion volume was strongly correlated with the proportion by which ventricular potential decreased after ablation. No damage to major epicardial arteries was detected when the catheter tip was positioned 5 mm away from CA.
Conclusions: In the vicinity of CA, RF ablation with cooling is more effective than that without and is safe if ablation sites are sited 5 mm away from major CA.

P1146 Long-term clinical outcome of ablation of ventricular arrhythmia from the distal purkinje arborization in patients after myocardial infarction

L.J. Szumowski[1], M.J. Orczykowski[2], P. Derejko[1], P. Urbanek[1], R. Kepski[1], E. Szufladowicz[1], A. Przybylski[1], F. Walczak[1]. *[1]Instituite of Cardiology, Warsaw, Poland; [2]Institute of Cardiology, Electrophisiological Laboratory, Warsaw, Poland*

The aim of this study was to describe long-term follow up of Purkinje origin ventricular arrhythmia ablation in patients (pts) after myocardial infarction (MI).
Group and method: The group consisted of 13 pts (twelve males; avg.age 60±10) that underwent ablation of frequent or incessant ventricular arhytmias despite revascularization and antiarrhythmic treatement. 5 pts demonstrated polymorphic ventricular tachycardia initiated by ventricular premature beats (VPBs) and have had up to 100 DC shocks before RFCA. Four pts had frequent monomorphic ventricular tachycardia (mVT), and 4 had up to 51000/24h (avg. 31000/24h) VPBs and non sustained VT (nsVT). Activation and pace mapping were used to identify the earliest site of VPB or VT ractivity. The presence of a sharp Purkinje potential preceding VPB/VT activation as well as sinus rhythm beats defined its origin from the Purkinje network. Electroanatomic voltage mapping was performed to delineate the extent of MI.Follow up was base on ICD memory, or at least 3 Holter recordings in pts without ICD.
Results: During 32-57 (avg.46 months) FU of the whole group 77% pts were free of ablated arrhythmia. 2 pts had a reduction in arrhythmia occurrence. One patient died due to heart failure.In group with prior PVT, one patient 36 months after the first ablation has had mVT and underwent successful second procedure.In group with mVT, one pt had 4 ICD interventions and another one has multiple ATP interventions and is planned for a second procedure. In group with nsVT an VPBs at least 3 Holter ECG recordings were done after the procedure. The reduction of VPBs/nsVT occurrence was over 95% (avg. 399 VPBs/24h compared to 31000 before ablation).None of the pts had major complications during or after procedure.
Conclusions: Ablation of the local Purkinje network localized in the border zone of MI allows suppression of ventricular arrhythmia (VPBs, mVT, PVT) in long term follow up.

P1147 Idiopathic dilated cardiomyopathy predicts adverse long-term outcome in patients with electrical storm treated by radiofrequency catheter ablation

M. Santamaria[1], C. Carbucicchio[2], N. Trevisi[2], G. Maccabelli[2], P. Della Bella[2]. *[1]Catholic University of the Sacred Heart, Cardiovascular Department, Campobasso, Italy; [2]University of Milan, Centro Cardiologico Monzino, Milan, Italy*

Purpose: Electrical storm (ES) in implantable cardioverter-defibrillator (ICD) patients (pts) is associated with adverse prognosis. Catheter ablation (CA) may be effective but the long-term prognosis is unknown. Purpose of this study was to investigate whether the underlying heart disease aetiology affects long-term outcome in the ES pts treated by CA.
Methods: Ninety five consecutive pts with coronary artery disease (CAD; 72), idiopatic dilated cardiomyopathy (IDCM; 10), arrhythmogenic right ventricular dysplasia (ARVD; 13), undergoing CA for drug refractory ES were prospectively evaluated. Acute efficacy of CA was defined by the prevention of inducibility of all clinical ventricular tachycardias (VTs). Long-term analysis primarily addressed ES recurrence and cardiac death (CD).
Results: ES was suppressed in all pts; CA was acutely effective in 85 pts (89%). At a mean follow up of 22±13 months, 87 pts (92%) were free from ES. Eleven pts died for cardiac causes (12%), 4 for sudden CD (SCD) due to ES recurrence. The rate of CA acute efficacy was significantly lower in IDCM vs. non-IDCM pts (70% vs. 92%, p=0.033). The incidence of ES recurrence (30% vs. 6%, p=0.027), CD (50% vs. 7%, p=0.002) and SCD (30% vs. 1%, p=0.007) was significantly higher in IDCM vs. non-IDCM pts. In 3 IDCM pts refractory to a conventional endocardial CA, an epicardial approach was performed; in all these pts a suppression of all clinical VTs at the programmed electrical stimulation and a prevention of VT and ES recurrence over the long-term were obtained. There was no significant difference in outcome between ARVD and CAD pts.
Conclusions: CA can be successfully applied to a population of pts with a variety of underlying heart disease suffering from ES. The presence of IDCM significantly impairs long-term prognosis. Our data suggest however that acute and long-term

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

outcome of CA can also be improved in IDCM pts if a combined endo-epicardial approach is applied as a first line strategy.

P1148 Long term outcome of catheter ablation of Atrial TachyArrhythmias in patients with congenital heart defects guided by 3-dimensional electro-anatomical mapping

N.M.S. De Groot, W.K. Chang, M. Rahantaipur, N.A. Blom, E.E. Van Der Wall, M.J. Schalij. *Leiden University Medical Centre, Cardiology Dept., Leiden, Netherlands*

Introduction: Catheter ablation has evolved as a possible curative treatment modality for post-operative atrial tachyarrhythmias (AT) in patients with congenital heart disease (CHD). This study was aimed at evaluating the procedural outcome of 3-dimensional electro-anatomical mapping guided catheter ablation of AT in a large cohort of patients with CHD and to study the incidence of AT during a long-term follow-up period of 45±26 months.
Methods: The study population consisted of 50 consecutive patients (24 male, 37±14 yrs) with CHD and post-operative, drug refractory AT referred for ablation. Mapping was guided by the electro-anatomical mapping system (CARTOTM) in all patients.
Results: Mapping revealed 74 AT, including 29 atrial flutter (AFL (CL= 278±81 ms), 31 intra-atrial re-entrant tachycardia, (IART, CL= 303±65 ms), 12 focal atrial tachycardia (FAT, CL= 372±99 ms) and 2 focal atrial fibrillation (AF). IART were most frequently observed in patients with tricuspid atresia (52.9%) and transposition of the great arteries (100%). Multiple AT, all originating from distinct atrial sites, were ablated in 12 pts; the underlying mechanism causing the AT was different for each AT in 6 pts. Ablation was successful in 52% of the IART, 93% of the AFL and all FAT and focal AF. During the follow-up period 5 patients died due to progressive pump failure. Rhythm prior to death was sinus rhythm (N=1) or AF (N=4). One patient was lost to follow-up, the remaining patients had either sinus rhythm (N=30), AT (N=4) or AF (N=10). Twenty-three patients (70%) who were successfully ablated were in sinus rhythm. Surprisingly, 41% of the patients who did not have a successful ablation (no termination during ablation, conversion to AF or another AT) remained in sinus rhythm during the follow-up period. Anti-arrhythmic drugs were used by 19 (63%) patients with sinus rhythm.
Conclusion: Focal and reentrant mechanisms underly late post-operative AT in patients with CHD. Successive AT within a pt may be caused by different mechanisms. The complexity of the reentrant circuit is associated with the complexity of the CHD and corresponding extensiveness of surgical procedures. Ablative therapy guided by a 3 - dimensional mapping technique is a successful treatment modality in this patient group. The incidence of sinus rhythm increases over time after ablative therapy of IART due to late cures.

P1149 Comparison of radiofrequency ablation with cryoablation using an 8 mm tip ablation catheter for the ablation of common atrial flutter - a randomized study (CRYOTIP)

M. Kuniss[1], T. Vogtmann[2], R. Ventura[3], J. Vogt[4], G. Groenefeld[5], S. Hohnloser[6], B. Zrenner[7], B. Lemke[8], J. Neuzner[9], H.F. Pitschner[6]. *[1]Kerckhoff-Klinik, Dept. of Cardiology, Bad Nauheim, Germany; [2]Charite University Hospital, Cardiology, Berlin, Germany; [3]University Hospital Eppendorf, Cardiology, Hamburg, Germany; [4]Heart Center North Rhine-Westphalia, Cardiology, Bad Oeynhausen, Germany; [5]Asklepios Hospital Barmbek, Cardiology, Hamburg, Germany; [6]JW Goethe University Hospital, Cardiology, Frankfurt, Germany; [7]German Heart Center, Cardiology, Muenchen, Germany; [8]Maerkische Kliniken, Cardiology, Luedenscheid, Germany; [9]Klinikum Kassel, Cardiology, Kassel, Germany*

Introduction: Recent studies show that pain-free cryoablation is comparable with radiofrequency (RF) ablation regarding short and long-term clinical success rates and safety in the treatment of common atrial flutter (AFL). Long-term success depends on persistence of bidirectional conduction block (BCB) in the inferior cavotricuspid isthmus (CTI). Aim of this present study is to compare RF ablation to cryoablation using similar ablation tip sizes with emphasis on acute success rates and persistence of BCB in the CTI.
Methods: In this prospective multicenter trial patients were randomly assigned to ablation with RF using conventional 8-mm tip catheter or cryoablation with 8-mm tip. Written informed consent was obtained from all patients prior to ablation. Acute success rate, clinical long-term success rate and persistence of BCB were defined as primary endpoints. By now data of 163 pts has been analyzed (122m, age 63.5±9.7years). 8 pts had to be excluded, 79 pts were treated with RF, 76 pts with cryo. Cryoenergy was delivered once at each catheter tip site for a maximum duration of 240s, max duration of RF application was 120s, max power 60W. The ablation endpoint was defined as complete BCB in the CTI 30 min after last energy delivery. A maximum of 30 Cryo/RF applications were allowed to achieve ablation endpoint. Persistence of BCB in the inferior CTI was controlled by repeat EP study 3 months post ablation including a clinical follow up, which was also performed in patients refusing the repeat EP study.
Results: The preliminary data show acute success rates of 92.4% in the RF group (73/79 pts) and of 93.4% (71/76 pts) in the Cryo group, respectively ($p>0.05$). Repeat EP study was performed in 53/73 pts treated with RF, in 45 pts (84.9%) BCB was persistent, in 8 asymptomatic pts conduction recovered, no clinical recurrence of AFL. In 52/71 pts treated with Cryo repeat EP study was performed showing persistence of BCB in 33 pts (63.5%), p=0.015. In 14 asymptomatic pts conduction recovered, 5 pts developed a recurrence of AFL. Due to a clinical asymptomatic status 20 pts in the RF group and 19 pts in the Cryo group refused repeat EP study.
Conclusions: Both energy forms are showing similar acute success rates. Clinical long-term success rate and rate of persistence of BCB were significantly different with reduced efficacy concerning the long term outcome in patients treated with Cryo.

P1150 Left-sided accessory pathway ablation without a fluoroscopy system

J.L. Merino, M. Gonzalez Vasserot, R. Peinado, O. Quintero, H. Roa, E. Macia, J.A. Sobrino, J.L. Lopez-Sendon. *Hospital Universitario "La Paz", Cardiac Electrophysiology Unit, Madrid, Spain*

Catheter ablation is the therapy of choice for patients with AV accessory pathways. However, fluoroscopy radiation to both patients and electrophysiology laboratory staff may be relevant. In addition, dependence on fluoroscopy protection and equipment is inconvenient and may limit the availability of these procedures.
Methods: 21 consecutive patients with a left sided AV accessory pathway were prospectively included in the study. The fluoroscopy system was switched off and all lead protective items (aprons, led glasses) withdrawn. A conventional ablation catheter was introduced through the femoral vein and moved into the right atrium guided just with a non-fluoroscopic digital navigation system. The anatomical representation of the right atrium and the coronary sinus was obtained with the digital system and 3 tetrapolar catheters were introduced and placed in the coronary sinus, the right ventricle and the His bundle area. Following conventional electrophysiological evaluation, the ablation catheter was withdrawn from the right chambers and introduced percutaneously through the right femoral artery into the left ventricle guided only with the non-fluoroscopic digital navigation system. The anatomical representation of the left ventricle was obtained with the digital system and the ablation was performed by conventional means without fluoroscopy.
Results: Ablation was successful accomplished with no fluoroscopy at all in all patients but one. There were no complications. A retrograde aortic approach was used in all but one with patent foramen ovale. Ablation was achieved with a median 2 (range 1-6) radiofrequency applications. The mean number of radiofrequency applications was significant lower (1.9±1.3 vs 4.1±3.7, $P<0.05$) than that used in the last 20 consecutive patients who underwent conventional left-sided accessory pathway ablation by the same operator before the design of this research project.
Conclusions: percutaneous ablation of left sided accessory pathways without fluoroscopy is feasible, safe, and may be more precise for radiofrequency lesion creation than the conventional fluoroscopy approach.

ABLATION OF ATRIAL FIBRILLATION

P1151 Asymptomatic arrhythmia relapse in patients underwent circumferential pulmonary vein isolation: incidence, recurrent arrhythmia types and predictors

X.P. Liu, D.Y. Long, Y. Tian, J.Z. Dong, C.S. Ma. *Beijing Anzhen Hospital,Capital University of, Department of Cardiology, Beijing, China, People's Republic of*

Background: Regarding the issue of asymptomatic recurrence after catheter ablation of AF (AF), most studies concerned with Pappone's approach. In recent years, another AF ablation approach, so-called circumferential pulmonary vein isolation (CPVI), has gained more popularity. However, the incidence, types and predictors of asymptomatic atrial tachy-arrhythmia (ATa) relapse after this approach are less known.
Methods: This prospective study enrolled 42 consecutive patients (male 26 patients, mean age: 58.2±13.7) with AF, including paroxysmal AF in 25 patients and non- paroxysmal AF in 17 patients. After the initial CPVI procedure, all patients were followed with series continuous 48 hours Holter recordings, which performed at 1, 3 and 6 months respectively. Predictors of asymptomatic ATa relapse were determined by Logistic regression analysis for eight variables as follows, age, gender, AF type (paroxysmal or non-paroxysmal), structural heart disease, diameter of left atria, left ventricular ejection fraction, procedure time and SDNN pre-procedure.
Results: At 1,3 and 6 months after CPVI, the incidence of asymptomatic ATa recurrence which revealed by 48 hours Holter recording was 8%, 16%, 16% in paroxysmal AF group, as well as 5.9%, 11.8%, 23.5% in non- paroxysmal AF group. The incidence of asymptomatic ATa recurrence in non- paroxysmal AF group was significant higher than that in paroxysmal AF group at 6 month follow-up CPVI ($P<0.05$). AF is the dominant (50%) arrhythmia type among asymptomatic recurrence ATa, while atrial tachycardia constitutes the major (33.3%) arrhythmia in symptomatic recurrent ATa. The independent predictors of asymptomatic ATa recurrence after CPVI includes non-paroxysmal AF (OR 4.162, 95% CI 1.757-43.186, P=0.028) left atrial enlargement (OR 12.149, 95% CI 3.489-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

101.723, P=0.036), and decrease of SDNN (OR 0.185, 95% CI 0.054-2.625, P=0.042).
Conclusions: (1) Asymptomatic ATa relapse is common after CPVI, particularly in patients with non-paroxysmal AF, left atrial enlargement or decrease of SDNN. (2) The dominant type of asymptomatic recurrent arrhythmia after CPVI was AF, rather than atrial tachycardia.

P1152 Basal plasmatic neuro-hormonal activation predicts the success of circumferential pulmonary veins ablation of atrial fibrillation

B. Benito, L.L. Mont, D. Tamborero, A. Berruezo, W. Tarifa, X. Freixa, M. Matiello, J. Brugada. *HOSPITAL CLINIC UNIVERSITY OF, ARRHYTHMIAS SECTION, Barcelona, Spain*

Recent data suggest that renin-angiotensin system may act as a local profibrotic factor promoting and perpetuating atrial fibrillation (AF).
The aim of the study was to analyze, in patients undergoing circumferential pulmonary veins ablation (CPVA) for treatment of drug-refractory AF, if basal plasmatic neuro-hormonal activation is related to the success of the procedure.
Methods: Pre-procedural basal plasmatic neuro-hormones (renin activity, angiotensin-II (AT-II), aldosterone, AT-II converting enzyme and atrial natriuretic peptide) were determined in patients undergoing a first procedure of CPVA. Patients with structural heart disease were excluded from the study. Success of the ablation was defined as the absence of AF after a blanking period of 1 month.
Results: A series of 45 consecutive patients were included. Of them, 36 have completed a minimum of a 4-month follow up and are presented. Mean age of the study population was 52±13 years, and 72% were males. Hypertension was present in 39% of patients, and 33% were endurance sport practitioners. In the remaining patients AF was considered idiopathic. AF was paroxysmal in 25 patients (69%), persistent in 7 (19%) and permanent in 4 (11%). Mean left atrial diameter was 40.5±6 mm. After a mean follow-up of 7.6±3 months, 25 patients (69.4%) remained in sinus rhythm. The univariable analysis showed that patients with AF recurrences showed a trend to higher basal plasmatic levels of AT-II (15.7±17 vs. 9.4±3 pg/mL, p = 0.06) and had significant higher levels of aldosterone (12.3±4 vs. 5.3±2 ng/dL, $p < 0.001$). Cox regression confirmed the basal plasmatic levels of aldosterone as the only independent predictor for AF recurrence in this series, with a hazard ratio of 1.58 (95% confidence interval 1.17-2.14; p= 0.003). The area under the ROC curve for basal aldosterone was of 0.89, and levels of aldosterone higher than 11.35 ng/dL had a sensitivity of 74% and a specificity of 100% for identifying patients with AF recurrences after CPVA.
Conclusions: Basal levels of aldosterone predict AF recurrences after CPVA in patients without structural heart disease, and may help identifying patients with a worse outcome. These results suggest that having a profibrotic milieu may contribute to perpetuate AF and may worsen the success rate of CPVA.

P1153 Left atrial remodelling and function after pulmonary vein encircling for atrial fibrillation: a real-time 3D echocardiography study

V. Delgado, B. Vidal, M. Sitges, N. Calvo, D. Tamborero, L. Mont, M. Azqueta, C. Pare, J. Brugada. *Hospital Clinic - Thorax Institute, Cardiology, Barcelona, Spain*

Background: Pulmonary vein encircling (PVE) has demonstrated its effectiveness in the treatment of atrial fibrillation (AF). However, its impact on atrial remodelling and function has not been studied extensively.
Objectives: Our aim was to evaluate the effect of PVE on left atrial (LA) volumes and function with the use of real-time 3D echocardiography (RT3DE).
Methods and Results: 34 pts with paroxysmal (n=16) or persistent (n=18) AF were treated with PVE with 3-dimensional electroanatomic mapping/ablation system (CARTO). LA volumes (maximum, pre-A and minimum) and function (reservoir, conductance and active contraction) were assessed with RT3DE before and 4.8 ±2.7 months after PVE. All patients underwent 24 hours ECG Holter registry at follow-up and were consequently divided into successful PVE patients (sinus rhythm) or failed PVE. LA volumes and LA function are shown in Table 1.

Table 1

		Vmax (ml)	Vmin (ml)	ActEF	VTIA	LACF
ALL (n=34)	pre	55±16	28±13	25±20	6±3	28±18
ALL (n=34)	post	48±16*	26±11	28±19	6±3	37±15
Successful PVE (n=24)	pre	50±11	26±14	25±21	6±3	32±19
Successful PVE (n=24)	post	45±10*	24±8	26±21	6±2	37±16
Failed PVE (n=10)	pre	64±18†	32±12	23±19	7±4	20±15
Failed PVE (n=10)	post	52±22*	30±15	18±11	6±2	37±14

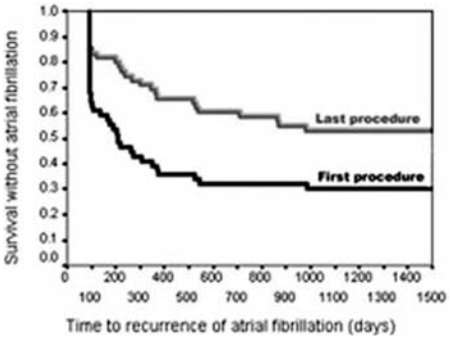
Vmax = Maximum LA volume; Vmin = Minimum LA volume; ActEF = Active LA emptying fraction; VTIA = velocity time integral A wave; LACF = left atrial conduit function; *$p<0.05$; †$p < 0.05$ vs pre- in successful PVE.

Conclusions: PVE induces a reduction in LA size without a significant impact on its function. RT3DE could be a useful imaging method to assess LA geometry and function after PVE.

P1154 Long-term efficacy and late arrhythmia recurrences with wide circumferential electrically isolating pulmonary vein ablation for persistent and permanent atrial fibrillation

S.C. Seow, T.W. Lim, C.H. Koay, D.L. Ross, S.P. Thomas. *Westmead Hospital, Cardiology, Sydney, Australia*

Introduction: Early recurrences of atrial arrhythmia after wide electrically isolating ablation for atrial fibrillation (AF) are well described but the long-term risk of recurrence for patients with persistent and permanent AF has not been studied in detail.
Methods: 56 consecutive patients (45 men [80.4%], age 55.9±8.7 years) with persistent (39 [69.6%]) or permanent (17[39.4%]) AF were followed up for 21.6±8.8 months following ablation. AF duration prior to ablation was 6.4±5.6 years. Electrically isolating lesions encircling the left and right pulmonary veins in pairs were created, guided by electroanatomical mapping.
Results: After 1.5±0.7 procedures, 48 (85.7%) were in sinus rhythm (SR) at 21.6±8.8 months follow-up. This was achieved with 1 procedure in 27(56.3%) and without anti-arrhythmics in 30(62.5%). AF recurrence was observed in 69.6% following the first and 46.4% after the last procedure. 90% of these occurred by 12.1 months following the first and 28.6 months following the last procedure. Of those with late recurrences (>3 months) following the last procedure, most (18, 69.2%) did not have any early recurrences. Pre-procedural AF duration (p=0.007) and female gender (p=0.005) were independent predictors of recurrence following the last procedure.



Survival Curves

Conclusions: Circumferential pulmonary vein isolation is effective for the majority of patients with persistent or permanent AF. However, repeat procedures are frequently required. Late recurrences are common and not precluded by the absence of early post-procedural arrhythmias.

P1155 Recovered sinus node function after catheter ablation of paroxysmal atrial fibrillation in sick sinus patients with prolonged sinus pauses

Y. Xia[1], Y. Yang[2], L. Gao[2], S. Zhang[2], D. Yang[2], S. Li[2], X. Yin[2], Z. Lin[2]. *[1]Lund, Sweden; [2]Dalian Medical University, Dept of Cardiology, Dalian, China, People's Republic of*

Objective: Paroxysmal atrial fibrillation (PAF) could be observed in many patients with sick sinus syndrome, whom we commonly called brady-tachy syndrome. On the other hand, the successful rate of catheter ablation of PAF remains increasingly high in recent years. In this study we observe the sinus rate in a selected group of brady-tachy patients before and after elimination of PAF.
Methods and Results: In 235 PAF patients underwent catheter ablation in our center, 16 with refractory paroxysmal AF and Holter recorded sinus pauses (>3 seconds) on termination of AF (9 female, mean age 59.2±8.0ys) were enrolled in this study. Six of them experienced dizziness and near syncope, and the rest 10 patients with syncope attacks, in which 5 of them received pacemaker therapy due to the dizziness and syncope 2.0±1.6 years before the ablation. Besides the sinus pause, frequent episode of atial premature complex, atrial tachycardia and PAF could be observed in their Holter recordings. The routine segmental pulmonary vein isolation or circumferential ipsilateral pulmonary vein ablation was applied in these patients, and during the procedure 2 cases with 'criminal' supra vena cava were also isolated. After the procedure, sinus node function was assessed during the first day, and at 1, 3, and 6 months, by 24 to 48-hour ambulatory monitoring to determine the mean heart rate and heart rate range. In 10 of the 11 cases without pacemaker, no PAF recurred and the mean heart rate and heart rate range recovered to normal, whereas cardiac pacemaker was implanted in the rest patient due to the PAF recurrence even after 3 times of ablation. In the 5 with pacemaker implanted before, the pacing rates were 42-76% decreased compared to that before the ablation, and mainly happened during the sleep. During the follow up of 24.3±3.2 months, none of these patients sufferred dizziness or syncope attack.
Conclusion: In some patients with brady-tachy syndrome, PAF can be eliminated by catheter ablation, and normal sinus node function could be restored after the procedure, which argues the necessity of the pacemaker implantation in a subset

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

of brady-tachy syndrome patients. Further studies are needed to assess the relationship of PAF and sinus node, and classify which part of theses patients could avoid the possible pacemaker implantation.

P1156 End-point for ablation of complex fractionated atrial electrograms (CFAEs) in patients with persistent atrial fibrillation: is acute sinus rhythm a predictor for mid-term success?

H. Estner[1], I. Deisenhofer[2], A. Luik[1], A. Konietzko[1], E. Uecer[1], B. Zrenner[1], G. Hessling[1]. *[1]German Heart Center Munich, Deutsches Herzzentrum Munchen, Munchen, Germany; [2]German Heart Center Munich, Munich, Germany*

Background: Catheter ablation of areas with complex fractionated atrial electrograms (CFAE) in the left or right atrium is a new approach for the treatment of atrial fibrillation (AF). We prospectively assessed if termination of AF to sinus rhythm during ablation of CFAE is a predictor for mid-term success (presence of stable sinus rhythm during 7-day-Holter at 3-month follow-up) in patients with persistent AF.
Methods: CFAE was performed in 30 symptomatic patients (pts) with persistent AF (23 male, mean age 62±8.5 years). Additional pulmonary vein isolation (PVI) was perfomed after CFAE In 22/30 pts (73%). After this single ablation procedure, a 3-month follow-up evaluation including a 7 –day Holter ECG was performed in 28 of the 30 pts (1 pt lost to follow-up, 1 pt died during follow-up due to cerebral bleeding).
Results: Termination or regularisation of AF during ablation of CFAE was acutely achieved in 24/30 patients (80%). AF termination and sinus rhythm occurred in 9/30 pts (30%; Group A). In 21/30 pts (70%; Group B) no termination but regularisation of AF to atrial tachycardia (n=15) or no effect (n=6) was observed.
At 3-month follow-up, stable sinus rhythm was present in 12/28 pts (42%), regular atrial tachycardia was found in 8/28 pts (29%) and AF relapsed in 8/28 pts (29%). In Group A, 7/9 pts (77%) were in stable sinus rhythm at follow-up whereas in Group B only 7/19 pts (37%) were in stable sinus rhythm (p=0.016). Group B included 4 pts with AF regularization and 3 pts with no effect during CFAE ablation. Additional PVI had no effect on the presence of stable sinus rhythm after 3 month in both groups (p=ns).
Conclusion: CFAE acutely leads to termination or regularisation of persistent AF in 80% of patients. After three months, significantly more pts were in sinus rhythm after intraprocedural termination of AF into sinus rhythm compared to pts in whom regularisation to atrial tachycardia or no effect was achieved during procedure.

P1157 Early complications of catheter ablation for atrial fibrillation

F. Zoppo[1], G. Stabile[2], C. Tondo[3], A. Colella[4], R. Mantovan[5], G. Senatore[6], N. Bottoni[7], G. Carreras[8], L. Coro[9], E. Bertaglia[6] on behalf of Italian Perspective Registry on atrial fibrillation procedural safety. *[1]Mirano (Venezia), Italy; [2]Maddaloni (Caserta), Italy; [3]Milano, Italy; [4]Firenze, Italy; [5]Treviso, Italy; [6]Cirie (Torino), Italy; [7]Reggio Emilia, Italy; [8]Napoli, Italy; [9]Conegliano, Italy*

Background: Data about procedural safety of left atrium (LA) ablation for atrial fibrillation (AF) are not yet consistent. Our aim was to perspectively assess the early complications of LA radiofrequency (RF) catheter ablation in unselected patients (pts) with AF.
Methods: From April 2005 to October 2006, 1011 (74% males) consecutive pts were collected in 10 Italian Centers for AF ablation. Electroanatomic mapping was used in 78%, cooled tip catheter in 89.5%. Mean procedure time was 197.9 (±88) min. Early complications were defined as occurred during the ablation up to the 30th post procedure day.
Results: Non deaths recorded. Complications occurred in 41 patients (4.0%): 13 (1.3%) peripheric vascular complications; 8 (0.8%) pericardial effusion; 6 (0.6%) cardiac tamponade successfully drained; 5 (0.5%) cerebral embolisms (CE) (four major strokes and one TIA); and 4 (0.4%) PV stenosis >50% and one was a total PV occlusion. Other isolated events were: 1 aortic puncture; 1 AV complete block, 1 transient phrenic nerve paralysis; 1 pneumothorax; and 1 pleuric hematic effusion. In the 5 cases of CE ablation a cooled catheter was used in 4; 4 (3 strokes and the TIA) occurred on the day after the procedure while switching to oral anticoagulation; only 1 during the procedure.
At the univariate analysis, the 27 patients (2.7%) with hemorrhagic complications (defined as pericardial or vascular) presented more frequently a history of structural heart disease (SHD) (50.0% vs 22.2%, p>0.001), in particular of coronary disease (23.1% vs 7.7%, p<0.005). In these patients a not cooled tip catheter was more frequently used (23.1% vs 10.2%, p<0.03), the procedure was significantly shorter (164.3±87.6 min vs 198.7± 77.3 min, p<0.02), and frequently performed by a less experienced operator (< 50 procedures done; 42.3% vs 19.3%, p<0.004).
At the multivariate analysis, only history of SHD (OR 2,700, 95% CI 1,138 to 6,409, p<0.03), and ablations performed by a less experienced operator (OR 2,716, 95% CI 1,117 to 6,602, p<0.03) continued to characterize patients who presented hemorrhagic complications We did not find any variable that significantly identify the 5 patients (0.5%) who presented CE, and the 4 patients (0.4%) who had significant PV stenosis.
Conclusions: Ablation for AF appears safe in an unselected population too. Early post-procedural days seem critical for thromboembolic events while shifting to oral anticoagulation. Particular care should be taken in patients with structural heart disease.
Complications are more frequent during the early phase of the learning curve.

P1158 Thoracoscopic bipolar RF isolation of the pulmonary veins as treatment for atrial fibrillation

L.V.A. Boersma, W.J. Van Boven, E.F.D. Wever, J.A.M. Defauw. *St.Antonius Hospital, Cardiology, Nieuwegein, Netherlands*

Introduction: Pulmonary vein (PV) catheter ablation has become first line treatment for drug-refractory AF. However, recurrence rates of up to 50% are reported, related to complexity of the substrate and incomplete ablation lines. Minimally invasive surgical ablation could provide an alternative approach to achieve transmural ablation lines to isolate the PVs.
Methods: Selected pts were enrolled for surgery if they were ineligible for or had failed a previous catheter ablation. Pre-operative MRI and echocardiography were performed to exclude major structural disease. Under general anesthesia, video-assisted thoracoscopic surgery was performed, both from the right and left side through a lateral chest wall incision. With the AtriCure bipolar RF clamp an ablation was performed at the antrum of the right and left PVs. Electrical isolation from the atrium was confirmed by stimulation and mapping of the PVs. Also, the nervus plexi were localized by high frequency stimulation and ablated, and the left atrial appendage was removed. Follow-up was performed through ECG recording, Holter recording, and telephonic interview for symptomatic AF.
Results: From November 2005 to February 2007, 41 pts (13 female) were enrolled (mean age 58±9 yrs, range 34-75 yrs). Seven had documented AF recurrence after a prior catheter ablation. AF was paroxysmal in 58% and persistent/permanent in 42%. All but 1 pt underwent a confirmed successful surgical RF isolation of both left and right PVs with removal of the appendage. Isolation was achieved with a median of 4 applications for the right PVs and left PVs, requiring less than 1 min per application. The median operating time was 2.5 hours, ranging from 2.0 to 4 hrs. All pts left the hospital within 5 days after surgery. Periprocedural complications consisted of 2 phrenic nerve lesions, while in 1 pt the procedure had to be discontinued due to bleeding. At discharge 92% of pts were in SR, while 4 pts received successful electrical cardioversion within 1 month, and 2 pts underwent a successful RFCA for typical flutter. After a blind period for arrhythmias of 3 months and a median follow-up of 5 months (range 1-16), 87% of pts are still in SR without a documented recurrence of AF.
Conclusions: Thoracoscopic bipolar RF isolation of the PVs and nervus plexi is a feasible surgical procedure. In selected pts with AF the success rate is 87%, with a low complication rate. Minimally invasive surgery may provide a valuable alternative approach to endocardial ablation.

P1159 Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation

A. Berruezo, L. Mont, D. Tamborero, B. Benito, M. Matiello, P. Berner, J. Brugada. *HOSPITAL CLINIC UNIVERSITY OF BARCELONA, Arrhythmia Section, Barcelona, Spain*

Background: The success rate of circumferential pulmonary vein ablation (CPVA) to treat atrial fibrillation (AF) ranges from 60 to 90% depending on the series. The objective of the study was to identify predictors of AF recurrence after a standardized CPVA procedure.
Methods and Results: A series of 148 consecutive patients undergoing CPVA for symptomatic paroxysmal (60.8%), persistent (23.6%) or permanent (15.5%) AF were included in the study. CPVA with creation of supplementary block lines along the posterior wall and mitral isthmus was performed and a minimum of six months follow-up completed in all patients. Structural heart disease was present in 19.6% and hypertension in 33.8% of patients. After 13.1±8.4 months follow-up, 73.6% of patients were free of AF recurrences after a mean of 1.18±0.45 procedures/patient. Univariable analysis showed that patients with AF recurrence were older (50.6±11.0 mm vs 55.1±10.4, p=0.031), had more often permanent AF (11,9% vs 25.6%, p=0.042) and previous hypertension (53.8% vs. 26.6%, p=0.002), larger anteroposterior left atrial diameter (LAD) (43.9±5.8 mm vs. 40.4±5.3 mm, p=0.001) and larger left ventricular end systolic diameter (LVESD) (34.4±4.5 mm vs. 32.0±5.2 mm, p=0.029). Cox regression analysis showed that hypertension (OR=2.8; 95% CI: 1.5-5.4; p=0.002) and LAD (OR=1.1; 95% CI: 1.05-1.19; p<0.001) were independent predictors of AF recurrence. The mean predicted proportion of patients with AF recurrence after CPVA of the multivariable model showed a linear relationship with the increase of LAD previous to the procedure. The presence of hypertension further increased the mean predicted proportion of patients with AF recurrence at each LAD.
Conclusions: Hypertension and LAD are independent pre-procedural predictors of AF recurrence after CPVA to treat AF. These data may help in patient selection for AF ablation.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1160 Holter ECG recording period after AF catheter ablation- how long is necessary?

S. Weis, C. Piorkowski, G. Hindricks. *Herzzentrum Leipzig, Rhzthmology, Leipzig, Germany*

Introduction: Currative ablation approaches to treat atrial fibrillation (AF) have been increasingly developed. Circumferential left atrial pulmonary vein (PV) abalation is commonly used today. Different follow-up strategies have been suggested. So far it is unclear which recording period is necessary for detection of most AF recurrencies.
Methods: 554 Patients with known highly symptomatic atrial fibrillation underwent radio- frequency (RF) catheter ablation from May 2005 to February 2007 at our institution. Follow-up was performed by 7-day Holter-ECG monitoring before ablation, after ablation and after 3; 6 and 12 months, respectivly. 243 patients who had completed the 6 months follow-up were included into this study. To assess the diagnostic value of different Holter-ECG recording intervals at the 6 month follow-up, the number of AF- recurrences after 1;2;3;4;5 and 6 days of recording were compared to the total 7-day ECG recording period.
Patients characteristics are as follows: sex: 75% male; 25% female, mean age all patients included 56.7 years, no strucutal heart disease 80.8%, no prior ablation therapies 65.7%.
Results: During the 7-dHolter-ECG at the 6 month follow-up 177/243 (72.9%) patients showed a stable sinus rhythm. 66/243 patients (27.2%) had recurrent episodes of AF and/or atrial flutter. 54 patients (21.4%) had recurrent AF episodes only. Using a shorter Holter-ECG recording period of less than 1day would have reduced the number of patients detected with AF recurrences to 26 (10.7%; $p<0.001$), of less than 2 days to 34 (14%; $p<0.00$), of less than 3 days to 39 (16%; $p<0.001$), of less than 4 days to 46 (19%, p=0.08), of less then 5 days to 49 (20.1%; p=0.63), of less then 6 days to 51 (21%, p=0.25); of less then 7 days to 53 (21.8%; p=1.00), respectively.
Discussion: According to our data, shorter periods of ECG-Holter monitoring at the 6 month follow-up after AF-ablation, can reduce the number of patients detected with AF recurrences up to 62% if monitored for 1 day only, as compared to a 7-day protocol the current gold standard of 7-d-Holter-ECG monitoring. Every recording period of less than 5 days resulted in a detection of significantly less patients with AF recurrences.

P1161 Medium term efficacy of radiofrequency catheter ablation on non-pulmonary vein originated atrial fibrillation

Y. Xia[1], Y. Yang[2], L. Gao[2], S. Zhang[2], D. Yang[2], S. Li[2], X. Yin[2], Z. Lin[2]. *[1]Lund, Sweden; [2]Dalian Medical University, Dept of Cardiology, Dalian, China, People's Republic of*

Background: Pulmonary vein (PV) has been demonstrated to be important for initiation of paroxysmal atrial fibrillation (PAF), and PV isolation has become a major strategy for treatment of PAF. Non-PV foci also play essential roles in some PAF patients. However, only limited data could be found in evaluation of the medium-term efficacy on non-PV foci ablation.
Methods and results: Two hundred and fifty six cases with PAF (62 female, mean age 53±2 ys.) were included. During the electrophysiologic study, twenty-seven patients (10.5%) were found with ectopic foci in non-PV areas (Group NPV), including the superior vena cava (16, 59.3%), left atrial posterial wall (4, 14.8%), crista terminalis (2, 7.4%), coronary sinus (2, 7.4%), fossa ovalis (1, 3.7%), left appendage (1, 3.7%), left atrial anterior wall (1, 3.7%). The rest patients were defined as Group PV, though their foci might not originate from PV in some cases. In Group NPV, all the non-PV foci were successfully eliminated during the first procedure. Second procedure was needed in 4 cases (14.8%), with 3 foci from SVC and one from left atrial posterior wall, whereas in Group PV 52 cases received second procedure (22.7%). Six cases received the third procedure, but no one is from Group NPV. During a follow-up period of 28±14 months, the 25 patients from Group NPV were free of PAF recurrence (92.6%), as compared to 185 without PAF recurrence in Group PV (80. 8%) after follow up of 32±14 months.
Conclusions: Identification and elimination of non-PV foci are important in treatment of a subset of PAF patients. Ablation in patients with non-PV foci clearly found could lead to a higher successful rate compare to those with PV isolation being routinely performed.

P1162 Significance of early recurrence of atrial fibrillation following pulmonary vein isolation

E.L. Mittmann-Braun, L.M. Lickfett, J. Schmidt, J.W. Schrickel, J.O. Schwab, M. Linhardt, B. Bellmann, A. Yang, G. Nickenig, T. Lewalter. *University of Bonn, Cardiology, Bonn, Germany*

Background: The relevance of early recurrence of atrial fibrillation (AF) within 14 days following pulmonary vein (PV) isolation (PVI) as a predictor for ongoing AF activity is until now controversial. We assessed the significance of an early recurrence of AF during the first 2 weeks after successful PVI in predicting a long term failure of the procedure.
Methods: The study cohort consisted of 48 pts (38 men, 57±10 yrs, 41 paroxysmal, 7 persistent AF, LVEF: 56±9%) and 53 PVI procedures (184 PVs were ablated, 3.5 PV's ablated per pt, radiation time: 61± 15 min, procedure duration: 196±44 min). Radiofrequency catheter ablation was performed in 48 and cryoablation in 5 procedures (6 pts with additional linear left atrial lesions). Daily and event-triggered ECG recording with transtelephonic transmission (ECG- TT) was performed during the first 3 months after ablation. All pts were further monitored with ECGs and repetitive Holter for AF recurrences over a mean period of 8 (1-18) months.
Results: We studied two cohorts separately: (Group A) Pt with no AF recurrence within the first 14 days after ablation and Pt with an AF recurrence within 14 days (Group B). The 1st and the 2nd ablation procedures in 7 pts were include in group A or B depending on the rhythm of the ECG-TT. There were no significant demographic differences in both groups. A complete isolation could be obtained in 90/91 PVs in group A and 87/93 PVs in group B. We analyzed 1430 ECGs (53±23/Pt) after 27 ablation procedures in group A and 1431 (56±26/Pt) after 26 ablation procedures in B. The first episode of AF occurs after 4±8 day after ablation in the total population. The frequency of AF during the first 3 months after ablation was 5±12 episodes in A and 23±21 episodes in B ($P < 0.001$). 20/27 (74%) pts in A and 4/26 (15%) pts in B were free of AF ($P< 0.001$). 5/27 pts (19%) of A and 22/26 (85%) of B got a new PV ablation procedure after 3 months because of AF recurrences.
Conclusions: The absence of AF during the first two weeks following PVI indicates a high positive predictive value for a further AF free survival and a clinical success of the ablation procedure. On the contrary, early AF recurrence after PVI is a strong indicator for further AF activity in 85% of these patients leading to a reablation procedure in the majority of this patient cohort.

P1163 Persistent iatrogenic atrial septal defect after pulmonary vein isolation. Is it really an emerging problem?

A. Rillig, U. Meyerfeldt, R. Birkemeyer, M. Kunze, W. Jung. *Schwarzwald-Baar-Klinikum, Internal Medicine Cardiology, Villingen-Schwenningen, Germany*

Purpose: At present time pulmonary vein isolation (PVI) is widely practiced for treating atrial fibrillation due to its increasing safety and efficacy. Transseptal access is necessary with one, two or even more transseptal sheaths to perform PVI. In recent studies a raising problem of persistent iatrogenic atrial septal defects (iASD) has been observed.
Methods: In this prospective study all patients were examined with transoesophageal echocardiography (TEE) before, directly after and in a 3, 6 and 12 months follow up period for evaluation of PV-stenosis and iASD. Interatrial shunt was characterized by echocardiographic parameters. We evaluated the characteristics and outcome of iASD after transseptal puncture in the period from August 2005 to April 2006. All patients were studied after placement of two transseptal 8F sheats in the left atrium. One sheath was used to introduce a multipolar mapping catheter into the PVs for mapping purposes. The second sheath was used for the ablation catheter.
Results: 26 patients underwent PVI with double transseptal puncture.
In all patients TEE was performed before PVI. Directly after the procedure there was seen an iASD in 77% (n=20) of the patients with a maximum diameter of 1.0 mm (mean 0,75 mm ±0,25mm). In 95% (n=19) of the patients with iASD there was an intermittent left to right shunting, in one patient we found a continuous left to right shunting. A right to left shunting could not be documented in any of the patients.
After 3 months there could not be found any iASDs in the patients, who showed an iASD directly after the intervention.
During 6 month follow-up period no patient died or suffered from cerebral or cardiac embolism and no PV-stenosis was detectable.
Conclusions: In contrast to previous studies we were only able to find small iASDs with left to right shunting directly after PVI (77% of the treated patients) but none with right to left shunting. No patient was found with a persistent iASD in the 3 month-follow-up period or later. Iatrogenic ASD was not associated with a higher rate of embolism or death.

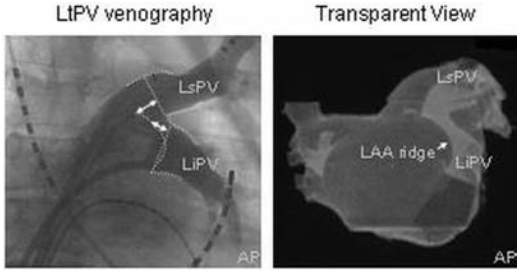
P1164 Accurate discrimination of the left atrial appendage ridge and left pulmonary vein ostium

K. Tanimoto, K. Soejima, K. Fukumoto, Y. Hagiwara, T. Sato, S. Miyoshi, S. Ogawa, M. Yamada, M. Jinzaki, S. Kuribayashi. *Keio University School of Medicine, Cardiology Division, Department of Medicine, Tokyo, Japan*

Background: The extensive encircling pulmonary vein (PV) isolation has been recently used for treatment of atrial fibrillation (AF). Making ablation lesions at the ridge between the left PVs and left atrial appendage (LAA ridge) is important to avoid the PV stenosis and to isolate the antrum. We developed the novel image-processing technique to reconstruct the unique three-dimensional images (Transparent View), which could visualize the LAA ridge easily.
Purpose: The purpose of this study was to identify the LAA ridge by Transparent View and LtPVos by PV venography.
Methods: Consecutive 21 patients who underwent catheter ablation for AF had preoperative ECG-gated 64-detector row computed tomography. The Transparent View was subsequently reconstructed by our novel volume rendering technique. Before the ablation, simultaneous venography of the left superior and inferior PV

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

was performed and the LtPVos was identified. The distance between the LtPVos and the LAA ridge verified by the Transparent View was compared to the distance measured by the PV venogram with the AP projection.
Results: Typical superior and inferior bifurcated PVs, PVs with left middle PV, and left common trunk were observed in 16, 1, 4 patients, respectively. The LAA ridge was deviated from the LtPVos by 6.8±3.7mm. The distance between the LAA ridge and left superior PVos was significantly longer than that between LAA ridge and left inferior PVos (7.1±3.5 vs. 3.4±3.2mm (P<0.05)). The distance between the LAA ridge and the left common trunk os was 6.7±3.9mm.



LtPV venography and Transparent View

Conclusion: There was the significant gap between LtPVos and LAA ridge. Accurate identification of the LAA ridge using the Transparent View may facilitate safer and more efficient ablation of AF.

P1165 Value of blanking time after isolation of pulmonary veins

U. Scholz, J. Vogt, L. Luong Thanh, D. Horstkotte, A. Dorszewski. *Dept Cardiology, Heart Center NRW, Kardiologie, Bad Oeynhausen, Germany*

Purpose: Following substrate modification in the treatment of paroxysmal atrial fibrillation (AF), different blanking times are used to evaluate the success of the procedure. Cryoisolation of pulmonary veins (PV) using the Arctic Front cryoballoon also includes the ablation of parts of the venous antrum. The present study investigates the value of early 7-day Holter monitoring following ablation with regard to long-term recurrences.
Methods: Between 8/2005 and 10/2006, 80 pts (24 women, mean age 59±10 years, 72 with paroxysmal, 8 with persistent AF, LA diameter 42±4 mm, 35 with lone AF, 30 with hypertension, 15 with minor structural heart diseases) underwent cryoisolation of PV. Isolation was performed following PV angiography using the 23/28 mm balloon (Arctic Front, Cryocath, Canada). In each patient (pts), all PV were isolated either with balloon only or with an additional touch up of rest potentials. One day after the procedure and at a 3-month interval, 79 patients underwent 7-day Holter monitoring. 52 pts (66%) had sinus rhythm (SR), 27 pts (34%) showed early recurrences of AF.
Results: 58 pts (39 with initial SR, 19 with early recurrence of AF) were within a mean follow-up period of 6 months. While only 14 of 39 pts (36%) with initial SR showed AF recurrences during their further course, 15 of 19 pts (79%) with early recurrences of AF developed further recurrences. Of 14 pts with AF recurrence and initial SR, 3 pts underwent re-ablation. 11 pts showed a significant reduction of AF burden and had sinus rhythm under antiarrhythmic medication. Of 15 pts with early and repeat AF recurrences, 6 pts were reisolated, 8 pts underwent medical therapy with a reduction of AF burden.
Conclusion: After cryoballoon isolation of PV, an early rhythm analysis provides information on the further course. The evidence of an early recurrence of AF is predictive for later recurrences and supports the necessity of a complete elimination of PV triggers. However, the presence of SR during the first 7 days is associated with a significantly better outcome. A blanking time is not useful.

P1166 Variation of the characteristics of clinical episodes of paroxysmal and persistent atrial fibrillation after ostial disconnection of pulmonary veins

G. De Ambroggi, C. Esposito, L. Vitali Serdoz, S. Foresti, M. Pittalis, P. Francia, M.C. Tavera, P. Lupo, L. De Ambroggi, R. Cappato. *IRCCS Policlinico San Donato, Milan Univ., Clinical Arrhythmias and Electrophysiology, San Donato Milanese (Milan), Italy*

Purpose: While pulmonary veins (PVs) have been shown to contribute in the maintenance of sustained atrial fibrillation (AF) during electrophysiological investigation, less is known about their role in the chronic clinical setting. The a im of our study was t o investigate clinical variations of paroxysmal (PAR) and persistent (PERS) AF in response to a prospectively designed multi-procedural radiofrequency (RF) catheter ablation approach that increases through subsequent steps the number of isolated PVs.
Methods and Results: One-hundred-nineteen consecutive patients with drug-refractory symptomatic PAR (72) or PERS (47) AF with no or mild heart disease underwent 317 procedures. Significantly more patients with paroxysmal AF (31 [43.7%]) than with persistent AF (11 [24.4%], p <0.01) were cured after isolation of the superior PVs only (first ablation step), but success rates became similar in the two patient groups (57 [80.2%] vs 36 [80.0%], p = 0.8) after additional isolation of the inferior PVs during a second ablation step, 5.7±3.1 months later, and after RF consolidation of the PV isolation design during a third ablation step (65 [91.5%] vs 39 [86.62%], p = 0.6), 6.6±3.0 months after the second step. After the first ablation step, 24-hour Holter monitoring revealed shorter episodes (from 14.4±12.0 to 8.8±7.2 hours, p = 0.03) in the 40 (56.3%) patients with recurrent PAR AF, whereas PERS AF turned into paroxismal self-terminating AF in 13 (27.7%) patients. Freedom from AF and shortening of AF duration correlated with the number of isolated superior PVs (25.8% vs 16.2% of all targeted PVs; p < 0.005). Moreover, significantly longer cumulative atrial to PV conduction times of the superior PVs were observed in the 13 patients with PERS AF and post-ablation self terminating AF (49.2±44.0 msec) as compared to those who remained in PERS AF (17.1±27.9 msec, p < 0.03).
Conclusions: These findings outline the role of PVs as critical determinants for arrhythmia onset and maintenance of clinical episodes of PAR and PERS atrial fibrillation.

P1167 Selection of catheter ablation method of paroxysmal atrial fibrillation according to number and localization of atrial ectopic foci using P-wave analysis

D. Lebedev, E. Mikhailov. *Almazov Heart, Blood and Endocrinology Centre, Saint-Petersburg, Russian Federation*

Background: Paroxysmal atrial fibrillation (PAF) can be treated with segmental ostial ablation of the pulmonary veins (SOA) and with circumferential left atrial ablation around the pulmonary veins (CLAA). There is no unified rule to select one of these approaches.
Purpose: The aim of the present study was to demonstrate the possibility to select the catheter ablation method using Holter monitoring and a special ectopic P-wave analysis.
Material and methods: 58 symptomatic patients (pts) (34 male; age 56±17 years) were included in the study. Holter monitoring was performed in 12 leads in all patients. Early "P on T" premature atrial contractions (PAC) were assessed using pre-ectopic T wave subtraction. Using vectorial and morphologic analysis we could determine localization of ectopic premature beats and number of arrhythmogenic foci. SOA was performed using Lasso catheter (group A) and CLAA was performed using Carto navigation system (group B).
Results: According to ectopic P-wave analysis 16 (27.6%) pts had only one "P on T" ectopic P-wave form, 27 pts (46.6%) had two ectopic P-wave forms, 15 (25.8%) had three forms. 28 pts underwent SOA (12 with one ectopic P-wave form, 11 with two forms and 6 with three forms). CLAA was performed in 30 pts (4 with one ectopic P-wave form, 16 with two and 11 with three forms). During 12±6 months we could observe recurrences of PAF and necessity of repeat ablations. In group A all 6 pts with three forms of ectopic P-waves (100%) had symptomatic recurrence of PAF and underwent repeat ablation, 4 of 11 (36%) pts with two ectopic P-wave forms underwent repeat ablation and only 1 pts with one form (8%) needed a repeat procedure. In group B only 2 patients (7%, both with three ectopic P-wave forms) had non significant benefit of the first procedure and needed repeat ablation.
Conclusion: In pts with PAF number of atrial triggering ectopic foci can play significant role in SOA effectiveness. In pts with more than two atrial ectopic foci can be recommended CLAA to get more effective catheter treatment.

P1168 Single centre UK experience of cryoablation ballon for paroxysmal AF

A.J. Sandilands, K. Woodburn, P.A. Boreham, T.R. Cripps. *Bristol Royal Infirmary, Cardiology, Bristol, United Kingdom*

Background: Radiofrequency ablation (RFA) for paroxysmal atrial fibrillation (AF) has developed into an effective and safe procedure. However, the efficacy of balloon cryoablation (Arctic Front, CryoCath) has not yet been established.
Methods and Results: We report the first 20 consecutive patients (16 male, mean age 54 years) undergoing balloon cryoablation between December 2005 and November 2006. Each patient had documented symptomatic paroxysmal AF with failure of at least 1 anti-arrythmic (mean 2, range 1-4) and 2 patients had AF suppression pacemakers. Following transeptal puncture, pulmonary vein (PV) anatomy was identified using contrast injection and PV potentials (PVP's) were mapped with a circular catheter. Balloon cryoablation was performed (12 patients 28mm, 7 patients 23mm with 1 patient both 23 and 28mm balloons) in each active PV ostia for up to 5 minutes, mean procedure time 154 mins, mean screening time 47.2 mins. Post ablation mapping demonstrated 86/90 PV's were electrically isolated (1 already silent, persistent PVP's in the remaining 3). 4 patients also underwent typical right atrial flutter ablation (2 as repeat procedure). A single patient had RFA to a single PV. Complications included 3 mechanical balloon failures necessitating new balloons, 4 phrenic nerve palsies (2 minor which reversed, 2 partially reversed but patients asymptomatic), 1 tamponade requiring drainage and a single patient with lobar collapse following general anaesthetic. With a mean follow up of 7 months, 9 (45%) patients were AF free on no medication, 3 (15%) patients had minor symptoms on no medication and 4 (20%) had

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

minor symptoms on medication. 4 (20%) patients had minor or no improvement in symptomology and are awaiting re-do. Patients were generally satisfied with the outcome using a postal questionnaire with mean scoring 4/5 (range 0-5).
Conclusion: It would therefore appear that balloon cryoablation for PAF is a safe and promising alternative to RF ablation.

P1169 Impact of ablation focused on the complex fractionated atrial potential on vagal modulation to atria

P. Jiang, S. Zhang, L. Gao, Y. Dong, D. Yang, Y. Xia, Y. Yang. *Dalian Medical University, Department of Cardiology, Dalian, China, People's Republic of*

Background: Ablation targeting complex fractionated atrial potential (CFAP) has been demonstrated to be effective for atrial fibrillation(AF). Some promising observation have shown that the distribution of CAFP has a relationship with the efferent vagal innervation to atria. This study aimed to investigate the impact of CAFP ablation on vagal modulation to atria and vulnerability to atrial fibrillation.
Methods: Ten adult mongrel dogs were involved in this study. Bilateral cervical sympathovagal trunks were decentralized. Metoprolol was given to block sympathetic effects. Multipolar catheters were placed into the right and left atrium and coronary sinus. CAFP was recorded by multipolar catheters during atrial fibrillation induced by S1S2 stimulation during sympathovagal trunks stimulation. Ablation was performed in right atrium and left atrium via trans-septal procedure guided by multipolar catheters. Atrial effective refractory period (ERP), vulnerability window (VW) of AF, and sinus rhythm cycle length (SCL) were measured at right atrial appendage (RAA), left atrial appendage (LAA), distal coronary sinus(CSd) and proximal coronary sinus(CSp) at baseline (without vagal stimulation) and during vagal stimulation before and after ablation. The underlyingtissue were excised from ablative sites and the same sites without ablation as control specimens. Serial sections were taken and stained with hematoxylin and eosin for microscopic examination.
Results: (1) SCL shortening during vagal stimulation significantly decreased after abaltion(18±8 vs 107±19 beats per minute,$P < 0.001$). (2) ERP shortening during vagal stimulation significantly decreased after ablation (17±24 vs 65±22ms at RAA, $P < 0.001$; 6±14 vs 41±19ms at LAA, $P < 0.001$; 9±10 vs 63±23ms at CSd, $P < 0.001$; 4±16 vs 61±21ms at CSp, $P < 0.001$). (3) AF was difficult induced at baseline before and after ablation in all sites (VW close to 0), While VW of atrial fibrillation to vagal stimulation significantly decreased after ablation (18±29 vs 58±13ms at RAA, $P < 0.001$; 19±22 vs 31±24ms at LAA, $P < 0.001$; 11±20 vs 52±28ms at CSd, $P < 0.001$; 7±15 vs 62±35ms at CSp, $P < 0.001$). (4) The architecture of individual ganglia was significantly altered after ablation.
Conclusions: The decreased SCL and ERP shortening to vagal stimulation after CFAP ablation indicates that CFAP ablation attenuate the vagal modulation to atria, thereby suppressing atrial fibrillation mediated by enhanced vagal activity.

P1170 Electrophysiological aspects of pulmonary vein circumferential ablation. Pulmonary vein disconnection rate after modification of ablation end points according to antrum electrogram characteristics

A. Arenal, E. Gonzalez-Torrecilla, F. Atienza, T. Datino, L. Atea, J. Almendral, A. Sanchez, F. Fernandez-Aviles. *Hospital Gregorio Maranon, Cardiology, Madrid, Spain*

Background and objectives: Pulmonary vein (PV) disconnection provides high success rate in patients with atrial fibrillation (AF). Circumferential pulmonary vein ablation (CPVA) is a simple an effective procedure but less than 60% of PVs are disconnected. The purpose of this study is to determine if the modification of CPVA electrophysiological end points increases the PV disconnection rate.
Methods and Results: Forty consecutive patients were analyzed. Study I: In 15 patients the characteristics of antrum electrograms at the PV- left atrium (LA) connection site before and after CPVA and disconnection rate were evaluated when standard ablation end points (80% reduction in electrogram amplitude or 0.1 mV) were achieved. Fifty five PV were analyzed, 17 during sinus rhythm (SR) and 38 during A F. PV-LA connection site electrograms were characterized by multiple components without isoelectric line (0.45+ 0.43 mV, 77+21 ms). After blind CPVA 55% of PV were disconnected, 70% in SR and 47% on A F ($p<0.1$). In 85% of non disconnected vein multicomponent electrograms (0.11+0.02 mV range 0.08 to 0.14 mV and 56+ 13 ms range 40 to 80 ms) were recorded at the site where circumferential mapping guided ablation disconnected PV. Study II: 25 consecutive patients (95 PV, 52 during AF and 43 during SR) underwent blind CPVA under modified ablation end points: 1) Single component electrograms: Voltage reduction by 80% or 0.1 mV and 2) Multi-component electrograms: Disappearance of the late component and voltage reduction to <0.05mv. Eighty five per cent of PVs were disconnected (95% in SR and 77% in AF ($p<0.01$).
Conclusions: PV-LA connection site electrograms were characterized by multiple components without isoelectric line. Modification of CPVA end points according to electrogram characteristics increases the PV-LA disconnection rate.

P1171 Duration of the A(H)A(Md) interval predicts occurrence of conduction block during radiofrequency ablation of the slow pathway

M. Stuehlinger[1], K. Etsadashvili[2], X. Stuehlinger[1], T. Berger[1], F.X. Roithinger[1], O. Pachinger[1], F. Hintringer[1]. *[1]Medical University of Innsbruck, Cardiology, Innsbruck, Austria; [2]Medical University of Innsbruck, Cardiology, Innsbruck, Austria*

Introduction: Modification of the slow pathway using radiofrequency (RF) is currently the most effective treatment for atrioventricular nodal reentry tachycardia (AVNRT). However, transient or permanent atrioventricular conduction block (AVB) may be a serious complication of this therapy. The risk of occurrence of ventricular-atrial conduction block (VAB) during rapid junctional activity (JA) and consecutive AVB during RF delivery is estimated by the radiologic distance on X-ray (XR) between the ablation catheter and the His-electrode. Since XR depends on the angle of the base of the triangle of Koch, its value in predicting AVB was compared with the electrical A(H)A(Md) interval, which was measured from beginning of the atrial signal on the His-bundle electrode to the one on the ablation catheter right before the start of RF delivery.
Methods: X-ray distance between the ablation and the His-catheter (XR), A(H)A(Md) interval as well as the occurrence of VAB during JA, transient or permanent AVB were analyzed retrospectively for 1585 RF deliveries in 393 patients diagnosed with AVNRT between 1999 and 2005 (58% female, 42% male) at our institution.
Results: A mean of 2.7 RF therapies were delivered per patient and A(H)A(Md) was closely correlated with the number of ablations per patient ($R=0.144$; $p<0.0001$) and XR ($R=0.165$; $p<0.0001$). VAB during JA was found during 348 ablations, and 38 cases of transient AVB (9 AVB I, 13 AVB II, 16 AVB III) and 13 cases of permanent AVB (8 AVB I and 5 AVB III) were documented. In a multivariate analysis A(H)A(Md) was the best predictor for VAB or AVB ($p<0.0001$), followed by the number of ablation ($p=0.015$) and XR ($p=0.05$). The risk of occurrence of transient or permanent AVB after an ablation was furthermore significantly elevated, if A(H)A(Md) was ≤21ms (15.5%) than if it was longer than 20ms (3.7% for 21-25ms; 1.4% for 25-30ms; 2.2% for 31-35ms; 2.8% for 36-40ms).
Conclusion: A(H)A(Md) interval is a better predictor for occurrence of conduction block during or after ablation of the slow pathway than the radiological distance from the ablation catheter to the compact AV-node. Specifically an interval <21ms increases the development of AV-Block 5-10fold. Therefore A(H)A(Md) measurements before RF delivery should be performed to avoid AV conduction block as a consequence of slow-pathway ablation.

P1172 Feasibility and safety of remote magnetic navigation for ablation of atrial fibrillation

X. Chen, S. Pehrson, J. Hastrup Svendsen. *Rigshospitalet, University of Copenhagen, Medical Department, Cardiology B-2014, Copenhagen, Denmark*

Purpose: The purpose of the current study was to evaluate the feasibility and safety in ablation of atrial fibrillation (AF) by remote magnetic navigation using a 4 mm tip magnetic catheter.
Methods: Forty-two consecutive patients (mean age 57±12 years, 30 male) underwent catheter ablation for AF using a remote magnetic navigation system (Niobe II, Stereotaxis). Ablation was performed with a 4-mm tip magnetic catheter. The power limit was set to 40 watts and RF time to 20 seconds, with the preset temperature of 60-65 °C in the first 5, and 55°C in the last 37 patients. A 3-D map was created using either integrated CARTO RMT system (n=31) or non-integrated NaVx system (n=11). For paroxysmal AF (n=29) circumferential pulmonary vein (PV) isolation and superior linear ablation were performed. For persistent/permanent AF (n=13) multi linear and fractional potential ablation were added.
Results: Complete circumferential PV isolation was achieved in 39 of 42 patients. The total procedure time was 140±39 min. The total procedure time was slightly shorter in the last 22 cases, but there was no significant difference between the first 20 and last 22 patients. The mapping/ablation time was 85±34 min, and the RF application time was 34±8 min. The total fluoroscopy time was 9,7±5,1 min. Ablation was performed during AF in 15 patients. AF was terminated during RF application in 4 of them. Small coagulum was found in 4 of the first 5 patients with higher temperature setting, but only in 3 of the last 37 patients with lower temperature setting. No acute complications were observed during or after the procedures.
Conclusions: Remote magnetic navigated ablation of AF ablation using a 4 mm tip magnetic catheter is feasible and safe. The total procedure time and fluoroscopy time are comparable with manual ablation, or even shorter.

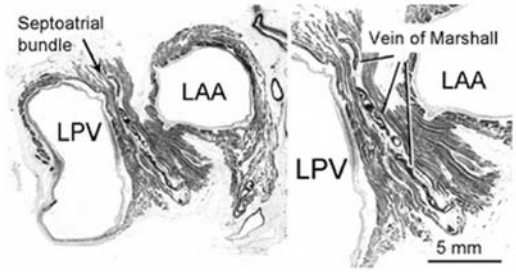
P1173 The architecture and structural content of the left postero-lateral ridge: more than a simple fold of the left atrium of implications for atrial fibrillation ablation

J.A. Cabrera[1], V. Climent[2], Y. Ho[3], A. Fernandez-Ruiz[2], D. Sanchez-Quintana[1]. *[1]Hospital Quiron Madrid, Cardiology, Madrid, Spain; [2]Facultad de Medicina. UEX, Anatomia Humana, Badajoz, Spain; [3]Royal Brompton Hospital, Cardiac morphology, London, United Kingdom*

Introduction: The postero-lateral ridge of the left atrium (LA) is a target of cur-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

rently used ablation procedures when encircling the orificies of the left pulmonary veins (PVs) in patients with atrial fibrillation (AF). The myocardial architecture and structural content of this anatomic structure has not been previously examined in the human heart.
Methods: In 32 normal human heart (24 males, 46±18 years) we examined by gross inspection and disecction technique the architectural arrangement of myocardial bundles forming the LA ridge. The vascular and autonomic nervous system content of the ridge, and its anatomic relations with the Marshall structures were also analyzed by histological sections Results: Epicardially the broad bundle that forms the LA ridge is in continuity with the uppermost and distal part of the interatrial band (Bachmann bundle). Endocardially, the myocardial content is the prolongation of leftward fibres from the septoatrial bundle that run toward the orifices of the left-sided PVs and the mouth of the appendage. The oblique vein of Marshall or its ligament courses obliquely in the epicardial aspect of the ridge and can be traced in 73% of specimens at a distance less than 3 mm from the endocardium (figure). In relation with the ridge we observed in all specimens small muscular bundles and abundant nerves and ganglions of the autonomic nervous system that crossed the vein to connect with the endocardial aspect of the LA ridge.



Arquitecture of the lef atrial ridge

Conclusions: The left postero-lateral ridge is more than a simple endocardial fold of the lateral wall of the LA. The close anatomic relation of the ridge with the autonomic nervous system, vessels and Marshall structures has not been previously reported and may be of potential relevance during catheter ablation of AF.

P1174 Cooled intra-esophageal balloon to prevent thermal injury of esophageal wall during radiofrequency ablation

M. Scanavacca, C.F. Pisani, S. Neto, W. Tamaki, R. Santos, C. Guirao, H. Oyama, V. Aielo, A. Leiner, E. Sosa. *Heart Institute, Arrhytmia Clincal Unit, Sao Paulo, Brazil*

Introduction: Atrio-esophageal fistula is a rare, but potentially lethal complication of atrial fibrillation (AF) radiofrequency (RF) catheter ablation. Theoretical mathematical models suggested that esophageal luminal cooling could be effective to prevent thermal injury of the esophageal wall. The aim of this study was to evaluate the protector effect of an esophageal cooled irrigated balloon on the esophageal injury caused by RF delivery.
Methods: The study was conducted in four dogs under anesthesia and controlled ventilation. A right thoracotomy was performed, exposing approximately 8 to 10 cm of the esophagus. A polyethylene esophageal balloon with 6 cm length and 3 cm diameter was positioned inside the esophageal lumen through an orogastric tube. RF pulses were delivered on the external esophageal surface, by a 4-mm tip catheter, controlled by temperature (between 60 and 85°C) in three dogs and controlled by power (4 and 8W) in one dog, in two different moments: (A) empty esophageal balloon and (B) cooled (10°C) saline solution filling the esophageal balloon. Histological measurements of the muscular layer lesion extension (necrosis and edema) were performed using Leica Qwin software.
Results: Fifteen esophageal lesions were analyzed. No difference on the thickness of muscular layer (1351±218μm) was observed among the samples. When RF delivery was controlled by catheter tip temperature (mean of 66.9±8.0°C), the mean power was 3.7±3.8W in the control group (A) and 4.0±3.3W in the cooled balloon group (B), (P=0.89). The depth of muscular layer lesion was higher in cooled balloon group (2262±289μm) when compared to control group (1540±485μm; P=0.035). When RF energy power was controlled (mean of 6.7±1.9 Watts), the mean catheter tip temperature was 80.0±0°C (A) and 70.4±9.8°C (B), (P=0.25). No difference was observed in the lesions depth in both groups (A= 2779±311μm vs. B= 2410±405μm; P=0.308).
Conclusions: The supposed protector effect against thermal injury by chilling the esophagus during RF delivery was not observed in this study. In fact, it suggests that there is an increase in the lesions depth when RF delivery is controlled by temperature of the catheter tip.

P1175 High success rate in cryoisolation of pulmonary vein ostia and antrum with balloon technique in paroxysmal atrial fibrillation

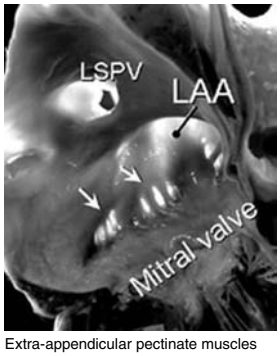
J. Vogt, A. Dorszewski, J. Heintze, U. Scholz, H. Buschler, L. Luong Thanh, D. Horstkotte. *Dept Cardiology, Heart Center NRW, Kardiologie, Bad Oeynhausen, Germany*

Purpose: In treatment of paroxysmal atrial fibrillation (af) circumferential substrate modification of the antrum of pulmonary veins (pv) seems superior in comparison to segmental methods. However with radiofrequency energy a risk of pv stenoses and esophago–left atrial fistula exists. This study reports on the success rate in isolating pv ostia and parts of antrum with the cryoballoon technique.
Methods: After pv angiography isolation was performed with best fitting 28/23mm balloon (Arctic Front, Cryocath, Canada).After inflation the over a wire balloon occludes the venous ostium and parts of venous antrum and freezes down to -50 to – 75 ° C 6 minutes two times per vein with nitrous oxide. Lasso mapped rest potentials were eliminated with additional balloon freezes or with the 9 french Freezor Max catheter.Patients were followed three monthly with the 7 day holter.
Results: We treated 94 p (30 women, mean age 59±10 years,84 with paroxysmal,10 persistent af,left atrium 42±4 mm,41 with lone af,37 hypertension,16 mild structural heart disease) with 23/28 mm balloon. Mean vein diameter was 18.9±4 mm angiographically. With a mean number of 2,4±0,6 impulses we could increase pv isolation up to 93% of the left pv and the right upper pv and 84% of the right lower pv and in up to 60% of the p all 4 pv with balloon only. After touch up of rest potentials we isolated 100% of all pv. The procedure time was 195±36 min, the x ray burden 36±9 min. We observed phrenic nerve palsy in 4 p with the 23 mm balloon recovered within 6 months. During a mean follow up of 6 months and 1.1 procedures per p(8 redos) of 58 p controlled with serial 7 day holter and symptoms 77% (39 p) were free of af without blanking time! 29% (17 p) showed marked reduction of af burden. In the 8 redos 76%(16) of the 21 reconducting veins were initially isolated with the 28 mm balloon.
Conclusion: Cryoisolation of ostia and antrum of the pv with the 23/28 mm balloon is safe and showed a favourable outcome. The superiority in comparison to substrate modification with RF may be an early and first line therapy of left atrial disease. Avoidance of phrenic nerve lesion and focus on different efficacy of balloon diameter may be essential.

P1176 The extra-appendicular posterior pectinate muscle: a new anatomic finding relevant to atrial fibrillation ablation

J.A. Cabrera[1], V. Climent[2], Y. Ho[3], A. Fernandez-Ruiz[4], D. Sanchez-Quintana[1]. *[1]Hospital Quiron Madrid, Cardiology, Madrid, Spain; [2]Facultad de Medicina. UEX, Anatomia Humana, Badajoz, Spain; [3]Royal Brompton Hospital, Cardiac morphology, London, United Kingdom; [4]Hospital Quiron Madrid, Cardiologia, London, Spain*

Introduction: Recent reports have shown the contribution of different atrial regions on the fibrillatory process and to the maintenance of atrial fibrillation (AF). Ablation of extrapulmonary vein triggers arising around or inside the left atrial appendage (LAA) may be requiered to avoid recurrences after pulmonary veins (PV) isolation.
Methods: In 32 normal human heart (24 males, 46±18 years) we examined by gross inspection and histological sections the muscular junction and connections between the LAA and the venous component of the left atrium (LA).
Results: The myocardial LA ridge and an inflection of the endocardial surface bounded the ostial borders of the LAA in most hearts. In the LA the pectinate muscles are mostly confined within the LAA. They form a complicated network of muscular strips lining the endocardial surface. In some 28% of our human heart the anterior ostial margin of the appendage does not present as a clear-cut border and muscular trabeculations can be found extending inferiorly from the appendage to the vestibule of the mitral valve (figure). These extra-appendicular myocardial bands correspond to the small posterior set of pectinate muscles originating from the septoatrial bundle to embraces the left appendage. In those hearts with extra-appendicular posterior pectinate muscles the areas in-between the muscular trabeculas had the thinnest muscular wall (0.5±0.2 mm). In other



Extra-appendicular pectinate muscles

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

specimens (15%) we found remnants of pectinate muscles between the ostium of the left inferior pulmonary vein and vestibule of the mitral annulus.
Conclusions: The presence of extra-appendicular posterior pectinate muscles found in 28% of our hearts and the thinnest muscular wall in-between the muscular trabeculas are anatomic finding of clinical relevance during ablation of patiens with AF

P1177 Comparison between three-dimensional mapping systems for atrial fibrillation ablation: a prospective randomized study

R. Mantovan[1], M. Crosato[1], V. Calzolari[1], L. Sacchetti[2], L. Montagna[3], D. Favarato[2], V. Rizzato[2], Z. Olivari[2].
[1]Cardiovascular Department, Treviso, Italy; [2]St Jude Medical, Agrate Mi, Italy; [3]Biosense, Webster, Milano, Italy

Three-dimensional mapping systems are useful tools for atrial fibrillation (AF) ablation. Aim of this study was to compare in prospective, randomized manner, procedural findings of AF ablation performed either with Carto (Biosense) or with NavX (St Jude) mapping systems.
Methods: 60 consecutive patients (pts) (mean age 55±8 years, female 21; 35%) affected by drug refractory paroxysmal (38), persistent (18) and permanent (4) AF underwent pulmonary veins (PV) ablation. AF history lasted from 6.3±4 years; 6 pts (10%) had experienced ischemic cerebral accidents. All pts underwent PV disconnection with an integrated approach performed by the same operator. Wide encircling lesions were performed around all PVs ostia using irrigated tip catheter. Electrical disconnection was confirmed by circumferential catheter. 30 pts (mean age 52±10 years, female 9) were randomized to Carto (C group) and 30 pts (mean age 57± 7 years, female 12) to Navx (N group). Open irrigation catheters (Thermo Cool, Biosense) were employed in C group, while pts in N group were further randomized to open irrigation catheters (Coolpath, St Jude-IBI) and internal irrigation catheters (Chilli II, Boston). The following procedural and fluoroscopy time were evaluated: 1-mapping time (time to create the anatomical reconstruction), 2- radiofrequency (RF) time (time to achieve all PVs disconnection), 3-total procedural time. Other linear lesions and/or lesions performed at fragmented potentials were excluded form this analysis. Time for electrical isolation of PVs with each catheter were evaluated.
Results: Clinical basal characteristics were comparable in both groups. A median of 4 PVs were disconnected in all pts. Procedural and fluoroscopy mapping time were 34±8 and 9.6±3 min (C group), 38±8 and 9.8±4 min (N group) respectively (ns). Procedural and fluoroscopy RF time were 110±6 and 25±4 min (C group), 105±10 and 24± 10 min (N group) respectively (ns). Total procedural and fluoroscopy time were 185±13 and 43±9 min (C group), 181±16 and 41± 13 min (N group) respectively (ns). Mean time for electrical isolation of PVs was 37±9 min with Thermo Cool open irrigation catheter, 38± 10 min with Coolpath open irrigation catheter and 39±11 min with Chilli II internal irrigation catheter (ns). One patient developed cardiac tamponade (N group, Coolpath catheter).
Conclusion: Three dimensional Carto and Navx mapping systems are equally effective in PVs isolation for AF ablation. Moreover both internal and open irrigation catheters seem equally efficacious and safe.

P1178 Segmental pulmonary vein ablation: success rates with and without exclusion of areas in close anatomical relationship to the esophagus

K. Kettering, H. Weig, M. Busch, R. Laszlo, J. Schreieck. *University of Tuebingen, Cardiology, Tuebingen, Germany*

Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation (AF). The occurrence of an atrioesophageal fistula is a rare but serious complication after AF-ablation procedures. This risk is also present during segmental pulmonary vein (PV) ablation procedures because the esophagus does frequently have a very close anatomical relationship to the right or left PV ostia. The aim of the present study was to analyse whether the exclusion of areas with a close anatomical relationship to the esophagus does have a significant effect on the success rates after segmental PV ablation procedures.
Methods: 47 consecutive pts. with symptomatic paroxysmal AF were enrolled in this study. In all pts., a segmental PV ablation procedure was performed. The procedures were facilitated by an online visualization of the Lasso catheter using the Navx system (open irrigated tip ablation catheter; 43 °C; 30 W). In 25 pts., a complete PV isolation was performed regardless of the anatomical relationship between the ablation sites and the esophagus (group A). In the remaining 22 pts., the esophagus was marked by a stomach tube and areas in close anatomical relationship to the esophagus were excluded from the ablation procedure (group B). After discharge, patients were scheduled for repeated visits at the arrhythmia clinic at 1 and 3 months after the ablation procedure.
Results: The segmental PV ablation procedure could be performed as planned in all patients. In group A, all PVs could be isolated successfully in 18 out of 25 pts. (72%). The main reasons for an incomplete PV isolation were: small diameter of the PVs, side branches close to the ostium or poorly accessible PV ostia. In group B, all PVs could be isolated successfully in only 12 out of 22 pts. (55%). This was mainly due to a close anatomical relationship to the esophagus. The ablation strategy had to be modified in 16/22 pts. in group B because of a close anatomical relationship between the left (n=10) or right (n=6) PV ostia and the esophagus. After 3 months, the percentage of patients free from an AF recurrence was not significantly different between the two groups (72 vs. 77%). There was no evidence for an atrioesophageal fistula and there was no PV stenosis post ablation.
Conclusions: The exclusion of areas with a close anatomical relationship to the esophagus results in a higher percentage of incompletely isolated PVs. However, it does not have a significant effect on the AF recurrence rate during midterm follow-up. The long-term performance of these patients is currently evaluated.

P1179 Cryothermal balloon ablation isolates the pulmonary veins and modifies the electrical properties of the atrium

Y. Van Belle, M. Rivero-Ayerza, E. Jessurun, P. Knops, P. Jansse, M. Miltenburg, K. Nieman, L. Jordaens on behalf of Electrophysiology Thoraxcentre Rotterdam. *Thoraxcentre, Clinical Electrophysiology, Rotterdam, Netherlands*

Purpose: Isolation of the pulmonary veins (PV) with balloon cryoablation (BCA) yields excellent results for patients (pts) with paroxysmal atrial fibrillation. To study whether BCA modifies the substrate in the left atrium (LA), we analysed the electroanatomical map (EAM) before and after BCA.
Methods: 17 consecutive pts were included, using 23 or 28 mm cryothermal balloons. Voltage mapping was performed; the earliest site of LA activation was labeled, and the conduction analysed with a propagation map. In 13/17 pts a good quality double EAM was available.
Results: In the 17 pts isolation was achieved in all targeted PV's. All 13 pts with double EAM were isolated with the balloon alone (in 4 cases a 28 mm, in 9 pts a 23 mm balloon). The EAM after BCA significantly changed. It showed a wide antral area of low voltage (<0.5mV) in 9pts (including all 28 mm cases), and a small area in 3 pts; the voltage map remained unchanged in one patient. In 7 of 9 pts with substantial voltage modification, this was restricted to either the left or the right side alone. The activation pattern changed markedly in 6, and moderately in 2 of the 14 pts in whom it could be assessed, irrespective of the size of the balloon. It was mainly the high septal region which was affected, shifting the earliest activation to other sites.
Conclusion: BCA is effective for achieving complete PV isolation. Substrate modification of the LA antrum is also observed, with a significant reduction of voltage. The pattern of LA activation changes in more than 50% of the pts, confirming that cryoablation with either the 23 or the 28 mm balloon modifies the atria as well.

P1180 Focal atrial tachycardia arising from the non-coronary aortic sinus

C. Kriatselis[1], M. Roser[1], S. Goetze[1], G. Evangelidis[2], M. Hoeher[2], D. Martinovic[3], E. Fleck[2]. *[1]German Heart Institute, Cardiology, Berlin, Germany; [2]Klinikum Bayreuth, Cardiology, Bayreuth, Germany; [3]Areteion Hospital, Heart Surgery, Nicosia, Cyprus*

Introduction: The majority of focal atrial tachycardias (FAT's) arise either in the right atrium (preferably crista terminals and coronary sinus ostium) or in the left atrium (pulmonary veins, close to mitral annulus). We describe 6 patients with FAT arising from the non-coronary aortic sinus.
Methods: 6 patients (p.) (2 females, age 54±12, 29 to 63 yrs) have been referred for electrophysiological study (EPS) because of paroxysmal palpitations. In 3 of them a regular narrow-QRS complex tachycardia had been documented. 2 p. had already an EPS and unsuccessful ablation attempt elsewhere. A long-standing hypertension was known in one p., otherwise the individuals were healthy.
Results: During the EPS a FAT (CL 418±57 ms) could easily be induced by atrial burst in all p. During tachycardia the earliest activation site was distal His. Proximal His, coronary sinus ostium and high right atrium were activated 7±2, 25±12 and 44±20 ms after distal His activation. Activation of the coronary sinus occured from proximal to distal. Mapping of the left atrium in 4 p. showed earliest activation in the septal region (22±10 ms later than distal His). No ablation was attempted at His side. The ablation catheter was retrograde introduced in the ascendant aorta and detailed activation mapping was performed in the aortic root. Both right and left coronary aortic sinus (AS) were activated almost simultaneously to distal His (left AS-distal His 4±9 ms, right AS-distal His 5±7ms). Activation in the non-coronary aortic sinus was 33±9 ms earlier than at distal His. RF-application (30 Watt, 40±12 sec) in this side terminated the FAT in less than 2 sec in 5 p. and in less than 6 sec in all p. After successful ablation FAT could not be induced in any of the p. A coronary angiogram after ablation excluded coronary spasm or thrombosis. No acute or late complication occurred in any of the p. During a follow-up of 6±2 months all p. remained free of symptoms.
Conclusion: In case of FAT with earliest atrial activation at His site, a detailed activation mapping in the aortic root and especially in the non-coronary aortic sinus should be performed. Radiofrequency ablation at this side is safe and effective in permanently eliminating the tachycardia.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1181 Four-year results of prospective follow-up after circumferential pulmonary veins catheter ablation in atrial fibrillation

I. Wozniak-Skowerska, A. Wnuk-Wojnar, S. Nowak, A. Hoffmann, C. Czerwinski, M. Trusz-Gluza. *Medical University of Silesia, I Department of Cardiology, Katowice, Poland*

Background: Catheter ablation has recently become a more widely used and evaluated method of treatment in highly symptomatic patients (pts) with drug refractory atrial fibrillation (AF). However, long-term results (> 1 yr) were not systematically assessed.
The aim of the study was to review the clinical data obtained from the 1 and 4 year prospective follow-up in AF pts after catheter ablation.
Methods: A group of consecutive 84 pts (47 males, mean age 54 + 9 yrs) with AF undergoing circumferential pulmonary veins catheter ablation (CPVA) according to Pappone technique from 2002 to 2003 was followed-up every three months up to 4 years after procedure. At baseline structural heart disease was noted in 27%, hypertension in 57% of pts. Symptoms, other clinical data and results of ECG, Holter or event recordings and echocardiography were collected.
Results: Antiarrhythmic drugs were mostly used as a "pill in the pocket" strategy. No late complications were found.

The results

	1 yr - %	4yrs - %	p
Improvement	75	60	NS
No AFrecurrence	24	13	NS
AFpermanent	12	27	NS
Pacemaker	7	14	NS
Re-ablation	1	8	NS
Revascularization	1	5	NS
Antiarrhythmicdrugs	80	62	NS
Beta blockers	55	45	NS
Anticoagulation	78	80	NS
Structuralheart disease	32	50	NS
Hypertension	63	77	NS

Conclusions: CPVA for drug-refractory atrial fibrillation is not a curative procedure but provides a clinical success in most of pts which persists up to 4 year follow-up in majority of pts. AF recurrence in some of pts was connected with progressing of structural heart disease.

P1182 The impact of linear ablation along the coronary sinus on the outcomes of catheter ablation for permanent atrial fibrillation

K. Rajappan, P. Kistler, S. Kalra, M. Kalla, M.J. Earley, S. Harris, D. Gupta, D. Abrams, S.C. Sporton, R.J. Schilling. *St Bartholomew's Hosp/Queen Mary University, Department of Cardiology, London, United Kingdom*

Introduction: The success of catheter ablation (CA) in permanent atrial fibrillation (AF) is inferior to paroxysmal AF. The appropriate strategy for additional atrial ablation following wide encirclement of pulmonary vein (PV) pairs in patients with chronic AF remains to be determined. We report the single procedure outcomes of adding linear ablation along the coronary sinus (CS) to the ablation strategy in patients with chronic AF.
Methods & Results: 71 consecutive patients (60±10 years, 55M) with permanent AF underwent FIRST-TIME CA guided by electroanatomic mapping and CT integration. Following double trans-septal puncture wide encirclement of PV pairs was performed using irrigated radiofrequency ablation with the endpoint of electrical isolation. In the first 34 patients (control group) linear ablation was performed at the left atrial (LA) roof, right atrial isthmus and complex fractionated LA electrical activity was targeted. In the subsequent 37patients (study group) ablation along the inferior LA parallel to the CS catheter and ablation within the CS (30 Watts) was performed with the endpoint of electrical disconnection. If AF persisted on completion of the lesion set internal DC cardioversion was performed. Procedure times were similar in both groups (268±61 [control] vs. 270±71 minutes [study]; p=ns). There were no additional complications from CS ablation. There was no difference in the number of patients who needed DC cardioversion at the end of the procedure (22 control vs. 25 study). All patients were in SR at the end of the procedure and on the 1st day afterwards. At follow up (19±12 weeks) 16/34 patients (47%) were free of AF in the control group compared with 16/37 patients (43%) in the study group (chi-squared=0.10; p=ns). Of those with recurrence 26 had AF (15 control vs. 11 study) and 13 had atrial tachycardia (3 control vs.10 study). (AF vs. atrial tachycardia for the two groups chi-squared=4.18; p< 0.05)
Conclusions: The addition of CS linear ablation for CA of permanent AF did not improve acute or medium term outcomes. There was a lower recurrence of AF and more atrial tachycardia in the linear CS ablation group. Atrial tachycardia may be more amenable to further ablation and hence improve outcome in the longer term.

P1183 Early recurrence of PV conduction following PV isolation: incidence, predictors and practical implications

N. Perez Castellano, J. Perez-Villacastin, J. Moreno Planas, J. Salinas Arce, M. Vega Olvera, S. Garraza, R. Morales, M. Doblado, E. Ruiz, C. Macaya. *San Carlos University Hospital, Arrhythmia Unit, Cardiovascular Institute, Madrid, Spain*

Despite controversial data in the literature, recent evidence supports the importance of achieving persistent pulmonary vein (PV) conduction block to succeed in atrial fibrillation (AF) ablation.
Methods: This study analyzed prospectively the incidence of early recurrence of PV conduction following ostial PV electrical disconnection. After each PV disconnection, PV conduction was periodically assessed during the ablation procedure. Monitoring was extended by a minimum of 30 minutes after the latest PV isolation. Data are presented as median [P25-P75].
Results: A total of 113 PVs from 34 patients referred for AF ablation were targeted. Bidirectional block was achieved in every PV. PV conduction was monitored during 68 [31-110] min following electrical disconnection. Early recurrence of PV conduction was observed in 16 PVs (14%) from 15 patients (44%). Early recurrence of PV conduction was more frequent in patients with structural heart disease (67% vs 32%; P=0.1), persistent atrial fibrillation (71% vs 33%; P=0.09), and PV with a common ostium (33% vs 11%; P=0.03). There were no differences in power and temperature delivered to patients with or without early recurrence of PV conduction. Survival analysis showed that the incidence of PV conduction recurrence increases lineally within the first 2 hours following isolation. At this time-frame, the rate of PV conduction recurrence is 25% (95% confidence interval = 19-31%).
Conclusions: Early recurrence of PV conduction following PV isolation is frequent (25% within the first 2 hours following isolation). PV conduction monitoring and re-ablation in case of recurrence might improve the efficacy of AF ablation.

P1184 An occluding cryoballoon for circumferential pulmonary vein isolation: feasibility and efficacy

Y. Van Belle, P. Jansse, M.J. Rivero-Ayerza, D.A.M.J. Theuns, E.R. Jessurun, L. Jordaens on behalf of Erasmus Thoraxcentre. *Thoraxcentre, Clinical Electrophysiology, Rotterdam, Netherlands*

Aim: To assess safety, feasibility and short term efficacy of pulmonary vein (PV) isolation in paroxysmal atrial fibrillation (PAF) with a cryoballoon.
Methods: We consecutively treated 57 patients with a double lumen 23 or 28mm cryoballoon. The acute results, complications and follow-up over the first three months were analysed, using a comprehensive and intensive follow-up period.
Results: During 57 procedures, 185 of 220 targeted PV's were successfully isolated using the cryoballoon (84%) (balloon group, 33 patients). In 33 veins (15%) an additional segmental isolation (hybrid group, 24 patients) was necessary with a standard cryocatheter to achieve isolation. In both groups the average procedure times were respectively 211±108 and 261 ±83 minutes (p=NS), the average fluoroscopy times were 66±33 and 52±36minutes (p=NS). The number of balloon applications did not differ between both groups: respectively a median 9 (4-18) and 10 (5-17) (p=NS). We observed twice phrenic nerve paralysis after ablation of the right superior PV, one recovered after 3 months, one persisted up to 6 months. There was one pericardial effusion which required surgical drainage. A daily transtelephonic rhythm recording showed a significant drop in mean AF burden from 24% to 10%, 9% and 5% during the three consecutive months of follow-up (all p<0.01). 39 patients (68%) were completely free from AF after a single procedure.
Conclusion: Balloon cryoablation of the pulmonary veins with additional segmental isolation if necessary, is a good approach for patients presenting with PAF, showing a successrate of 68%. The major complication seems to be phrenic nerve paralysis after ablation of the right superior PV, but this is potentially reversible over several months.

P1185 Comparison of the efficacy between circumferential pulmonary vein ablation and segmental pulmonary isolation for treatment of paroxysmal atrial fibrillation

D. Yang, S. Zhang, L. Gao, Y. Xia, Y. Wang. *Dalian, China, People's Republic of*

Objectives: Data on the comparison of the circumferential pulmonary vein ablation (CPVA) and the segmental pulmonary vein isolation (SPVI) for treatment of paroxysmal atrial fibrillation (PAF) are little. We hypothesized that CPVA approach was superior to SPVI approach.
Methods: One hundred patients with highly symptomatic PAF were randomly assigned to undergo either CPVA (n=50) or SPVI (n=50). Freedom from atrial tachyarrhythmias in a 24 hour Holter monitoring at 3rd month, 6th month, 9th month and 12th month after ablation was the primary end point. Secondary end points were post-ablation atrial reentrant tachycardia and a composite of pericardial tamponade, thromboembolic complications, and pulmonary vein stenosis (safety end point).
Results: On the basis of the results of the 4 times 24 hr Holter monitoring, 42 patients (84%) after CPVA and 41 patients (82%) after SPVI (p>0.5) were free of

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

atrial tachyarrhythmia episodes. No significant difference was found in the safety end point (2 versus 2 events; $p>0.5$) in CPVA group versus SPVI group, respectively. However, there were more post-ablation atrial reentrant tachycardia in CPVA group than SPVI group (5 versus 0, $p<0.02$)
Conclusions: This study demonstrates no superiority of CPVA over SPVI for treatment of PAF in terms of efficacy and safety. CPVA may give rise to post-ablation atrial reentrant tachycardia.

P1186 Clinical utility of periprocedural transoesophageal echocardiography during pulmonary vein isolation for atrial fibrillation

A.M. Martellotto[1], R.A. Lawrance[2], S. Kimber[1], S. Gulamhusein[1], J.B. Choy[1], A. Pantano[1]. *[1]University of Alberta Hospital, Division of Cardiology, Edmonton, Canada; [2]University of Alberta Hospital, Adult Cardiology, Edmonton, Canada*

Background: Despite anticoagulation, thromboembolic events during pulmonary vein isolation (PVI) for atrial fibrillation occur at rates of up to 10%. Peri-procedural transeosophageal echocardiography (TOE) can rule out left atrial (LA) clot. Recent reports suggest that thrombus may form on the trans-septal sheath and may have important consequences.
Objectives: We sought to determine if TOE would be useful in the identification of sheath thrombus during trans-septal puncture, and whether or not anticoagulation influenced the rate of its formation.
Methods: Between July 2004 to January 2007, 51 consecutive patients (61 procedures) underwent PVI. TOE was used to guide the trans-septal puncture as well as to rule out LA clot and clot on the trans-septal sheath.
Results: TOE detected the presence of clot on the trans-septal sheath prior to the puncture in 3 patients (in 2 of 31 where INR <2, and 1 of 30 where INR ≥ 2). One LA appendage clot was detected in one patient whose INR <2 leading to abandonment of the procedure. Clot was confirmed by aspiration from the sheath which was then removed and cleaned. None of the patients had clinical evidence of thromboembolism, and there were no complications from the TOE.

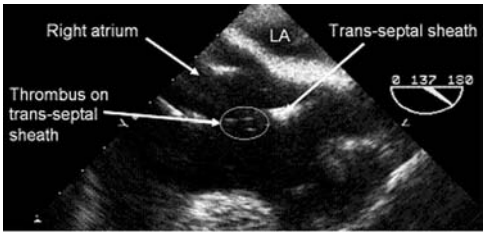


Figure 1. TOE clot on trans-septal sheath

Conclusion: Despite adequate anticoagulation prior to PVI, clot can form on the trans-septal sheath. Routine TOE is a safe and clinically useful tool during trans-septal puncture, both to guide accurate positioning of the sheath for trans-septal puncture and to allow for detection of LA clots and those on the trans-septal the sheath whilst still in the right atrium. This is likely to have clinical importance in the prevention of thromboembolic complications during PVI.

P1187 Proximal coronary sinus as critical part of atrial flutter during re-do ablation of atrial fibrillation patients

A. Ardashev[1], E. Zhelyakov[2], D. Mangutov[1], A. Konev[1]. *[1]Burdenko Head Clinical & Military Hospital, Interventional Cardiology Dept., Moscow, Russian Federation; [2]Moscow, Russian Federation*

Purpose: to access role of coronary sinus (CS) as component of atypical atrial flutter (AAF) reentry circuit after radiofrequency ablation (RFA) of atrial fibrillation (AFib) pts.
Methods: Study was conducted on 102 consecutive patients (44 women, 54.3±13.6 years of age) with the paroxysmal (51%), persistent (22%) and chronic (27%) AFib underwent circumferential radiofrequency ablation (RFA) procedure guided by CARTO system. AAF manifested in 22 (22%) pts after primary RF-ablation session in the period of 23±15 days. Electrical and/or drug cardioversion was effective in 13 pts. Repeated RFA was performed in 9 (9%) pts with sustained drug-refractory AAF.
Results: Activation mapping guided by CARTO system revealed reentry circuits (cycle length – 220 and 230 ms) at the vicinity of right pulmonary veins in 2 pts and atrial perimitral reentry with mean cycle length of 240±15 ms in 7 pts. Left mitral isthmus – dependent AAF was verified by entrainment technique and successfully ablated in those 7 cases. Distal CS RF-isolation (12-1 to 3 clock on LAO projection) was performed in all cases as first step without any corresponding cycle length changes of AAF. As a second step AAF was terminated during left mitral ablation only in 2 pts. As a third step linear RF-lessions from right pulmonary vein ostium to mitral annulus was performed and turned out to be associated with increasing of AAF cycle length (from 240±10 ms to 340±20 ms, $p<0.001$) in 5 cases. Additional RF-application applied inside the proximal CS roof (fourth-step) terminated AAF in 5 pts. There was no arrhythmias induction while of control left auricular burst and programmed stimulation. Follow up was 6.7±2.4 mos. There were neither atrial fibrillation nor atrial flutter during follow up period observed.
Conclusion: Structures of proximal coronary sinus corresponding to low common pathway insertion could be critical component of reentry circuit in some cases of atypical atrial flutter after RFA of atrial fibrillation pts.

P1188 Increased NT-pro-B-type natriuretic peptide is associated with poor outcome following catheter ablation of atrial fibrillation

B. Nilsson[1], J.P. Goetze[2], X. Chen[2], S. Pehrson[2], J.H. Svendsen[2]. *[1]The Heart Centre, Rigshospitalet, Department of Cardiology, Copenhagen, Denmark; [2]Clinical Biochemestry, Rigshospitalet, Department of Clinical Biochemistry, Copenhagen, Denmark*

Purpose: This study aimed to investigate whether measurement of plasma NT-pro-B-type natriuretic peptide (NT-proBNP) before ablation treatment and after exercise testing has predictive information regarding the clinical outcome following pulmonary vein isolation in patients known with atrial fibrillation (AF).
Methods: The study population consisted of a subgroup of patients undergoing catheter ablation for AF from November 2002 to November 2004. Before ablation, a symptom limited exercise testing was performed on a cycle ergometer. Plasma samples for NT-proBNP analysis were obtained prior the ablation (before and after exercise test), and repeated in those who displayed sinus rhythm at 1, 3, and 12 months after the final procedure.
Results: A total of 51 patients (paroxysmal AF: 34; persistent AF: 17) were included of which 41 patients underwent an exercise test. At study entry the median NT-proBNP level was found to be 14 pmol/L (quartiles: 8 and 27), with no significant difference between patients with paroxysmal end persistent AF. After the exercise test, the mean NT-proBNP value increased from 13 pmol/L (quartiles: 7.5 and 26) to 15 pmol/L (quartiles: 9 and 34), $P<0.001$. Following a maximum of two ablations, 22 patients were free of recurrences and 29 patients experienced recurrent AF. In patients with successful ablation, the mean proBNP at baseline was 10 pmol/L (quartiles: 7 and 22.25) compared to 22 pmol/L (quartiles: 12 and 34.5) in patients with treatment failure, P=0.02. With respect to exercise testing (n=41), a borderline significance was observed with a higher increase during exercise in patients with recurrent AF (n=23) compared to patients without (n=18): 2 pmol/L (quartiles: 1 and 7) vs. 1.5 pmol/L (quartiles: 0 and 3), P=0.07. Three months following the final ablation procedure, the overall NT-proBNP concentration decreased from 14 pmol/L (quartiles: 8 and 27, n=51) to 9 pmol/L (quartiles: 4 and 16, n=41), P=0.002. However, subgroup analysis revealed that a reduction in NT-proBNP concentration was only seen in patients with no recurrent arrhythmia following ablation(s) (P=0.009) and in patients being free of arrhythmia when a previously ineffective antiarrhythmic drug were added as well as recurrent AF (P=0.002).
Conclusions: Following successful ablation treatment, a significantly lower NT-proBNP concentration at baseline and a trend towards a diminished increase during exercise was seen compared to patients with recurrent AF. The NT-proBNP concentration declined in patients with no recurrent AF after successful ablation with/without subsequent antiarrhythmic medication.

VENTRICULAR FUNCTION

P1189 Timing and extent of longitudinal and circumferential strain of the left ventricular myocardium by 2D-speckle tracking echocardiography

E. Tosoratti, L.P. Badano, D. Pavoni, N. Pezzutto, R. Marinigh, M. Cinello, P. Gianfagna, C. Capelli, P.M. Fioretti. *Az. Osp-Univers. S. Maria della Misericordia, Cardiopulmonary sciences, Udine, Italy*

Purpose: Two-Dimensional Ultrasound Speckle Tracking Imaging (2DSTI), a newly developed, angle of insonation independent echo-technique, allows assessment of both longitudinal and circumferential strain, whose reference values have not been reported so far.
Methods: We acquired (average frame rate 63±11 fps) 4-, 2-chamber and long-axis apical views, and basal, mid-ventricle and apical short axis views of the LV in 80 normal volunteers (35±13 years, range 15-63 years, 53% males) to assess global LV longitudinal (LS) and circumferential (CS) strain, and assess the time from Q wave to peak strain (ttp) (Table 1).

Table 1

Global Longitudinal strain (%)	4 chamber view	-17.95±2.81
	2 chamber view	-18.70±3.32
	Long axis view	-16.42±2.97
Global Circumferential strain (%)	Base	-15.50±2.93
	Mid-ventricle	-15.99±2.81
	Apex	-20.09±4.86
Time to peak-Global Longitudinal strain (ms)	4 chamber view	418±43
	2 chamber view	413±42
	Long axis view	416±36
Time to peak-Global Circumferential strain (ms)	Base	459±62
	Apex	428±48

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: No significant difference was observed in extent and time to peak for LS among the 3 apical views. LS was similar in males and females (-17.1±2.5 vs -19.0±2.9%, respectively, p= 0.575). No relationship was found between LS and age (r= -0.09), heart rate (r= 0.03), body mass index (r= 0.06), systolic blood pressure (r=-0.002). Conversely, peak CS was higher (p=<0.0001) and occurs earlier (p=0.0013) at the apex than at the base.
Conclusions: We provide reference values for 2DSTI estimation of LV LS and CS, new echocardiographic parameters of LV systolic function. Our results may help echocardiographers to identify myocardial dysfunction and dyssynchrony when assessing LV performance in terms of LV deformation and mechanical activation.

P1190 Resveratrol protects against insulin resistance syndrome and improves left ventricular contractile functions by activating estrogen receptor

J.Y. Deng, L.M. Hung. *Chang Gung University, Dept of Life Science, Tao-Yuan, Taiwan*

Epidemiological studies have shown that red wine consumption is associated with reduced in cardiovascular mortality in the general population and diabetic patients. It has been reported that resveratrol protects against insulin resistance by activating SIRT1 and PGC-1 a. The aim of this study was to investigate whether resveratrol can attenuate insulin resistance syndrome (IRS), improve IRS-induced cardiac contractile dysfunctions, and delineated its underlying mechanisms. Male Sprague-Dawley rats were given high cholesterol-fructose (HCF) diet for 15 weeks; the rats developed insulin resistance syndrome characterized by elevated blood pressure, hyperlipidemia, hyperinsulinemia, impaired glucose tolerance, and insulin resistance. Oral gavage fed with resveratrol (1 mg/kg/day, 15 weeks) significantly reduced blood pressure, plasma insulin, triglyceride, and cholesterol levels as compare to HCF. Resveratrol also attenuated plasma glucose elevation and improved insulin responses during glucose tolerance test (GTT). Furthermore, insulin-stimulated plasma glucose lowering effects were significantly improved by resveratrol during insulin tolerance test (ITT). The 2-deoxyglucose uptake and membranous GLUT4 (glucose transporter 4) protein levels were dose-dependently increased by resveratrol in C2C12 cells. Pretreatment with estrogen antagonist (ICI 182,780) completely antagonized resveratrol-stimulated glucose uptake and membranous GLUT4 protein levels.
Our results show that cardiac output, e jection fraction, and s troke volume were significantly diminished in IRS individuals. The rats with IRS showed decrease the left ventricular end systolic elastance, whereas the effective arterial elastance (Ea) was increased. In addition, the relaxation time constantof left ventricle pressure (tau) was prolonged in the HCF group. Interestingly, the IRS-induced left ventricular contractile dysfunctions were significantly alleviated by resveratrol. The i nsulin-stimulated GLUT4 membrane translocation and protein kinase B (Akt) phosphorylation were dramatic reduced while fatty acid transporter 1 (FATP1) protein levels were enhanced in HCF rats. In resveratrol treated group, phosphorylated Akt and membranous GLUT4 protein levels were significantly enhanced as compare to HCF group. Overall, these results indicate that resveratrol protect against cardiac insulin resistance may through estrogen receptor pathway and may contribute to preservation of left ventricular contractile functions in insulin resistance individuals.

P1191 In DOCA-salt rat plasma concentrations of matrix metalloproteinase-2, tissue inhibitor of metalloproteinases-1 and osteopontin are correlated with impairment of left ventricular contractility

F. Kramer[1], P. Ellinghaus[1], A. Kretschmer[1], M. Klein[1], P. Sandner[1], H. Milting[2], T. Krahn[1]. *[1]BayerHealthCare AG, TD-Translational Medicine/Biomarker, Wuppertal, Germany; [2]Herz-und Diabeteszentrum NRW, Bad Oeynhausen, Germany*

Background: The matrix metalloproteinases (MMPs) and their endogenous inhibitors, the tissue inhibitors of metalloproteinases (TIMPs) play a key role in extracellular matrix maintenance and are altered in the failing heart. As the common diagnostic markers of heart failure (HF), atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) primarily reflect increased pressure loading, determination of heart-derived MMPs, and TIMPs in plasma as well as determination of the emerging fibrosis marker osteopontin (OPN) might be valuable tools to detect and assess heart fibrosis. Here, the effect of spironolactone-treatment (50 mg/kg/d) on MMP2, TIMP1 and OPN plasma levels were assessed in a HF animal model.
Methods: Unilaterally nephrectomized Wistar rats received subcutaneous injection of 100 mg deoxycorticosterone-acetate (DOCA) once per week and 1% (w/v) NaCl in drinking water (n=10). Blood pressure (BP) was monitored weekly and blood samples were collected retro-orbitally after 1, 2 and 4 weeks. After 6 weeks, left ventricular contractility (LVC) and mRNA expression in the left ventricle were assessed.
Results: DOCA-treatment increased plasma TIMP1, MMP2 and OPN levels whereas spironolactone-treatment suppressed the DOCA effect (TIMP1: controls: 9.4+2.1 ng/mL, DOCA: 28.2+7.2 ng/mL, Spiro.:19.2+4.8ng/mL all p<0.001; MMP2: controls: 132.5+2.7 ng/mL, DOCA: 188.6+8.3 ng/mL, Spiro.: 169.4+4.2 ng/mL all p<0.001; OPN: controls: 15.7+0.5 ng/mL, DOCA: 37.4+0.9 ng/mL, Spiro.: 24.8+3.3 ng/mL, control vs. DOCA p<0.001; Spiro vs. DOCA p<0.05). Increase of plasma marker levels after DOCA-treatment correlated with deteriorated LVC (8409+509 mmHg/sec controls: 6297+462 mmHg/sec, p<0.05). Spironolactone-treatment significantly reduced the impairment of LVC by DOCA (Spiro.: 7626+518 mmHg/sec, DOCA: 8409+509 mmHg/sec, p<0.05). MMP2, TIMP1 and OPN plasma concentrations of placebo- and spironolactone-treated animals paralleled increase of BP. Increased expression of TIMP1 and OPN mRNA in the left ventricle mirrored circulating concentrations of TIMP1 and OPN protein, whereas MMP2 mRNA expression was not elevated by either DOCA or spironolactone-treatment after 6 weeks.
Conclusions: In DOCA-salt rats plasma concentrations of MMP2, TIMP1 and OPN paralleled with increases in BP and were inversely correlated with the LVC. Based on these findings, it seems reasonable to use these plasma markers to monitor development of HF in DOCA-salt rats. It remains to be established, whether in human HF patients, circulating levels of aforementioned markers correlate with cardiac fibrosis as determined by imaging.

P1192 Dyslipidemia in combination with type II diabetes has no additional effect on contractility and relaxation, but increases ventricular stiffness in leptin-deficient mice

A. Van Den Bergh, P. Holvoet, W. Flameng, P. Herijgers. *KULeuven, Dept. Cardiovascular Diseases, Leuven, Belgium*

Purpose: Type II diabetes, often associated with abdominal obesity, frequently leads to heart failure. Clinical and epidemiological evidence suggests that supplemental dyslipidemia aggravates the cardiovascular outcome. The impact of dyslipidemia on top of type II diabetes on left ventricular function however remains incompletely defined.
Methods: We studied left ventricular function in vivo using pressure-volume analysis in obese diabetic mice with leptin deficiency (ob/ob), non-obese dyslipidemic mice with LDL-receptor deficiency (LDLR-/-) and obese diabetic dyslipidemic mice with combined leptin and LDL-receptor deficiency (DKO), and compared them with wild-type (WT) mice.
Results: LDLR-/- mice did not differ from WT. Both ob/ob and DKO mice displayed a comparable impaired contractility and early relaxation in comparison with WT, as determined by respectively the preload-recruitable stroke work (58±7 in ob/ob; 55±8 in DKO; 74±10 mmHg in WT) and tau (7,8±1,6 in ob/ob; 6,6±1,0 in DKO; 5,4±1,1 ms in WT). A differential pattern of remodelling was observed in the mouse models. Whereas ob/ob mice developed an eccentric hypertrophy, we demonstrated a concentric hypertrophic cardiomyopathy in DKO mice. Parameters of compliance/stiffness differed between both mouse models. DKO mice developed a higher end-systolic elastance (6,6±2,8 mmHg/μL), arterial elastance (6,3±2,7 mmHg/μL) and end-diastolic pressure-volume relationship (0,4±0,2 mmHg/μL) when compared with ob/ob mice (resp. 2,9±1,1; 2,2±0,5; 0,1±0,02 mmHg/μL), indicating increased vascular-ventricular stiffening. Cardiac output was increased in ob/ob mice, whereas it was decreased in DKO mice (12,5±3,1 in ob/ob; 5,8±2,3 in DKO; 8,2±2,1 mL/min in WT).
Conclusion: Type II diabetes in mice leads to impaired contractility and relaxation, but only when dyslipidemia is superimposed, increased vascular-ventricular stiffening develops, leading to a worsening of overall hemodynamic characteristics.

P1193 Heart failure with preserved ejection fraction in Ibadan, Nigeria

A. Adebayo, O.S. Ogah, A.A. Adebiyi, O.O. Oladapo, A. Aje, D.B. Ojji, A.O. Falase. *University College Hospital, Medicine Dept., Ibadan, Nigeria*

Purpose: The study aimed to determine the frequency and characteristics of heart failure with normal ejection fraction (EF) in a native African population with heart failure.
Methods: Subjects were 177 consecutive individuals with heart failure and 90 apparently normal control subjects. All the subjects underwent transthoracic echocardiography. The group with heart failure was further subdivided into heart failure with normal EF (EF ≥50)(HFNEF) and heart failure with low EF(EF <50)(HFLEF).
Results: The subjects with heart failure have a mean age of 52.3±16.64 years vs 52.1±11.84 years in the control subjects; p=0.914. Other baseline characteristics except blood pressure parameters and height were comparable between the group with heart failure and the control subjects. Compared with the HFLEF group, the HFNEF group have a smaller left ventricular diameter (in diastole and systole): (5.2±1.22cm vs 6.2±1.39cm; p<0.0001 and 3.6±1.24 cm vs 5.4±1.35cm;p<0.0001) respectively, a higher relative wall thickness and deceleration time: (0.4±0.12 vs 0.3±0.14 p<0.0001 and 149.6±72.35 vs 110.9±63.40 p=0.001) respectively. The two groups with heart failure differed significantly from the control subjects in virtually all echocardiographic measurements except aortic root diameter, LV posterior wall thickness(HFLEF), and late mitral inflow velocity(HFNEF).HFNEF accounted for 70(39.5%) of the cases of heart failure in this study. Hypertension is the underlying cardiovascular disease in 134(75.7%) of the combined heart failure population, 58(82.9%) of the HFNEFgroup and 76(71%) of the HFLEF group. Females accounted for 44 (62.9%) of the HFNEF subjects against 42(39.3%) in the HFLEF group(p=0.002).
Conclusions: The frequency of heart failure with normal EF among native African

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

subjects with heart failure is comparable with the frequency in other populations. These groups of patients are more likely female, hypertensive with concentric pattern of left ventricular hypertrophy.

P1194 Assessing left ventricular dyssynchrony in heart failure patients by real time three-dimensional echocardiography: a comparison with tissue Doppler imaging

J. Cui[1], X.H. Shu[2], C.Z. Pan[1], J.B. Ge[1]. [1]*Shanghai, China, People's Republic of;* [2]*Zhongshan Hospital, Fudan University, Department of Cardiology, Shanghai, China, People's Republic of*

Background: Echocardiographic assessments of mechanical dyssynchrony by echocardiography may predict response to cardiac resynchronization therapy. Several echocardiographic methods can be used to quantify left ventricular systolic asynchrony, but it is unclear how the different methods should be applied.
Objective: To compare the ability of real time three-dimensional (3D) echocardiography with tissue Doppler imaging (TDI) in assessing left ventricular mechanical dyssynchrony in patients with chronic heart failure(HF).
Methods: Tissue Doppler imaging (TDI) and 3D full-volume data acquisition were performed during sinus rhythm (Philips iE33 with Qlab 5.0 software) in 30 patients with advanced heart failure (NYHA III/IV, LVEF $\leq$ 35%), and 9 of them had wide QRS complex. 30 healthy subjects were enrolled as controls. Segmental LV time-volume curves were calculated by semi-automated contour analysis and thesystolic dyssynchrony index (SDI) was derived from the dispersionof time to minimum regional volume for all 16 LV segments. The 3D results were compared with Ts-SD (standard deviation of time to peak velocity) of the 12 basal and middle LV segments by TDI.
Results: In healthy subjects, the SDI and Ts-SD were 1.85±0.44 and 18.93±4.70 respectively, and there was a significant correlation between them (r =0.7147, p= 0.005). In HF patients with wide QRS complex, SDI and Ts-SD were significantly increased with good correlation (SDI: 9.18 ±2.61, Ts-SD: 55.06±12.14, r= 0.6062, p=0.0077). In HF patients with narrow-QRS complex, SDI was increased with poor correlation with Ts-SD (SDI: 8.05±3.02, Ts-SD: 39.08±10.17, r= 0.3260, p= 0.045),
Conclusions: Mechanical asynchrony by TDI and 3D results were comparable in patients with advance heart failure as well as wide QRS complex, SDI by 3D echocardiography may be similar to Ts-SD by TDI in assessing left ventricular systolic asynchrony.

P1195 Effects of prolonged combined therapy with Erythropoietin and Granulocyte Colony-Stimulating Factor on left ventricular mechanics in a closed-chest porcine ischemia-reperfusion model

Y. Yeghiazarians, F.S. Angeli, M. Shapiro, N. Amabile, G. Orcino, S.C. Burjonroppa, Y. Zhang, S.A. Glantz, K. Chatterjee, W. Grossman. *University of California, Medicine-Division of Cardiology, San Francisco, United States of America*

Purpose: Although Erythropoietin (EPO) and Granulocyte Colony-Stimulating Factor (G-CSF) function were reported previously to prevent cardiac remodeling after myocardial infarction (MI), the effects of prolonged combined therapy on left ventricular (LV) mechanics and hemodynamics remain unclear.
Methods: Antero-apical MI was induced in anesthesized swine by a 90 minute balloon occlusion of the left anterior descending artery. Animals were divided between treatment groups with EPO-GCSF combination therapy (bolus of EPO 0.9ug/kg and GCSF 10ug/kg at time of reperfusion, followed by 5 doses of GCSF 5ug/kg, from day 5 to 9, and 4 doses of 0.45ug/kg EPO once per week starting at day 1, n=8) or control (saline injections, n=8). LV pressure volume (PV) data were collected via a 12 electrode, 7-segment conductance catheter at steady state and during transient inferior vena cava occlusion prior to AMI, and at 1 and 6 weeks post-MI. Volumes were calibreted using transthoracic echocardiographic data. Pigs were under beta-blockade for the duration of the experiment. Hemoglobin (Hgb), hematocrit (Hct) and whole blood viscosity were assessed. Values are reported as least-squares means and SEMs.
Results: MI size was the same in both groups as assessed by the values of post-MI CPK peak and LV ejection fraction (EF %) at week 1. EPO-GCSF therapy induced a significant increase in Hgb (11±1 vs. 13±1 g/dl) and Hct (32±1 vs. 41±2%), peak at 4 weeks ($p<0.01$), with no changes in blood and arterial resistance, or in arterial pressure. EPO-GCSF attenuated systolic dysfunction at week 6 compared to controls: EF% (41±1 vs. 27±2, $p<0.05$), dP/dtmax (1006±33 vs. 842±38 mmHg/s, $p<0.01$), and stroke volume (31±2 vs.20±2 ml, $p<0.01$), stroke work (2088±171 vs.1433±209 mmHg/ml, $p<0.05$), and mechanical efficiency (0.53 vs.0.45, $p<0.05$) were increased. Diastolic function was preserved in the EPO-GCSF group at 6 weeks: Tau (56±2 vs. 63±2 ms, $p<0.05$), dp/dtmin (-1022±22 vs. -902±38 mmHg/s, $p<0.05$), exponential beta coefficient of the ED-PVR (0.07±0.01 vs. 0.16±0.04, $p<0.05$). Although the slope of linear ESPVR (Ees) showed no significant changes, we found a significant rightward shift of the linearly derived Vo in the control group compared to EPO-GCSF ($p<0.05$).
Conclusion: Together, these findings suggest that the beneficial effect of EPO-GCSF prolonged therapy over time is related to reduced impairment of systolic function and preservation of diastolic function. Morever, the potential negative effects of EPO on rheologic variables did not change the outcome in this model.

P1196 The total heart volume starts to increase before the end of systolic ejection and decreases before the end of diastole

M. Carlsson, M. Ugander, H. Arheden. *Clinical Physiology, Lund University Hospital, Lund, Sweden*

Purpose: We aimed to quantify the increase in total heart volume (THV) before the end of systolic ejection (late ejection filing volume, LEFV), and to quantify the volume decrease caused by atrial contraction (atrial wave reversal volume, AWRV).
Methods: Eleven healthy volunteers underwent cardiac cine MRI and MRI flow measurement in all vessels leading to and from the heart.
Results: The LEFV is marked by diagonal lines in Fig. 1A and is defined as the volume resulting from the difference in the inflow to and outflow from the heart between time point 1 (when inflow exceeds outflow) and time point 2 (when systolic outflow is zero). Between time point 1 and 2 the LEFV was 11.4±1.3 ml or 1.4±0.1% of THV, with no difference between the left and right side of the heart (p=0.92). The LEFV results in an increase in THV concomitant with decreasing Left Ventricular (LV) and Right Ventricular (RV) volumes, this can be appreciated in Fig. 1B between time point 1 and 2. The flow from the heart in the veins during atrial contraction is seen in Fig 1A and the resulting volume decrease of the THV and increase in LV and RV volumes in Fig. 1B, between time point 3 and 4. The total AWRV was 0.8±0.1% of THV. The AWRV through the caval veins was greater (4.3±0.6 ml, $p<0.05$) than through the pulmonary veins (2.6±0.7 ml).

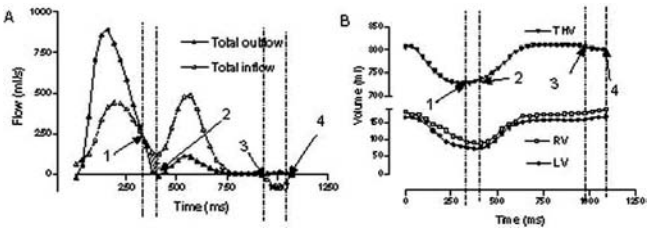


Figure 1

Conclusions: The heart is smallest before the end of systole and largest before the end of diastole. The volume difference which occurs in the atria before the end of systolic ejection (LEFV) was previously unknown and have been identified and quantified. LEFV might be important for understanding the coupling of systolic to diastolic function. Also, the late diastolic decrease in total heart volume caused by atrial contraction has been quantified.

P1197 Altered expression of beta1 integrin in relation to ADAM proteins in pressure overload hypertrophy and dilated cardiomyopathy

L. Delrue, M. Vanderheyden, F. Casselman, F. Wellens, S. Verstreken, E. Van Schuerbeeck, L. Mortier, M. Goethals, J. Bartunek. *OLV-Hospital, Cardiovascular Center/Molecular Cardiology, Aalst, Belgium*

Background: Integrin signalling regulates mechanotransduction-dependent cardiac growth. ADAM (A Disintegrin And Metalloproteinase) proteins are cell surface proteins that regulate cell-cell and cell-matrix interactions and by shedding integrins may participate in the mechanotransduction and cardiac remodeling.
Aim: We investigated whether LV gene expression of ADAM proteins in relationship to the expression of muscle specific β1D-integrin is altered in patients (pts) with established pressure overload LV hypertrophy due to aortic stenosis (AS) and idiopathic congestive cardiomyopathy (CCMP).
Methods: LV biopsies were obtained perioperatively in 9 pts with CAD with normal LV function (Control, C) and in 11 AS pt and in 15 CCMP pts at cardiac catheterization. LV message levels of ADAM 9, 10, 12, 15 and 17 proteins and β1-integrin message levels were determined by real time quantitative TaqMan PCR (relative units).
Results (see Table *$p<0.05$ vs Control by ANOVA):

	Control (n=9)	AS (n=11)	CCMP (n=15)
ADAM9/GAPDH	0.27±0.05	0.33±0.05	0.39±0.03
ADAM10/GAPDH	0.71±0.12	0.77±0.17	1.32±0.11*
ADAM12/GAPDH	0.22±0.09	0.71±0.13*	1.08±0.16*
ADAM15/GAPDH	0.11±0.03	0.22±0.03*	0.18±0.19*
ADAM17/GAPDH	0.29±0.06	0.38±0.04	0.45±0.04*
β1D/GAPDH	0.25±0.04	0.47±0.04*	0.37±0.03*

LV β1D message levels were higher in AS and CCMP pts. LV ADAM 12 and 15 were increased in both CMP and AS vs C. LV ADAM 10 and 17 were upregulated only in CCMP vs C. Note, the ratio of ADAM 9, 10, 12 and 17 to β1D expression was significantly higher in CCMP vs AS pts. In the entire population, a significant

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

relationship was noted between LV ADAM 10 and 12 message levels and LV end-diastolic volume index (r=0.41, p<0.01 and r=0.49, p<0.01 respectively). On the other hand, an inverse relationship was noted between both proteins and LV ejection fraction (r=-0.59, p<0.01 and r=-0.39, p<0.05, respectively).
Conclusion: Altered expression of ADAM proteins relative to β1-integrins may contribute to LV remodelling and systolic dysfunction in overloaded and failing human hearts.

P1198 The heart rate lowering per se is beneficial in chronic heart failure management: a pilot study

D. Logeart[1], V. Ciobotaru[2], F. Rouzet[3], J.P. Gueffet[4], F. Pousset[5], A. Cohen Solal[6], G. Jondeau[2]. *[1]A.P Hopital Lariboisiere, Service De Cardiologie, Paris, France; [2]APHP Hopital Georges Pompidou, Paris, France; [3]APHP Hopital Bichat, Paris, France; [4]CHU Nantes, Nantes, France; [5]APHP Hopital Pitie Salpetriere, Nantes, France; [6]APHP Hopital Lariboisiere, Paris, France*

Background: It has been suggested that heart rate (HR) lowering could be beneficial in chronic heart failure (CHF) management because of effects on filling, perfusion as well as on the bioenergetics of failing ventricles. So far, direct evidence of such effetcs in humans have missed.
Aim: To compare the effects of two HRs in patients with CHF, left ventricular (LV) systolic dysfunction and permanent cardiac pacing.
Methods: The inclusion criteria were: NYHA 2-3, LV ejection fraction (LVEF) ≤ 0.35, stable medication for more than 3 months, permanent cardiac pacing with HR depending on pacing > 90% of beats for more than 3 months. Patients were randomised to be paced at either 55 or 75/min for 3 months. The pacing-mediated HR was then inverted for a second 3-month period. The HR dependency on pacing was checked using Holter ECG recordings during each period. After each 3-month period, gated blood pool SPECT, echocardiography, blood samples and clinical data were obtained for centralized and blinded measurements of the following: LVEF, LV dimensions and function, BNP levels as well as NYHA class. Data were analysed using paired t-test.
Results: Twelve patients (68±8 years, LVEF 0.23±0.10) completed the study. Main results are given in the table below.

	LVEF (%)	BNP (pg/ml)	LV end-diastolic diameter (mm)	Doppler E/Ea Doppler E/Ea	NYHA NYHA
55/min	25.3±9.4	327±135	70.0±6.2	14.7±3.3	2.1±0.5
75/min	20.6±8.4	420±173	69.4±6.2	15.2±3.2	2.7±0.4
Delta 55/min–75/min	+4.7±3.0	-93±84	-0.6±2.3	+0.58±1.4	-0.7±0.5
p value	0.0002	0.003	0.19	0.40	0.0007

Conclusion: This pilot study suggests that HR lowering per se is beneficial in patients with CHF and low LVEF.

P1199 Relation between exercise induced changes of right ventricle systolic function and exercise tolerance in heart failure patients

P. Rubis[1], P. Podolec[2], L. Tomkiewicz-Pajak[2], G. Kopec[1], P. Herod[1], B. Sobien[1], W. Tracz[1]. *[1]Department of Cardiac And Vascular Disease, Krakow, Poland; [2]Department of Cardiac and Vascular Disease, Krakow, Poland*

Aim: To asses impact of exercise induced changes of right ventricle (RV) isovolumic contraction and ejection phase parameters by stress echocardiography (stress-echo) on exercise tolerance in heart failure (HF) patients (pts).
Material and Methods: 75 consecutive pts with chronic, stable HF [due to ischemic (n=52) or non-ischemic (n=23) cardiomyopathy], 63 male, mean age of 57.9±8.8 (21-79) years. The following RV systolic parameters were measured at baseline and peak exercise during stress-echo (15 – 25 Watts, 2-min increments): myocardial velocity during isovolumic contraction (IVV), myocardial acceleration during isovolumic contraction (IVA), myocardial velocity during ejection phase (S') and myocardial acceleration during ejection phase (S'acc). Parameters were derived from septal and lateral border of the tricuspid annulus in the apical four chamber view. Simultaneously during stress-echo peak oxygen uptake (VO_2 peak) was measured. Pts were divided into two groups according to VO_2 peak value: group 1 (<14 ml/kg/min) and group 2 (>14 ml/kg/min).
Results: There were no differences of IVV, IVA, S' and S'acc values at rest in both groups. However, peak exercise values of analysed indices were significantly higher in group 2.

Table 1

VO_2 peak (ml/kg/min)	< 14	> 14	p-value
Number of patients	32	43	
IVV rest (cm/s)	7.77±4.1	8.41±3.2	NS
IVA rest (m/s^2)	1.61±0.88	1.81±1.01	NS
S' rest (cm/s)	9.21±4.8	9.52±3.6	NS
S'acc rest (m/s^2)	1.31±0.81	1.29±0.79	NS
IVV peak exercise (cm/s)	8.55±2.2	12.1±5.6	0.05
IVA peak exercise (m/s^2)	2.14±1.1	3.51±2.3	0.05
S' peak exercise (cm/s)	8.98±4.3	13.2±4.1	0.05
S'acc peak exercise (m/s^2)	1.73±0.7	2.6±0.55	0.05

Conclusions: Measurement of RV isovolumic contraction and ejection phase parameters by stress-echo is a precise method for assessing exercise induced changes of RV systolic function. Rest values of RV systolic function parameters did not separate pts with worse functional capacity. However, preserved RV residual myocardial contractile reserve is related to better exercise tolerance.

P1200 Clinical value of B-type natriuretic peptide for the assessment of left ventricular filling pressures in patients with systolic heart failure and non conclusive tissue doppler indexes

A. Karavidas[1], G. Lazaros[1], D. Farmakis[2], J.T. Parissis[1], C. Michailidis[2], D. Avramidis[2], E. Matsakas[2]. *[1]Geniko Kratiko Hospital, Athens, Greece; [2]Attikon University Hospital, Athens, Greece*

Background: Invasive hemodynamic monitoring with a Swan-Ganz catheter in heart failure may lack prognostic value and may also be hazardous. We assessed the clinical utility of B-type natriuretic peptide (BNP) in estimating left ventricular (LV) filling pressures in patients with non-conclusive tissue Doppler indexes.
Methods and Results: Fifty patients with systolic heart failure and an early transmitral velocity to early diastolic mitral annular velocity ratio (E/Ea) between 8 and 15 were studied; 25 of them had been admitted for acutely decompensated heart failure (group A) and the remainders were clinically stable outpatients (group B). All patients underwent simultaneous invasive pulmonary capillary wedge pressure (PCWP) determination, BNP measurement and echocardiography (Table). In group A, BNP correlated with PCWP (r=0.803, p<0.001), deceleration time (DT, r=-0.602, p=0.001) and end-systolic wall stress (SWS, r=0.565, p=0.003). In multivariate analysis, BNP was the only parameter independently associated with PCWP (p=0.023). In group B, no correlation was found between BNP and PCWP or SWS, while DT correlated significantly with both PCWP (r=-0.817, p<0.001) and BNP (r=-0.8, p<0.001).

Table 1

	Group A (n=25)	Group B (n=25)	p value
LV end-diastolic diameter, mm	67±5	67±4	NS
LV end-systolic diameter, mm	58±5	59±5	NS
LV ejection fraction. %	25±5	26±7	NS
SWS, kdyn/cm^2	476±97	419±92	<0.05
E, m/sec	1.10±0.24	1.03±0.19	NS
A, m/sec	0.44±0.17	0.46±0.18	NS
E/A	2.45±1.19	2.34±1.15	NS
DT, msec	118±9	171±20	<0.001
Ea, m/sec	0.09±0.03	0.10±0.02	NS
E/Ea	10.80±2.10	10.00±1.50	NS
PCWP, mmHg	23±3	15±3	<0.001
BNP, pg/mL	879±145	130±126	<0.001

Conclusion: BNP may be a useful non-invasive tool for the assessment of LV filling pressures in patients with acutely decompensated heart failure and non conclusive tissue Doppler indexes.

P1201 Identifying myocardial dysfunction with two-dimensional ultrasound speckle tracking imaging. Reference values for rotation and torsion of the left ventricle

E. Tosoratti, L.P. Badano, M. Cinello, R. Marinigh, D. Pavoni, P. Gianfagna, N. Pezzutto, C. Capelli, P.M. Fioretti. *Azienda Ospedaliero-Universitaria di Udine, Scienze Cardiopolmonari, Udine, Italy*

Purpose: torsional deformation of the left ventricle (LV) is the twisting motion of the heart due to contraction of its obliquely spiraling fibers. Two-Dimensional Speckle Tracking Echo (2DSTE), an angle of insonation independent echotechnique whose accuracy has been demonstrated in comparison with magnetic resonance imaging and sonomicrometry, has been recently accepted as a novel method to estimate LV torsion. However, reference values for LV rotation and torsion obtained with 2DSTE have not been reported so far.
Methods: we acquired basal, papillary and apical short axis views of the LV in 80 normal volunteers (35±13 years, range 15-63 years, 53% males) with no history of heart disease, no cardiovascular risk factor, and a normal resting electrocardiogram to assess LV rotation dynamics (i.e. extent and velocity of rotation), estimate LV torsion (i.e. apical LV rotation – basal LV rotation) (Table) and assess the time from Q wave to peak rotation.
Results: systolic LV rotation was clockwise at the apex, and counterclockwise at

		Early Systole	Late Systole
Heart Rate (bpm)	68±12		
Systolic Blood Pressure (mmHg)	123±13		
Basal Rotation (deg)		2.87±1.59	-5.50±2.70
Papillary Rotation (deg)		1.45±2.06	-0.32±4.63
Apical Rotation (deg)		-2.56±1.52	9.32±4.46
Torsion (deg)	14.79±4.81		
Basal Rotation Velocity (deg/s)	-67.32±23.21		
Papillary Rotation Velocity (deg/s)	-16.26±52.17		
Apical Rotation velocity (deg/s)	73.43±29.92		

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

basal level, while the average systolic rotation at the papillary level was close to zero. No significant difference was found in the time to systolic peak rotation between basal and apical level (395±70 ms and 408±59 ms, respectively, p=0.31). The rotation rate was opposite in versus but similar in amplitude at the two LV levels (P=0.46).
Conclusions: our study provides reference values for 2DSTI estimation of LV torsion, a new echocardiographic index of LV performance. Our results may help echocardiographers to identify myocardial dysfunction when assessing LV performance in terms of LV torsion and rotation.

P1202 The MACH 2 trial: safety and feasibility of left ventricular support with the Impella LP 2.5 device in patients with acute ST-segment Elevation Myocardial Infarction

K.D. Sjauw, M. Remmelink, J. Baan Jr, R.J. Van Der Schaaf, M.M. Vis, K.T. Koch, J.G.P. Tijssen, J.J. Piek, R.J. De Winter, J.P.S. Henriques. *Academic Medical Center, Cardiology, Amsterdam, Netherlands*

Background: Unloading the left ventricle (LV) may in addition to reperfusion therapy reduce infarct size in STEMI patients. It may also give the myocardium time to recuperate from ischemic stunning. Hence, mechanical LV support could reduce mortality. These effects might particularly apply to cardiogenic shock (CS) patients, who often present with a large ischemic area at risk. The Impella LP 2.5 device is a percutaneous implantable left ventricular assist device (LVAD). Before initiation of a trial in CS patients the safety and feasibility of Impella support should be determined in haemodynamical less ill patients.
Methods: The study is a single center non-randomized controlled open trial in 20 consecutive patients with a first anterior STEMI. After primary PCI they were alternately assigned to either 3 days support with the Impella or to routine care. The primary endpoint was safety and feasibility of Impella support. Secondary endpoints were quantitative parameters of myocardial function and the extent of myocardial infarction obtained from echo and MRI at baseline and 4 months follow-up.
Results: All patients underwent primary PCI. Placement of the Impella pump was successful in all cases. The device did not induce aortic valve regurgitation. There were no device related adverse events during Impella implantation or operation. Hemolysis occurred only within the first 24 hours of support. Impella support decreased pulmonary artery wedge pressure and increased cardiac output. No significant differences were observed in infarct size and left ventricular ejection fraction at 4 months. However, compared to the control group the Impella group showed to be in worse antecedent clinical condition.
Conclusions: The findings, concerning the safety and feasibility of prolonged Impella support in the setting of STEMI are encouraging. In addition to hemodynamic support, its unloading capacity might influence infarct size and post-infarct remodelling. Larger randomized studies are warranted.

P1203 Non-invasive determination of cardiac output by the inertgas rebreathing method compared with magnetic resonance tomography

J. Saur, F. Trinkmann, J. Weissmann, D. Dinter, T. Papavassiliu, M. Borggrefe, J.J. Kaden. *University Hospital Mannheim, 1st Department of Medicine, Mannheim, Germany*

Background: The cardiac output (CO) is an important parameter in the diagnosis and therapy of cardiac diseases. The current standard methods for the determination of the CO, however, are either invasive (e.g. right heart catheterization) or technically expendable and expensive (magnetic resonance tomography, MRT). The traditional non-invasive methods of determining the CO by rebreathing of carbon dioxide are easily carried out but suffer from methodical inaccuracies. Therefore the aim of the study at hand was to evaluate a new method for determining the CO by means of the inert gas rebreathing method.
Methods: We prospectively included 109 consecutive patients who were scheduled to undergo cardiac MRT. The CO of reclining patients was determined by inert gas rebreathing with dinitric oxide and sulfur hexafluoride immediately before or after the MRT. The data determined by MRT for CO and for stroke volume served as reference values. The statistic comparison of the methods was drawn by means of Bland-Altman analysis.
Results: The 109 patients consisted of 74 men (aged 17 to 79 years, median 54 years) and 35 women (aged 16 to 79 years, median 54 years). The CO by means of MRT was 5.1±1.4 l/min (mean ± SD, minimum 2.5 l/min, maximum 9.0 l/min), the CO by means of Innocor was 4.9±1.3 (minimum 2.0 l/min, maximum 8.1 l/min). Bland-Altman analysis showed a good correspondence of the two methods for the CO with an average deviation of 0.2±1.0 l/min. Comparing the CO (MRT) and the pulmonary blood flow, the deviation was 0.3±1.1 l/min. The determination of the stroke volume resulted in an average deviation of 4±16 ml (Innocor versus MRT).
Conclusion: The rebreathing method with dinitric oxide and sulfur hexafluoride allows a reliable non-invasive determination of the CO. The future importance of the method for diagnosing and treating cardiac diseases remains to be assessed by further studies.

P1204 Hemodynamic effects of mild hypothermia in vivo

H. Post, J. Schmitto, R. Holland, J. Christoph, R. Wachter, F. Schoendube, B. Pieske. *Universitatsklinikum Goettingen, Zentrum Innere Medizin Kardiologie, Goettingen, Germany*

Introduction: The induction of mild hypothermia (33°C, MH) after cardiopulmonary resuscitation has become a therapeutical standard to attenuate hypoxic brain injury. While MH exerts a positive inotropic effect in vitro, the hemodynamic effects of MH in vivo are largely unkown. We thus tested the hemodynamic effects of MH by the conductance catheter technique during vena cava occlusioin in pigs in vivo.
Methods: 5 anaesthetized (fentanyl, midazolam, isoflurane, pancuronium) female domestic pigs (68±7 kg) were instrumented for the measurement of pressure-volume loops (conductance catheter), cardiac output (thermodilution), and for vena cava inf. occlusion. Controlled MH was induced by an invasive approach (V. cava inferior cooling catheter).
Results: After induction of MH (from 37°C to 33°C), heart rate (91±6 vs 77±4 bpm) and whole body oxygen consumption (225±13 vs 151±13 ml/min) decreased (both $p<0.05$), while arterial lactate concentration and mixed-venous oxygen saturation remained constant. Cardiac output tended to decrease (5.1±0.4 vs 4.5±0.4 l/min, p=0.11), and end-diastolic volume, stroke volume, peak systolic pressure and dP/dtmax did not change significantly. dP/dtmin decreased (-1558±77 vs -1002±114 mmHg/s, $p<0.05$), and the time constant of isovolumetric relaxation (tau) was prolonged (50±1 vs 98±14 ms). To assess parameters of inotropy and lusitropy independent from load, end-systolic and end-diastolic pressure-volume relationsships were derived from short episodes of vena cava inf. occlusion before and after induction of MH. The end-diastolic volume corresponding to an end-systolic pressure of 100 mmHg did not change with MH (56±6 v 54±11 ml), while the end-diastolic volume corresponding to an end-diastolic pressure of 5 mmHg tended to decrease (96±16 vs 72±14 ml, p=0.07).
Conclusion: MH negatively affects diastolic function, which, however, is compensated for by a parallel decrease of spontaneous heart rate. Considering the 33% decrease of whole body oxygen consumption, the induction of MH during cardiogenic shock warrants further studies.

P1205 Assessing left ventricular systolic function in atrial fibrillation: blinded comparison of echocardiography and radionuclide ventriculography

A.U. Khand, D. Motherwell, G. Mccurach, J. Mcgowan, J.G.F. Cleland, A. Colette, W. Martin. *Glasgow Royal Infirmary, Cardiology, Glasgow, United Kingdom*

Background: Assessment of left ventricular function in chronic atrial fibrillation (CAF) is an important but difficult determination due to beat to beat variation in ejection fraction. No previous studies have directly compared two of the most commonly employed techniques in daily use for assessment of ventricular function, namely echocardiography and radionuclide ventriculography (RNVG), in patients with CAF
Methods: 38 patients with CAF and symptoms of heart failure had both echocardiography and technetium based RNVG < 4 weeks apart. Left ventricular ejection fraction (LVEF) was calculated with echo, in a blinded fashion by two experienced operators, using a validated wall motion index (WMI). Similarly two experienced observers determined LVEF by RNVG. An assessment was also made of wall motion scores in 10 segments using a 5 point scale in the 40° and 70° (Left Anterior Oblique) LAO projections of RNVG. The equivalent area in segments in echo (apical 4 chamber and apical 2 chamber) were also scored.
Results: Paired data for WMI/LVEF was available for 38 patients undergoing echocardiography and in 36 undergoing RNVG. Repeatabillity co-efficient for LVEF by echo (a measure of interobserver variability) was 17.4% whereas it was 7.4% by RNVG (ejection fraction units). Paired wall motion scores for equivalent regions in echo and RNVG were available in 37 patients (370 segments). Of these segment 269/370 (73%) and 363/370 (98%) of segments were seen and scored by echo and RNVG respectively. There were fair measures of agreement (κ 0.35 for echo and κ 0.38 for RNVG) (table)

Parameter	Echo agreement for LVEF	RNVG agreement for LVEF	Agreement for Wall motion scoring	
			Echo	RNVG
N	38	36		
Mean diff	2.4%	1.5%		
Kappa values	–	–	0.35	0.38
Repeatability coefficient	17.4%	7.4%		

Conclusion: This is the first study to directly compare echocardiography and RNVG for the assessment of left ventricular function in patients with CAF. Whilst repeatability of regional wall motion scores is similar there is large interobserver variability for the calculation of ejection fraction by echocardiography compared to RNVG in CAF. Echocardiography is an inappropriate technique for serial measurement of LVEF in CAF

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1206 QRS duration: does it influence diastolic dyssynchrony in heart failure patients

A.M. Hamdy[1], H.M. Fereig[1], M.A. Nabih[2], O.H. Al-Khatib[2]. *[1]Al-Azhar University, Cardiology, Cairo, Egypt; [2]Ain-Shams University, Cardiology, Cairo, Egypt*

Background: Several studies dealt with systolic dyssynchrony and its relation to QRS duration in congestive heart failure patients (pts). We aimed to study the presence of diastolic dyssynchrony in those pts and to determine its relation to QRS duration.
Methods: 60 pts with dilated myopathic hearts (EF: 27.5±6.6%) & 10 age matched normal (NL) persons were subjected to evaluation of parameters of diastolic dyssynchrony by tissue Doppler. Patients were divided into 3 groups according to QRS duration (G1: <120 ms, G2: 120-140 ms, and G3>140 ms). Using offline analysis of 12 segments, we measured time to peak early diastole (Te) in ms, calculated as the difference between time from onset of QRS to peak Em minus time from onset of QRS to peak systolic wave (to reduce the effect of associated systolic dyssynchrony). Parameters of diastolic intra-ventricular dyssynchrony included diastolic dyssynchrony index (Te-SD) calculated as standard deviation of Te of the 12 segments, maximum difference of Te (Te-max) between any 2 of the 12 segments, and diastolic basal lateral to basal septal delays (Te-BL-BS). Diastolic inter-ventricular delay between LV & RV basal segments (Te-LV-RV) was also measured.
Results: All diastolic intra-ventricular dyssynchrony parameters were significantly higher in each of the 3 groups (table 1) as compared to NL (for Te-SD & Te-max: $p<0.0001$ in G1, G2 or G3 versus NL; for Te-BL-BS: $p<0.005$ in G1 and G3 versus NL & p=0.01 in G2 versus NL). There was no significant difference between any 2 pts groups as regards intra-ventricular diastolic dyssynchrony parameters. Te-LV-RV was higher in G3 compared to NL, G1 or G2 ($p<0.05$ in all comparisons) and was not significantly different in G1 or G2 compared to NL.

Table 1

	G1	G2	G3	NL
Te-SD	46.2±14.3	44.7±18.6	48.9±24.4	20.1±8.9
Te-max	145.2±46.5	141.6±57.7	153.6±71.3	64±27.2
Te-BL-BS	59.3±50.8	52.6±42	65.7±47.8	14±14.3
Te-LV-RV	58.2±52	52.1±44.4	103.6±71.1	42±25.3

Conclusion: Heart failure patients have both intra and inter-ventricular diastolic dyssynchrony. Intra-ventricular diastolic dyssynchrony has no relation to QRS duration. In contrast, inter-ventricular diastolic dyssynchcrony is related to the presence of wide QRS.

P1207 Left ventricular hypertrabeculation is associated with left ventricular dyssynchrony: a cardiac magnetic resonance study

Z. Yousef, S. Chalil, R. Smith, K. Khadjooi, F. Leyva. *Good Hope Hospital, Cardiology, Sutton Coldfield, United Kingdom*

Background: Left ventricular hypertrabeculation (LVHT) is a morphological feature of left ventricular non-compaction (VNC). We explored whether, in the absence of systolic dysfunction, LVHT is associated with left ventricular dyssynchrony.
Methods: 14 patients with LVHT [age 53.6±3.6, LVEF = 52.7±2.5%, (mean ± SEM)] and 17 healthy controls underwent cardiovascular magnetic resonance (CMR). LV short-axis stacks were divided into 6 slices, from base to apex. The phase time to maximum wall thickening(T_{thick}) for each of the 6 segments in each slice was measured. In-slice dyssynchrony was quantified in terms of the standard deviation of T_{thick} (CMR-T_{thick} SD) for the 6 segments in each slice. The standard deviation of T_{thick} for all imaged segments was used as a global measure of dyssynchrony. The distribution of non-compacted myocardium (NC) in relation to underlying compacted (C) myocardium was determined using 2 chamber views (steady-state free precession sequence).
Results: In patients with LVHT, NC was most pronounced at the apical segments (basal-septal 21%, midseptal 100%, apicoseptal 100%, apical 100%, apicoinferior 100% and basal inferior 0%). The global CMR-T_{thick} SD was higher in IVNC than in controls (130.1±13.5 v 50.8±2.3 ms, $p<0.0001$). In patients with LVHT, in-slice CMR-T_{thick} SD increased from basal slices (mainly C) to apical slices (mainly NC), from 74.6 to 171.2 ms ($p<0.0001$). In controls, there was no difference in CMR-T_{thick} SD between basal and apical slices (38.2 and 39.6 ms, respectively).
Conclusions: LVHT is associated with global LV dyssynchrony, even in the presence of a normal LVEF. The correlation between the distribution of NC and regional dyssynchrony provides evidence for an untoward mechanical effect of NC on underlying C.

P1208 Evidence of LV wall movement actively decelerating aortic blood flow

C.M. Page[1], A.W. Khir[1], M.Y. Henein[2] on behalf of Brunel Institute of Bioengineering. *[1]Brunel University, Biomedical instituite for Bioengineering, London, United Kingdom; [2]West Middlesex University Hospital, Cardiology Department, Middlesex, United Kingdom*

Purpose: It has been reported that aortic flow deceleration towards end systole is dominated by a forward suction wave (FSW) that is generated by the left ventricle (LV). Neither the time nor LV mechanical activities underlying the generation of the FSW have yet been thoroughly investigated.
Hypothesis: As blood is incompressible, intraventricular circulation accompanies regional wall movement throughout the cardiac cycle. During LV ejection, both longitudinal (major axis) and circumferential (minor axis) contract (shorten). Therefore, we hypothesise that the time of maximum shortening speed of both axes should coincide with the onset of the FSW as measured by wave intensity analysis (WIA). Furthermore, the shortening rate following the point of maximum shortening speed of the LV axes is expected to influence the magnitude of the FSW.
Methods: 11 mongrel dogs were anaesthetised, endotracheally intubated and mechanically ventilated. Pressure (P) and flow (U) were measured in the ascending aorta using a high fidelity pressure catheter and ultrasonic flow probe. LV axes dimensions were measured using ultrasound crystals, and all measurements were sampled at 200Hz for 30 seconds. Wave speed in the aorta was calculated using the PU-loop method and was utilised to determine WIA, which was then used to identify the onset of the FSW. Correlations were calculated using paired t-test and $p<0.05$ was considered significant.
Results: LV minor axis maximum shortening velocity occurred 0.06±0.02s after the onset of ejection and coincided with the arrival of the reflected wave ($r=0.82$, $p<0.05$). LV major axis maximum shortening velocity occurred 0.09±0.03s after the onset of ejection and coincided with the onset of the FSW ($r=0.73$, $p<0.05$). The FSW was observed to have a slow and then rapid stage. The rapid stage occurred 0.012±0.04s after the onset of ejection, coincided with peak P and an inflection point on the U waveform. The energy carried by FSW correlated with the LV major axis decelerated shortening ($r=0.42$, $p<0.05$).
Conclusion: The aortic FSW detected in end systole is generated by the LV as its major axis shortening velocity starts to fall. This follows the fall in minor axis shortening velocity. Reflected waves instigate aortic flow deceleration, but the FSW causes an increase in the falling rate of aortic U, inducing an inflection point on the descending limb of the U waveform. The significant relationship between the decline of wall speed and the FSW suggests that LV contraction in late systole influences the energy carried by this wave which itself enhances flow deceleration.

P1209 The sarcolemmal calcium pump mediates lipopolysaccharide-induced myocardial dysfunction in mice

D. Oceandy, S. Prehar, M. Zi, T. Mohamed, E. Cartwright, L. Neyses. *University of Manchester, Cardiovascular and Endocrine Sciences, Manchester, United Kingdom*

Cardiac contractile dysfunction is one of the major problems in septic shock syndrome that may cause mortality. During septicaemia, bacterial lipopolysacharide (LPS) or endotoxin is released into the systemic circulation and induces the production of proinflammatory substances such as TNF-alpha, interleukin-1 and nitric oxide (NO). An excessive inflammatory response may then cause global vasodilatation, circulatory collapse and myocardial dysfunction. The plasma membrane calcium ATPase (PMCA) is a ubiquitously expressed calcium pump that regulates intracellular calcium signalling. Previous studies suggest the involvement of PMCA4 in TNF-alpha and NO-mediated signalling. We therefore investigated whether PMCA4 is involved in the development of cardiovascular dysfunction during endotoxemia.
PMCA4 knockout (PMCA4-/-) mice and wildtype littermates were treated with LPS (20 mg/kg body weight) for 16 hours. PMCA4-/- mice displayed significantly reduced cardiac contractility after LPS treatment compared to wildtype controls (dP/dt max: PMCA4-/-, 3048±470 mmHg/s, wildtype, 6383±1470 mmHg/s, $P<0.05$, $n\geq5$). The cardiac relaxation speed was also prolonged in PMCA4-/- mice as indicated by dP/dt min and Tau values. PMCA4-/- mice exhibited a greater systemic inflammatory response as indicated by higher serum TNF-alpha level after LPS treatment(PMCA4-/-,205±75 ng/ml; WT, 68±9 ng/ml; $P<0.05$, $n\geq5$). To test whether modulation of NO signalling might be the possible mechanism, we performed analysis using neonatal rat cardiomyocytes. We found that overexpression of PMCA4 reduced the production of NO as indicated by staining with NO-sensitive probe DAF-AM.
In conclusion, the present study demonstrates that PMCA4 is involved in the development of myocardial dysfunction during endotoxemia. It is possible that modulation of NO signalling by PMCA4 is the mechanism responsible for this finding.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1210 Effect of an integrated approach to care in heart failure patients with compromised or preserved left ventricular function

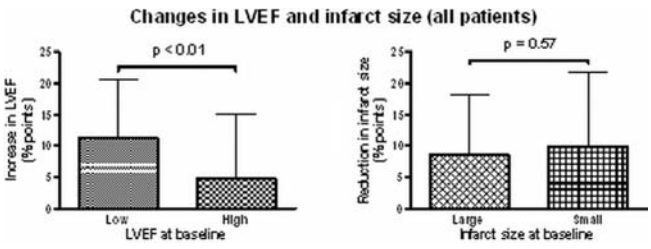
D. Degli Esposti, E.R. Cosentino, A. Dormi, S. Bacchelli, E.R. Rinaldi, D. De Sanctis, D. Maione, M.G. Prandin, E. Ambrosioni, C. Borghi.
S.Orsola Hospital-University of Bologna, Internal Medicine Department, Bologna, Italy

Heart failure (HF) is a major public health challenge. HF patients (pts) in fact, still have a bad prognosis and need frequent hospitalizations.
Aim of this study was to evaluate the effect of 1 year of an integrated programme care, comprehensive of systematic assessment and management, counselling and education of patients, on NYHA class and hospitalization of out HF pts with preserved (P: ejection fraction-EF $>$ 40%) or damaged (D: EF $\leq$ 40%) left ventricular (LV) systolic function.
Study pts were required to have clinical characteristics of HF, according to the new approach to the classification of HF; we in fact also considered pts in stage A. At entry and after 1 year we evaluated the NYHA class and the number of hospitalizations in the previous 12 months.
In a 5 year period we evaluated 672 consecutive HF pts, 439 with LV EF determination [239 M, 200 F, 92 pts (21%) with EF $\leq$ 40%, 72$\pm$10 years; 347 pts (79%) with EF $>$ 40%, age 73$\pm$9], of which 241 had at least 1 year control [129 M, 112 F, 59 pts (24.5%) with EF $\leq$ 40%, age 72$\pm$11; 182 pts (75.5%) with EF $>$ 40%, age 74$\pm$8; p=ns for age].
At entry, 47 Dpts (79.6%) and 112 Ppts (61.5%) had at least 1 hospital admission because of HF, whilst 17 Dpts (28.8%) and 29 Ppts (15.9%) had $\geq$ 3 admissions. After 1 year 4 Dpts (6.8%) and 11 (6%) Ppts were admitted once and nobody had $\geq$ 3 readmissions; 3 Dpts died.
At entry 3 Dpts (5.1%) and 81 Ppts (44.5%) were in NYHA class I, 39 Dpts (66.1%) and 74 Ppts (40.7%) in NYHA II, 17 Dpts (28.8%) and 27 Ppts (14.8%) in NYHA III; no pts was in NYHA IV. After 1 year 35 Dpts (59.3%) and 60 Ppts (33%) improved their NYHA class, 1 Dpts (1.7%) and 9 Ppts (4.9%) showed a worse NYHA class, 23 Dpts (39%) and 113 Ppts (62.1%) maintained the same NYHA class ($p < .0001$ in Dpts, $p < .001$ in Ppts for improving trend; p = ns for worsening trend in both LV systolic function groups).
In conclusion, the specific care and educational/support intervention programme was effective in reducing readmission and in ameliorating NYHA class of all HF pts, independently on their LV systolic function. Albeit HF pts with preserved LV systolic function showed a better quod vitam prognosis (nobody died in this group in our study), they nevertheless had frequent hospitalization before entry in our programme and, after 1 year of our programme implementation, they showed a reduction in admissions, and an improving in clinical conditions as well as pts with compromised LV systolic function. Specific care and support seem therefore to be a good tool in the global management of HF public health challenge.

P1211 Changes in LVEF and infarct size after acute myocardial infarction. Relation to baseline values and bone marrow cell treatment

K. Lunde[1], S. Aakhus[1], S. Solheim[2], J.G. Fjeld[1], H. Arnesen[2], K. Forfang[1] on behalf of ASTAMI investigators. *[1]Rikshospitalet-Radiumhospitalet Univ.Hospital, Cardiology, Oslo, Norway; [2]Ullevaal Univ.Hospital, Cardiology, Oslo, Norway*

Purpose: To investigate if the changes in left ventricular ejection fraction (LVEF) and infarct size after acute myocardial infarction(AMI) are different for patients with high and low values of these parameters at baseline, and if these changes are influenced by mononuclear bone marrow cell (mBMC) treatment.
Methods: Patients with a first anterior wall ST-elevation AMI treated with PCI with stent on LAD culprit lesion 2-12 hours after onset of symptoms were randomised to intracoronary administration of autologous mBMC after 4-8 days (n=50) or control (n=50). ECG-gated SPECT was performed at baseline (4$\pm$1days) and repeated after 6 months.
Results: There were no statistically significant differences between the groups for the studied parameters at baseline. We dichotomized the material according to the median baseline values for LVEF (47%) and infarct size (46.7%) respectively. LVEF increased with 11.2$\pm$9.3%points in the baseline low group, and with 4.7$\pm$10.3%points in the baseline high group, $p < 0.01$. The reduction in infarct size was not different between those with large and small infarcts at baseline. These changes were similar also for only the mBMC and only the control group, respectively.
Conclusion: After AMI, the improvement in LVEF is greater for patients with low LVEF at baseline, whereas the reduction in infarct size is independent of the baseline value. The increase in LVEF and reduction in infarct size after 6 months are not influenced by mBMC treatment, regardless of the baseline values.



P1212 The cardiac consequence of electrolyte disturbance and endocrine disorder in heart failure patients

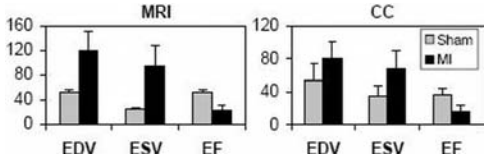
K.-D. Schlueter[1], I. Tastan[2], Y. Abdallah[2], R. Schreckenberg[2].
[1]Justus-Liebig-Universitat, Physiology Dept., Giessen, Germany; [2]Justus-Liebig-University, Giessen, Germany

Background: Endocrine disorders in patients with heart failure are well recognized in the past years. Disturbed electrolyte composition contributes to this phenomenon. A loss in free plasma calcium in patients with heart failure (NYHA IV: -6.5%) and plasma sodium (NYHA IV: - 4.9%) are leading to small increases in plasma parathyroid hormone (PTH) and aldosterone (ALDO). This study was aimed to investigate to which extent long term exposure of cardiomyocytes to PTH or ALDO modifies the contractile performance of cardiomyocytes specifically in the context of altered electrolyte composition.
Results: Isolated adult ventricular rat cardiomyocytes were used and paced at 0.5 to 2.0 Hz. Cell shortening was detected by a cell edge detection sysmtem. Calcium transients were monitored by FURA/AM loading. Cells were exposed to PTH and ALDO for 24 h. Low calcium (0.9 mM) and low sodium (136 mM) buffers were adjusted to the small changes observed in patients with heart failure and compared to normal values (calcium: 1.1 mM, sodium: 143 mM).
Results: Low concentrations of synthetic PTH(1-34) (200 pM) increased cell shortening by up to 34.4$\pm$4.3% (n=48). The effect of PTH was cAMP-dependent, PKC-independent, specific for PTH (i.e. could not be evoked by PTHrP or osteostatin, two other members of the peptide family), and was found in a similar way for full length recombinant PTH. PTH treatment did not impair maximal responsiveness to beta-adrenoceptor stimulation. PTH increased resting cell calcium (by 7%) and systolic peak values (by 7.4%). The cardiac improvement caused by PTH was inversely correlated with the external calcium concentration. ALDO caused a concentration-dependent effect as well, and increased cell shortening and resting calcium. The ALDO effects were more pronounced at low sodium and low calcium concentration. The effects of ALDO and PTH were not additive.
Conclusion: Cardiomyocytes chronically exposed to PTH and ALDO significantly improve cell shortening via a higher resting cell calcium. This effect is more relavant in the presence of slighty reduced plasma calcium and sodium levels. The slightly elevated plasma concentrations of PTH and ALDO are adaptive processes for the cardiomyocytes.

P1213 Assessment of left ventricular function in the failing mouse heart by magnetic resonance imaging and conductance catheter

E.M. Winter, R.W. Grauss, D.E. Atsma, M.J. Schalij, A.C. Gittenberger-De Groot, P. Steendijk. *Leiden University Medical Center, Anatomy & Embryology, Leiden, Netherlands*

Purpose: The murine myocardial infarction (MI) model is widely used to test novel heart failure therapies. Magnetic resonance imaging (MRI) and conductance catheter (CC) both enable cardiac phenotyping under physiological, closed-chest conditions. We performed a head-to-head comparison of MRI versus CC in the ischemic failing mouse heart.
Methods: In 42 mice MI was created by LAD ligation, 18 mice received a sham operation. The animals were studied 2 weeks later by MRI (day 14) and CC (day 15). MRI was performed with a 9.4 Tesla Brucker DRX. We scanned 6-9 continuous 1-mm short axis slices (18-22 frames/beat) and left ventricular end-systolic volume (ESV), end-diastolic volume (EDV) and ejection fraction (EF) were calculated. CC measurements used a 1.4F Millar pressure-conductance catheter introduced via the right carotid artery. Parallel conductance was obtained by central hypertonic saline injections and slope factor alpha was assessed in vitro.
Results: Comparison between MRI and CC for all pooled data by orthogonal linear regression revealed good correlations: EDV: CC=0.60MRI+11.1 (R=0.44); ESV: CC=0.59MRI+13.4 (R=0.59); EF: CC=0.80MRI-3.2 (R=0.80). CC-derived volumes and EF were consistently lower than those by MRI, but differences between study groups were comparable with both methods (Fig).



Conclusion: Volumes and EFs obtained in normal and failing mouse hearts showed good correlation between MRI and CC, albeit with systematically lower values for CC. Both techniques adequately evaluated changes in function induced by MI but the modalities were not interchangeable. MRI and CC have important additional complementary characteristics: MRI provides anatomic information and regional function, whereas CC provides detailed functional hemodynamics including on-line pressure-volume relations.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1214 Antibody-titers against Troponin I correlate with improvement of left ventricular function after acute myocardial infarction

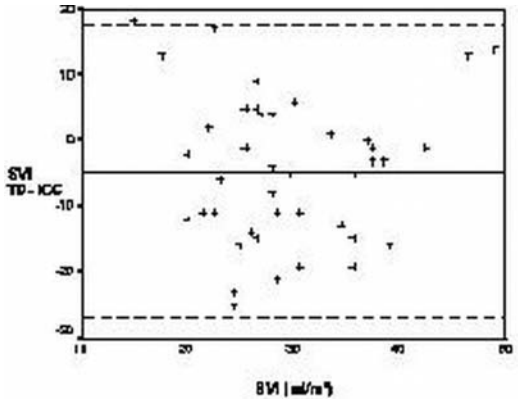
F. Leuschner[1], S. Goeser[1], H. Steen[1], L. Reinhardt[1], K. Hallermayer[2], R. Oettl[2], G. Pfitzer[3], E. Giannitsis[3], H.A. Katus[3], Z. Kaya[3]. *[1]University of Heidelberg, Innere Medizin Iii, Kardiologie, Angiologie, Heidelberg, Germany; [2]Roche Diagnostics, Innere Medizin Iii, Kardiologie, Angiologie, Penzberg, Germany; [3]University of Cologne, Innere Medizin Iii, Kardiologie, Angiologie, Cologne, Germany*

Background: Cardiac troponins in blood are the most preferred markers of myocardial damage. It has been shown that the application of antibodies against cardiac troponin I (cTnI-Ab) can induce dilation and dysfunction of the heart in mice. Furthermore we recently demonstrated that immunization with troponin I induces severe inflammation and fibrosis in the myocardium. In the presented study we performed a clinical trial to investigate the presence of cTnI-Ab in patients with acute myocardial infarction and their effect on the improvement of left ventricular function (LVF) over a period of 6-9 month.
Methods and Results: 33 patients with acute myocardial infarction were included in this study. Every patient underwent coronary angiography and was treated according to the current guidelines. LVF was determined by magnetic resonance imaging (MRI) conducted on a 1.5-T whole-body system 4-7 days and 6-9 months after myocardial infarction. An ELISA-Assay to measure cTnI-Ab-titers was established and serum from each patient was screened for the presence of cTnI-Ab. Out of 33 tested patients 4 had positive cTnI-Ab-titers and 29 were negative. LVF of patients with positive cTnI-Ab-titers decreased over the follow up period of 6-9 month (-8,5% ±6,1). In contrast patients with negative cTnI-Ab-titers showed improvement of LVF (+6,9% ±2,6; p=0,04).
Conclusion: We demonstrate for the first time that the prevalence of cTnI-Abs in patients with acute myocardial infarction has an impact on the improvement of the LVF over a study period of 6-9 months.

P1215 Noninvasive measurement of stroke volume index using impedance cardiography (ICG) in patients with chronic heart failure

A.G. Kieback[1], A.C. Borges[2], G. Baumann[1], M. Laule[1]. *[1]Universitaet Greifswald, Klinik Fur Innere Medizin, Greifswald, Germany; [2]Charite- Universitaetsmedizin Berlin, Medizinische Klinik, Berlin, Germany*

Purpose: This study was conducted in order to find out if noninvasive measurement of stroke volume index using impedance cardiography (ICG) results in sufficient agreement with invasive thermodilution measurements.
Methods: 13 patients- all of them were admitted to the cardiac intensive care unit with severe chronic heart failure (NYHA III- IV) and in whom a Swan-Ganz catheter was positioned- received noninvasive impedance cardiography (ICG) measurements together with the invasive hemodynamic thermodilution (TD)measurements. The agreement between the ICG and TD values for the stroke volume index was defined as primary endpoint. A descriptive statistical evaluation using Bland-Altmann-plots was performed. The differences between the ICG and TD values for the stroke volume were plotted against the mean values of both measurements. Correlation coefficients were calculated according to Pearson.
Results: The results are demonstrated in figure 1. There were huge differences between ICG and TD values for the stroke volume index. The correlation coefficient r was 0.29. An analysis of data from those patients without or with only mild tricuspid regurgitation yielded similar results (r= 0.38).



Agreement between the ICG and TD values

Conclusions: Noninvasive measurement of stroke volume index using impedance cardiography did not result in sufficient agreement with the results from invasive thermodilution measurements in this study with patients suffering from severe chronic heart failure.

P1216 Non Invasive estimation of pulmonary artery diastolic pressure in patients with chronic heart failure

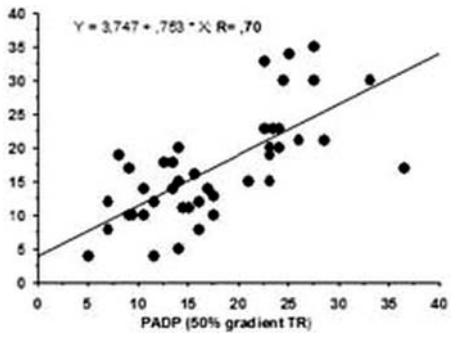
T. Damy, D. Morris, P.F. Lesaut, J.L. Monin, E. Vermes, P. Gueret, J.L. Dubois Rande, L. Hittinger. *Hopital Henri Mondor, Federation De Cardiologie, Creteil, France*

Purpose: Pulmonary artery diastolic pressure (PADP) has prognosis value in heart failure (HF). The objective of our study was to evaluate the accuracy of three echocardiographic methods to estimate PADP.
Methods: 55 patients (51±12 years, 83% men, 40% ischemic) with systolic left ventricular dysfunction (LVEF: 28±8%) underwent right heart catheterization (cathe) and echocardiography(echo) within 24 hours. PADPecho was evaluate by three methods: PADP1 was estimated from the gradient of the end diastolic pulmonary regurgitation (PR) velocity; PADP2 was estimated from the gradient velocity of the tricuspid regurgitation (TR) at the time of pulmonary valve opening; PADP3 was estimated using a formula based on the correlation of catheterization measurement of pulmonary artery systolic pressure (PASP cathe) and PADPcathe: PADPcathe=0,5xPASPcathe (R=0.92). PADP3= 0.5 x (gradient peak TR echo). The three PADPecho estimation were correlated to of the PADP cathe.
Results: PR and TR regurgitation were successively detected in 42% and 78% of the patients. The best method was PADP3 which have a good correlation and agreement with PADPcathe.

PADP echo and cathe correlation

N: 55	Methods	Patients	Correlation PADPecho/cathe	Mean PADP Cathe (mmHg)	Mean PADP Echo (mmHg)
PADP 1	PR	23 (42%)	R= 0.76 p=<0.0001	18.9±9	18.7±6, p=0.73
PADP 2	TR at pulmonary valve opening	43 (78%)	R= 0.52 p =0.0004	17.1±7	15±6.5, p=0.08
PADP 3	0,5xTR	43 (78%)	R=0,70 p<0.0001	17.1±7	17.8±7,p=0.47

PR: pulmonary regurgitation; TR: tricuspid regurgitation.



Correlation PADP cathe and echo (0.5xTR)

Conclusions: The estimation of PADP based on 50% of the gradient peak of TR may provide a easily and reliably method to evaluate the PADP in HF.

P1217 Non-invasive echocardiographic assessment of aorto-ventricular elastance matching in normals and chronic heart failure patients

L. Zhong[1], T.T. Le[1], R.S. Tan[1], D.N. Ghista[2], R. Zannoli[3]. *[1]National Heart Centre, Cardiology, Singapore, Singapore; [2]University of New South Wales Asia, Science, Engineering and Technology, Singapore, Singapore; [3]University of Bologna, Bologna, Italy*

Background & aim: We propose a novel aorto-ventricular elastance matching index (AVEM), ratio of aortic (E_a) and left ventricular (LV) end-systolic elastances (E_{es}), to define LV contraction-aortic impedance interaction. High E_{es} coupled to low E_a is optimal for LV energy generation and transfer. We aim to compare AVEM in chronic heart failure (HF) patients and normals.
Methods: We performed echocardiography (echo) on 10 volunteers (Group A) and 10 HF patients with ischemic cardiomyopathy (Group B), and calculated AVEM in all. We solved for aortic compliance C_a (= $1/E_a$) in the equation governing aortic pressure, P(t): $(1 + R_{av}/R_p)I(t) + C_a R_{av} dI(t)/dt = P(t)/R_p + C_a dP(t)/dt$. I(t) is LV outflow; R_{av}, aortic valve resistance; R_p, peripheral resistance (= mean arterial pressure/cardiac output). All terms were derived by measuring heart rate, brachial systolic (P_s) and diastolic (P_d) blood pressures (BP), and stroke volume (SV) using echo. E_{es} was expressed in terms of estimated normalized LV end-

Table 1. Ea, Ees and AVEM in Groups A and B

Parameter	Group A	Group B	p values
Age (years)	50±11	52±10	0.6
EF (%)	64±7	19±7	<0.0001
E_a (mmHg/ml)	0.86±0.25	0.84±0.25	0.8
E_{es} (mmHg/ml)	2.62±0.59	0.71±0.18	<0.0001
AVEM (E_a/E_{es})	0.33±0.084	1.25±0.47	<0.0001

Values expressed as means ± SD.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

diastolic elastance, E_{Nd}: $E_{es} = (P_d - E_{Nd}\ P_s)/(E_{Nd}\ SV)$; and $E_{Nd} = 0.0275 - 0.165EF + 0.3656(P_d/P_s) + 0.515.Sum(a_i\ ri)$. a_i denotes the constants 0.35695, -7.2266, 74.249, -307.39, 684.54, -856.92, 571.95, -159.1; r, ratio of pre-ejection to total systolic durations; EF, LV ejection fraction.
Results: Group B had significantly lower EF, E_{es} and higher AVEM versus Group A (table 1).
Conclusion: We determined AVEM from non-invasive BP and echo data. HF patients had high AVEM due to low E_{es}. AVEM may be used to monitor integrated LV-aortic function during HF treatment.

P1218 Disproportionate shortening of left ventricular diastolic duration in patients with dilated cardiomyopathy

G. Plehn[1], J. Vormbrock[1], C. Zuehlke[1], C. Perings[1], A. Meissner[1], S. Perings[2], H.J. Trappe[2]. *[1]University of Bochum, Cardiology Dept, Herne, Germany; [2]Institute of Cardiology, Tangramhaus Duesseldorf, Germany*

Introduction: Cardiac performance can be characterised in terms of the relative duration of systole and diastole. In pediatric patients with dilated cardiomyopathy a disproportionate shortening of left ventricular diastole was observed. Our study was intended to reproduce these findings in an adult patient group and to evaluate exercise related changes of both time intervals.
Methods: We used exercise radionuclide angiography in 61 patients with IDCM, The phases of the cardiac cycle were derived from a radionuclide time-activity curve with high temporal resolution. The control group consisted of 26 patients referred for ventricular function assessment with radionuclide angiography before cardiotoxic cancer treatment.
Results: When the duration of systole was expressed as the product of systolic time and heart rate DCM patients exhibited a significant increase in LV systolic time at rest (23.9 vs 21.5 s/min; p = 0.02) and during peak exercise (29.2 vs 26.7 s/min; p = 0.03). The prolongation of LV systole at peak exercise was evident although the peak heart rate was significantly lower in the patient group than in the control group (118 vs 127/min; p = 0.04). In DCM patients t he diastolic time loss per beat was further quantified using a regression equation obtained from the healthy control group. A significant shortening of LV diastolic time was confirmed during peak exercise. Furthermore, a progressive loss in diastolic time per beat from rest to peak exercise was noted.
Conclusion: Cardiac cycle abnormalities of patients with dilated cardiomyopathy are characterised by a prolongation of LV systole and an abnormal shortening of LV diastole. The systolic-diastolic mismatch is accentuated during exercise and has the potential to impair the cardiac reserve in these patients by restricting ventricular filling and perfusion.

DIASTOLIC DYSFUNCTION

P1219 Effects of left ventricular diastolic dysfunction on adrenergic tone and baroreflex control in essential hypertension

G. Seravalle[1], C. Cuspidi[2], F. Quarti Trevano[3], G. Brambilla[3], G.B. Bolla[4], G. Grassi[3], G. Mancia[3]. *[1]Ospedale St. Luca - Istituto Auxologico Itali, Cardiology Dept, Milan, Italy; [2]Policlinico di Monza, Cardiology, Monza, Italy; [3]S. Gerardo Hpt, Clinica Medica, Monza, Italy; [4]University di Milano, Centro Interuniversitario Fisiologia Clinica, Milan, Italy*

Objective: Several studies have provided evidence that left ventricular (LV) hypertrophy exacerbates the hyperadrenergic state characterizing essential hypertension. No information is available on whether and to what extent sympathetic function is altered by LV dysfunction, i.e. a cardiac functional abnormality which is detected in hypertension and carries an adverse prognostic relevance.
Design and Methods: In 47 male untreated moderate essential hypertensives (age 48.6±1.6 yrs, mean±SEM) and in 15 age-matched healthy male normotensives (C), we measured beat-to-beat blood pressure (Finapres), heart rate (EKG), and muscle sympathetic nerve traffic (microneurography, MSNA) at rest and during arterial baroreceptor stimulation and deactivaction via the vasoactive drug technique. Measurements also included echocardiographic assessment of LV geometry and function (LV septal wall tickness, posterior wall tickness, LV mass index, LV diameters and ejection fraction as well as Doppler evaluation of E wave, A wave and E/A ratio).
Results: Based on the results of the echocardiographic evaluation, hypertensive patients were classified as with no LV hypertrophy (HT, n=14, LV mass index 106±7 g/m^2, E/A ratio 1.04±0.03), with LV diastolic dysfunction (HTD, n=8, LV mass index 114±8 g/m^2, E/A ratio 0.69±0.09), with LV hypertrophy (HTH, n= 14, LV mass index 136±10 g/m^2, E/A ratio 1.01±0.06) and with LV hypertrophy coupled with LV diastolic dysfunction (HTHD, n=11, LV mass index 140±11 g/m^2, E/A ratio 0.64±0.06). LV ejection fraction was >50% in all groups. For blood pressure values superimposable in the 4 hypertensive groups MSNA was significantly greater in HT than in C (52.1±2.8 vs 39.8±2.6 bs/100hb, p<0.02) and more so in HTD and HTH (62.4±3.0 and 63.2±2.9 bs/100hb, p<0.03). In HTDH the concomitant presence of LV diastolic dysfunction and hypertrophy induced a further MSNA increase(70.2±3.2 bs/100hb, p<0.03). Compared to C, baroreflex heart rate control was impaired in all the 4 hypertensive groups, the degree of impairment being more marked in HTHD. In contrast, baroreflex modulation of MSNA was preserved in HT and in HTH but significantly reduced in HTD and in HTHD (-27±6 and -35±7% respectively, p<0.05 for both).
Conclusions: We can conclude that in HT the impairment of LV diastolic function is associated with a marked sympathetic activation and a baroreflex impairment. These alterations, which appear to be potentiated when diastolic dysfunction is associated with LV hypertrophy, may account for by the increased cardiovascular risk observed when this functional cardiac alteration is present.

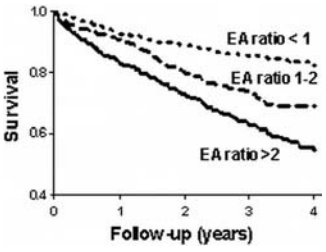
P1220 The prognostic significance of E:A ratio in patients with chronic heart failure: can E:A alone predict survival?

G.A. Whalley[1], A.L. Klein[2], C.M. Yu[3], M. Quintana[4], S. Ghio[5], D.L. Prior[6], P.L. Temporelli[7], R. Troughton[8], K.K. Poppe[8], R.N. Doughty[8] on behalf of The MeRGE HF Collaborators. *[1]The University of Auckland, Medicine, Auckland, New Zealand; [2]The Cleveland Clinic, Cleveland, United States of America; [3]Prince of Wales Hospital, Hong Kong, China, People's Republic of; [4]Karolinska University Hospital, Stockholm, Sweden; [5]Fondazione IRCCS Policlinico S Matteo, Pavia, Italy; [6]St Vincent's Hospital, Melbourne, Australia; [7]Salvatore Maugeri Foundation, Veruno, Italy; [8]Otago University, Christchurch, New Zealand*

40% of heart failure (HF) patients (pts) have restrictive diastolic filling (RF): an important predictor of mortality. But most pts have non-RF. Some studies suggest pts with pseudonormal (PN) filling have intermediate risk, but detection of PN filling requires advanced techniques that are not routinely used. We hypothesise that an E:A>1 in HF pts may be considered PN and this might identify a group of pts at intermediate risk.
Methods: The MeRGE collaboration includes prospective data from 17 studies in chronic HF. This analysis includes 2344 pts, classified into 3 groups: 1) E:A <1; 2) E:A 1-2; 3) E:A >2. Time to first event (all-cause death at 4 years) was analysed by Kaplan-Meier method and Cox Proportional Hazards model and repeated in pts with reduced EF (n=2084).
Results: 467 deaths occurred: mortality was different across the groups. In multivariate analysis, E:A(HR:1.12, CI:1.09,1.16), EF(HR:0.96, CI:0.95,0.97) and Age (HR:1.04, CI:1.03,1.04) predicted death. Similar results were seen pts with EF<40%.

Group event rate and characteristics

	E:A <1	E:A 1-2	E:A >2
Deaths/Number at risk	127/1037	143/673	197/637
Age, years	62.3	59.4	56.3
EF, %	30.9	29.6	25.6



Kaplan Meier Survival

Conclusion: In pts with HF, it is possible to identify pts at intermediate risk of death by using E:A alone, without further clarification of PN filling. The study highlights the important of diastolic assessment and its role in prognostication in pts with HF.

P1221 Diastolic function and exercise induced QTdispersion changes in subjects with athletic and pathological LV hypertrophy

N. Sharashidze[1], Z. Pagava[2], G. Mamaladze[2], T. Kishmareia[2]. *[1]Tbilisi, Georgia, Republic of; [2]Institute of Cardio9logy, Tbilisi, Georgia, Republic of*

The purpose of the present work was to study interrelation between LV diastolic function and exercise induced QT dispersion changes in subjects with athletic and pathological LV hypertrophy.
Methods: 52 soccer players (I group), 30 hypertensive patients (II group) and 15 healthy volunteers (III group) were studied. LV mass and function was evaluated by echocardiography. Exercise tests were performed on treadmill; QTd was calculated at rest, peak exercise and during recovery period.
Results: In all groups LV-mass,Edd-end diastolic diameter,LV diastolic filling velocities: V_E -Early peak flow velocity, V_A- Atrial flow velocity were measured.V_E/V_A was calculated. V_E in I group was 48±5,1 cm/s (95%CI 65-102), 48±3,2 cm/s (95%CI 32-67) and 70±3,8 cm/s (95%CI 63-77) in II and III groups respectively. V_A was 48±5,1 cm/s (95%CI 39-56,4) in I group, 55±8,0 cm/s (95%CI 34-68)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

and 30±4,3 cm/s (95%CI 22-40) in II and III groups respectively. V_E/V_A in I group 1,1±0,9 (95%CI 0,5-2,58), 0,85±0,33 (95%CI 0,43-1,161) and 1,12±0,3 (95%CI 0,72-1,52) in II and III groups. Comparison showed, that group of athletes is more heterogeneous depending on standard deviation and wide variation of 95% CI of study parameters. From I group 15 subjects were separated. In all of them variation of indices significantly exceeded the variations in control group. This 15 athletes formed group Ia. After separation I group became more homogeneous (group Ib). In Ia group V_E was 67±2,8 cm/s (95%CI 0,56-1,44) and 88±3,6 m/s (95%CI 80,7- 95) in Ib group. V_E/V_A in Ia group was 1,0±0,25 (95%CI 0,56-1,44) and 2,2±0,28 (95%CI 1,1-2,7). In Ib group LV mass growth is associated with heart function enhancement, while in Ia group large LV mass and signs of impaired diastolic function was found, like in patient's group. During treadmill test QTd reduced at exercise peak in Ib group as well as in control group. In contrast, Ia and patient groups QTd increased at exercise peak and remained extended in recovery period.

Conclusions: In subjects with LV hypertrophy and signs of diastolic dysfunction QTd increases during physical exercise, when in athletes with LV hypertrophy and preserved diastolic function, as well in healthy subjects QTd decreases during exercise. Hence, QTd enhancement during exercise test might be indicator of LV diastolic dysfunction.

P1222 Brain natriuretic peptide level in the prediction of severity of left and right ventricular diastolic dysfunction and survival in patients with chronic heart failure and preserved systolic function

L.R. Tumasyan[1], A.B. Nargizyan[2], K.G. Adamyan[1]. *[1]Institute of Cardiology, Heart Failure, Yerevan, Armenia; [2]Institute of Cardiology, Heart Failure, Yerevan, Armenia*

Background: Prognostic value of brain natriuretic peptide (BNP) level and its relation with left (LV) and right ventricular (RV) diastolic function in patients (pts) with non-systolic chronic heart failure (CHF) has not been established.

The aim of study was to assess the usefulness of BNP in the prediction of mortality and severity of LV and RV diastolic dysfunction in CHF pts with preserved systolic function.

Methods: 68 pts (age 63.1±0.9) with NYHA III class diastolic CHF in sinus rhythm were prospectively studied. Peak early (Em and Et) and late (Am and At) transmitral and transtricuspid filling velocities, Em/Am and Et/At ratios and the deceleration times of the E waves (DTm and DTt, ms) were obtained using echocardiography. BNP plasma levels (pg/ml) were assessed simultaneously.

Results: During mean follow-up of 37±0.7 months from cardiac causes died 22 (32.4%) pts. Survivors had lower BNP level (267±72 vs. 598±93), Em/Am (0.8±0.2 vs. 2.3±0.3), higher Et/At (1.25±0.08 vs. 0.84±0.07), longer DTm (240±12 vs. 120±7.7) and shorter DTt (139.2±9.1 vs.196.9±12.1) than died pts, ($p<0.001$ for all). Pearson analysis revealed significant correlation of BNP level with Em/Am (r=0.67), Et/At (r=-0.65), DTm (r=-0.71), and DTt (r=-0.72) ($p<0.01$, for all), but not LV EF (r=0.2). Multivariate Cox stepwise analysis revealed that BNP level, Em/Am, Et/At, and DTm and DTt were the significant independent predictors of cardiac death. Groups of patients with abnormal, pseudonormal and restrictive filling patterns were not significantly different for baseline parameters, except BNP levels (252±25, 388±37 and 572±51, respectively, $p<0.01$ for all). Kaplan-Meier survival curves demonstrated a survival rate of 84.6% in 26 pts with abnormal filling pattern. 22 pts with restrictive filling represented the highest risk group with survival rate 45.5%. In this subset pts who died had shorter DTm (96±3.1 vs. 115±4.1), longer DTt (198±10.3 vs.152±6.1), higher Em/Am (3.3±0.15 vs. 2.2±0.3) and lower Et/At (0.81±0.05 vs. 1.1±0.07), ($p<0.01$ for all), than survivors. 20 pts with pseudonormal filling pattern had an intermediate risk of cardiac events (survival rate 60%).

In conclusions, BNP levels and parameters of LV and RV diastolic dysfunction are the powerful independent predictors of survival in pts with CHF and preserved systolic function. Moreover, BNP level is useful marker of severity of diastolic dysfunction and prognosis in such pts.

P1223 Loss of diastolic time as a mechanism of left atrial pressure rise in patients with dilated cardiomyopathy

G. Plehn[1], J. Vormbrock[1], C. Zuehlke[1], C. Perings[1], S. Perings[2], A. Meissner[2], H.J. Trappe[2]. *[1]University of Bochum, Cardiology Dept, Herne, Germany; [2]Kardiologie am Tangramhaus, Duesseldorf, Germany*

Introduction: Cardiac performance can be characterised in terms of the relative duration of systole and diastole. A disproportionate shortening of left ventricular diastolic time has been demonstrated in systolic and diastolic heart failure. However, little is known about exercise related changes of the relative duration of LV systole and diastole and its impact on hemodynamic variables in patients with idiopathic dilated cardiomyopathy (IDCM).

Methods: We used exercise radionuclide angiography with simultaneous right heart catheterisation for hemodynamic characterisation of 57 patients with IDCM. The phases of the cardiac cycle were derived with high temporal resolution from the left ventricular time-activity curve. In patients with IDCM t he loss of diastolic time per beat (DT) was quantified using a regression equation obtained from a healthy control group (n=26). According to the median DT at peak exercise patients were divided into two groups: group A with a DT $<$ 21 ms and group B with a DT $>$ 21 ms.

Results: The peak exercise values of DT observed in the entire patient group with IDCM were significantly shorter than those predicted as normal diastolic time heart rate relation (274 vs 296 ms; p = 0.02). Group A and B patients did not differ in their baseline and exercise characteristics of LV performance or loading conditions. A significant elevation of the peak exercise pulmonary artery wedge pressure/end-diastolic volume ratio (0.19 vs 0.13 mmHg/ml; p = 0.04) as well as a higher increment in pulmonary artery wedge pressure and a reduced stroke volume reserve were obvious in group A patients (13.9 vs 8.7 mmHg; p = 0.01 and 7.1 vs 13.7 ml/m^2; p = 0.04). The duration of exercise (9.4 vs 11.4 min; p = 0.01) was significantly reduced in group A patients.

Conclusion: An abnormal shortening of diastolic time during exercise can restrict left ventricular filling to an extent that is sufficient to limit left ventricular stroke volume reserve and to cause pulmonary congestion in patients with IDCM. Evaluation of b asic time elements of the cardiac cycle during exercise may contribute to a more comprehensive description of cardiac function in heart failure patients.

P1224 Left atrial function in different grades of diastolic dysfunction

A. Maestroni, G. Gentile, A. Volpi. *A.O. Ospedale Civile di Vimercate, U.O. Cardiologia Giussano, Giussano, Milano, Italy*

Aim: A progressive severity of diastolic dysfunction has been shown to be related with a progressive increase in left atrial (LA) volume. The objective of this study is to describe LA function in patients with different grade of diastolic dysfunction.

Methods: LA function was assessed with echocardiography in three groups: 14 subjects with normal diastolic function; 19 patients with abnormal left ventricle (LV) relaxation (E/A $<$ 0,75 and E/e' $<$ 15) and 14 patients with increased LV filling pressure (E/e' $>$ 15). Patients with atrial fibrillation and significant heart valves diseases were excluded.

LA maximum volume (LAvol MAX), pre-P wave volume (LAvol P) and minimum volume (LAvol MIN) were measured in each group. Estimates for LA reservoir function (LAvol MAX - LAvol MIN), LA conduit function (LV stroke volume - LA reservoir volume), LA passive emptying (LAvol MAX - LAvol P) and LA active emptying (LAvol P - LAvol MIN) were calculated.

LA volumes were measured according to the Guidelines of the American Society of Echocardiography.

Results: LAvol MAX, LAvol P and LAvol MIN increased with severity of diastolic dysfunction (observed values respectively were 27±8 ml/m^2, 19±7 ml/m^2, 14±6 ml/m^2 in normal subjects; 32±12 ml/m^2, 28±11 ml/m^2, 17±9 ml/m^2 in patients with abnormal LV relaxation and 48±18 ml/m^2, 41±18 ml/m^2, 33±17 ml/m^2 in patients with increased LV filling pressure). The differences between abnormal LV relaxation group and increased LV filling pressure group are statistically significant with p $<$ 0,02.

LA reservoir and conduit functions did not differ in the three groups. Patients with abnormal LV relaxation showed lower LA passive emptying compared with normal subjects (5±4 vs 8±3; p $<$ 0,01) and with those with increased LV filling pressure (5±4 vs 7±5; p NS) and higher active emptying compared with normal subjects (10±4 vs 6±3; p $<$ 0,001) and with those with increased LV filling pressure (10±4 vs 8±8; p NS).

The LV systolic function was not different in the three groups.

Conclusions: Maximum, pre-P and minimum LA volumes increase progressively with severity of diastolic dysfunction. No relation was found between LA reservoir and conduit function and diastolic dysfunction grade. In patients with abnormal LV relaxation reservoir volume is mainly supported by active rather than passive emptying.

P1225 Age-related increase in the prevalence of diastolic dysfunction is associated with elevated E over e'lat. and NT-proBNP values

A. Kockskaemper, S. Kleta, R. Wachter, L. Binder, B. Pieske on behalf of German Competence Network Heart Failure Study Group. *University of Goettingen, Cardiology & Pneumology, Goettingen, Germany*

Introduction: Diastolic heart failure is now recognized as an important clinical entity, but diagnosis of early stages of the disease remains elusive. We determined the prevalence of diastolic dysfunction in patients at risk and evaluated the role of novel parameters (echocardiography: tissue doppler; natriuretic peptides: NT-proBNP) in the diagnosis of asymptomatic diastolic dysfunction (diaDF) or symptomatic diastolic heart failure (diaHF).

Methods: We established a prospective cohort of 1344 ambulatory general practice patients (583 male, 761 female) with at least one risk factor for diastolic dysfunction (hypertension, diabetes, sleep apnoea; no history of coronary artery disease). After clinical work-up, diastolic function was assessed by comprehensive echocardiography according to current American Society of Echocardiography recommendations (including E/e'lat. reflecting left ventricular end-diastolic pressure). NT-proBNP levels were measured in parallel. Clinical heart failure was diagnosed according to Framingham criteria.

Results: 6.9% of the patients had previously unknown systolic dysfunction (EF $<$50%) and were evaluated separately. The overall prevalence of isolated diaDF

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

was 85.7%. It increased with increasing age (51-60 years: 69.8%, ≥80 years: 95.6%). Older patients more often suffered from symptoms of heart failure. Isolated diaHF was diagnosed in 32.6% of 51-60 year old patients and in 70.0% of patients ≥80 years. Using established echocardiographic staging parameters, >80% of diaHF patients were classified stage I (mild) diastolic dysfunction despite signs and symptoms of heart failure. In patients with diaDF, there was a significant increase in E/e'lat. and NT-proBNP values with increasing age (51-60 years vs ≥80 years; E/e'lat.: 8.6±0.2 vs 12.1±0.7; NT-proBNP: 78.8±7.3 vs 307.0±35.0 pg/mL; both $p<0.001$). In older age groups (>70 years), E/e'lat. values were significantly higher in patients with diaHF compared to patients with diaDF without signs of heart failure (71-80 years: 10.8±0.3 vs 9.5±0.2; ≥80 years: 12.6±0.9 vs 11.3±0.8; both $p<0.05$). In contrast, NT-proBNP values did not significantly differ between diaDF and diaHF patients.
Conclusion: In this large prospective cohort, the prevalence of diaDF was high. Prevalence of diaDF and resulting diaHF increased with age. While both tissue doppler and NT-proBNP indicate more severe diaDF, only tissue doppler was able to differentiate between diaDF and diaHF. These novel markers may help in the prognostic evaluation and diagnosis of patients at risk for diastolic heart failure.

P1226 NT pro BNP levels correlate with LV compliance and LV remodelling in patients with HEFNF: an endomyocardial biopsy and pressure volume loop based study in heart failure with normal ejection

C.T. Tschope, D. Westermann, M.K. Kasner, S.J. Jager, H.P.S. Schultheiss, M.P. Pauschinger. *Berlin, Germany*

Background: We investigated the plasma NT-proBNP and its cardiac precursor, proBNP, in patients with heart failure symptoms despite regular EF (HEFNF) and correlated them with diastolic parameters of pressure-volume (PV)-loop analysis and LV collagen content.
Methods: 52 Pat. (aged 52±10 years) with reduced exercise tolerance despite preserved systolic function (EF 68±8%) were invasively investigated using a conductance-catheter-system to reveal PV-loops at rest and during pacing (120/min). Cardiac performance were derived from LV PV-data obtained both at steady state and during transient preload reduction induced by transient occlusion of the inferior abdominal vena cava. Diastolic performance was measured by peak dP/dt min., the time constant of isovolumic pressure relaxation (tau), LVEDP and the diastolic stiffness constant b (EDPVR). Simultaneously, plasma ProBNP levels were determined. In a subgroup of patients cardiac Pro-BNP (n/12) and Sirius red had been performed from endomycardial biopsies (n/30) and analyzed by immunohistological staining.
Results: Cardiac proBNP levels correlated significantly with plasma NT-proBNP levels. In 34/52 (65%) patients NT-proBNP levels were increased (>125pg/ml), which was associated with a reduction in cardiac output despite regular systolic function. These patients showed pathological LV relaxation and compliance already at rest indicated by a prolongation of Tau (44 [41 – 48] vs. 55 [48 – 67] ms; $p<0.001$) and an increase in LV stiffness (0.011 [0.009 – 0.017] vs. 0.030 [0.019 – 0.039]; $p<0.001$); LVEDP: 9.2 [5.7 – 12.0] vs. 16.5 [10.7 – 22.3] mmHg; $p=0.005$), respectively. NT-proBNP levels correlated significantly with Tau, LVEDP, and LV stiffness both at rest and during pacing-induced stress. The strongest correlation was found between NT-proBNP and the degree of LV compliance (LV stiffness: $r=0.49$; $p=0.002$; LVEDP: $r=0.54$; $p<0.001$) and the degree of LV collagen content, which also correlated with LV stiffness.
Conclusion: NT-proBNP plasma levels correlate with the degree of LV compliance and matrix remodelling in patients with HFNEF. We conclude that NT-proBNP is a useful biomarker in the difficult diagnosis of HFNEF.

P1227 Left ventricular diastolic dysfunction predicts increased risk of cardiovascular events in patients on chronic hemodialysis with preserved left ventricular systolic function

H. Takase[1], T. Okado[1], T. Toriyama[1], S. Tanaka[1], F. Suzuki[1], T. Terada[1], M. Kaneko[1], G. Kimura[2], Y. Dohi[2]. *[1]Enshu General Hospital, Dept. of Internal Medicine, Hamamatsu, Japan; [2]Nagoya City University, Internal Medicine and Pathophysiology, Nagoya, Japan*

Purpose: Cardiovascular disease is the main cause of mortality in patients on chronic maintenance hemodialysis. Recent studies demonstrated that an elevation of B-type natriuretic peptide (BNP) predicts cardiovascular events in dialyzed patients without clinical signs of cardiovascular diseases. We hypothesized that an impairment of diastolic function contributes to BNP elevation and increased risk of cardiovascular events in this population. The present study was designed to investigate a possible contribution of left ventricular diastolic dysfunction to BNP elevation in patients on chronic hemodialysis with preserved left ventricular systolic function.
Methods: Patients on chronic maintenance hemodialysis with a stable condition at least for the last 3 months were screened for the eligibility. Patients with normal systolic function (ejection fraction in echocardiograms ≥50%) and post-hemodialytic cardiothoracic ratio on chest X-ray <50% in males and <55% in females were enrolled in the present study (n=94, male/female=55/39, 65.5±12.0 years old). The exclusion criteria were: ischemic heart disease, valvular heart disease, congestive heart failure, severe arrhythmia, and atrial fibrillation. Their BNP concentrations were measured and left ventricular diastolic function was assessed by echocardiography after hemodialysis. Diastolic function was assessed by analyzing patterns of transmitral flow in echocardiograms [1].
Results: Echocardiography revealed that 38 out of the 94 patients had diastolic dysfunction. BNP levels were higher in patients with diastolic dysfunction (319±166 ng/l [median±median absolute deviation]) than in those without diastolic dysfunction (127±80 ng/l, $p<0.01$). Multiple regression analysis adjusted by age, gender, body mass index, blood pressure, hemoglobin, left ventricular mass index, and the presence of diabetes mellitus demonstrated that diastolic dysfunction was the only significant predictor of BNP elevation in dialyzed patients ($p<0.01$).
Conclusions: Elevated BNP is associated with impaired diastolic function in patients on chronic maintenance hemodialysis. Poor prognosis in dialyzed patients with elevated BNP may be at least in part attributable to diastolic dysfunction. Approaches to improve diastolic dysfunction may improve the prognosis in this population. Reference: [1] Lubien E, et al. Circulation. 2002;105:595-601

P1228 Effects of K201 (JTV-519) on excitation-contraction coupling and Ca^{2+} release in rat ventricular cardiomyocytes

N. Otani[1], R. Matsuda[2], S. Toyoda[1], T. Matsuda[1], N. Kaneko[1], C.M. Loughrey[3], G.L. Smith[3]. *[1]Dokkyo Medical university School of Medicine, Cardiology & Pneumology, Tochigi, Japan; [2]Dokkyo Medical University School of Medicine, Dept. of Cardiology & Pneumology, Tochigi, Japan; [3]University of Glasgow, Veterinary Medicine, Glasgow, United Kingdom*

Purpose: We have shown the effects of norepinephrine and Ca^{2+} overload on diastolic function on rat hearts in vivo. K201 has novel actions on sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA) mediated SR Ca^{2+} uptake and ryanodine receptor-2 (RyR2) mediated Ca^{2+} leak. K201 (JTV-519), a 1,4-benzothiazepine derivative, was found to prevent diastolic dysfunction induced by calcium overload and norepinephrine, but the cellular mechanism remains unclear.
Methods: We studied that Ca^{2+} spark and wave measurements were made to load 10 μmol/L Fluo-3AM (Km 488 nmol/L) on isolated rat cardiomyocytes using confocal microscopy.
Results: Raising extracellular Ca^{2+} (4.75 mM) and adding 150 nM isoprenaline caused spontaneous Ca^{2+} release and the generation of Ca^{2+} waves during diastole. Addition of 1 μM K201 reduced the incidence of Ca^{2+} wave in diastole and decreased the number of initiating events. Similar results were observed in the presence of increased extracellular Ca^{2+} (4.75 mM). In single rat cardiomyocyte exposed to both high calcium and norepinephrine the production of diastolic calcium waves is prevented by 1 μM K201. This is in good correlation with the effects at the whole animal level. The action of K201 was evident only when spontaneous Ca^{2+} waves were present. Under conditions of lower calcium loads, when only calcium sparks were evident, K201 did not significant affect diastolic calcium.
Conclusions: Our data suggest that K201 can limit diastolic dysfunction by altering Ca^{2+} handling by the SR, in particular preventing the abnormal release of SR of calcium during diastole.

P1229 Matrix Metalloproteinase-9 and Tissue Inhibitor of Matrix Metalloproteinase-2 Affect Left Ventricular function after Acute Myocardial Infarction

K. Yajima[1], N. Ohte[2], T. Yoshida[1], M. Oguri[1], K. Kato[1], T. Hibino[1], K. Yokoi[1]. *[1]Gifu Prefectural Tajimi Hospital, Department of Cardiology, Tajimi, Japan; [2]Nagoya City Univ Graduate Sch of Med Sciences, Dep of Int Med and Pathophysiology, Nagoya, Japan*

Turnover of extra cellular matrix proteins is mediated by a family of matrix metalloproteinases (MMPs). Tissue inhibitor of matrix metalloproteinases (TIMPs) can inhibit the function of MMPs by forming complexes with them. MMPs and TIMPs have been reported to play an important role that provokes to ventricular dysfunction and remodeling after myocardial infarction. Pathophysiology of left ventricular (LV) dysfunction, especially diastolic dysfunction, in patients with acute myocardial infarction (AMI) has not been fully elucidated. Thus, we investigated the association between serum levels of MMPs and TIMPs and LV dysfunction.
Method: We studied 81 consecutive patients with an AMI successfully treated with primary percutaneous coronary intervention (PCI). They did not have a prior myocardial infarction. We measured serum levels of MMP-9 and TIMP-2 just after PCI on the first hospital day with Enzyme-Linked Immunosorbent assay method. LV function was evaluated by cardiac catheterization 2 weeks after the onset of AMI. We calculated a time constant of LV relaxation (tau) from the LV pressure waves obtained with a catheter-tipped micromanometer. LV ejection fraction (EF) was obtained from contrast left ventriculography. Correlations between serum levels of MMPs and TIMPs and cardiac function indexes were evaluated by Peasons rank correlation test.
Result: Serum level of MMP-9 was significantly and inversely correlated with LVEF ($r=-0.39$, $p<0.001$). Serum level of TIMP-2 revealed a significant and inverse correlation with tau ($r=-0.31$, $p<0.005$).
Conclusion: This study demonstrates that a high serum level of MMP-9 is associated with greater magnitude of LV systolic dysfunction. In contrast, a high serum level of TIMP-2 is associated with less impaired LV relaxation time constant, suggesting that it may renovate LV early diastolic dysfunction.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1230 Changes in cardiac function and structure following administration of aldosterone in rats: mechanisms involved

B. Martin-Fernandez, M. Miana, N. De Las Heras, S. Ballesteros, V. Cachofeiro, V. Lahera. *School of Medicine. Universidad Complutense, Department of Physiology, Madrid, Spain*

Aim: To investigate the role of aldosterone in the development of functional and structural cardiac alterations, as well as the mechanisms involved in these processes.
Design and methods: Aldosterone was administered for 21 days to male Wistar rats at three doses (10 m g, 100 m g and 1000 m g/kg/day s.c.). Rats received NaCl 1% as drinking water. At the end of the treatment, a catheter was advanced into the left ventricle through the right carotid artery. Systolic (SAP) and diastolic arterial pressure (DAP), heart rate (HR), left ventricular end-diastolic pressure (LVEDP), left ventricular systolic pressure (LVSP), + dP/dt and - dP/dt were measured. Ratio heart/body weight was used as index of cardiac hypertrophy. Cardiac gene expression of inflammatory mediators (TNF- alfa and IL-1 beta), growth factors (TGF-beta and CTGF), p22phox subunit of NADP (H) oxidase and eNOS were measured by real-time RT-PCR.
Results: Aldosterone increased relative heart weight ($p<0.001$) in a dose-dependent manner, reaching significant differences with the last two doses when compared with controls. A similar pattern was observed with SAP ($p<0.01$), DAP ($p<0.01$) and LVEDP ($p<0.001$). Only the highest dose of aldosterone reduced –dP/dt ($p<0.001$). No changes were observed in either HR, LVSP or +dP/dt with respect to their controls.

Table 1

	Control	ALDO 10 mg	ALDO 100mg	ALDO 1000mg
TNF-alfa	100±10,6	111,8±16,8	224,6±42*#	224,8±35,2*#
IL-1beta	100±16,5	104±18,7	178±29,3	270±53,9*#
CTGF	100±13,7	108±8,5	127±21,4	222±48,2*#+
TGF-beta	100±15,5	104±11,3	115±12,7	188±40,3*
p22phox	100±15,11	97,6±6,2	155±20,4*#	177,1±31,6*
eNOS	100±8,4	105,2±17,1	127,8±12	167±23,7*

Data expressed in relative expression (%) *vs CT, #vs ALDO 10, +vs ALDO 100.

Summary: Aldosterone produced a dose-dependent arterial pressure increase, cardiac hypertrophy and diastolic dysfunction. Aldosterone, increased the expression of inflammatory mediators and growth factors and is associated with an increase in oxidative stress as well as in NO production. All these data suggest that both hemodynamic and non-hemodynamic molecular mechanisms participate in the functional and structural cardiac alterations induced by aldosterone in rats.

P1231 Prevalence and determinants of systolic and diastolic dysfunction in dialysis patients

J.W.L. Hartog[1], F. Salachova[1], F.M.E. Hoekstra[2], R.M. Huisman[1], D.J. Van Veldhuisen[2], A.A. Voors[2]. *[1]University Medical Center Groningen, Cardiology Dept., Groningen, Netherlands; [2]Dialysis Center Groningen, Medicine, Groningen, Netherlands*

Background: Cardiovascular morbidity and mortality are high in dialysis patients. Systolic and diastolic dysfunction are frequent echocardiographic abnormalities in these patients. We investigated the prevalence and determinants of systolic and diastolic dysfunction in haemodialysis and peritoneal dialysis patients.
Methods: A total of 168 patients (126 haemodialysis, 42 peritoneal dialysis, 38% female) aged 59±16 years from the Dialysis Centre Groningen, who underwent standard echocardiography, were included. Systolic dysfunction was defined by a left ventricular ejection fraction $\leq$ 55%. Diastolic dysfunction was defined as either a tissue velocity imaging (TVI) $\leq$ 8 cm/sec and/or an abnormal E/A ratio, isovolumetric relaxation time (IVRT), deceleration time (DCT), and the parasternal long axis diameter of the left atrium.
Results: Systolic dysfunction was present in 53 (32%) patients. Multivariate linear regression analysis revealed that it was associated with myocardial ischemia (p=0.003)and cerebrovascular accident (CVA) in medical history (p=0.04), smoking (p=0.03), and higher age (p=0.01). Ninety-two(70%) patients had diastolic dysfunction. Patients with diastolic dysfunction were older ($p<0.0001$), had a lower Kt/V urea (marker for dialysis quality; p= 0.026), a lower calcium-phosphate product (p=0.017), higher plasma triglycerides (p=0.018), and higher use of angiotensin converting enzyme inhibitors (p=0.03).
Conclusion: Both systolic and diastolic dysfunction were frequently present in dialysis patients. Systolic dysfunction was related to a history of and risk factors for cardiovascular disease. In addition to age, calcium-phosphate product, triglyceride levels, and the use of ACE inhibition, diastolic dysfunction was most interestingly related to dialysis quality. These data may help understand why dialysis patients develop systolic and diastolic dysfunction. As both are adverse prognostic factors for survival in dialysis patients, early detection and treatment of these echocardiographic abnormalities may decrease the risk to develop congestive heart failure.

PULMONARY EMBOLISM AND CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

P1232 Pulmonary embolism - problems with diagnosis

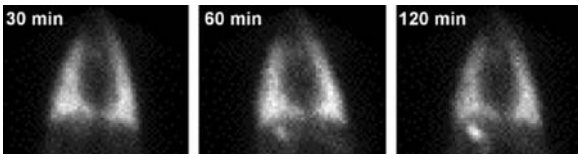
D.E. Lacka, K. Rejner, M. Kaczorowska. *Medical University of Warsaw, Warsaw, Poland*

Introduction: Since 1922, when Wharton and Pierson described radiographic features of pulmonary embolism, the constant development of technology has offered clinicians new diagnostic tools, such as angiography, scintigraphy, CT, MRI. Despite such variety of available tests, clinical diagnosis of pulmonary embolism still causes many problems and the number of diagnosed cases constitutes a minimal percentage of real morbidity confirmed by autopsy.
Aims: – To analyze the frequency of occurrence of pulmonary embolism in autopsy protocols and to analyze its pathogenetic factors.
– To analyze clinico-pathological discrepancies in diagnosis of pulmonary embolism.
– To find out which diseases was pulmonary embolism most frequently confused with.
Methods: 10 000 autopsies from the years 1980-2006 were analyzed.947 cases of PE diagnosed post mortem were encountered. From these, 2 groups of patients were created: group 1 with clinical diagnosis of PE and group 2 without clinical diagnosis of PE
Results: PE occurred in 10% of patients that were examined by autopsy (n=947) and was the main cause of death in 68% of cases.
From the analyzed pathogenetic factors:
– venous thrombosis occurred in 23% of cases,
– cancer in 17%,
– atrial fibrillation in 14%,
– decubitus or paralysis (expression of immobilization) appeared in 11% of patients,
– 8.5% underwent a major orthopaedic surgery or bone fracture,
– 7.4% of patients had right heart thrombosis.
Group 1(clinically diagnosed PE) comprised 22% of analyzed cases and group 2 (without clinical diagnosis of PE) 78% of cases In the second group PE was the cause of death in 65% of patients.
In patients who died because of PE that was not clinically diagnosed, the most frequently stated clinical cause of death was acute circulatory and respiratory insufficiency (40%). Myocardial infarction was stated in 17%, apoplexy in 17% as well. In 16% the cause of death was attributed to cancers other than lung tumour, while lung cancer was mistakenly diagnosed in 7% of patients.
Conclusions: In the analyzed autopsies pulmonary embolism constituted 10% of all diagnoses.
Only $\frac{1}{4}$ of patients among this group were clinically correctly diagnosed.
Venous thrombosis, cancer disease and atrial fibrillation were the most frequent coexisting pathogenetic factors.
Pulmonary embolism that was not detected in lifetime, was most often clinically diagnosed as circulatory insufficiency, myocardial infarction or apoplexy.

P1233 Use of a chelated adrenomedullin derivative for molecular imaging of the pulmonary circulation

F. Harel[1], Y. Fu[2], A. Caron[2], M. Letourneau[1], Q.T. Nguyen[2], L. Perreault[2], A. Fournier[1], J. Dupuis[2]. *[1]Montreal Heart Institute, Montreal, Canada; [2]INRS-Institut Armand Frappier, Pointe-Claire, Canada*

Background: Adrenomedullin (AM) is a vasodilator peptide predominantly cleared by the pulmonary circulation through specific endothelial receptors. We developed a chelated human AM derivative (AM) using diethylenetriaminepentaacetic acid (DTPA) radiolabeled with 99mTc. We evaluated the biodistribution, plasma kinetics and utility of 99mTc-DTPA-AM as a pulmonary vascular imaging agent.
Methods and Results: The radiochemical purity of 99mTc-DTPA-AM was 92±2%. A hemodynamically inactive dose of the compound was intravenously injected to anesthetized dogs (n=6) and the tracer activity serially determined in blood samples as well as in various regions of interest using external detection with a gamma camera. The capacity to image vascular perfusion defects was evaluated after surgical pulmonary lobe ligations. 99mTc-DTPA-AM was rapidly cleared from plasma following a two-compartment model with a very rapid distribution half-life of 1.75 min (95% confidence interval: 1.31-2.65). The lungs retained most of the activity after 30 minutes (27±3%, $p<0.001$), as compared to kidneys (19±3%), liver (12±1%), heart (7± 2%), bladder (6±2%) and gallbladder



Molecular imaging of lung perfusion

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(1.0±0.4%). Lung retention was mildly reduced with time but sustained up to 4 hours after the injection (16±2%). After pulmonary lobe ligations, anatomically corresponding perfusion defects were easily detectable by external imaging.
Conclusion: 99mTc-DTPA-AM displays important and extended lung retention and is a promising new agent for pulmonary vascular imaging. This novel molecular imaging agent enables detection of anatomical perfusion defects, but also has the inherent potential for the detection of functional vascular perfusion abnormalities.

P1234 What is the prevalence of free-floating thrombi in the right heart complicating acute pulmonary embolism?

I. Abi Nasr, N. Mansencal, R. Nguetta, J.C. Farcot, T. Joseph, P. Lacombe, O. Dubourg. *Ap-Hp, Hopital Ambroise Pare, Boulogne-Billancourt, France*

Background: Free-floating thrombi in the right heart is considered as exceptional in acute pulmonary embolism (PE). Studies evaluating such complications are rare. The aim of this study was to estimate the prevalence of free-floating thrombi in the right heart in a population of patients presenting with acute PE.
Methods: We studied 195 consecutive patients with confirmed PE (by CT-scan or lung scintigraphy) and all these patients underwent transthoracic echocardiography. We systematically assessed: 1) right to left ventricular end-diastolic area ratio using 2D echo in apical 4-chamber view and a right ventricular dilation was defined as a ratio $>$ 0.6; 2) systolic pulmonary arterial pressure (SPAP) using CW Doppler and 3) the presence of free-floating thrombi in the right heart using 2D echo and we separated thrombi prolapsing into the tricuspid valve from those less mobile in the right atrium.
Results: Mean age was 66±18 yo (range: 16-95), 76 men and 119 women. Using transthoracic echocardiography, 81 patients (42%) presented with right ventricular dilation, SPAP was measurable in 138 patients (71%) and mean SPAP was 42±12 mmHg. Eleven patients had free-floating thrombi in the right heart. The prevalence of free-floating thrombi in the right heart in our population was 5.6%. The characteristics of free-floating thrombi in the right heart were as follows: the thrombus was serpentine, very mobile and prolapsing into the tricuspid valve in 9 patients and was less mobile and spherical in 2 patients; all patients had also right ventricular dilation and mean SPAP was 50±5 mmHg (p=0.03).
Conclusion: Our study suggests that the prevalence of free-floating thrombi in the right heart in acute PE is 5.6%. This complication is not so unusual in acute PE and should be systematically assessed using transthoracic echocardiography.

P1235 Pulmonary embolism following cardiac surgery: retrospective analysis of 7783 patients

E. Eleuteri, C. Marcassa, R. Campini, P. Calza, F. Scapellato, P.L. Temporelli, P. Giannuzzi. *Fondazione Salvatore Maugeri, IRCCS, Cardiology, Veruno (No), Italy*

Purpose: Pulmonary embolism (PE) is a relatively uncommon but severe complication of cardiac surgery, with a 1%-3% prevalence. The evenience of PE can significantly prolong hospital stay, with a consequent significant raise of expence. We tried to evaluate the incidence of PE a large group of pts in a cardiac rehabilitation setting.
Methods: From 1995 to 2003, 7783 patients entered our Institution within 30 days from cardiac surgery (coronary artery bypass gtafting, CABG, heart valve replacement, HVR, or both, CABG+HVR), for a programmed rehabilitation period. All records were surveyed for type of surgery, clinical characteristics and most frequent complications. Along the rehabilitation period, PE was suspected in 165 pts (2.1%). The diagnosis has been confirmed in 67 pts (0.9%), by clinical and scintigraphic data according to PIOPED criteria. PE pts were older (70±7 vs 65±9 years, p $<$.001). Pts that had undergone HVR had a lower incidence of PE (0.5%) as compared to pts with CABG (CABG, 0.9%) or CABG+HVR(1.1%), but these differences didn't reach statistical significance. At univariate analysis no conventional risk factor, namely smoking abit, hypertension, diabetes, hyperlipidemia, showed significant correlation with PE. On the contrary, surgery complications had significant positive predictive value (1.8% vs 0.3%, p $<$.0001), namely myocardial infarction (MI) (3% vs 0.8%,p$<$.0001), respiratory distress with need of prolonged ventilation (2.1% vs 0.8%, p$<$.05), atrial fibrillation or atrial flutter (AF/AFF) (1.3% vs 0.8%, p $<$.05), mechanical assistence (3.3% vs 0.8%, p$<$.001), need of inotropic therapy (2.5% vs 0.8%, p$<$.001). At multivariate analysis, only MI during surgery (p = .001) and AF/AFF (p = .03) resulted as significant predictors of PE.
Conclusions: In our retrospective analysis, PE is quite uncommon after cardiac surgery (incidence 0.9%) during the rehabilitation period. Variables associated with PE are mainly older age and peri-operative complications, AF/AFF and MI being the only clinical predictors of PE. We believe that, at least in subgroup of pts at higher risk of developing PE, pharmacological prophylaxis with unfractioned heparin or low molecular weight heparin should be considered as a routine prevention measure. Trials on wide populations are needed.

P1236 Acute pulmonary embolism: EKG value in the identification of patients with right ventricular dysfunction/overload

P. Magno, S. Baptista, A. Freitas, V. M Gil. *Hospital Fernando Fonseca, Cardiology, Amadora-Lisbon, Portugal*

Introduction: There are ECG signs typical of pulmonary embolism (PE). Though not widely accepted, some authors believe they suggest right ventricular (RV) dysfunction/overload (DO), a feature of poor prognosis.
Objective: To verify if there is any relation between typical ECG signs of PE and echocardiographyc signs of RV DO.
Population and methods: Retrospective analysis of admission's ECG and echocardiography data from 107 consecutive patients with PE. Patients were divided in 2 groups, according to the presence (A – 61) or absence (B – 46) of ECG typical of PE. ECG was considered typical of PE if at least one of the following was present: S1Q3T3, inverted T wave in V1-V4, right bundle branch block, right axis and/or clockwise rotation of electrical axis. RV DO was defined as the presence of at least one of the following: RV dilation, D-shaped left ventricle, McConnel's sign.
Results: Groups A and B, respectively, were not significantly different (p=NS) in what concerned age (53,5±18,6vs60±17,1 years), sex (men 37,7vs34,8%), cardiac (3,3vs4,3%) and lung (14,8vs30,4%) disease, previous PE (4,9vs13%) or clinical presentation: syncope (31,1vs28,3%), dyspnea (93,4vs80,4%), hypotension (23vs26,1%), cardiac arrest (3,3vs6,5%). The ECG typical of PE was significantly more frequent in patients with RV-DO (93,4vs63,4%; p$<$0,001). Its specificity and sensibility were, respectively, 78,9% and 64,8%, being its positive and negative predictive values 93,4% e 32,6%.

Table 1

n (%)	**RV DO (n=88)	**RV DO (n=19)
*Negative T wave in V1-V4	31 (55,7)	3 (15,8)
*Right bundle branch block	19 (34,4)	2 (10,5)
*S1Q3T3	18 (31,1)	1 (5,3)
*Right axis deviation	10 (16,4)	0
*Clockwise axis deviation	8 (13,1)	0
**Group A	57 (93,4)	4 (6,6)
**Gruoup B	31 (67,4)	15 (32,6)

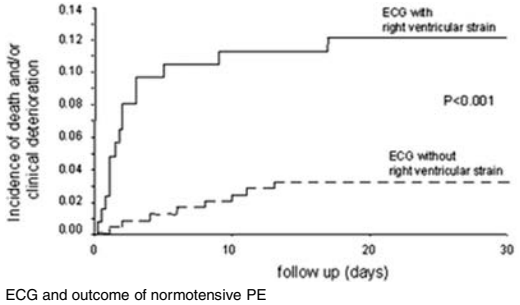
*no. of cases/(%) **no. of patients/(%).

Conclusion: Despite low sensibility and specificity the ECG criteria considered as typical of PE was significantly more frequent in patients with RV-DO, being its positive predictive value high. This criteria may be useful in selecting patients with PE candidates to urgent echocardiography due to the suspicion of RV DO.

P1237 Right ventricular strain pattern at ECG predicts adverse short term outcome and right ventricular dysfunction persistence in patients with acute pulmonary embolism and normal blood pressure

S. Vanni, G. Polidori, P. Nazerian, S. Magazzini, B. Paladini, M. Zanobetti, G. Giannazzo, A. Conti, S. Grifoni. *Emergency Department, AOU Careggi, Emergency Department, Firenze, Italy*

Background: In patients with acute pulmonary embolism (PE) and normal blood pressure echocardiographic evidence of right ventricular dysfunction (RVD) on admission and persistent RVD at discharge has important prognostic implications. However, echocardiography may be not routinely available in the emergency setting. Electrocardiography (ECG) has a widespread use and it is easily interpreted. Present study was planned to investigate the prognostic value of ECG in patients with acute PE and normal blood pressure.
Methods: Consecutive patients with PE and normal blood pressure were included in the study. ECG and echocardiography were performed in a blinded fashion on admission and at discharge. Primary study outcomes were clinical deterioration and/or death at 30 days and persistent RVD at hospital discharge.
Results: Three hundred eighty-six patients with a mean age of 67±16 years were included in the study. On admission, the ECG of 130 patients (31%) showed at least one of the following: right ventricular branch block, S1Q3T3, negative T wave in V1-V4. During follow-up 23 patients (6%) had clinical deterioration, 12 (3%) patients died and 72 (19%) showed RVD persistence at hospital discharge. At multivariate logistic regression analysis right ventricular strain at ECG was as-



ECG and outcome of normotensive PE

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

sociated with the presence of RVD on admission (OR 4.98; CI 95% 2.82-8.79) and of RVD persistence at hospital discharge (OR 4.68; CI 95% 2.54-8.62). At multivariate Cox survival analysis right ventricular strain pattern was an independent predictor of clinical deterioration and/or death at 30 days (HR 3.64, CI 95% 1.53-8.63).
Conclusions: Right ventricular strain pattern at ECG is an independent predictor of adverse short term clinical outcome and of persistent RVD in patients with acute PE and normal blood pressure.

P1238 Platelet function in chronic thromboembolic pulmonary hypertension

R. Sadushi[1], S. Panzer[2], D. Bonderman[2], N. Skoro-Sajer[2], W. Klepetko[3], I.M. Lang[3]. *[1]Internal Medicine II, Division of Cardiology, Vienna, Austria; [2]Department of Blood Group Serology, Vienna, Austria; [3]Division of Cardiothoracic Surgery, Vienna, Austria*

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by thrombotic obstruction of pulmonary arteries. The role of platelets in the pathogenesis of CTEPH is unknown.
Patients and Methods: Because circulating heterotypic aggregates between monocytes and platelets (MPA) and platelets and leukocytes (LPA) represent reliable markers of platelet activation in vivo, we investigated MPA by FACS in 13 patients (pts) with CTEPH [median (interquartile range): 59 (43-72)] at the time of diagnosis, when patients were off anticoagulation. Thirteen matched healthy volunteers served as controls (ctrls).
Results: MPA-formation measured by CD14+/CD41+% [CTEPH: 65.28(39.92-90.97) versus ctrls 25.92(2.46-36.39); $P<0.05$] and PLA-formation assessed byco-expression of CD45+/CD41+% [median (interquartile range); CTEPH: 12.96(6.43-22.44) versus ctrls 6.61(1.02-10.02); $P<0.05$] were significantly higher in patients with CTEPH (Figure 1). After activation with Thrombin Receptor Activating Peptide-6 (TRAP) MPA [CD14+/CD41+%: 93.30(65.72-98.79) versus ctrls 69.92(26.18-96.95); $P<0.05$] and PLA [CD45+/CD41+: 33.34(17.40-41.86) versus ctrls 16.26(3.02-32.42); $P<0.05$] were increased in CTEPH. In addition, platelet surface coverage and average size of aggregates measured by the cone and platelet analyser Impact R (CPA) were significantly higher in CTEPH pts [SC%, 12(1.2-18); ACμm^2, 52(25-125)] than in ctrls [SC%, 9 (4.8-20); ACμm^2,34(21-137), $P<0.05$].

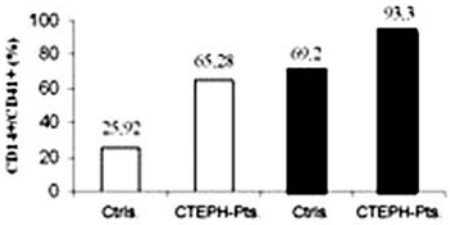


Figure 1 MPA measured by CD14+/CD41+ at (baseline [white bars] and after activation with TRAP [black bars])

Conclusion: In stable pts with CTEPH, functional platelet tests revealed a state of activation. Further experiments are directed at the understanding of how activated platelets contribute to a failure of thrombus resolution.

P1239 Incidence of hyperhomocisteinemia and methylentetrahydrofolate reductase 677 genotypes in patients with pulmonary thromboembolism

N. Antonijevic[1], A. Beletic[2], D. Mirkovic[1], V. Sango[3], I. Novakovic[3], V. Djordjevic[4], S. Obradovic[5], J. Perunicic[1], B. Jakovljevic[5], Z. Vasiljevic[1]. *[1]Clinical Center of Serbia, Cardiovascular Diseases, Belgrade, Serbia; [2]Clinical Center of Serbia, Medical Biochemistry, Belgrade, Serbia; [3]School of Medicine, Biology, Belgrade, Serbia; [4]Inst. of Molec. Genet. and Gen. Engineering, Belgrade, Serbia; [5]Military Medical Academy, Urgent Medicine, Belgrade, Serbia*

Purpose: Methylentetrahydrofolate reductase (MTHFR) 677 T/T genotype is possibly associated with a higher risk of venous thrombosis and, also, one of the causes of hyperhomocysteinemia (HHcy). Hyperhomocysteinemia, itself, is an important risk factor for pulmonary thromboembolism (PTE).The purpose of this study is to determine the differences in HHcy incidence, homocysteinemia levels and distribution of all the three MTHFR 677 genotypes (C/C, C/T and T/T) between patients with PTE and healthy persons.
Methods: The study enrolled 64 patients and 50 controls. Homocysteine was measured using HPLC method with fluorescent detection and HHcy was defined as homocysteinemia above 12 μmol/L. PCR amplification and digestion with restrictive endonuclease Hinf I were employed for determination of MTHFR 677 genotype. Statistical analyses included chi-square and Mann-Whitney U tests.
Results: Median homocysteinemia value was significantly higher (p=0.017) in patients (12.10 μmol/L) than in controls (10.35 μmol/L). The comparison of HHcy incidence between patients (51.5%) and controls (30.0%) revealed significant difference (p=0.021). There was no statistically significant difference in distribution of MTHFR 677 genotypes between patients and controls. In patients, homocysteinemia was significantly higher (p=0.002) in men (14.05μmol/L) than in women (10.08 μmol/L). HHcy was present in 67.6% of men with PTE, which was significantly higher (p=0.006) than the incidence in women with PTE (33.3%). Healthy males had significantly higher (p=0.001) homocysteinemia (12.54 μmol/L) than healthy females (9.39 μmol/L). Significant difference (p=0.031) was observed between the incidences of HHcy in healthy males (44.0%) and healthy females (16.0%). There were no statistically significant gender-specific differences in distribution of MTHFR 677 genotypes in both groups.
Conclusion: We conclude that the incidence of hyperhomocysteinemia and homocysteinemia level are significantly higher in all the patients compared with healthy persons, as well as in both healthy males and males with PTE compared with healthy females and female patients. On the contrary, no statistically significant difference was observed in distribution of the aforesaid MTHFR 677 genotypes betweenpatients and controls. This may indicate that HHcy findings in PTE are likely to have a greater clinical importance than MTHFR 677 genotype.

P1240 Elevated D-dimer concentration identifies patients with incomplete recanalization of pulmonary thromboemboli despite 6 months of anticoagulation after the first episode of acute pulmonary embolism

A. Kaczynska, M. Kostrubiec, R. Pacho, L. Grabowska-Derlatka, J. Kunikowska, L. Krolicki, M. Jelenska, P. Pruszczyk. *Medical University of Warsaw, Dept. of Internal Medicine and Cardiology, Warsaw, Poland*

Background: Despite long-term anticoagulation in some patients after acute pulmonary embolism (APE) pulmonary thrombi are not completely resolved which may lead to chronic thromboembolic pulmonary hypertension. Elevated D-dimer concentration may indicate incomplete pulmonary thrombi resolution after 6-month anticoagulation after the first episode of PE.
Methods: 55 patients aged 54,7±18,6 years were observed. In acute phase 4 patients (7,2%) received thrombolysis. For 6 months patients were anticoagulated (74,5% -acenocumarol and 25,5% - low molecular weight heparin). Then spiral computed tomography (sCT), lung perfusion scintigraphy and D-dimer assessment were performed.
Results: Incomplete recanalisation of pulmonary circulation was detected in 38 (69,1%) patients - thrombi at sCT and/or $\geq$ 1 wedge-shaped perfusion defect at scintigraphy. Age, sex, rate of unprovoked APE, thrombophilia, malignancies, thrombolysis in the acute phase and type of long term anticoagulation were similar in patients without and with complete recanalization. D-dimer at follow-up but not on admission was higher in patients with then without incomplete recanalization (340 (80-2280) vs 160 (60-590) ng/ml, p = 0,02). All 11 (20%) patients with D-dimer level > 500 ng/mL at follow-up did not resolve thromboemboli completely. ROC analysis showed that D-dimer at follow-up identified patients with incomplete recanalization (AUC 0,709, 95% CI (0,560-0,831), p = 0,007). Multivariable analysis confirmed that D-dimer >350 ng/mL at follow-up and right ventricle dysfunction at the diagnosis were predictors of incomplete recanalization (OR 18,58 (95% CI 1,97-175,19) and 7,03 (95% CI 1,43-34,6), respectively, p = 0,0006).
Conclusion: Elevated D-dimer after 6-month anticoagulation and right ventricular dysfunction at the diagnosis predict incomplete recanalization of pulmonary circulation.

P1241 Trombophilia and pulmonary endarterectomy

J. Lindner[1], P. Jansa[1], E. Mayer[2], T. Grus[1], T. Palecek[1], D. Rubes[1], K. Kubzova[1], M. Aschermann[1], J. Blaha[1], A. Linhart[1]. *[1]General University Hospital, Department of Cardiovascular Surgery, Prague, Czech Republic; [2]Johannes Gutenberg University, Cardiothoracic and Vascular Surgery, Mainz, Germany*

Objectives: There have been only a few reports of surgically treated patients with chronic tromboembolic pulmonary hypertension (CTEPH) and trombophilia. In US study trombophilia was found in 10% of patients, in Japan's study in 32% and in our study even in 48%. The aim of the present study was to compare groups of patients with and without trombophilia undergoing pulmonary endarterectomy (PEA).
Methods: 39 patients with CTEPH together (19 with trombophilia 12 males and 7 females) underwent PEA using cardiopulmonary bypass (CPB) and deep hy-

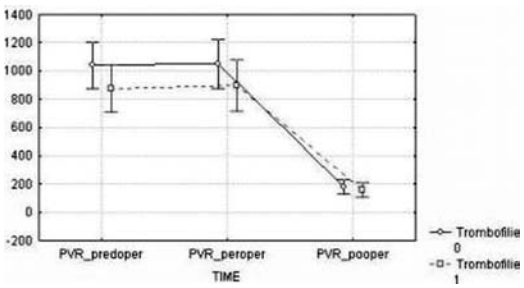


Figure 1. Pulmonary vascular rezistance (PVR)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

pothermic circulatory arrest. Four patients had antiphospolipid syndrome, 4 Leiden mutation factor V, 3 mutation factor II-protrombin, 2 deficit C protein, 2 suffer with hyperhomocystenemia and 11 patients had Methylenetetrahydrofolate Reductase (MTHFR) gene mutation.
Results: After operation there was a considerable improvement of haemodynamic parameters (mPA, CI, PVR) in both groups without statistic difference (Figure 1).
Within one month there was a considerable improvement or normalisation of haemodynamic parameters and an increase walking distance on the six-minute walking test.
Conclusions: PEA is a curative method for patients with CTEPH with a surgically accessible obstruction of the pulmonary artery. Early results patients with accompanied trombophilia after PEA are compable to patients without trombophilia with clinical and hemodynamic improvement.

P1242 Misguided thrombus resolution and bacterial infection in chronic thromboembolic pulmonary hypertension

D. Bondermann, J. Jakowitsch, B. Redwan, H. Bergmeister, M.K. Renner, A. Panzenboeck, C.H. Adlbrecht, A. Georgopoulos, W. Klepetko, I. Lang. *Vienna, Austria*

Background: Acute pulmonary emboli usually resolve within 6 months. However, a proportion of 0.5-3.8% undergo organization with permanent obstruction of the pulmonary vascular bed. The resulting condition is chronic thromboembolic pulmonary hypertension (CTEPH). Based on the observation that CTEPH lacks traditional risk factors for venous thromboembolism, we hypothesized that thrombus persistence in CTEPH is due to delayed resolution rather than abnormal plasmatic thrombosis. Furthermore, because CTEPH occurs in association with Staphylococcus aureus-infected intravenous lines, we tested whether bacterial infection may be involved in the vascular remodeling of delayed thrombus resolution.
Methods: In a first step, CTEPH thromboemboli were sterilly harvested during pulmonary endarterectomy (PEA) and subjected to histologic analyses and Staphylococcus-specific PCR. Secondly, a murine model of thrombus resolution was utilized to examine the effects of bacterial infection on thrombus organization.
Results: Staphylococcal DNA was detected in 7 of 26 PEA specimens. In the mouse model, Staphylococcal infection delayed resolution of thrombi parallel with an up-regulation of the profibrotic genes transforming growth factor beta and connective tissue growth factor expressions.
Conclusions: Bacterial infection enhances fibrotic vascular remodeling after thrombosis, resulting in misguided thrombus resolution. Thrombus infection may be a key pathogenetic event in the evolution of CTEPH.

P1243 Splenectomy is associated with misguided thrombus resolution

M.K. Renner, B. Redwan, H. Panzenboeck, J. Jakowitsch, R. Sadushi, J. Kellermair, D. Bonderman, I.M. Lang. *Medical University Vienna, Cardiology Dept., Vienna, Austria*

Purpose: Chronic thromboembolic pulmonary hypertension (CTEPH) is a vascular disorder characterized by organizing venous thromboemboli obstructing the major pulmonary arteries. Previous studies have demonstrated that prior splenectomy is associated with an increased risk of CTEPH. However, pathomechanisms of altered thrombus formation and resolution after splenectomy are still unclear.
Methods: To compare venous thrombus formation and resolution, we utilized a mouse model of venous thrombosis. At fixed time points, (days 3,7,14 and 28 after vena cava ligation performed three months after splenectomy) thrombus and blood cells were harvested.
Results: Cross-sectional analysis showed that thrombus areas of splenectomised mice were significantly larger than those of control thrombi at all time points (day 28: 0,08±0,02 vs 0,03±0,02 mm^2, n=8,p<0,03, Fig. 1). Thrombi of splenectomised mice demonstrated a higher cell density (day 28: 21416±1299 vs 11173±1040 cells/mm^2,p<0,03) and more collagen than control thrombi (day 28: 29,2±3,1 vs 12,3±1,5% of thrombus area, p<0,03). Smooth muscle cells and macrophages accumulated within the thrombi by day 28. FACS analysis revealed a higher amount of CD41-positive thrombozytes (day 28: 16013±5484 vs 4738±401 cells/µl,p<0,03) and leucozyte/platelet aggregates with an increased proportion of activated platelets (CD11b/CD41,day 28: 65,1±4,4 vs 49,4±5,8%,p<0,03 and CD11b/CD62P, day 28: 7,5±1,4 vs 5,2±0,9%, n.s.).
Conclusion: We demonstrate that splenectomy leads to altered thrombus resolution in a mouse model. Our data provide evidence that alterations of the coagulation and immune systems occur after splenectomy. Further studies will clarify the detailed pathomechanisms which mediate delayed thrombus resolution after splenectomy.

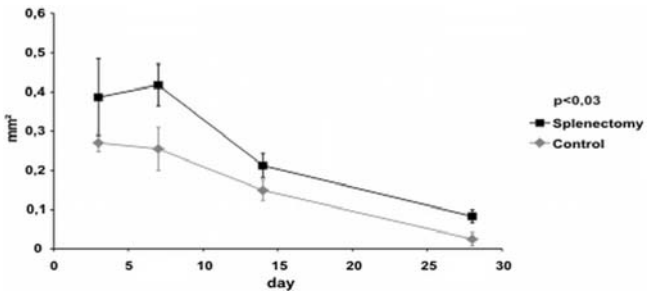


Figure 1: Thrombus area

P1244 Outcome after pulmonary thromboendarterectomy over a 30-month period- a single center experience

M.W. Wieteska[1], A. Biederman[2], M. Kurzyna[2], W. Dyk[1], M. Szturmowicz[2], L. Wawrzynska[2], J. Burakowski[2], B. Hajduk[2], A. Torbicki[2]. [1] *Institute of Tuberculosis And Lung Diseases, Department of Chest Medicine, Warsaw, Poland;* [2] *Institute of Cardiology, First Division of Cardiosurgery, Warsaw, Poland*

Background: Patients suffering from thromboembolic pulmonary hypertension usually develop progressive right heart failure that poorly respond to medical treatment. Selected patients with proximal CTEPH can be successfully treated by pulmonary tromboendarterectomy (PTE). In this study mid-term effects on survival, functional status and echocardiography were assessed.
Methods: Fifty five patients (41 male and 14 female, mean age 51 years, range 25 to 76, preoperative WHO functional class II/III/IV: n=6/35/14, with mean pulmonary artery pressure mPAP 49.4±9 mmHg) were re-evaluated 3-117 months (mean 32 month) after PTE surgery.
Results: Four patients died early after the intervention (7,2%). One late death in the second year of follow-up due to progressive left ventricle failure was unrelated to pulmonary endarterectomy. The actual survival rate, including early hospital mortality, at 12, 24, 36 months remained the same 92,4% (95%CI:85.2-99.6). Fifty one patients survived and presented significant postoperative hemodynamic improvement. The mean pulmonary artery pressure (mPAP 48.2±8 vs. 26.3±7.9 mmHg, p<0.001) and pulmonary vascular resistance (PVR 743.8±252.4 vs.135.3±63.7dyne ·s ·cm-5, p<0.001) decreased while cardiac index increased (CI 2.40±0.49 vs. 3.4±0.9 l/min/m^2, p<0.001). All survivors reported marked sustained improvement of their clinical status. At follow up 29, 19 and 3 patients were in WHO functional class I, II and III, respectively. The six minute walk distance increased from 359.9 m ±125.3 to 464.1±115.5, p<0.001 with less marked arterial oxygen desaturation at end-exercise (pre-op 86.0± 7.0 vs. 92.0±4.6% post-op, p<0.001). Borg dyspnea score decreased from 1.6±1.9 to 0.5±1.2, p<0.001. Echocardiographic examinations revealed sustained significant decrease of the right ventricular (RV) diastolic dimension from 38.2±6.8 to 28.8±4.6 mm, p<0.001), decrease of RV/LV dimension ratio from 0.93±0.3 to 0.61±0.14 and decrease of tricuspid regurgitation peak velocity from 73.7±19.4 to 31.1±12.3 mmHg, p<0.001). The acceleration time of RV ejection increased from 58.1± 9.1 to 94.0±14.9 ms, p<0.001).
Conclusions: PTE is treatment of choice in selected patients with CTEPH with acceptable surgical mortality and excellent mid-term survival. It also leads to sustained improvement of clinical condition, six-minute walk distance and echocardiographic signs of right ventricular dysfunction.

P1245 Abnormal hemodynamic response to exercise in patients after successful pulmonary endarterectomy

D. Bondermann, A. Martischnig, M. Nikfardjam, B. Meyer, R. Sadushi, G. Heinz, W. Klepetko, I.M. Lang. *Vienna, Austria*

Background: Pulmonary endarterectomy (PEA) provides potential cure for patients with chronic thromboembolic pulmonary hypertension (CTEPH). Successfully operated patients have been shown to normalize exercise capacity and hemodynamic parameters in long-term studies. The aim of the present study was investigate whether pulmonary hypertension can be provoked by exercise in CTEPH patients at least one year after successful PEA.
Methods: 13 successfully operated CTEPH patients and 6 age-matched controls without pulmonary arterial hypertension underwent right heart catheterization at rest and after 10 minutes of submaximal supine bicycle-exercise. Hemodynamic parameters and invasively measured systemic blood pressure were recorded. Between-group differences were compared utilizing an unpaired t-test. P-value <0.05 was considered statistically significant.
Results: There were no differences between patients and controls with respect to resting hemodynamic parameters. However, after 10 minutes of submaximal exercise -as a physiological reaction- mean pulmonary vascular resistance dropped in control subjects (-38.8±26.4 dynes·s·cm^{-5}), but increased in CTEPH patients (+4.9±32.1 dynes·s·cm^{-5}, p=0.01). Accordingly, a more pronounced increase in mean pulmonary arterial pressure was measured in CTEPH patients (+11.9±5.9 mmHg) as compared to controls (+5.0±4.9 mmHg, p=0.024).
Conclusions: CTEPH patients after successful PEA demonstrate an abnormal hemodynamic response to exercise. There is a need for studies to investigate whether symptomatic CTEPH patients would benefit from vasodilator therapies.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

PULMONARY HYPERTENSION

P1246 The value of electrocardiography in the diagnosis of pulmonary hypertension

A. Martischnig, P. Wexberg, R. Sadushi, N. Skoro-Sajer, I.M. Lang, D. Bondermann. *Vienna, Austria*

Background: Current guidelines for pulmonary hypertension (PH) recommend invasive hemodynamic evaluation of patients with echocardiographic systolic pulmonary pressures (sPAP) >36mmHg. The growing awareness for PH, a high prevalence of postcapillary PH and the inability to discern between pre- and postcapillary PH by echocardiography (TTE), have led to an excessive amount of invasive hemodynamic measurements in unaffected individuals. The aim of the present study was to test the ability of 12-lead ECG to discriminate between pre- and postcapillary PH in a pre-selected patient population with clinical and TTE suspicion of PH.
Methods: This retrospective study was performed at a tertiary referral center for PH. Admission ECGs of 49 patients were analyzed. The diagnostic value of ECG findings compatible with precapillary PH were evaluated, such as 1) R/S-ratio in V_1, 2) QRS-axis, 3) QRS duration, 4) right ventricular strain (RVS) defined as negative T-wave in V_2 and V_3, 5) P-wave amplitude, 6) right bundle branch block (RBBB) and 7) P-wave axis. Sensitivity, specificity and Youden's index (sensitivity + specificity - 1) were calculated.
Results: In multivariate analysis, sPAP ($p < 0.0001$), RVS ($p = < 0.0001$) and RBBB (p=0.006) remained predictors of precapillary PH. The presence of RVS or RBBB was predictive for precapillary PH (96% or 100%, respectively). Both parameters displayed low negative predictive values (56% and 43%). When combining the diagnostic performance of TTE-sPAP (Youden's index 0.65) with RVS (Youden's index 0.61) the index improved to 0.77 (Table).

Table 1

Parameter	Sensitivity	Specificity	Youden's Index
sPAP>60mmHg	0.79	0.86	0.65
RBBB	0.41	1.00	0.41
RVS	0.68	0.94	0.61
sPAP>60mmHg or RBBB	0.84	0.86	0.70
sPAP>60mmHg or RVS	0.91	0.86	0.77
sPAP>60mmHg or RBBB or RVS	0.91	0.86	0.77

Conclusions: In contrast to the current perception that ECG is not a valuable diagnostic tool in PH, our data suggest that the synergistic use of TTE and ECG in pre-selected patients provides incremental diagnostic information compared with either method alone.

P1247 Diagnosing pulmonary arterial hypertension with a novel 12-lead ECG parameter

I.R. Henkens[1], A. Vonk Noordegraaf[2], A. Boonstra[2], C.A. Swenne[3], R.W.C. Scherptong[1], A.P. Wijnmalen[1], J.W. Twisk[3], E.E. Van Der Wall[1], M.J. Schalij[1], H.W. Vliegen[1]. *[1]Leiden University Medical Centre, Cardiology, Leiden, Netherlands; [2]VU Medical Center, Pulmonology, Amsterdam, Netherlands; [3]Leiden University Medical Center, Cardiology, Leiden, Netherlands*

Background: Pulmonary Arterial Hypertension (PAH) requires an invasive diagnosis. Optimal selection of patients with suspected PAH for right heart catheterization requires a simple yet reliable test to prevent a dramatic rise in cost and patient burden. Classic ECG parameters are considered unsuitable for this purpose. We propose a new ECG parameter that is highly accurate in diagnosing PAH.
Methods: An electrocardiogram (ECG) of 26 Idiopathic PAH patients (QRS duration ≤100 msec), recorded <30 days before diagnostic heart catheterization, was matched for sex and QRS duration with two ECGs from healthy control subjects (n=52). Accuracy in diagnosing PAH was tested for classic ECG criteria, criteria derived from an inverse Dower matrix synthesized vectorcardiogram, and a novel 12-lead ECG criterion: net QRST area in lead I (= QRS and T area above the baseline minus QRS and T area below the baseline).
Results: Classic ECG criteria had high specificity, yet poor sensitivity for PAH. In comparison, the vectorcardiographic spatial ventricular gradient (VG) magnitude and spatial VG vectorial projection on the X-axis through the heart showed high sensitivity and specificity for PAH. The composite vectorcardiographic parameter (spatial VG magnitude * spatial VG vectorial projection on the X-axis) had 100% sensitivity and 100% specificity for PAH. This composite measure correlated well with the 12-lead ECG derived net QRST area in lead I ($r=0.82$, $P<0.001$). Two independent observers, blinded to the origin of the ECGs determined a 96-100% sensitivity and 94-98% specificity for a net QRST area < 16 mV*ms (=four small squares of ECG paper) for diagnosis of PAH ($\kappa=0.92$, $P<0.001$).
Conclusion: Combined spatial ventricular gradient magnitude and orientation from vectorcardiographic analysis as well as from a standard 12-lead ECG shows excellent diagnostic accuracy for Pulmonary Arterial Hypertension. These findings warrant further research regarding the ECG as a potential screening tool for patients at risk for developing Pulmonary Arterial Hypertension.

P1248 Screening of patients at risk for pulmonary arterial hypertension: role of exercise stress echocardiography

R. Maier[1], G. Kovacs[1], S. Scheidl[1], C. Hesse[1], W. Salmhofer[1], R. Stauber[1], F. Fruhwald[1], E. Aberer[1], E. Gruenig[2], H. Olschewski[1]. *[1]Graz, Austria; [2]Heidelberg, Germany*

Background: Pulmonary arterial hypertension (PAH) is frequently associated with collagen vascular diseases and portal hypertension. Unfortunately, PAH often remains unrecognised over years and may finally end up in right heart failure. In the early stage of the disease no significant changes may be observed at rest, however, remodelling of small pulmonary arteries leads to insufficient vasodilatation and elevated pulmonary artery pressure during exercise. To assess pulmonary artery pressure non-invasively during exercise, we performed exercise stress echocardiography in patients at risk for PAH.
Patients and methods: We examined 47 patients (13 male (28%), 34 female (72%); mean age 54±13 years) with systemic sclerosis, CREST syndrome, systemic lupus erythematosus and liver cirrhosis, respectively. All patients underwent transthoracic echocardiography at rest and during exercise as well as cardiopulmonary exercise test. Estimated systolic pulmonary artery pressure (SPAP) was calculated from peak tricuspid regurgitant flow velocity using the simplified Bernoulli equation. In patients with an estimated SPAP >40 mmHg at rest or exercise, right heart catheterisation (RHC) was recommended.
Results: From these 47 patients, 28 (60%) had a normal SPAP at rest and during exercise (22±2 mmHg and 28±6 mmHg, respectively). In 1 patient SPAP was already elevated at rest (54 mmHg), which could be confirmed by RHC (SPAP 44 mmHg). 18 patients (38%) had a normal SPAP at rest (27±5 mmHg), but an elevated SPAP during exercise (55±8 mmHg). Out of these 18 patients, 8 underwent RHC so far. These examinations revealed 1 patient with elevated SPAP already at rest (47 mmHg), while estimated SPAP by echocardiography was 29 mmHg in this particular patient. In 6 patients exercise caused elevation of SPAP (26±4 vs. 56±16 mmHg), as predicted by echocardiography (29±5 vs. 59±9 mmHg). 1 patient was found with normal SPAP at rest as well as during exercise (21 and 28 mmHg, respectively), while estimated SPAP by echocardiography was 33 and 66 mmHg, respectively.
Conclusion: In patients at risk for PAH, exercise stress echocardiography seems to be able to identify the disease in a very early stage. RHC confirmed exercise induced elevation of pulmonary artery pressure in 7 of 8 patients (87.5%). Whether these preliminary results can also be shown in a larger patient cohort, is under investigation now in our ongoing screening program. Exercise stress echocardiography might become a key screening tool for early diagnosis of PAH.

P1249 Risk of pulmonary hypertension in patients with atrial septal defect

H. Helgason[1], M. Dellborg[2], P. Eriksson[2]. *[1]Landspitali, University Hospital, Pediatrics, Reykjavik, Iceland; [2]Sahlgrenska University Hospital, Ostra, Cardiology, Gothenburg, Sweden*

Introduction: Atrial septal defect (ASD) is a congenital heart defect commonly diagnosed in adulthood. Closure of the defect at any age is generally considered the treatment of choice.
Purpose: To determine the risk of presenting with pulmonary hypertension (PH) in patients with an ASD.
Materials and methods: From 2001 through 2005 (5 years) 90 patients underwent cardiac catheterization with intention to close the defect. Hemodynamic data was available in 83 patients, (27 male and 56 female patients, age 18 – 80 years) for evaluation. The size of the defects was measured by a measuring balloon, the mean pulmonary artery pressure (pPA), calculated pulmonary vascular resistance (Rp) and the pulmonary to systemic vascular resistance ratio were evaluated (Rp:Rs). We arbitrarily divided the group into three age groups: group I: 18-39 years (n=21), group II: 40 – 59 years (n=28) and group III: 60 and older (n=34) and compared the three groups (table I).
Results: The mean size of the defects in the whole group was 22,8±6,3 mm. The size of the defects was 25,8±6,3 mm in group I, 22,2±6,7 mm in group II and 21,6±5,7 mm in group III. There was no significant difference in Qp:Qs of the size of the defects between the three groups. The value for pPA, Rp, Rp:Rs and Qp:Qs is shown in table I.

Table I

	Mean pPA (mmHg)	Rp (Wood Units)	Rp:Rs ratio	Qp:Qs
Group I	16,0±3,5 [1), 2)]	0,9±0,6 [1), 2)]	4,4±2,2 (x10^{-2}) [1), 2)]	3,0±1,4
Group II	18,8±9,1 [1), 3)]	2,0±1,6 [1), 3)]	7,2±5,5 (x10^{-2}) [1), 3)]	2,0±0,7
Group III	22,5±6,0 [2), 3)]	1,8±1,1 [2), 3)]	7,5±4,6 (x10^{-2}) [2), 3)]	2,4±1,2

When group I and group II were compared: 1) p=NS; 2) p<0,01. When group I and III were compared: 2) p<0,01. When group II and group III were compared: 3) p=NS.

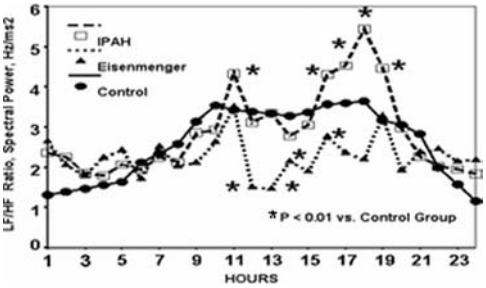
Conclusion: The risk of presenting with PH is low in patients with ASD even in patients above the age of 40 with a large left-to-right shunt. Although the mean pPA, Rp and Rp:Rs increases with age the values are still within normal limits. The risk of developing irreversible PH thus seems to be low.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1250 Circadian modulation of heart rate variability in idiopathic pulmonary hypertension and Eisenmenger syndrome

M. Rosas, J. Sandoval, T. Pulido, F. Attie. *Instituto Nacional de Cardiologia, Cardiologia Dipt, Mexico, Mexico*

Purpose: We sought to establish the circadian sympathovagal modulation of heart rate variability (C-HRV) in two distinct groups of pulmonary arterial hypertension (PAH).
Methods: 24-hr Holter monitoring studies were recorded in 34 patients with severe idiopathic PAH (IPAH), and in 32 with PAH associated with Eisenmenger syndrome (ES). Forty four gender and age-matched normal subjects were used as a control. Both, time (mean, SDNN, SDANN, rMSSD, PNN5O) and spectral parameters (LF, HF, LF/HF ratio) of HRV were analyzed during three periods: 24-hr, day (08:00 to 22:00) and night (23:00 to 07:00).
Results: C-HRV parameters were: LF/HF (day) 5.9:1, 2.5:1, and 4.2:1 for IPAH, ES, and control group, respectively ($p < 0.001$). At night LF/HF ratios were 2.8:1, 1.5:1, and 1.2:1, ($p = 0.034$). SDANN was the only different time-domain parameter among groups (114±22 vs. 68±24 vs. 136 ±32, $p < 0.001$)



Conclusions: Patients with PAH have an altered autonomic modulation of HRV. In IPAH, C-HRV is lost due to an increase in sympathetic tone. ES patients showed a different and somehow unexpected pattern of depressed sympathetic activity. A better hemodynamic profile and/or the existence of chronic arterial hypoxemia in ES may explain the differences in C-HRV in these PAH groups.

PLATELET FUNCTION AND ANTI-PLATELET TREATMENT

P1251 Comparison of outcomes between patients undergoing percutaneous coronary stent implantation with eptifibatide and abciximab: an analysis using propensity score methods

J.P. Dery[1], J. Griffin[2], K.S. Pieper[1], R.A. Harrington[1], J.E. Tcheng[1]. *[1]Quebec Heart Institute, Cardiology, Quebec City, Canada; [2]Duke Clinical Research Institute, Cardiology, Durham, Nc, United States of America*

Purpose: Platelet glycoprotein (GP) IIb/IIIa inhibitors reduce ischemic complications in patients undergoing PCI. However, the superiority of abciximab or eptifibatide in this setting remains unsettled, with no direct comparisons between the two in randomized controlled trials. This study was conducted to compare the effect of abxicimab with that of eptifibatide in patients undergoing elective percutaneous coronary intervention (PCI) with stent implantation.
Methods: All consecutive patients who underwent PCI with stent implantation between January, 1999 and July, 2002 were identified using the catheterization laboratory database. After excluding patients with acute ST-segment elevation myocardial infarction (MI) and those undergoing vein graft intervention, we compared outcomes in patients receiving abciximab with those receiving eptifibatide. Logistic regression and Cox proportional hazards regression were used to model 30-day and 1-year outcomes, respectively. Baseline covariates and propensity scores were used to adjust for differences in baseline characteristics.
Results: Of the 3112 patients included in the analysis, 1549 patients received abciximab and 1569 were treated with eptifibatide. At 1 year, 73 patients in each group had died. There was no difference in rates of death/MI at 1 year across the two treatment groups (unadjusted (abciximab vs eptifibatide) hazard ratio (HR) 0.96, 95% confidence limits (CL) [0.75-1.23]). Adjustment for baseline characteristics with and without propensity score methods also demonstrated no treatment effect on rates of death/MI at 1 year (Covariate-adjusted: HR 0.86, 95%CL [0.67-1.11]; Propensity-adjusted: HR 0.91, 95%CL [0.60-1.34]. Severe thrombocytopenia and clinically apparent bleeding were more common in the abciximab group. However, the incidences of blood transfusion (abciximab: 2.7%; eptifibatide: 3.3%) and hemoglobin drop >3g/l (abciximab and eptifibatide: 4.3%) were similar in both groups.
Conclusion: In this cohort of patients undergoing PCI with stent implantation, the use of abciximab or eptifibatide resulted in similar rates of Death/MI at 1-year.

P1252 Platelet glycoprotein IIb/IIIa polymorphism and prediction of cardiovascular events in stable coronary artery patients

F. Addad[1], F. Abderrazek[1], T. Chakroun[1], Z. Dridi[1], S. Maoui[1], K. Ben Hamda[1], H. Gamra[1], F. Maatoug[1], M. Ben Farhat[1], I. Elalamy[2]. *[1]University Hospital, Cardiology Dept., Monastir, Tunisia; [2]University Hospital, Tenon, hematology, Paris, France*

Background: Platelet glycoprotein (GP) IIb/IIIa is a membrane receptor for fibrinogen and von Willebrand factor which plays a key role in the development of thrombotic complications of coronary artery disease (CAD). However, there is considerable controversy regarding the clinical role of the GPIIb/IIIa PIA1/A2 as a risk factor for myocardial infarction. The aim of the current study was to investigate the association between PI(A) GPIIIa polymorphism and cardiovascular events at one year.
Methods: We prospectively included 188 post-ACS patients (183 men) aged 59±10 years and receiving daily aspirin (250 mg/day). All subjects had significant coronary artery stenosis confirmed by elective coronary angiography. The clinical outcome at one year was the composite of non fatal MI, stroke, recurrent unstable angina or cardiac death. Acute vascular events were defined by the association of unstable angina, MI or ischemic stroke. Screening for the PI(A) GPIIIa genotypes was performed by polymerase chain reaction of genomic DNA, followed by NciI digestion and agarose gel electrophoresis.
Results: The genotype distribution of the PI(A) GPIIIa polymorphism in our study group was PI(A1/A1)-55%, PI(A1/A2)-44% and PI(A2/A2)-1%. The incidence of cardiac death and the composite endpoint of the homozygous PI(A1/A1) genotype were significantly higher in comparison to PI(A2/A2) and PI(A1/A2) patients (see table below). Multivariate analysis identified the following predictive of cardiac death: age older than 65 years (OR=6.8, [1.4-34, 95% CI]; P=0.018), EF<50% (OR 8.6, [1.7-42.6 CI 95%]; P=0.008) and homozygous PI(A1/A1) genotype (OR 8.6, [1.0-78.6 CI 95%]; P=0.05.

	PLA1/A1	PLA2/A1 and PLA2/A2	OR[IC95%]	p value
cardiac death	10 (9.6%)	1 (1.2%)	4.1[1.2-71]	0.014
Recurrent acute coronary syndrom	5(4.8%)	1 (1.2%)	4.1[0.5-37]	0.16
Acute vascular events	5(4.8%)	2(2.4%)	2.1[0.4-10.9]	0.38
composite endpoints	15 (14.4%)	3 (3.6%)	4.5[1.2-16]	0.012

Conclusions: Our results suggest, that the PI(A1/A1) genotype of PI(A) GPIIIa polymorphism is associated with a poor prognosis at one year. This study might have implications for antiplatelet therapy of patients with MI.

P1253 Assessment of ADP-induced platelet aggregation with optical aggregometry and multiple electrode platelet aggregometry before and after clopidogrel loading

D. Sibbing, S. Braun, S. Jawanski, A. Schomig, A. Kastrati, N. Von Beckerath. *Deutsches Herzzentrum Muenchen, Muenchen, Germany*

Purpose: The level of platelet aggregation, measured with optical aggregometry in platelet rich plasma (PRP), has been shown to predict outcomes after percutaneous coronary intervention (PCI). However, measuring parameters of platelet function with optical aggregometry is time consuming. Thus, a fast, reliable and simple method to individually assess clopidogrel responsiveness would be of great value for clinical practice. A new method, multiple electrode platelet aggregometry (MEA), to rapidly measure platelet aggregation in whole blood has been developed recently. The aim of this study was to correlate results of MEA with optical aggregometry before and after clopidogrel loading with 600 mg.
Methods: Blood samples of 36 patients scheduled for coronary angiography were taken before and at least 2h after administration of 600 mg clopidogrel. Maximal ADP(5 μM)-induced platelet aggregation was measured with optical aggregometry in PRP. ADP (6.4 μM)-induced platelet aggregation was also assessed in whole blood with MEA on the Multiplate Analyzer (Dynabyte, Munich, Germany).

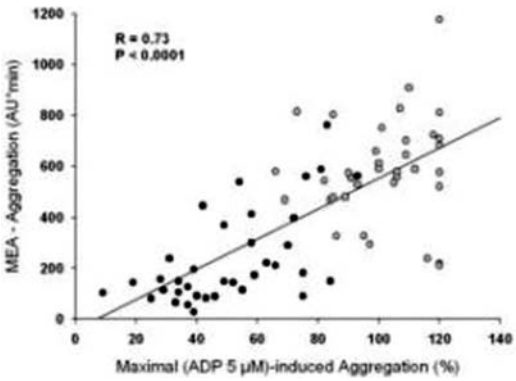


Figure 1

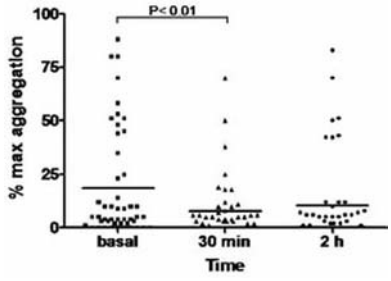
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Aggregation with MEA was quantified as area under the curve of arbitrary units (AU*min).
Results: The correlation coefficients describing the correlation of AU and AU*min measured by MEA with ADP(5 μM)-induced aggregation in PRP were 0.74 and 0.73 respectively. As shown in Fig. 1, MEA strongly correlated with ADP-induced aggregation in PRP (grey dots=untreated, black dots=after 600 mg clopidogrel).
Conclusion: MEA is a reliable method to individually assess platelet function prior to and under clopidogrel therapy. Thus, MEA may be helpful in tailoring antiplatelet regimes in patients scheduled for PCI. Further studies with clinical endpoints are needed to assess the predictive values of the measurements obtained with MEA.

P1254 Inhibitory effect of coffee on platelet aggregation

G. Renda, M. Zurro, G. Malatesta, A. Tatasciore, A. Sciartilli, M. Gravina, M. Zimarino, R. De Caterina. *G. D'annunzio University, Institute of Cardiology, Chieti, Italy*

Introduction: The effect of coffee on platelet function is debated. Aim of this study was to evaluate whether caffeine or the whole coffee drink affect platelet aggregation.
Methods: We recruited 54 male healthy volunteers, moderate caffeine consumers, avoiding coffee for the 24h preceding the study and aspirin in the week before study. Each participant was administered a 40mL volume of a decaffeinated coffee preparation spiked with either 3mg/kg caffeine (about 2 cups of espresso)(whole coffee), or the corresponding vehicle. Platelet (Plt) aggregation was evaluated before, 30min and 2h after coffee assumption by the Born's method and the PFA-100 device. The same protocol was repeated 24h later, after the alternative drinking.
Results: After 30min from consumption of whole coffee, ADP(0.75μM)-induced Plt aggregation was significantly decreased (% max aggregation = 8±13 at 30min vs. 19±25 at baseline, $P<0.01$), with a partial recovery at 2h (see Figure). Epinephrine (EPI)(0.2μM)-induced Plt aggregation showed a slight reduction at 30min and a significant reduction at 2h (12±21 at 2h vs. 24±29 at baseline, $P<0.05$). Similarly, at 30min from drinking of decaffeinated coffee alone, ADP(0.75μM)-induced Plt aggregation was significantly decreased (9±17 at 30min vs. 17±25 at baseline $P<0.05$), but here the reduction of EPI(0.2μM)-induced Plt aggregation was not statistically significant. Plt aggregability detected by the PFA-100 device with both collagen-ADP and collagen-EPI cartridges did not change significantly after coffee drinking.



ADP-induced Plt aggregation after coffee

Conclusions: Coffee consumption exerts an inhibitory effect on platelet aggregation. This effect cannot be attributed to caffeine because also observed after decaffeinated coffee. Components of coffee other than caffeine are involved in the antiplatelet effect.

P1255 Effect of increasing doses of aspirin on aspirin resistance in patients with diabetes mellitus

Y. Dogan[1], M.A. Duzenli[2], K. Ozdemir[2], N. Aygul[2], A. Soylu[2], M. Tokac[2], A. Aribas[2]. *[1]selcuk universty of medical faculty, cardiology, Konya, Turkey; [2]Selcuk University Meram Faculty of Medicine, Cardiology Department, Konya, Turkey*

Objectives: Aspirin is recommended for primary and secondary prevenrion in diabetes mellitus, however platelets of diabetic patients have been reported to be less sensitive to aspirin. Aspirin-induced suppression of platelet thromboxane synthesis is lower in diabetic patients than nondiabetic individuals and a higher incidence of aspirin resistance in diabetic patients has been reported. Therefore, low-dose aspirin might be inadequate for inhibition of platelet function in diabetic patients. The aim of this study is to compare a medium (300 mg/day) and low (100 mg/day) dose of aspirin on platelet function in diabetic patients.
Method: We studied 57 type 2 diabetic patients who have taken 100 mg of aspirin daily for at least 10 days. Platelet functions were evaluated by optical agregometry using ADP, collagen, and epinephrine as platelet agonists. Patients whose aggregation percentages were above the upper limit for each agonist were accepted as aspirin resistant (>69% for ADP, >70% for collagen, >78% for epinephrine). Patients who had no resistance to three agonists were accepted as sensitive. Patients who were resistant to one agonist were accepted as mild,two agonist were accepted as moderate, three agonist were accepted as severe aspirin resistant. Patients who had aspirin resistance contiuned the aspirin therapy at a dose of 300 mg daily for seven days, and agregation tests were again performed.
Results: Thirty-three (57.9%) of 57 were aspirin responder, 12 (21.1%) patients had mild, 7 (12.3%) patients had moderate and 5 (8,8%)patients had severe resistance. Of 24 patients who had aspirin resistance, 12 (50%) became aspirin sensitive after 300 mg of aspirin intake. Mean aggregation percentages decreased for collagen from 81.7 to 52.8, for ADP from 76.0 to 56.1 and for epinephrine from 66.4 to 26.9 ($p<0.01$, $p=0.01$, $p<0.01$ respectively).
Conclusion: Low dose (100mg/day) aspirin therapy may not be sufficient for a certain percentage of patients with diabetes mellitus. In these patients may show a greater platelet agregation with the use of 300 mg aspirin. The long term follow-up studies are need to explain this hypothesis.

P1256 Clinical determinants of platelet function in patients with cad undergoing coronary angiography and treated by dual antiplatelet therapy

R. Marcucci[1], R. Paniccia[2], A.M. Gori[1], E. Romano[1], S. Poli[1], P.G. Buonamici[1], D. Antoniucci[1], G.F. Gensini[1], R. Abbate[1]. *[1]University of Florence, Heart And Vessels Department, Florence, Italy; [2]University of Florence, Heart and vessels, Florence, Italy*

Introduction: We sought to evaluate the clinical determinants of platelet function in a large cohort of patients undergoing PCI on dual antiplatelet therapy.
Methods: We measured platelet function by both a point-of-care assay (PFA-100) and platelet aggregation (PA) with two agonists (arachidonic acid, AA, 0.5 mg/mL and ADP 2 and 10 microm/L) in 868 adult patients with coronary artery disease: 386 with acute coronary syndromes undergoing a primary PCI (group A) and 482 coronary artery disease patients scheduled to undergo an elective PCI (group B).
Results: PFA test detected 265/868 (30.5%) aspirin resistant patients (CT/EPI<203 sec). In a multivariate model, ACS (OR:1.5, 95% CI 1.1-2.1, p=.01) and chronic use of aspirin (OR:0.4, 95% CI 0.3-0.6, p=.0001) were significant and independent predictors of response to aspirin detected by PFA-100. Leukocytes and ESR were significantly higher in patients with aspirin resistance both in patients of group A and B. PA induced by AA detected 271/868 (31.2%) aspirin resistant patients (AA-PA;20%). In a multivariate model, ACS (OR:1.7, 95% CI 1.2-2.4, p=.001) and chronic use of aspirin (OR:0.4, 95% CI 0.3-0.6, p=.0001) were significant and independent predictors of response to aspirin detected by AA-PA. Leukocytes and ESR were significantly higher in patients with aspirin resistance both in patients of group A and B. 54/868 (6.2%) patients were clopidogrel resistant by ADP 2 μM and 192/868 (22.1%) by ADP 10 μM. In a multivariate model, previous use of clopidogrel (OR:0.6, 95% CI 0.3-0.9, p=.02) and diabetes (OR:1.5, 95% CI 1.1-2.2, p<.05) were significant and independent predictors of response to clopidogrel detected by ADP-PA.
Conclusions: Our data demonstrated that diabetes, ACS, chronic use of antiplatelet agents are independent predictor of the platelet response to both aspirin and clopidogrel. We provided the first evidence of a possible involvement of the inflammatory processes in the development of laboratory resistance to aspirin.

P1257 Real time thrombosis profiler: a novel assay to measure differential effects of anti-platelet drugs on thrombus initiation, propagation and stability

G. Stephens, D. Gao, D.R. Phillips, P. Andre. *Portola Pharmaceuticals Inc., Department of Biology, South San Francsico, United States of America*

Predication of anti-platelet activity in patients has proven to be one of the biggest challenges in anti-thrombotic drug development. Of particular note were the trials of the oral GPIIb/IIIa antagonists which failed to provide commensurate reductions in clinical end points, despite potent inhibition of platelet aggregation. In order to bridge the gap between in vitro pharmacodynamic activity assays and therapeutic dosing, we have adapted perfusion chamber technology to examine the effects of site-specific anti-platelet agents on the initiation, propagation and stabilization of thrombosis. Thrombosis was initiated by perfusion of Factor Xa-inhibitor anti-coagulated human whole blood through a collagen coated capillary at arterial shear rate (1600s-1). Thrombosis was measured by the rate of deposition of fluorescently labeled platelets in real time (Fluorescent Unit/s) and capillary patency. Data are expressed as Mean±SEM, one way ANOVA. In untreated blood, thrombi formed rapidly (3.0±0.35 FU/s) and occluded all capillaries (6 of 6 occluded). Cox-1 inhibition (aspirin) had no effect on the rate of thrombus formation (2.7±0.22 FU/s, p=ns) but inhibited thrombus stability to allow initiation of a cyclic thrombotic process, preventing thrombus stabilization and capillary occlusion (0 of 8 occluded). Addition of a P2Y12 antagonist (PRT060128 1.1μM) to aspirin treatment caused inhibition of the rate of thrombus formation (1.8±0.24 FU/s, $p<0.01$), further reducing the size of thrombi formed. Inhibition of GPIIb-II Ia at clinically relevant concentrations (2.4μM eptifibatide) prevented thrombus growth in all capillaries (0.3±0.06 FU/s, $p<0.01$). In contrast, moderate inhibition of GPIIb-IIIa (0.5μM eptifibatide), representing a level of platelet inhibition achieved in failed clinical trails of oral GPIIb-IIIa antagonists, reduced the rate of thrombus growth (1.83±0.3 FU/s, $p<0.05$) but did not prevent the formation of stable thrombi, allowing 4 of 8 to occlude. Thus, real time monitoring of thrombosis has shown that while GPIIb-IIIa is involved in thrombus growth, Cox-1

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

and P2Y12 are involved in thrombus stability. In addition, cyclic thrombotic process, as characterized by the combination of a P2Y12 antagonist and aspirin, can be detected in this assay, a limitation of other platelet pharmacodynamic assays available. Since sub optimal inhibition of GPIIb-IIIa (<80%) only retards the rate of thrombus growth, these data, in part, explain the clinical failures observed by the use of oral GPIIb-IIIa antagonists. Use of this assay may provide more accurate predictions of therapeutic activity levels.

P1258 Rosuvastatin inhibits platelt-collagen interaction

B. Molins[1], E. Pena[1], T. Padro[1], C. Mendieta[2], L. Badimon[1]. [1]*Cardiovascular Research Center, CSIC-ICCC, Barcelona, Spain;* [2]*School of Dentistry, University of Barcelona, Periodontics, Barcelona, Spain*

Background and Objective: Rosuvastatin, an inhibitor of HMG-CoA reductase, is an effective lipid-lowering agent. As other statins, rosuvastatin has shown to exert other vascular protective effects beyond cholesterol reduction. The aim of the present study was to evaluate the acute effect of rosuvastatin on platelet-collagen interaction under flow conditions followed by a proteomic analysis to identify the potential proteins involved in the inhibitory mechanisms of rosuvastatin in platelet function.
Methods: Citrated porcine blood was incubated with mepacrine to render platelets fluorescent, and with rosuvastatin at different concentrations (2 μM, 4 μM, 8 μM). In vitro perfusions were carried out over collagen type I-coated slides using a flat perfusion chamber at wall shear rates of 300/s and 1500/s. Images of platelet deposition were acquired by confocal inverted laser microscope. Thrombus height was calculated acquiring crossectional images of the proximal section. The area covered by platelets was evaluated using Image 1.61 Software, and expressed as μm^2/field analyzed. Perfused effluent blood was collected and platelets were obtained after centrifugation. Platelet pellets were sequentially extracted based on differential protein solubility (cytosolic-enriched fraction, and cytoskeleton/membrane-enriched fraction) and two dimensional gel electrophoresis was performed. PD-Quest software was used for analysis of differential protein pattern, and proteins were identified by mass spectrometry (MALDI-TOF).
Results: Rosuvastatin yielded an immediate reduction of platelet deposition at 300/s and 1500/s. At 300/s in vitro rosuvastatin treatment (2, 4, 8μM) decreased platelet deposition by 50%, 47%, and 60%, respectively ($p<0.0001$), and reduced thrombus height by 30% at any rosuvastatin concentration ($p<0.05$) versus untreated blood. At 1500/s, rosuvastatin 8 μM inhibited platelet deposition by 56% ($p<0.05$). Proteomic analysis revealed that rosuvastatin modulated the expression pattern of 10 proteins in the cytosolic fraction and 8 in the membrane-enriched fraction. Among them, rosuvastatin induced an increase in the expression level of GRP78, a member of the heat-shock protein family that attenuates cell surface tissue factor activation.
Conclusions: Rosuvastatin significantly reduced platelet-collagen interaction by decreasing platelet deposition, showing an inhibitory effect on platelet activation, independently of its cholesterol-lowering effects.

P1259 Fe-induced platelet aggregation measurement: a novel method to measure platelet function and comparison with existing platelet function tests

J.J.J. Smit[1], A.W.J. Van 'T Hof[1], J.P. Ottervanger[1], R.J. Slingerland[1], F. Zijlstra[2], W. Van Oeveren[3]. [1]*Isala Klinieken, cardiology, Zwolle, Netherlands;* [2]*University Medical Center, cardiology, Groningen, Netherlands;* [3]*Haemoscan, Groningen, Netherlands*

Purpose: Antiplatelet therapies have an increasing role in the treatment of acute coronary artery syndromes (ACS). However, the relationship between in vitro platelet aggregation and clinical outcome, especially subacute thrombosis after stenting, is unclear. Since most stents are made of stainless steel, providing a potent stimulus for platelet aggregation, we developed a platelet function test using stainless steel as an agonist.
Methods: In a subanalysis of the On-TIME-2 trial, we performed duplo measurement of Fe-induced aggregation (FIPA) on citrated blood, drawn from the femoral sheat during catheterisation before primary percutaneous coronary intervention of 111 patients presenting with a ST elevation myocardial infarction. Within one hour, the samples were added to 100 mg of low carbon steel and after 5 seconds mixture on a vortex incubated for 15 minutes. The ratio between the non-aggregated platelets in a platelet count in the agonist sample and a platelet count in a reference sample x100% was calculated as the platelet aggregation inhibition. FIPA was compared to platelet aggregation measurement using ADP as a stimulus and PFA-100.
Results: FIPA measurement proved to be reproducible (correlation coefficient R=0.942, $p<0.001$ between duplo samples). FIPA correlated with ADP induced platelet aggregation (R=0.83) and weakly with PFA-100 bleeding time (R=0.56). FIPA was the most potent agonist: there were no patients in which FIPA could not be measured whenever PFA-100 or ADP did measure platelet aggregation.
Conclusion: FIPA measurement is a feasable and easy method for platelet function measurement, using the same agonist for platelet aggregation as stents in coronary arteries. Furthermore, FIPA could be measured in patients using potent platelet inhibitors as GpIIb/IIIa blockers plus clopidogrel and acetylsalicylic acid in contrast to other methods of platelet function. Therefore, it might be a suitable test for measurement of platelet aggregation inhibition in patients with an ACS, using multiple antiplatelet regimes.

P1260 The significance of vasodilator-stimulated phosphoprotein for risk

R. Blindt, K. Iofina, A. De Taeye, F. Vogt, R. Mueller, P. Kiefer, M. Kelm, R. Hoffmann. *University Hospital Rwth Aachen, Medical Clinic I, Aachen, Germany*

Aims: Low-response to the P2Y12 adenosine diphosphate (ADP)-receptor antagonist clopidogrel was suggested to correspond to a higher incidence of stent thrombosis (ST). This prospective observational study assessed the capability of two platelet function assays, e.g. direct measurement of the phosphorylation status of vasodilator-stimulated phosphoprotein (VASP) and ADP-induced platelet aggregation for definition of the individual risk to develop ST.
Methods: 66 patients with an elevated high risk to develop ST were enrolled. All patients received a dual antiplatelet therapy consisting of 100-mg aspirin and 75-mg clopidogrel during an observation period of 6 months. Flow cytometry of VASP phosphorylation and densitometrically-determined measurement of ADP-induced platelet aggregation was performed 72-96 hours after stent implantation. These data were related to angiographically confirmed ST.
Results: Seven patients suffered from an angiographically confirmed ST (10.6%). The mean VASP-platelet reactivity indices in the ST group were significantly higher (59.4$\pm$14.4%) compared to patients without ST (43.4$\pm$16.0%, P=0.016), while ADP-induced platelet aggregation did not differ significantly. There was only a poor correlation between both methods using non-linear regression analysis (r2= 0.068). In a multivariate analysis, VASP was the only independent predictor of ST and was superior to previously identified angiographic parameters. ROC analysis revealed a cut-off value for VASP-PRI of $<$ 48% to be associated with low risk of ST.
Conclusions: Determination of VASP phosphorylation is superior to conventional platelet aggregometry and angiographic parameters for assessing the risk of ST. Patients with a VASP-PRI $>$ 48% seem to have a significantly increased risk.

P1261 Desensitization procedure in patients with aspirin sensitivity: safety and efficacy

R. Rossini, G. Musumeci, M. Scuri, P. Invernizzi, P. Ferrazzi, A. Gavazzi. *Ospedali Riuniti Di Bergamo, Cardiologia Dept., Bergamo, Italy*

Background: with the widespread of drug eluting stents (DES) in coronary percutaneous interventions (PCI), aspirin therapy has become mandatory. However, some patients (pts) are unable to tolerate acetylsalicylic acid (aspirin) due to sensitivity, which can limit percutaneous coronary revascularization.
Aim: to test safety and efficacy of a new standard desensitization procedure, using escalating low doses of aspirin in pts with acetylsalicylic acid sensitivity.
Methods and Results: Out of 801 pts with coronary artery disease, twenty-one (age 63.4$\pm$7.6 yrs; 16 male) had a history of aspirin sensitivity (2.6%). They were admitted for acute coronary syndrome (N=12) or stable angina (N=9). Seven pts had respiratory sensitivity (asthma and/or rhinitis), and 14 had experienced cutaneous reactions (urticaria and/or angioedema). All pts underwent the challenge-desensitization procedure. None received pretreatment with antihistamines or corticosteroids, and beta-blockers were withheld 24 hours before desensitization. Six sequential doses of aspirin (1, 5, 10, 20, 40, and 100 mg) were administered orally, with the procedure lasting 5.5 hours. Blood pressure, pulse, cutaneous, nasoocular, or pulmonary reactions were monitored closely until 4 hours after the procedure. The desensitization procedure was successful in 18 pts (85.7%). No serious adverse reaction occurred: two pts (both with a history of chronic idiopathic urticaria) developed cutaneous reaction which resolved with corticosteroids and antihistamines; one patient (with frequent asthma attacks) experienced shortness of breath associated with bronchospasm, which resolved immediately after the administration of corticosteroids. All pts but 2 underwent PCI (1.4 stent/pt, DES 76.1%, stent length 26.2$\pm$7.4 mm, multivessel PCI 38%) and were discharged on dual antiplatelet therapy. At six-month follow-up, all pts well tolerated aspirin. No major adverse cardiac event occurred.
Conclusions: this desensitization procedure seems to be safe and effective in the vast majority of pts with cutaneous or respiratory aspirin sensitivity. Complex PCI procedures can be performed also in such pts, without increasing the risk of stent thrombosis.

P1262 Differential response to heparinoids and glycoprotein IIb/IIIa inhibitors in acute coronary syndromes based on prior aspirin use: meta-analysis of randomized controlled trials

H. Jain, G. Lancaster, S. Zarich. *Bridgeport Hospital/Yale New Haven Health Sys, Cardiology, Bridgeport, United States of America*

Background: Even though prior aspirin use is included in the TIMI risk score to determine poor outcome in subjects presenting with ACS, there are no current guidelines or recommendations for treatment based on prior aspirin status.
Methods: We performed a systematic review of the literature and meta-analysis

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

of four large trials (n=18061) and studied the response to treatment between aspirin users and non users with standard unfractionated heparin (UFH) alone versus alternative use of low-molecular weight heparin (LMWH) or addition of glycoprotein IIb/IIIa inhibitor (GPI) to unfractionated heparin. Our main aim was to see if patients on prior aspirin respond differently to different anti-thrombotic/anti-platelet treatment as compared to patients not on aspirin at the time of presentation. Composite end points were death, myocardial infarction and revascularization. Heterogeneity between studies was quantified with I2 test.
Results: We identified 4 large clinical trials with a total of 18,061 subjects, 12,094 were reported to be on prior aspirin and 6045 received UFH. The combined end point was seen in a total of 2946 patients at an average follow-up of 23.5 days (7-43 days). Use of LMWH/GPI was associated with 20% reduction in end points in patients on aspirin as compared to patients who received standard UFH; combined OR 0.80, p<0.001, 95% CI 0.73-0.88. We did not notice any difference in patients not on aspirin (n=5967) and they responded similarly to the use of UFH or LMWH/GPI; OR 0.99, p=0.85, 95% CI 0.85-1.15.
Conclusion: Patients presenting with acute coronary syndrome who are already taking aspirin respond better to treatment with LMWH or addition of GPI to UFH compared to UFH alone. In subjects not on prior aspirin there is no difference in treatment response.

P1263 Prognostic implications of high platelet reactivity in patients with diabetes mellitus and coronary artery disease on chronic dual antiplatelet therapy

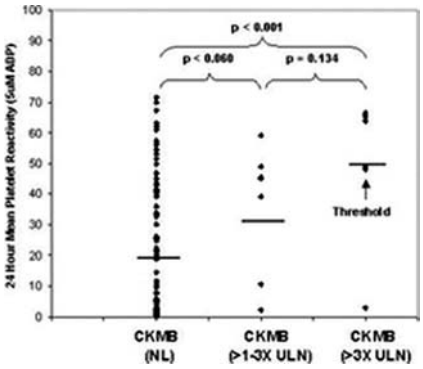
D.J. Angiolillo[1], E. Bernardo[2], M. Sabate[1], P. Jimenez-Quevedo[1], J. Palazuelos[1], R. Hernandez-Antolin[1], M.A. Costa[2], T.A. Bass[2], C. Macaya[1], A. Fernandez-Ortiz[1]. *[1]University of Florida-Shands Jacksonville, Division of Cardiology, Jacksonville, United States of America; [2]San Carlos University Hospital, Madrid, Spain*

Background: Patients with high platelet reactivity (HPR) have an increased risk of major adverse cardiovascular events (MACE) even while on dual antiplatelet therapy. To date most studies have evaluated the prognostic implications of HPR in the early phases of antiplatelet treatment and in patients undergoing percutaneous coronary interventions. Therefore, the impact of HPR in patients in their chronic phase of treatment warrants investigation. Type 2 diabetes mellitus (T2DM) patients have increased platelet reactivity compared to non-diabetics. Whether HPR specifically determined in T2DM patients is associated with MACE is unknown.
Methods: We prospectively studied 174 T2DM patients on chronic aspirin (100mg/d) and clopidogrel (75mg/d) therapy. HPR was defined as the upper quartile of platelet aggregation assessed by light transmittance aggregometry (LTA) following stimuli with 20μmol/L adenosine diphosphate (ADP). Additional LTA assays using collagen (6 μg/mL), epinephrine (20 μmol/L) and thrombin receptor agonist peptide (25 μmol/L) were also performed. Patients were followed for 2-years and MACE recorded. MACE included death secondary to cardiovascular cause, ST-segment elevation myocardial infarction (STEMI), non-ST segment elevation acute coronary syndrome (non-STEMI and unstable angina), and stroke.
Results: ADP-induced platelet reactivity quartile cut points for the 25th, 50th and 75th percentiles of the study population were 44.0%, 52.0%, and 62.0%. A total of 42 MACE occurred in 35 patients (20.1%) during the 2-year follow-up. MACE occurred in 11.1%, 18.6%, 11.1% and 37.7% of patients from the lowest to upper quartile of platelet reactivity, respectively (p=0.005). Receiver-operating characteristics analysis indicated that a cut-off value of 62% ADP-induced platelet reactivity was the best to predict MACE. MACE was significantly higher in patients platelet reactivity above this value [37.7% vs 13.9%; OR, 3.7; 95% CI, 1.7-8.2; p=0.001]. Multivariate Cox regression analyses showed HPR (HR: 3.16; 95% CI, 1.61-6.21; p= 0.001), renal failure (HR: 2.82; 95% CI, 1.37-5.78; p= 0.005), and NYHA class III-IV (HR: 2.72; 95% CI, 1.32-5.62; p= 0.007) to be independent predictors of MACE. Patients with MACE had higher platelet aggregation compared to patients without events (57.2±14.3% vs 50.9±13.4%; p=0.02). Patients with HPR showed increased platelet aggregation using all other LTA assays (all p-values <0.001).
Conclusion: HPR is an independent predictor of long-term MACE in T2DM patients. This suggess the need for more potent and tailored antithrombotic treatment regimens in these high risk patients.

P1264 Bivalirudin with and without eptifibatide for elective stenting: a pharmacodynamic study of platelet reactivity in relation to the occurrence of periprocedural myocardial infarction

P.A. Gurbel, K. Bliden, J. Dichiara, M. Antonino, W. Herzog, C. Cummings, B. Dubois, T. Gesheff, U.S. Tantry. *Sinai Center For Thrombosis Research, Center For Thrombosis Research, Baltimore, United States of America*

Background: Previously it was demonstrated that heparin and eptifibatide produced superior platelet inhibition and less myocardial necrosis than heparin alone in patients treated with clopidogrel (CLP) at the time of stenting. The primary objectives of the present study was to compare the effect of bivalirudin (B) + eptifibatide (E) vs. B alone on platelet reactivity and study the relation of reactivity to myocardial necrosis following elective stenting.
Methods: 150 patients undergoing elective stenting were randomly treated with B vs. B+E; all received CLP and aspirin. Serial measurements of platelet reactivity to multiple agonists by aggregometry and cardiac markers were performed over 24 hours.
Results: B+E compared to B produced superior inhibition of platelet aggregation to
5 μMADP, 20 μMADP, 15μMTRAP, 25 μMTRAP, collagen (p< 0.01 for all). B+E was associated with reduced myocardial infarction (8% vs. 2%). There was a platelet reactivity threshold for myocardial infarction.



Conclusions: An important relation exists between platelet reactivity and post-stent infarction, supporting a reactivity threshhold for infarction. Eptifibatide added to bivalirudin, produces superior platelet inhibition, drops all patients below the threshold, and reduces necrosis marker release.

P1265 The effect of duration of therapy on the benefit of fondaparinux over enoxaparin in acute coronary syndromes: insights from the OASIS 5 trial

S. Jolly[1], S.R. Mehta[1], L. Wallentin[2], R. Afzal[1], A. Budaj[3], K.A.A. Fox[4], J. Col[5], H.J. Rupprecht[6], C.B. Granger[7], S. Yusuf[5]. *[1]Hamilton Health Sciences, Population Health Research Institute, Hamilton, Canada; [2]Uppsala Clinical Research Centre, Cardiology, Uppsala, Sweden; [3]Grochowski Hospital, Warsaw, Poland; [4]The Chancellor's Building, Cardiovascular Research, Edinburgh, United Kingdom; [5]Clinique Universitaire St Luc, Cardiology, Brussels, Belgium; [6]GPR Klinikum Russelsheim, Cardiology, Russelsheim, Austria; [7]Duke University Medical Center, Department of Medicine, Durham, United States of America*

Purpose: There is great variability in the length of antithrombotic therapy for the treatment of acute coronary syndromes worldwide. The objective of this analysis was to determine if duration of therapy had an effect on the benefit of fondaparinux over enoxaparin, in the OASIS 5 trial, for reducing major bleeding and on the composite of death, MI and stroke.
Methods: Patients with non-ST elevation acute coronary syndromes (n=20 078) were randomized between fondaparinux and enoxaparin until hospital discharge or 8 days, which ever came first. Centers were divided into three tertiles based on median duration of therapy with either fondaparinux or enoxaparin and patients were divided into these three groups. A cox proportional hazard model was used to compare the composite of death, MI or stroke (primary endpoint) and major bleeding at 30 days in those treated with fondaparinux compared to enoxaparin in these three groups based on the center's median duration of therapy.
Results: The three tertiles of length of therapy by center were <4 days (n=5765), 4-6 days (n=6251) and >6 days (n=8062). The centers with the shortest duration of therapy were predominantly in North America and Australia and had higher rates of PCI and CABG. The rates of the composite endpoint of death, MI and stroke were similar between the enoxaparin and fondaparinux groups in all three tertiles (interaction p= 0.40, table1). However, fondaparinux was associated with a significant reduction in major bleeding over enoxaparin in all three tertiles with the largest benefit in the centers with intermediate and longer durations of therapy tertiles (interaction p= 0.09, table1).

Duration of Therapy and Outcomes

	Enoxaparin (%)	Fondaparinux (%)	HR	P value
Composite of Death, MI or Stroke				
<4 days (n=5765)	206 (7.2)	174 (6.0)	0.84	0.08
4-6 days (n=6251)	240 (7.7)	213 (6.8)	0.87	0.16
>6 days (n=8062)	306 (7.6)	284 (7.1)	0.93	0.40
Major Bleeding				
<4 days (n=5765)	178 (6.3)	141 (4.9)	0.78	0.025
4-6 days (n=6251)	174 (5.6)	88 (2.8)	0.49	<0.0001
>6 days (n=8062)	143 (3.6)	85 (2.1)	0.59	0.0001

Conclusions: Fondaparinux is associated with reductions in major bleeding regardless of center's median duration of therapy.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1266 Intravenous low-molecular-weight heparin compared with unfractionated heparin in percutaneous coronary intervention: quantitative review of randomised trials

R. Dumaine[1], M. Borentain[1], C. Bode[2], R. Gallo[3], H. White[4], J.-P. Collet[3], S. Steinhubl[5], G. Montalescot[3]. [1]*Pitie Salpetriere University Hospital, Paris, France;* [2]*Universitaetsklinikum Freiburg, Freiburg, Germany;* [3]*Montreal Heart Institute, Montreal, Canada;* [4]*Auckland City Hospital, Auckland, New Zealand;* [5]*University of Kentucky, Lexington, United States of America*

Purpose: A meta-analysis of randomised trials was performed to compare the efficacy and safety of intravenous low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH) in percutaneous coronary intervention (PCI).
Methods: Randomised studies comparing intravenous LMWH with UFH among patients undergoing PCI were identified and data on baseline characteristics and safety and efficacy outcomes were analysed. Safety endpoints included major bleeding, minor bleeding, and the composite of major and minor bleeding. Bleeding definitions were those used in the trials. Efficacy endpoints included the following ischemic events: death, myocardial infarction (MI), and urgent target vessel revascularization (UTVR). Efficacy assessment was expressed as a composite of these efficacy endpoints.
Results: Thirteen trials including 7318 patients were included in the meta-analysis. Of these, 4201 (57.5%) received LMWH and 3117 (42.5%) received UFH. In 11 trials, enoxaparin was the prescribed LMWH. Intravenous LMWH was associated with a significant 43% reduction in the risk of major bleeding compared with UFH (Table; P=0.002). A trend towards a reduction in minor bleeding was also observed. The incidence of death, MI, death or MI, urgent revascularisation and composite efficacy endpoint was similar between patients receiving LMWH and UFH (Table).

	LMWH	UFH	OR (95% CI)	P-value
Death	16/4201	7/3117	1.26 (0.57-2.81)	0.570
MI	187/3939	137/2819	0.97 (0.77-1.22)	0.794
UTVR	122/3747	90/2690	1.30 (0.97-1.75)	0.084
Death or MI	202/3939	144/2819	0.99 (0.79-1.24)	0.929
Composite efficacy	325/3939	255/2819	1.02 (0.85-1.22)	0.871
Composite efficacy/safety	381/3939	321/2819	0.91 (0.78-1.08)	0.288
Major bleeding	55/4201	68/3117	0.57 (0.40-0.82)	0.002
Minor bleeding	246/4121	275/3038	0.75 (0.47-1.20)	0.236
Major and minor bleeding	296/4121	338/3117	0.73 (0.50-1.05)	0.089

Conclusion: Compared with UFH, the use of intravenous LMWH during PCI is associated with a significant decrease in major bleeding events, confirming the safety results obtained in the STEEPLE trial. In this adequately powered analysis, ischemic event rates were similar between LMWH and UFH treated patients.

P1267 Effect of fondaparinux 2.5 mg once daily on all cause mortality: a meta-analysis of thromboprophylaxis trials

A.G.G. Turpie[1], J. Eikelboom[2]. [1]*HHS - General Division, Department of Medicine, Hamilton, Canada;* [2]*HHS - General Hospital, Thrombosis Service - McMaster Clinic, Hamilton, Canada*

Purpose: Compared with placebo, unfractionated heparin or low-molecular-weight heparins (LMWH), fondaparinux 2.5 mg once daily significantly reduced overall mortality by about 15% at 30 days in patients with acute coronary syndromes (OASIS-5 and -6). In order to determine whether this benefit was observed in other settings, we analyzed the effect of fondaparinux 2.5 mg on all-cause mortality in all phase III fondaparinux thromboprophylaxis trials.
Methods: We performed a meta-analysis of 8 randomized, double-blind trials in patients undergoing major orthopedic (EPHESUS, PENTHIFRA, PENTAMAKS, PENTATHLON 2000, PENTHIFRA-PLUS) or abdominal (PEGASUS, APOLLO) surgery or in medical patients (ARTEMIS). In 5 trials, fondaparinux 2.5 mg once daily was compared with approved regimens of LMWH; in 3 trials, the comparator was placebo. Fondaparinux and comparators were administered for up to 31 days. The efficacy outcome was all-cause mortality up to day 32.
Results: A total of 13,085 patients were analyzed. Compared with placebo or LMWH, fondaparinux demonstrated a non-significant reduction in all-cause mortality (p=0.069; test for heterogeneity: p=0.615). Consistent results were observed irrespective of the type of comparator (Table).

All-cause mortality at day 32

Day 32	Fondaparinux 2.5 mg	Comparator	Odds ratio (95% CI)
versus placebo	2.0% (28/1405)	2.8% (36/1409)	0.77 (0.46-1.26)
versus LMWH	1.5% (79/5133)	1.9% (99/5138)	0.80 (0.59-1.07)
All studies	1.6% (107/6538)	2.1% (135/6547)	0.79 (0.61-1.02)

Conclusions: In thromboprophylactic settings, fondaparinux 2.5 mg once daily given for up to 31 days tended to reduce all-cause mortality relative to placebo/LMWH. This result is consistent with the long-term reduction in mortality observed with fondaparinux 2.5 mg in patients with acute coronary syndromes.

P1268 Efficacy of bivalirudin in patients with non-ST elevation acute coronary syndrome undergoing percutaneous coronary intervention: a meta-analysis on 17,375 patients

A. Varma[1], A. Abbate[1], G.G.L. Biondi-Zoccai[2], G.W. Vetrovec[1]. [1]*Richmond, United States of America;* [2]*Turin, Italy*

Background: Direct thrombin inhibitors offer an advantage over unfractionated heparin (UFH) by the ability to inhibit clot-bound thrombin, therefore potentially providing for a more effective anticoagulation. We performed a meta-analysis of randomized controlled trials that compared bivalirudin to heparin both with provisional use of GpIIb/IIIa inhibitors in patients undergoing a percutaneous coronary intervention (PCI). Our goal was to evaluate the effects on the composite endpoint of death, myocardial infarction, and recurrent ischemia or target vessel revascularization, and of the composite endpoint plus major bleeding.
Methods: We performed a search of MEDLINE, the Cochrane database, and proceedings of major medical conferences for trials according to the following inclusion criteria: prospective randomized comparison of bivalirudin vs UFH in patients with Non-ST-segment elevation acute coronary syndrome (NSTEACS) undergoing PCI with or without gpIIb/IIIa inhibitor use. Exclusion criteria included: non-randomized allocation, use of fibrinolytics, ST-segment elevation, recent hemorrhage, shock or use of warfarin. Peto fixed effect odds ratios (OR) were calculated.
Results: We pooled data from 5 trials enrolling a total of 17,375 patients with a follow-up period of up to 6 months. We found that there was no difference, comparing bivalirudin vs UFH, in the incidence of the composite endpoint (OR 1.07 [0.96, 1.20] P=0.21) or in the incidence of the composite endpoint plus major bleeding (OR 0.98 [0.89, 1.08], P=0.70.
Conclusion: In patients with NSTEACS undergoing PCI, the use of bivalirudin was not associated with a statistically significant difference in the incidence of ischemic events compared to UFH with provisional IIb/IIIa inhibitors. However, inconsistencies in use of IIb/IIIa in terms of rates and choice of inhibitor need to be acknowledged. This is particularly relevant for high risk patients who benefit the most from abciximab

NEW ANTIPLATELET AGENTS

P1269 Efficacy of SCH 602539, a selective thrombin receptor antagonist, alone and in combination with cangrelor in a folts model of thrombosis in anesthetized monkeys

M. Chintala, S. Kurowski, S. Vemulapalli, Q. Li, A. Brown, J. Strony. *Schering-Plough Research Institute, Cardiovascular/Metabolic Diseases, Kenilworth, United States of America*

Background: Thrombin, the most potent physiological activator of platelets is reported to active platelets through novel G-protein coupled thrombin receptors also referred to as protease activated receptors (PAR's). SCH 602539 is a potent and selective antagonist of the PAR-1 receptor. We evaluated the efficacy of SCH 602539 alone and in combination with the ADP antagonist Cangrelor.
Methods: We used the Folts model of thrombosis in anesthetized cynomolgus monkeys where the carotid artery was subjected to mechanical injury and flow limiting stenosis. Increasing doses of SCH 602539, cangrelor or both were administered intravenously to the same animal in a sequential manner and the ability to inhibit cyclic flow reductions (CFR's) was monitored. Since these agents target distinct pathways of platelet activation we also evaluated if their antithrombotic effects were additive. Ex-vivo platelet aggregation to thrombin receptor agonist peptide (TRAP), ADP, collagen and thromboxane was also evaluatedResults: SCH 602539 is a potent and selective antagonist of the PAR-1 receptor with a Ki of 26 nM and inhibited platelet aggregation to TRAP in washed human platelets (IC_{50} of 0.18 μM) and ex-vivo platelet aggregation to TRAP in cynomolgus monkeys following oral dosing (0.1 mg/kg). In the present study, administration of SCH 602539 resulted in a dose related inhibition of CFR's from a baseline of 9 to 4, 2 and 2 (at 0.1, 0.3 and 1 mg/kg, i.v., bolus respectively). SCH 602539 selectively inhibited TRAP-induced platelet aggregation (1 μM) ex-vivo with complete inhibition observed at the two higher doses. Cangrelor also resulted in dose related inhibition to CFR's from a baseline of 10 to 6, 3 and 1 (0.1, 0.2 and 0.3 μg/kg/minX30 min, i.v. respectively) and inhibited ADP-induced platelet aggregation (10 μM) by 60% at the highest dose used. In a separate group of animals, co-administration of SCH 602539 (0.1 mg/kg) and cangrelor (0.1 μg/kg/min) significantly inhibited CFR's which were abolished in 4 of 5 animals. It must be pointed out that at these doses, SCH 602539 and cangrelor had modest activity when administered alone and did not abolish CFR's in any animal.
Conclusions: SCH 602539, a selective PAR-1 thrombin receptor antagonist inhibited thrombosis in a Folts model in monkeys and these findings were comparable to that of the ADP antagonist Cangrelor. We have also demonstrated that the efficacy of these agents are additive. These results suggest that PAR-1 antagonism may serve as a novel approach for the treatment of atherothrombosis and this hypothesis needs to be tested clinically.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1270 Rivaroxaban, a novel, oral, direct Factor Xa inhibitor, enhanced the antithrombotic effects of clopidogrel and acetylsalicylic acid in rats

E. Perzborn, E. Fischer, U. Lange. *Bayer HealthCare AG, Cardiovascular Research, Wuppertal, Germany*

Rivaroxaban (BAY 59-7939) is a novel, oral, direct Factor Xa inhibitor in advanced clinical development for the prevention and treatment of venous and arterial thromboembolic disorders. Patients likely to receive rivaroxaban include those with cardiovascular diseases, who may also take clopidogrel and acetylsalicylic acid (ASA). This study assessed the effects of intravenous rivaroxaban 0.1 mg/kg, oral clopidogrel 1 mg/kg, oral ASA 10 mg/kg, or their combinations, on arterial thrombosis and haemostasis. Effects on thrombosis were investigated in a rat arteriovenous-shunt model, with a shunt between the right common carotid artery and the left jugular vein. Bleeding times were measured in a rat tail transection model. Rivaroxaban, clopidogrel or ASA alone significantly inhibited thrombus formation without affecting haemostasis ($p<0.001$ vs control). There was an increased antithrombotic effect with the combination of rivaroxaban plus clopidogrel, and rivaroxaban plus ASA, but not with clopidogrel plus ASA (Table). Addition of rivaroxaban to the combination of clopidogrel and ASA significantly enhanced the antithrombotic effect ($p<0.01$). Bleeding time was unaffected by rivaroxaban, clopidogrel or ASA alone. Addition of rivaroxaban to the combination of clopidogrel and ASA did not further prolong bleeding time beyond the slight increase observed with all combinations containing clopidogrel. Clopidogrel and ASA did not influence the anticoagulant effect of rivaroxaban, as shown by the prothrombin time (PT).

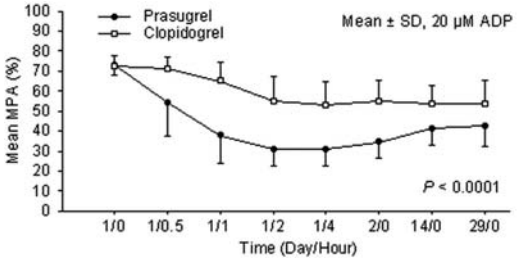
Group	Thrombus reduction (%; n=6)	Bleeding time (x-fold; n=10)	PT prolongation (x-fold)
Rivaroxaban	37±5	1±0.1	1.3±0.06
Clopidogrel	35±6	1.3±0.1	1.0±0.03
ASA	37±4	1.3±0.2	1.0±0.02
Rivaroxaban + clopidogrel	63±4	3.1±1.0	1.3±0.04
Rivaroxaban + ASA	59±3	1.2±0.1	1.2±0.03
Clopidogrel + ASA	36±5	2.4±1.0	1.0±0.04
Rivaroxaban + clopidogrel + ASA	75±2	4±2	1.4±0.04

In conclusion, these results suggest that concomitant administration of rivaroxaban, clopidogrel and ASA may have greater antithrombotic effect than the individual treatments, and may be superior to the combination of clopidogrel and ASA.

P1271 Greater inhibition of platelet aggregation with a prasugrel 60 mg loading dose compared with a clopidogrel 600 mg loading dose in aspirin-treated patients

C. Varenhorst[1], O. Braun[2], S. James[2], D. Erlinge[1], K.J. Winters[3], J.T. Brandt[3], J.A. Jakubowski[3], T. Costigan[3], A. Siegbahn[4], L.C. Wallentin[5]. *[1]Dept Cardiology, Uppsala Clinical Research Centre, Uppsala, Sweden; [2]Dept Cardiology, Lund, Sweden; [3]Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, United States of America; [4]Dept Clinical Chemistry, Coagulation Sciences, Uppsala, Sweden; [5]Uppsala Clinical Research Center, Cardiology Department, Uppsala, Sweden*

Purpose: Prasugrel, a new P2Y12 antagonist, has been previously reported to achieve more potent inhibition of maximal platelet aggregation (MPA) vs. conventional doses of clopidogrel. We evaluated MPA in aspirin-treated subjects with stable coronary artery disease comparing prasugrel with clopidogrel starting with a clopidogrel 600 mg loading dose (LD).
Methods: After a run-in on 75 mg aspirin, 110 subjects were randomly assigned to double blind treatment with either clopidogrel (n=55) 600 mg LD followed by 75 mg o.d. (once daily) maintenance dose (MD) for 28 days or prasugrel (n=55) 60 mg LD followed by 10 mg o.d. MD for 28 days. MPA to 20 μM ADP was measured by turbidimetric aggregometry at pre-dose and 30 minutes, 1, 2, 4 and 24h post-LD and repeated pre-dose at days 14 and 29.
Results: There was no significant difference in clinical characteristics or MPA level at baseline. 106 patients completed the study (54 on prasugrel and 52 on clopidogrel). Treatment was well tolerated in both groups. As illustrated in the figure the mean MPA levels were significantly ($p<0.0001$) lower with prasugrel at all time-points after start of treatment.



Conclusion: In aspirin-treated subjects with coronary artery disease prasugrel (60 mg LD and 10 mg MD) provides faster and greater inhibition of platelet aggregation as compared to 600 mg LD and 75 mg MD regimen of clopidogrel. The prasugrel regimen was associated with a significantly lower MPA as early as 30 minutes after the LD which might be advantageous in the PCI setting.

P1272 Co-administration of rivaroxaban - a novel, oral, direct Factor Xa inhibitor - and clopidogrel in healthy subjects

D. Kubitza, M. Becka, W. Mueck, M. Zuehlsdorf. *Bayer HealthCare AG, Institute of Clinical Pharmacology, Wuppertal, Germany*

Rivaroxaban is an oral, direct Factor Xa (FXa) inhibitor in clinical development for the prevention and treatment of thromboembolic disorders. Co-administration of rivaroxaban and clopidogrel in patients is likely; therefore, this study was performed to investigate the influence of clopidogrel on the tolerability, pharmacodynamics and pharmacokinetics (PK) of rivaroxaban. Healthy male subjects (N=27) received a single dose of clopidogrel 300 mg. Clopidogrel 'responders' (platelet aggregation <0.6 times baseline [tb] after 24 hours; n=14) were then randomized in a non-blinded, three-way crossover study to: A, 300 mg clopidogrel on day 1 and 75 mg clopidogrel on day 2; B, rivaroxaban 15 mg; or C, a combination of A and B (with rivaroxaban given on day 2). All treatments were well tolerated. Rivaroxaban alone inhibited FXa activity by a maximum of 33% and prolonged prothrombin time (PT) by 1.3 tb, whereas clopidogrel alone did not affect either parameter. There were no further effects on FXa activity or PT with the combination, compared with rivaroxaban alone. As expected, ADP-stimulated platelet aggregation was inhibited by clopidogrel alone, but not rivaroxaban. No further effect on platelet aggregation was observed with the combination, compared with clopidogrel alone: least-squares (LS)-means [90% CI] were 78.5% [72.4–84.5] with rivaroxaban; 21.1% [14.6–27.6] with clopidogrel; and 18.6% [12.1–25.2] with the combination. Bleeding time with the combination was significantly prolonged in four subjects, compared with either drug alone, which increased the overall LS-means [90% CI] to 3.77 tb [2.82–4.73] with the combination, compared with 1.13 tb [0.17–2.09] with rivaroxaban; and 1.96 tb [0.10–2.91] with clopidogrel. There were only minor variations in bleeding time between subjects with either drug alone. Co-administration of clopidogrel did not affect the PK of rivaroxaban (LS-means ratio for AUC was 0.98, 90% CI 0.85–1.12, and LS-means ratio for the C_{max} was 0.92, 90% CI 0.81–1.04). In conclusion, co-administration of clopidogrel did not affect the tolerability or PK of rivaroxaban in healthy subjects, nor did it affect inhibition of FXa activity, prolongation of PT, or platelet aggregation. Significant prolongation of bleeding time in a few subjects receiving the combination was observed; however, a similar effect has been reported in healthy subjects receiving clopidogrel and acetylsalicylic acid. These findings suggest it may be possible to administer rivaroxaban and clopidogrel together; this will be evaluated further in ongoing clinical studies.

P1273 Antithrombotic effects of nicorandil in platelet thrombi formed at site of FeCl3-induced endothelial injury in a mouse testicular artery detected by novel real time three-dimensional imaging system

H. Ishida, N. Higashijima, Y. Takahari, Y.U. Eguchi, Y. Kawamura, S. Goto. *Tokai University School of Medicine, Isehara, Japan*

Introduction: Nicorandil, a hybrid compound of an ATP-sensitive potassium channel opener and a nitric oxide donor, has been reported to preserve microvascular integrity in patients with reperfused myocardial infarction. Recently, nicorandil has been suggested to reduce the risk of thrombus formation. To elucidate this possibility, we examined the effect of nicorandil on the FeCl3-induced thrombi formed in a mouse testicular artery.
Methods: Arterial thrombosis was induced by endothelial injury caused by FeCl3 in mouse testicular artery. Platelet thrombi formed there were detected by newly developed real time three dimensional imaging system with the use of ultra-fast laser confocal microspe equipped with piezo-motor control unit. Mice were pretreated by nicorandil (15mg/kg/day as free drinking) or neither (control) for one week. Antiplatelet agent, anti-GP IIb/IIIa agents, tirofiban (0.3μmol/kg), was administered intravenously before the injury.
Results: Three-dimesional growth of thrombi, reaching to the complete occlusion within 12.3±2.5 min (n=32), was developed after endothelial injury by FeCl3 in control mice. Nicorandil significantly slowed the growth of thrombi, reaching to the

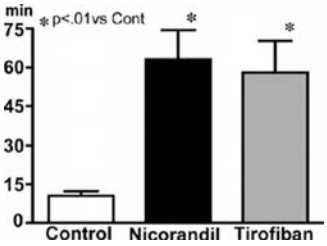


Figure 1

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

arterial occlusion in 54.6±10.8 min (n=11; p<0.01 as compared to the control). Tirofiban showed similar effect (58 ±12.4 min; n=5, Figure). Nicorandil did not inhibit a platelet aggregation under in vitro experiments.
Conclusion: This result suggests that nicorandil has the antithrombotic effects in vivo.

ALL AROUND CLOPIDOGREL

P1274 Optimising clopidogrel therapy: reducing the non-responder incidence by aggregometry-guided modification of therapy

H. Neubauer, S. Lask, J. Khandanpour, A. Muegge. *Ruhr-University-Bochum, Cardiology, Bochum, Germany*

Introduction: The platelet inhibitory effect of clopidogrel is insufficient in about 5-25% of patients. These "non-responders" bear a significantly higher risk of cardiovascular complications and stent thrombosis. The therapeutic options for non-responders who require a dual anti-thrombotic therapy are still undetermined. We examined the number of clopidogrel non-responders in patients after elective coronary stenting (PCI) and established a therapeutic algorithm.
Method: In 82 patients after PCI (mean age 65.9 years, 55 male/27 female; all on 100mg Aspirin daily), we performed aggregometry testing (Chrono-Log 590-2D) 48h after a loading dose of 600mg clopidogrel was taken, followed by 75mg clopidogrel daily (=standard regimen). The measurements were donein 5ml citrated whole blood. Platelets were stimulated with 5 and 20 m M ADP for at least 6 min. Clopidogrel "responders" and "non-responders" were defined on impedance values (< 5 ohm and > 5 ohm, respectively). Platelets of "non-responders" were further evaluated with the ADP $P2Y_{12}$ receptor agonist MeSAMP in order to disclose ADP receptor defects. In case of "non-responders" unrelated to ADP receptor defects, the clopidogrel loading dose (600 mg) was repeated followed by clopidogrel 75mg twice daily (=high dose regimen). If patients were not responding to the high dose regimen, the medication was changed to ticlopidine 250mg twice daily (=ticlopidine regimen).
Results: 66/82 patients (80.5%) were clopidogrel-responders, 16/82 patients (19.5%) were "non-responders". A defect of the ADP-receptor $P2Y_{12}$ was detected in 1/16 (6.25%) of the "non-responders". The majority of "non-responders" unrelated to the ADP receptor defect (10/15; 66.7%) could be effectively treated with the high dose clopidogrel regimen. The remaining "non-responders" were treated with ticlopidine, in 1/5 cases (20%) this regimen resulted in a normal suppression of ADP-induced platelet aggregation. Overall, a therapeutic suppression of ADP-induced platelet aggregation could be achieved in 77/82 patients (93.9%), however, 5/82 (6.1%) patients remained "true" non-responders.
Conclusion: In our study 19.5% of patients were initially clopidogrel "non-responders". Our aggregometer–guided therapeutic algorithm could reduce the incidence of initial clopidogrel "non-responder" from 19.5% to 6.1%. We recommend a regular monitoring of high-risk clopidogrel patients to evaluate if they are "non-responders". These "non-responders" should than be treated using a therapeutic regimen according to the outcome of aggregometric testing.

P1275 Assessment of the acute and chronic antiplatelet effects of clopidogrel in patients undergoing coronary intervention: comparison of the VerifyNow P2Y12 rapid analyzer with optical agggregometry

D. Trenk, W. Hochholzer, B. Mueller, F.-J. Neumann. *Herz-Zentrum Bad Krozingen, Abt. fuer Klinische Pharmakologie, Bad Krozingen, Germany*

A variable response to clopidogrel is consistently observed when either adenosine diphosphate (ADP)-induced platelet aggregation or the expression of surface proteins after stimulation with ADP is assessed. The EXCELSIOR study demonstrated a 7-fold risk for 30-day major adverse cardiac events in patients with inadequate platelet response to loading with 600 mg clopidogrel. Conventional platelet function tests are time consuming and require experienced laboratory staff. We, therefore, tested a point-of-care method (VerifyNow P2Y12 cartridge-based assay) in 44 patients and assessed the correlation with light transmission aggregometry in platelet rich plasma.
A bolus dose of 600 mg clopidogrel was administered to the patients at least 2 h before percutaneous catheter intervention (PCI). Patients were stratified according to the extent of platelet inhibition assessed 24 h after PCI either to conventional treatment (75 mg clopidogrel daily; n=24) or an intensified regimen (150 mg daily; n=20). Residual platelet aggregation was determined in platelet rich plasma by optical aggregometry 5 minutes after addition of 5 μM ADP and in whole citrated blood using the VerifyNow P2Y12 rapid analyzer. Assessments were performed 24 h (T1) as well as 14 days (T2) and 28 days (T3) after PCI.
Residual platelet aggregation was 10.5% (4.0-23.0%) [median; interquartile range] at 24 h after the bolus dose (T1), 10.0% (5.0-18.0%) at T2 and 7.5% (3.0-16.5%) at T3 during dose-adjusted chronic treatment with clopidogrel. P2Y12 Reaction Units (PRU) from the VerifyNow P2Y12 rapid analyzer decreased from 115 PRU (57.5-157.0 PRU) at T1 to 79.5 PRU (31.0-115.0 PRU) at T2 and to 89.0 PRU (47.5-132.0 PRU) at T3. Correlation analysis between P2Y12 Reaction Units and residual platelet aggregation by light transmittance aggregometry yielded significant correlations after the bolus dose of clopidogrel (Non-parametric Spearman correlation coefficient at T1: r=0.753; p<0.0001) as well as during maintenance treatment (T2: r=0.547, p=0.0001; T3: r=0.578, p<0.0001).
In summary, significant correlations were observed between measures of the antiplatelet effect of clopidogrel obtained by the easy to use point-of-care system VerifyNow P2Y12 rapid analyzer in whole blood and data obtained by conventional optical aggregometry after stimulation of platelet rich plasma with ADP 5μM.

P1276 Evaluation of premature interruption of dual antiplatelet therapy in the world of real practice

J.-P. Collet[1], P. Coriat[1], B. Napoleon[2], V. Trosini-Desert[3], D. Thomas[3], G. Montalescot[3]. *[1]Hopital Pitie Salpetriere, Institut De Cardiologie, Paris Cedex 13, France; [2]Clinique Sainte-Anne Lumiere, Gastroenterology SFED, Lyon 69003, France; [3]Hopital Pitie-Salpetriere, Pneumologie GELF, Paris Cedex 13, France*

Introduction: Exaggerated concern about increased procedure-related bleeding is one of the major factors for premature discontinuation of dual oral antiplatelet therapy (DOAT) that is detrimental after stent placement.
Aim: The REGINA survey was designed to evaluate how interruption of DOAT was handled in the real life.
Methods: A total of 2515 medical doctors were randomly selected out of 4581 to participate into a telephone interview. Scientific recommendations on how to manage DOAT were first appraised by 3 simple questions (table). Temporary interruption strategies of DOAT for invasive or surgical procedure were then evaluated after DES placement considering a high risk period (<30d) and a low risk period (>18 month). The rate of appropriate answers predefined by an expert panel was compared between these two situations and between the different categories of physicians.

Rate of good/appropriate answers (%)	Dentists N=437	Primary Care N=446	Anaesthesiol. N=469	Gastroenterol. N=440	Pneumologists N=453	Cardiologists N=457
Overall (%)	9	27	46	46	43	61*
What is a drug eluting stent?	7	39	56	43	40	95*
What is the minimum duration of dual OAT after DES placement?	7	17	20	17	15	54*
What is the minimum duration of dual OAT after BMS placement?	12	46	49	46	33	88*
Answers in the low risk situation	3	27	39	26	15	60*
Answer in the high risk situation Rate (%)	21	29	47	15	18	6*
Rate of discontinuation of one or both OAT? (%)	17	58	82	77	81	89*
Use of substitution therapy ? (%)	40	60	66	73	74	53*
Interruption < 5 days prior to procedure (%)	48	32	27	10	13	28*
Postponing invasive or surgical procedure (%)	79	36	4	13	23	20*

*indicates significant differences for all.

Results: The rate of appropriate answers was significantly lower among primary care physicians and dentists as compared to other physicians. Interruption of one or both OAT was frequent, most often more than 5 days prior to the procedure and the use of substitution therapy including low molecular weight heparin or NSAID was frequent. There was a significant difference in the rate of appropriate answers according to the period at risk for stent thrombosis. After multivariable analysis, independent correlates for appropriate answers were the type of speciality, public practice instead of private practice and gender.

P1277 High post-treatment platelet reactivity is related to adverse long-term outcome in patients with non-ST segment elevation acute coronary syndrome

A. De Miguel, A. Diego, B. Samaniego, D. Alonso, C. Cuellas, F. Fernandez-Vazquez, N. Alonso-Orcajo, R. Carbonell, C. Pascual, A. Perez De Prado on behalf of RASCA Investigators. *Hospital De Leon, Servicio De Cardiologia, Leon, Spain*

Purpose: To determine the relationship between clopidogrel-related inhibition of platelet aggregation (IPA) and post-treatment platelet reactivity (PPR) with outcomes in non-ST-segment elevation acute coronary syndrome (NSTEACS).
Methods: 179 patients with NSTEACS treated with a loading dose of 300 mg clopidogrel + 75 mg daily and an early coronary angiography were included. Primary end point was the 1-year occurrence of major adverse cardiac events (MACE). IPA and PPR were assessed with a point-of-care P2Y12 specific analyzer.
Results: 161 patients (90%) were followed-up (468±204 days). 18 patients (11%) incurred MACE (10 deaths, 6 myocardial infarctions, 2 strokes, 5 revascularizations). Variables significantly associated with MACE are detailed in the table. Independent predictors of long-term MACE identified with multivariate stepwise analysis were: PPR (p=0.006), use of unfractionated heparin (p=0.011) and previous percutaneous coronary intervention (PCI, p=0.019).
Conclusions: Heightened PPR and lower IPA in patients with NSTEACS are

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Table 1

	MACE (n=18)	No MACE (n=143)	p
Age; years, mean ± SD	73.6±7.1	66.9±10.9	0.001
Female gender	8 (44%)	33 (23%)	0.049
Hypertension	17 (94%)	78 (55%)	0.001
Active smokers	0	30 (21%)	0.026
Diabetes on treatment	9 (50%)	27 (19%)	0.006
Previous antiplatelet treatment	13 (72%)	50 (35%)	0.004
Previous myocardial infarction	9 (50%)	25 (17%)	0.002
Previous PCI	5 (28%)	15 (10%)	0.036
Previous CABG	4 (22%)	8 (6%)	0.031
TIMI risk score > 3	15 (83%)	73 (51%)	0.011
Creatinine clearance (mL/min)	51±28	78±29	0.016
Baseline haemoglobin (g/dL)	12.0±1.3	13.8±1.7	0.001
Unfractionated heparin use	13 (72%)	33 (23%)	0.001
Number of diseased vessels	2.3±0.9	1.6±1.1	0.006
Inhibition of platelet aggregation (IPA)	31±21%	43±21%	0.049
Post-treatment platelet reactivity (PPR), units	204±60	155±67	0.006

correlated with MACE. After adjusting for covariates, PPR predicts the occurrence of MACE.

P1278 Contribution of the P2Y1 ADP receptor to platelet reactivity in clopidogrel-treated cardiovascular patients

E. Toth Zsamboki, B. Beres, K. Vargova, N. Kiss, A. Kovacs, G. Kerecsen, I. Preda, R.G. Kiss. *HAS-SU and Nat. Cent. For Health Services, Res. Group for Infl. Biol. and Immunogen., Budapest, Hungary*

Clopidogrel, the platelet P2Y12 ADP receptor inhibitor is a key element of the therapy in ischemic heart disease patients with PCI. Since concomitant activation of the two platelet ADP receptor (the clopidogrel-target P2Y12 and the P2Y1) is required for platelet aggregation, our objective was to investigate contribution of the P2Y1 receptor to platelet reactivity in clopidogrel-treated cardiovascular patients (n=136).

Platelet aggregation was induced by ADP (1,25 μM, 5 μM), collagen (1 μg/ml) and epinephrine (2 μg/ml, citrated plasma, Born aggregometry); the specific P2Y1 inhibitor, MRS2179 was also used. The purely P2Y1-mediated ADP-induced shape change (SC) was recorded as well. Amplitude of SC was identical in healthy control (n=10) and in the patient cohort (Median:-7.8%, IQR:-6- -10%, vs.M:-8.43%, IQR:-10- -6%); 40 μM MRS2179 in controls fully, while in patients only partially (M:-4.0%, IQR:-1 - -6%, $p<0.05$) inhibited SC, indicating lower EC50 values in patient platelets. We found no significant difference between patients in the lowest/highest SC quartile in respect to ADP (M:58% vs. M:52%), collagen (M:22,8% vs. M:22,8%) and epinephrine-induced (M:31.4% vs. M:26,4%) aggregations. We found no correlation between SC and platelet aggregation induced by ADP, collagen or epinephrine. MRS2179 strongly inhibited both ADP (5 μM: M:52,3%, IQR:39-66% vs. M:23%, IQR:11-30%, $p<0.05$) and collagen-induced aggregations (M:24,6% IQR:6-32% vs. M:10,7%, IQR:2-14%, $p<0.05$) in patient platelets; when it was combined in vitro with 10 μM cangrelor, the specific P2Y12 inhibitor, platelet aggregations were fully (ADP 5 μM:1%, $p<0.005$) or greatly (collagen: M:4%, $p<0.0005$) blocked. The inhibitory efficacy of MRS2179 was significantly reduced in clopidogrel-treated patients in the highest ADP-aggregation quartile in contrast to the lowest quartile (average inhibitory effect: 1.25 μM ADP: 68% vs.78.5%, $p<0.005$; 5 μM ADP: 50%vs. 70%, $p<0.005$).

Based on these results, specific P2Y1 inhibitors reduce platelet aggregations significantly in clopidogrel-treated patients, indicating that the receptor - especially in combination with effective P2Y12 inhibition - might represent a new antiplatelet target. The P2Y1 receptor is a prerequisite for ADP-induced aggregations; however, extent of activation is essentially determined by the availability of the P2Y12 ADP receptor in clopidogrel-treated cardiovascular patients. In the future, measurement of the ADP-induced shape change EC50 value might help to identify the individual P2Y1 heterogeneity.

P1279 More reliable antipletelet effect using the 600 mg loading dose of clopidogrel in PCI

S. Hoffmann, R. Klamroth, D. Andresen. *Vivantes Friedrichshain, Berlin, Germany*

Purpose: Dual antiplatelet therapy with ASA and clopidogrel is the regimen of choice to prevent stent thrombosis. However, the inhibition of platelet function with these drugs shows a great interindividual variability with a potential lack of efficacy. Furthermore is the inhibitory effect of clopidogrel time dependent. Faster action is achieved due to a loading dose, however the value of loading dose of 300mg or even 600mg in elective PCIis yet not well defined.

Methods: We examined 40 pts with a loading dose of 300mg clopidogrel and 40 pts with a loading dose of 600mg one day before elective PCI in combination with aspirin. Blood samples were obtained immediately after PCI and platelet inhibition was studied by light transmittance aggregometry in platelet rich plasma using platelet poor plasma as a reference. We defined clopidogrel resistance as > 30% after induction with ADP.

Results: The median time interval between the loading dose and PCI was 20±6 h. In the 300 mg loading dose group 60% of the pts (24/40) showed insufficient platelet inhibition at the time of PCI. With 600 mg loading dose this rate decreased to 20% (8/40). The incidence of diabetes was 26%(21/80) with no difference in both groups. None of the diabetic pts showed sufficient platelet inhibition after loading dose, even the higher dose had no effect.

Conclusion: – The majority of patients scheduled for elective PCI did not show sufficient platelet inhibition despite the recommended loading dose of 300 mg Clopidogrel.

– The rate of sufficient platelet inhibition can be markedly increased with a higher loading dose of 600 mg Clopidogrel.

– Patients with diabetes did not show any Clopidogrel effect 24h after Clopidogrel bolus, so there is a need in additional platelet inhibition in this group with complex interventions.

P1280 Impact of high clopidogrel maintenance dosing on thrombin generation in patients with type 2 diabetes mellitus: insights of the OPTIMUS study

D.J. Angiolillo, M.A. Costa, S.B. Shoemaker, B. Desai, H. Yuan, L. Guzman, M. Zenni, T.A. Bass. *University of Florida-Shands Jacksonville, Division of Cardiology, Jacksonville, United States of America*

Purpose: Patients with type 2 diabetes mellitus (T2DM) have hyper-reactive platelets. Activated platelets not only lead to the formation of aggregates, but also play a pivotal role in triggering the coagulation cascade by inducing thrombin generation. The hypothesis of this study is that, in addition to enhancing platelet inhibition, more aggressive antiplatelet treatment regimens also reduce thrombin generation rates in DM patients with hyper-reactive platelets.

Methods: A subgroup of patients (n=30) enrolled in the OPTIMUS (Optimizing anti-Platelet Therapy in diabetes MellitUS) study were included. All patients were on chronic (>1 month) clopidogrel (75 mg/day) and aspirin (81mg/day) treatment. Patients with enhanced platelet reactivity (defined as > 50% maximum platelet aggregation following 20μmol/L adenosine diphosphate stimuli) were eligible for the study and randomized to either standard (75 mg/day) or high (150 mg/day) maintenance dose of clopidogrel therapy for one-month. In addition to platelet aggregation using light transmittance aggregometry, the onset of thrombin induced platelet-fibrin clot formation, a marker of the speed of thrombin generation was assessed by thrombelastography. Laboratory personnel were blinded to treatment assignment.

Results: Platelet aggregation (%) significantly reduced after one-month treatment in patients (n=15) randomized to the high maintenance dose (66.2±5 vs 51.0±13; $p<0.0001$), while no changes were observed in patients (n=15) on standard dosing (63.8±8 vs 62.0±7; p=0.5). The speed of thrombin generation (min) was prolonged (5.5±1.4 vs 6.6±1.4; p=0.03) in the high maintenance dose group, while no changes were observed in patients on standard dosing (5.8±1.4 vs 5.6±1.0; p=0.7). Intergroup group comparisons were also statistically significant for platelet aggregation (p=0.01) and thrombin generation (p=0.03) profiles.

Conclusions: In addition to enhancing platelet inhibition, the selective use of a high maintenance dose of clopidogrel in a high risk cohort of T2DM patients reduces thrombin generation, contributing to the overall antithrombotic properties of this drug.

P1281 Antiplatelet therapy resistance: a risc factor for stent thrombosis

S. Hoffmann[1], R. Klamroth[2], M. Orlovic[1], H. Landgraf[1], D. Andresen[1]. *[1]Vivantes Friedrichshain, Cardiology, Berlin, Germany; [2]Vivantes Fridrichshain, Hemostasiology, Berlin, Germany*

Purpose: Subacute sten thrombosis (SAT) is a rare, but often fatal complication after PCI. Dual antiplatelet therapy with ASA and clopidogrel has lead to a reduction of SAT to less than 2%. However, the inhibition of platelet function with these drugs shows a great interindividual variability with a potential lack of efficacy, called ASA or clopidogrel ressistance. The question remains if this resistance is linked to clinical events.

Methods: We examined 53 pts with SAT between day 2 and 30 post PCI despite adequate dual antiplatelet therapy. All pts received a loading dose of 300mg to 600mg clopidogrel followed by 75mg/d in combination with ASA 100mg/d. Platelet inhibition was studied by light transmittance aggregometry in platelet rich plasma using platelet poor plasma as a reference. We defined ASA resistance as platelet aggregation > 30% after induction with arachidonic acid and clopidogrel resitance as > 30% after induction with ADP. We compared these pts with 20 matched pts without SAT.

Results: In the SAT group 62% (33/53) had insufficient platelet inhibition despite the use of ASA and clopidogrel. We observed ASA resitance in 13% (7/53) and clopidogrel resistance in 53% (28/53). 3/53 (6%) of the pts did not show any antiplatelet effect despite the use of a combination therapy. In the matched control group without SAT we found only 1 ASA (5%) and 1 clopidogrel (5%) non-responder.

Conclusion: 1. Insufficient platelet inhibition is a likely reason of stent thrombosis.
2. Platelet function testing is able to detect insufficient platelet inhibition.
3. Early routine platelet function testing is a reasonable instrument to prevent coronary stent thrombosis.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1282 Triple antithrombotic treatment in patients with intracoronary stents who require oral anticoagulation

E. Guasch[1], J.C. Reverter[2], R. Andrea[2], P. Loma-Osorio[2], A. Sionis[2], M. Heras[2]. *[1]Thorax Institute - Hospital Clinic, Cardiology, Barcelona, Spain; [2]CDB - Hospital Clinic, Barcelona, Spain*

Introduction: Double antiaggregation with aspirin (ASA) plus clopidogrel (Clo) is mandatory in patients with intracoronary stents. Patients with comorbidities may require oral anticoagulants (OAC). There are no definite studies on the safety and efficacy of combining ASA, Clo and OAC.
Aim: To assess the bleeding complications of patients with triple antithrombotic therapy compared with dual antithrombotic treatment (OAC+ASA or Clo).
Methods: We identified retrospectively patients who were previously taking OAC, and who had an intracoronary stent implanted and were given ASA+Clo in addition to OAC. Efficacy was defined as the lack of emboli and stent occlusion and safety as the lack of haemorrhages. We have classified bleedings as: non-severe hemorrhage (NSH) when only required stopping anticoagulation therapy for at least 48 hours, and severe hemorrhage (SH) as those requiring hospitalization or transfusion. The safety and efficacy of the triple therapy (OAC+ASA+Clo) was compared with dual therapy (OAC+ 1 antiplatelet agent) in the same patients, using linearized rates (days of exposure to each treatment regimen).
Results: In one year, 33 patients were identified as having had triple therapy for variable periods of time. There were 28 men (84%), mean age 63.2 yr. Linearized rates for triple therapy were 4.42 patient-year in triple therapy and 52.58 patient-year for dual therapy. The absolute and linearized rates of bleeding, thrombotic episodes and % of adequate INR (2-3) are described in the table. INR was >3 in two bleeding episodes, none of them severe. The only stent thrombosis occurred after early withdrawal of clopidogrel.

	Triple Therapy		Double Therapy		p
	n=33	% Pt year	n=33	% Pt year	
NSH	4	90	2	3	<0.01
SH	0	0	1	1.5	ns
Intrastent thrombosis	0	0	1	1.5	ns
INR 2-3	63%		64.7%		ns

Conclusions: In this small study, patients who were on OAC (INR 2-3) and received an intracoronary stent, triple therapy was effective in avoiding thrombotic events, but was associated with an increase in non-severe bleedings that resolved uneventfully. In these patients, bare metal stents should be recommended.

P1283 Monitoring platelet inhibition in patients on high clopidogrel maintenance dosing using P2Y12 specific assays

D.J. Angiolillo, M.A. Costa, S.B. Shoemaker, B. Desai, H. Yuan, R.K. Charlton, L. Guzman, M. Zenni, T.A. Bass. *University of Florida-Shands Jacksonville, Division of Cardiology, Jacksonville, United States of America*

Purpose: Clopidogrel specifically inhibits the platelet adenosine diphosphate (ADP) P2Y12 receptor. ADP is used as an agonist in functional assays to determine the degree of clopidogrel-induced antiplatelet effects. However, this approach leads to stimuli of purinergic receptors (e.g. P2Y1) which are not inhibited by clopidogrel. Novel platelet function assays using PGE1 in addition to ADP are able to more specifically assess inhibition of the P2Y12 pathway. However, these assays have been primarily evaluated in patients receiving standard clopidogrel dosing, and if these may be implied for evaluation of antiplatelet effects achieved with high dosing regimens has not been explored.
Methods: A cohort of 23 patients on chronic clopidogrel (75 mg/day) treatment was studied. Platelet function was assessed before and after one month treatment with a high (150 mg/day) maintenance dose of clopidogrel. Assays combining ADP+PGE1 included a) the VerifyNow P2Y12 point-of-care assay and b) assessment of the phosphorylation (P) status of the vasodilator-stimulated phosphoprotein (VASP) using flow cytometric technique. The VerfiyNow P2Y12 assay measures changes in optical signaling, reported in P2Y12 Reaction Units (PRU), and allows to define percentage inhibition using a separate channel containing iso-TRAP. Measuring VASP-P levels allows to define the P2Y12 reactivity index (PRI).
Results: The percentage inhibition of PRU significantly increased from 31.2±15% to 46.1±21% and the PRI significantly reduced from 71.1±16% to 55.6±10% ($p<0.001$), both indicative of enhanced clopidogrel-induced platelet P2Y12 inhibition. A good correlation was observed between the 2 tests to identify enhanced clopidogrel-induced effects test (r=-0.64 [95% CI -0.84 to -0.28]; p=0.002). Accordingly inhibition of platelet aggregation profiles following 20μM ADP stimuli using gold standard light transmittance aggregometry increased by 22.4±15% with an absolute change from 67.4±6% to 52.3±12% ($p<0.001$).
Conclusions: A high maintenance dose of clopidogrel further enhances platelet inhibition in patients already on chronic clopidogrel therapy using standard dose regimens. In addition to standard platelet aggregation testing, the effects of more aggressive P2Y12 inhibition can be detected by novel and more specific platelet function assays.

P1284 Predictors of antiplatelet effects of a loading dose of clopidogrel 600 mg in patients undergoing coronary angiography with and without percutaneous coronary intervention

D. Trenk, W. Hochholzer, H.-P. Bestehorn, C.M. Valina, C. Stratz, P. Schmiebusch, H.J. Buettner, F.-J. Neumann. *Herz-Zentrum Bad Krozingen, Abt. fuer Klinische Pharmakologie, Bad Krozingen, Germany*

A marked interindividual variability in antiplatelet response is observed following administration of 600-mg loading doses of clopidogrel as well as during chronic therapy. The EXCELSIOR-study showed the impact of this variability on major adverse cardiac events (MACE: death, myocardial infarction (MI) and target lesion revascularization (TLR)) within 30 days following elective coronary stent implantation (PCI). Predictors for an insufficient antiplatelet effect of clopidogrel have so far not been defined.
This prospective study enrolled 1,987 patients either with coronary angiography (n=1,185) or PCI (n=802). All patients received clopidogrel 600 mg before angiography. We analyzed the impact of demographic and clinical characteristics as well as the effect of concomitant medication on residual platelet aggregation determined by optical aggregometry (ADP 5μM) at baseline and immediately before administration of contrast media.
Differences in baseline aggregation before clopidogrel accounted for 27% of the variability in platelet aggregation at angiography. Female patients (+3.0%, 95% confidence interval [CI]: 1.1-5.0%; p=0.003), elderly patients (per 10 years of age: +2.0%; 1.1-2.9%; $P<0.001$) and patients with a blunted response to ASS (+20.7%; 16.0-25.3%; $P<0.001$) had an exaggerated platelet aggregation at baseline. Demographic and clinical characteristics identified as predictors for an increased platelet aggregation at coronary angiography are summarized in the Table.
Patients treated with verapamil/diltiazem (+5.7%; 95% CI:1.6-9.8%; P=0.007; n=71) and diabetics with sulfonyl urea drugs (+6.6%; 95% CI:3.1-10.2%; $P<0.001$; n=94) had an increased platelet aggregation at coronary angiography.

	delta Aggregation (%) [95% CI]	p-value
Age per 10 years	2.2 [1.2-3.1]	P<0.001
Body weight per 10 kg	1.1 [0.5-1.7]	P=0.001
Diabetes mellitus	3.5 [1.3-5.7]	P=0.002
Coronary heart disease	2.2 [0.3-4.1]	P=0.023
Angiography within <2h after clopidogrel 600 mg	10.5 [8.8.-12.2]	P<0.001

The antiplatelet effect of clopidogrel 600mg administered to patients undergoing elective coronary angiography without/with PCI was altered by demographic and clinical characteristics as well as by the concomitant medication of the patients.

P1285 The Effect of Caffeine on the Response to Clopidogrel in Healthy Volunteers - a Crossover Study

E.I. Lev[1], M.E. Arikan[1], M. Vaduganathan[2], C. Alviar[2], A. Tellez[2], N. Mathuria[3], I. Del Conde[4], J.F. Granada[4], N.S. Kleiman[3]. *[1]The Methodist Hospital, The Methodist DeBakey Heart Center, Houston, United States of America; [2]The Methodist Hospital, The Methodist DeBakey Heart Center, Houston, Texas, United States of America; [3]Baylor College of Medicine, Cardiology, Houston, Texas, United States of America; [4]Brigham and Womens Hospital, Boston, United States of America*

Purpose: Clopidogrel inhibits the platelet P2Y12 receptor, leading to increased intra-cellular cyclic AMP levels. Methylxanthines, such as caffeine, also cause a rise in intra-cellular platelet cyclic AMP. We, therefore, aimed to test the effect of caffeine administration on the anti-platelet effect of clopidogrel in healthy subjects.
Methods: Twelve healthy subjects (25% women, age=33.5±6 years) were enrolled in a 2 week crossover study. Each week blood samples were drawn at baseline, 2,4 and 24 hrs following 300 mg clopidogrel intake. At the first week 6 subjects received caffeine (300 mg pill) 30 min after clopidogrel. At the second week the other 6 subjects received the caffeine. One month later the effect of caffeine alone (without clopidogrel) was tested in all subjects, 2 hos after caffeine (300 mg pill). Platelet function was evaluated by aggregation in response to 5,10 and 20 μM ADP and 1 μg/ml collagen and by flow cytomeric determination of P-selectin expression and PAC-1 binding.
Results: In the crossover study caffeine administration was associated with lower ADP-induced aggregation at 4 hrs after clopidogrel, and lower activation markers at 2 hrs after clopidogrel (Table). There were no differences in collagen-induced

Effect of clopidogrel +/- caffeine

	Baseline	2 hrs post clopidogrel	4 hrs post clopidogrel	24 hrs post clopidogrel
Aggr. ADP-5 no caffeine	74.6±18%	50.4±18%	49.3±13%*	48.1±12%
Aggr. ADP-5 with caffeine	71.3±14%	45.6±9%	35.1±10%*	46.2±11%
Aggr. ADP-10 no caffeine	86.3±13%	61.2±13%	60.5±13%*	57.1±11%
Aggr. ADP-10 with caffeine	82.9±8%	55.4±9%	44.1±12%*	53.8±10%
P-selectin no caffeine (MFI)	11.9±4	7.7±3.7**	5.4±2.2	5.2±2.6
P-selectin with caffeine (MFI)	12.1±4.3	5.6±3.4**	4.9±2.8	5.4±3
PAC-1 no caffeine (MFI)	5.9±1.1	4.5±1.6**	3.5±1.4	3.6±1.4
PAC-1 with caffeine (MFI)	5.6±1.2	3.3±1.6**	2.9±1.5	3.5±1.6

*P<0.05, **P<0.01, for comparison of effect with vs without caffeine, by ANOVA with repeated measures (aggr=aggregation, MFI=mean fluorescence intensity).

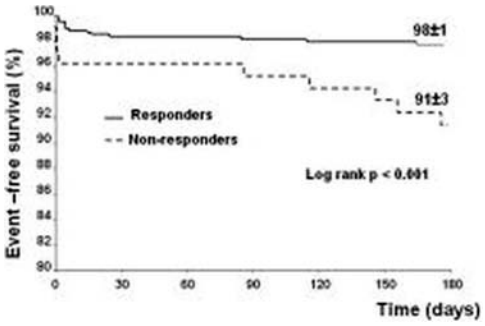
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

aggregation between the effects of clopidogrel with and without caffeine. Caffeine alone had no significant effect on platelet aggregation or activation.
Conclusions: Acute caffeine administration following clopidogrel loading appears to be associated with increased platelet inhibition 2-4 hrs after clopidogrel treatment, in healthy subjects.

P1286 Impact of platelet reactivity following clopidogrel administration on drug-eluting stent thrombosis

D. Antoniucci, P. Buonamici, R. Marcucci, A. Migliorini, G.F. Gensini, A. Santini, R. Paniccia, G. Moschi, A.M. Gori, R. Abbate. *Careggi Hospital, Department of Cardiology, Florence, Italy*

Purpose: To determine whether non-responsiveness to clopidogrel as revealed by high in vitro post-treatment platelet reactivity is predictive of drug-eluting stent thrombosis.
Methods: Prospective observational cohort study conducted from July 2005 to August 2006 in an academic hospital. A total of 804 patients who had successful sirolimus or paclitaxel-eluting stent implantation had the assessment of post-treatment platelet reactivity after a loading dose of 600 mg of clopidogrel. Patients with platelet aggregation by 10 μmol ADP $\geq$ 70% were defined as non-responders. All patients received chronic dual antiplatelet treatment (aspirin 325 mg and clopidogrel 75 mg daily) for 6 months. The primary endpoint was the incidence of definite/probable early, subacute and late stent thrombosis at 6-month follow-up.
Results: The incidence of 6-month definite/probable stent thrombosis was 3.1%. All stent thromboses were subacute or late. Out of 804 patients, 105 (13%) were non-responder to clopidogrel. The incidence of stent thrombosis was 8.6% in non-responders, and 2.3% in responders ($p < 0.001$). By multivariate analysis the predictors of stent thrombosis were: non-responsiveness to clopidogrel (HR 3.08, 95% CI 1.32-7.16; p = 0.009), left ventricular ejection fraction (HR 0.95, 95% CI 0.92-0.98; p = 0.001), total stent length (HR 1.01, 95% CI 1.00-1.02; p = 0.010), and ST-segment elevation acute myocardial infarction (HR 2.41, 95%CI 1.04-5.63; p = 0.041).



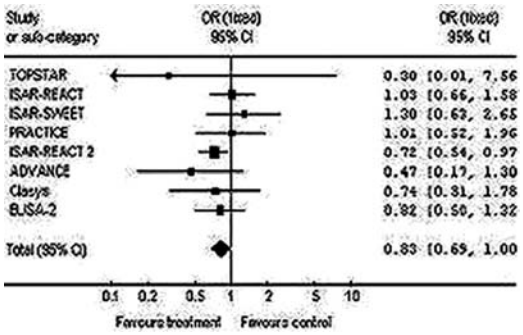
Event-Free Survival (Kaplan-Meyer)

Conclusions: Non-responsiveness to clopidogrel is a strong independent predictor of stent thrombosis in patients receiving sirolimus- or paclitaxel-eluting stents.

P1287 Do gp IIb/IIIa inhibitors add benefit during PCI in patients pre-treated with clopidogrel?. a meta-analysis

P. Loma-Osorio[1], X. Bosch[1], E. Guasch[1], J. Marrugat[2]. *[1]Thorax Institute. Hospital Clinic, Coronary Care Unit, Barcelona, Spain; [2]Institut Municipal dInvestigacio Medica, Unitat de Lipids i Epidemiologia Cardiovasc, Barcelona, Spain*

Background: Large clinical trials have demonstrated that glycoprotein IIb/IIIa inhibitors (IIb/IIIa) significantly reduce the risk of cardiac events in patients undergoing percutaneous coronary intervention (PCI). Current treatment strategies in this setting include routine double platelet inhibition with aspirin and clopidogrel before the procedure. The benefit obtained from additional glycoprotein IIb/IIIa inhibition is unclear. The aim of the study was to compare the effect of IIb/IIIa on 30-day major events (ME, death or myocardial infarction) in patients pre-treated with clopidogrel, and to assess if this effect is related to basal risk.
Methods: We performed a meta-analysis including all randomized controlled trials comparing intravenous IIb/IIIa with placebo administered during PCI in patients previously treated with clopidogrel at least 2 h before the procedure.
Results: Eight randomized trials including 6,098 patients were analyzed. Four of these trials with 3,156 patients were performed in stable coronary patients, three with 2,740 patients were performed in patients with acute coronary syndromes and one with 202 patients was performed in a mixed population. The 30-day incidence of ME ranged from 2% to 31%. The overall incidence of ME in the IIb/IIIa versus control group was 7.40% and 8.76%. This translates into a statistically significant 17% relative reduction of ME (OR: 0.83, CI 95%: 0.69-1.00, p=0.05). A significant correlation between baseline risk and effect of treatment was observed (R2= 97.8%).



Conclusions: The results of this systematic review show that further platelet inhibition with IIb/IIIa significantly reduces 30-day death or myocardial infarction in clopidogrel pre-treated patients. The magnitude of this effect is related to the basal risk of the patients.

P1288 Discontinuation of clopidogrel within the year following a non-ST-segment elevation acute coronary syndrome has a deleterious effect: evidence from the CURE trial

M.E. Bertrand[1], G. Montalescot[2], J.P. Collet[3], J.P. Bassand[4], S. Yusuf[5]. *[1]Lille Heart Institute, 59037, Lille, France; [2]Institut du Coeur, 75000, Paris, France; [3]INSERM U 856, 75000, Paris, France; [4]Dept of Cardiology, Besancon, France; [5]Hamilton General Hospital, Hamilton, Canada*

Objectives: To determine the effect of early permanent discontinuation of clopidogrel on subsequent clinical outcome in the CURE trial.
Background: In patients with non-ST-elevation acute coronary syndromes, long-term (up to 12 months) treatment with clopidogrel plus ASA significantly reduces the risk of cardiovascular death, MI, or stroke compared with ASA alone. However, the clinical impact of early clopidogrel discontinuation is unknown.
Methods: Clinical outcomes were compared for patients (n = 1,157) in the clopidogrel and placebo groups in CURE who permanently discontinued study drug due to consent withdrawal. Analyses were performed for the first (cardiovascular death, MI, or stroke) and second (cardiovascular death, MI, stroke, or refractory ischemia) co-primary endpoints. Among the patients who stopped medication for withdrawal of consent, 23% stopped the treatment within the first month after randomization, 41.7% between 2 and 4 months and one third between 5 and 12 months (33.7%). The median time for discontinuation of study drug was 3.0 months
Results: The event-free survival curves which markedly diverge over the first three months tend then to catch up gradually over time between 4 and 12 months of follow-up. For study drug discontinuation within one month of randomization, the incidence of the first co-primary endpoint was still lower in the clopidogrel discontinued group compared with the aspirin alone group (5.83% vs. 7.56%, hazard ratio = 0.76, 95% CI 0.45-1.28, p = 0.53). However, when study drug was discontinued in subsequent months, the primary endpoint occurred more frequently in the discontinued clopidogrel group than in the aspirin alone group (discontinuation during Months 2–4: 5.83% vs. 3.93%; HR = 1.51, 95% CI 0.59–3.93, p = 0.35; discontinuation during Months 5–12: 3.14% vs. 1.24%; HR = 2.58, 95% CI 0.46–18.7, p = 0.23). Finally, a complete loss of the early benefit was observed at one year in patients who stopped clopidogrel. Similar results were obtained for the second co-primary endpoint.
Conclusions: Discontinuation of clopidogrel in patients presenting with non-ST-segment elevation acute coronary syndromes has a deleterious effect characterized by the occurrence of major cardiovascular events at a rate higher than in patients treated with ASA alone.

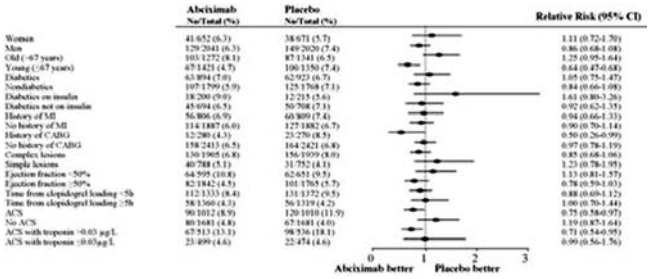
P1289 Abciximab for patients undergoing a percutaneous coronary intervention after pretreatment with 600 mg of clopidogrel: meta-analysis of individual patient data from 4 randomized clinical trials

J. Mehilli[1], P.B. Berger[2], G. Ndrepepa[1], A. Kalyanasundaram[2], S. Schulz[1], M. Seyfarth[1], A. Kastrati[1], A.: Schomig[1]. *[1]Deutsches Herzzentrum, Kardiologie Abt., Munich, Germany; [2]Geisinger Center for Health Research, Danville, United States of America*

A comprehensive analysis of the value of the glycoprotein IIb/IIIa inhibitor abciximab (A) as an adjunct therapy during percutaneous coronary intervention (PCI) after a high-dose pre-treatment with clopidogrel is lacking. We now report the results of a pooled analysis of 4 trials: ISAR-REACT, ISAR-SWEET, ISAR-SMART 2, and ISAR-REACT 2, performed in 8 hospitals that addressed this issue in various clinical settings.
Methods: Inclusion criteria common to all 4 trials were the presence of native coronary artery disease requiring a PCI procedure, and treatment with 600 mg of clopidogrel at least 2 hours prior to the coronary intervention. Patients (pts) were randomized to receive either A plus unfractionated heparin (UFH) (2693

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

pts) or placebo plus UFH (2691 pts). There was no significant difference in the frequency of the primary end point, combined incidence of death, myocardial infarction, and urgent target vessel revascularization within 30 days of randomization, between pts randomized to A (6.3%) and those randomized to placebo (6.9%), p=0.34. Abciximab was only beneficial among younger patients (P=0.012 for an age-A interaction) and those with an elevated troponin at study entry (P=0.014 for a troponin-A interaction), Figure. Major bleeding was similar between the two arms (relative risk 1.11, 95% CI 0.67-1.84), although the frequency of intracranial bleedings was significantly higher with A (relative risk 3.0, 95% CI 0.24-157.33). Moreover, minor bleeding, need for transfusion, and profound thrombocytopenia were all increased by A.



Conclusion: Among patients undergoing PCI after a high-dose pre-treatment with clopidogrel, abciximab reduces ischemic complications in the subsets of younger patients and of those with elevated troponin level.

P1290 Comparison of low-dose versus high-dose atorvastain in clopidogrel resistance after coronary stenting in patients with acute coronary syndrome

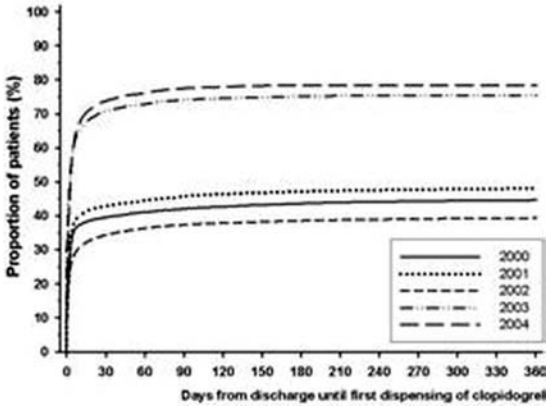
S.J. Hong, W.J. Shim, S.M. Park, H.J. Joo, S.Y. Shin, J.I. Choi, J.Y. Park, K.A. Kim, D.S. Lim. *Korea University Anam Hospital, Cardiology Department, Seoul, Korea, Republic of*

Background: Atorvastatin metabolized by cytochrome P450 3A4 reportedly reduce the metabolism of clopidogrel into active metabolite, thus attenuating its inhibition of platelet aggregation ex vivo. We compared the effect of atorvastatin 10 mg versus 40 mg in clopidogrel resistance and clinical events after coronary stenting in patients with acute coronary syndrome.
Methods: Platelet aggregation was measured before clopidogrel administration, 4 hours, 24 hours, and 5 days after the clopidogrel administration in 106 consecutive patients with acute coronary syndrome. Stented patients were randomly assigned to either atorvastatin 10 mg (n=53) or atorvastatin 40 mg (n=53), and received an oral loading dose of 300 mg of clopidogrel followed by 75 mg/d for 8 months. Measurement of platelet aggregation was done by the turbimetric method with the addition of adenosine diphosphate 5 μmol/L with continuous stirring at 1300 rpm. All patients received aspirin. Clinical events such as death, myocardial infarction, and target lesion revascularization (TLR) were compared during the 8-month follow-up.
Results: Percent platelet aggregation was 41.4±35.6, 52.2± 26.5, 42.1±29.5 (4 hours, 24 hours, and 5 days after 300 mg of clopidogrel pretreatment, respectively) in the Atorvastatin 10 mg Group. Percent platelet aggregation in the Atorvastatin 40 mg Group was 36.2±28.0, 47.6± 25.8, 44.3±28.5 (4 hours, 24 hours, and 5 days after 300 mg of clopidogrel pretreatment, respectively). No significant differences in percent platelet aggregation were noted between the 2 groups. Two cases of subacute stent thrombosis were found only in the Atorvastatin 40 mg Group. Clinical events such as death (p=0.534), myocardial infarction (p=0.882), and TLR (p=1.000) demonstrated no significant difference between the 2 groups during the follow-up.
Conclusion: Atorvastatin 10 mg and 40 mg coadministered with clopidogrel for 8 months does not effect the antiplatelet potency of clopidogrel and showed no significant difference in clinical events in patients with acute coronary syndrome.

P1292 Underuse of clopidogrel treatment in women, elderly and diabetics after acute myocardial infarction with or without percutaneous coronary intervention

R. Sorensen[1], G.H. Gislason[1], S.Z. Abildstrom[1], J.N. Rasmussen[2], S. Rasmussen[2], M. Madsen[2], L. Kober[3], T.S. Ken[4], M.L. Hansen[1], C. Torp-Pedersen[1]. *[1]Gentofte Hospital, Copenhagen, Denmark; [2]National Institute of Public Health, Copenhagen, Denmark; [3]Rigshospitalet, Copenhagen, Denmark; [4]Bispebjerg Hospital, Copenhagen, Denmark*

Purpose: Since 2001 international guidelines recommend clopidogrel treatment in most patients with myocardial infarction (MI) and for patients having a percutaneous coronary intervention (PCI). We studied initiation of clopidogrel treatment in an unselected population of MI patients with or without a PCI to identify likely targets for improvement.
Methods: By individual-level-linkage of nationwide administrative registers all patients surviving first hospitalization for MI in Denmark in 2000-2004 and their status of PCI were identified. Their use of clopidogrel was recorded. We used multivariable logistic regression models calculating odds ratio (OR) for initiation of treatment within 30 days after discharge, adjusted for age, sex and concomitant medical treatment.
Results: A total of 40,671 MI patients were included and of these 21,999 (54%) received a PCI. In 2001–2004 the prescription rate of clopidogrel increased from 22,0% to 61,5% among the MI patients without PCI and 88.6% to 96.6% for the MI patients with PCI. Treatment was mainly initiated within 30 days from discharge (Fig 1). In the adjusted model women (OR 0.86; 0.81-0.90), patients aged ≥70 years (OR 0.76; 0.72-0.81), patients with diabetes (OR 0.88; 0.81-0.95) and heart failure (OR 0.59; 0.56-0.63) were less likely to receive treatment.



MI patients initiation of clopidogrel

Conclusions: There was a high rate in clopidogrel use in MI patients with a PCI and also an increase in clopidogrel use in MI patients without PCI since 2001. This indicates that guidelines were generally followed. However among the MI population without a PCI a focused effort is needed to improve initiation of clopidogrel among women, elderly patients, and patients with heart failure and diabetes.

P1293 Effect of clopidogrel pretreatment on TIMI perfusion grade and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction

E.I. Lev, R. Kornowski, H. Vaknin-Assa, S. Fuchs, D. Brosh, A. Battler, A. Assali. *Rabin Medical Center, Cardiology, Petah-Tikva, Israel*

Purpose: Recent trials have shown that early clopidogrel treatment reduces ischemic complications in patients (pts) with ST-segment elevation myocardial infarction (STEMI) who receive fibrinolytic therapy. However, there is limited data on the value of clopidogrel pretreatment in pts with STEMI treated with percutaneous coronary intervention (PCI). We aimed to examine the effect of clopidogrel preloading on outcomes of primary PCI.
Methods: We used our database of all pts treated with primary PCI for STEMI between 03/2003-06/2006. Excluded were pts with cardiogenic shock. Pts (n=292) were allocated into 2 groups: those who received clopidogrel loading before PCI (in the emergency room or coronary care unit, n=165) and those who received the loading dose immediately after PCI (n=127). TIMI myocardial perfusion (TMP) grade at the end of PCI and clinical outcomes were assessed.
Results: Clinical characteristics, TMP grade (myocardial blush score) and 30 day outcomes are presented (Table).

	Clopidogrel pre-treatment (n=165)	No Clopidogrel pre-treatment (n=127)	P value
Women	22%	18%	0.5
Mean age (years)	60±14	61±13	0.5
Diabetes	25%	22%	0.3
Hypertension	46%	42%	0.5
Anterior Wall MI	42%	43%	0.6
LVEF<40%	35%	34%	0.9
Pre TIMI 0/1 flow	58%	63%	0.5
Post TIMI 3 flow	97.6%	94.5%	0.4
No reflow	1.8%	6.4%	0.06
GP IIb/IIIa use	80%	75%	0.3
TMP grade 3	85%	71%	0.01
30 day outcome			
Death	0.6%	1.6%	0.6
Re-infarction	0	3.2%	0.04
Stent thrombosis	0	2.4%	0.08

Conclusions: Pretreatment with clopidogrel was associated with increased rates of TMP grade 3 and reduced rates of re-infarction. These data support the early use of clopidogrel in pts with STEMI treated with primary PCI.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1294 Clopidogrel patterns of use in acute coronary syndrome patients undergoing percutaneous coronary intervention in 5 european countries

P. Mccollam[1], J.P. Bae[1], P. Nasuti[2], E. Yeung[2], B. Hamad[2]. [1]*Eli Lilly, Global Health Outcomes, Indianapolis, United States of America;* [2]*IMS Health, London, United Kingdom*

Purpose: Recently published data have increased interest in higher clopidogrel loading doses (>300mg) in acute coronary syndrome (ACS) patients undergoing percutaneous coronary intervention (PCI). The purpose of this study was to examine clopidogrel patterns of use in the hospital setting in ACS/PCI patients residing in Europe.
Methods: This was a retrospective study using the IMS Health Acute Cardiovascular Analyzer. This is a physician-reported registry in Germany, France, Italy, Spain and the UK. Data collection timeframe was December 2005 - November 2006. The standard dose clopidogrel group was defined as ≤300mg. Demographic and health characteristics were compiled for the entire cohort and by country.
Results: Over 400 cardiologists reported data on 4,278 ACS patients who received clopidogrel and underwent PCI. Patient count by country was: Germany-1142, France-970, Italy-736, Spain-913, UK-517. Mean age was 63±11.8 (SD) years, 42.6% were age >65; 69% were male. Common co-morbidities and risk factors were: hypertension 70%, dyslipidemia 75%, diabetes 33%, prior myocardial infarction (MI) 13%. Medications prior to admission were: clopidogrel 19%, statins 32%, aspirin 63%. The index diagnosis was: ST-elevation MI 43%, non ST-elevation MI 34% and unstable angina 23%. Timing of clopidogrel administration in relation to PCI was: 59.7% pre-PCI, 12.5% at PCI and 18.4% after PCI (9.5% not reported). Loading dose ranged from 75-900mg. Dosage ≤300mg by country was: Germany 55.2%, France 69.6%, Italy 90.5%, Spain 84.1%, UK 70.8%. Approximately 96% of patients were discharged on clopidogrel and the most commonly reported planned duration was 6-12 months (28%) followed by >12 months (15%).
Conclusion: These recent data indicate many patients received clopidogrel prior to PCI at the ≤300mg dose but some geographic variation was seen. The vast majority of patients received clopidogrel upon discharge, but the planned duration of therapy varied from 6-12 months or more. These data continue to be useful benchmarks for later comparison to treatment guidelines.

P1295 Incidence of clopidogrel resistance in high risk PCI patients using VASP-test

V. Letocart, P. Gueret, G. Le Coq, D. Boulmier, S. Mock, M. Bedossa, A. Ingels, H. Le Breton. *university hospital, Rennes, France*

Incidence of biological clopidogrel resistance (or insufficient response) occurs in about 30% of patient using platelet aggregometry or flow cytometry to measure the quantitative VASP protein phosphorylation (VASP test). The influence of a new loading dose in resistant patients (Pts) is still unknown.
Purpose: we used the VASP-test (Platelet VASP-FCM) to determine prospectively clopidogrel resistance incidence in high risk PCI procedures and to evaluate the benefit of a new 300 mg loading dose in so called resistant Pts.
Methods: Seventy seven Pts were included between september 2005 and february 2006 (mean age: 65,1±11,4 years) all pretreated by clopidogrel. High risk PCI concerned the followed situations: left main lesion, otial LAD lesion, three vessels desease, single patent coronary vessel, terminal renal failure, stent thrombosis and rotative atherectomy procedure. The first VASP-test was performed before the procedure. Pts were defined as resistant when they had a platelet reactivity index (PRI) higher than 60%. In those cases, Pts received a new 300 mg loading dose. A second Vasp-test was performed at least 6 hours after.
Results: Mean PRI was 48,2±19,5% with a high interindividual variability from 6 to 88,9%. Twenty six Pts (34%) were considered as resistant to clopidogrel (PRI = 70,5±7,5%; 60,4 – 88,9%). A new 300 mg loading dose was administrated to twenty-two of them. A second test was performed 18±6.5 hours after the new loading dose. Sixteen Pts (73% of the resistant Pts) became sensitive to clopidogrel with a mean decrease of the PRI of 25,1% whereas 6 Pts (27% of the resistant Pts) remained resistant with a decrease of only 3,7%. The 2 Pts admitted for stent thrombosis were resistant to clopidogrel (PRI = 74 and 80%). No resistance predictive factor was identified (body mass index > 25, statine treatment, CRP, diabete mellitus, acute coronary syndrome).
Conclusion: Using the VASP-test, thirty four percent of high risk PCI patients showed an insufficient response to standard doses of clopidogrel. Seventy three percent of them became sensitive after a new 300 mg loading dose and 27% remained resistant which represent only 8% of the global study population.

P1296 Duration of clopidogrel treatment after acute myocardial infarction with or without percutaneous coronary intervention

R. Sorensen[1], G.H. Gislason[1], S.Z. Abildstrom[1], J.N. Rasmussen[2], T.K. Schramm[3], F. Folke[1], M.L. Hansen[1], L. Kober[4], M. Madsen[3], C. Torp-Pedersen[1]. [1]*Gentofte Hospital, Copenhagen, Denmark;* [2]*National Institute of Public Health, Copenhagen, Denmark;* [3]*Bispebjerg Hospital, Copenhagen, Denmark;* [4]*Rigshospitalet, Copenhagen, Denmark*

Purpose: To analyze duration of clopidogrel treatment in relation to changes in guidelines during a 5 year period in a nationwide unselected cohort of patients with acute myocardial infarction (MI) with or without percutaneus coronary intervention (PCI).
Methods: Patients discharged alive after first hospitalization for MI with or without a following PCI procedure from 2000-2004, were identified by individual-level-linkage of nationwide administrative registers in Denmark. Patients claiming a prescription for clopidogrel within 90 days after discharge were included. Adherence to clopidogrel treatment was analyzed in three periods (2000-2001, 2002-2003 and 2004) by Kaplan-Meier plots. Factors affecting adherence were analyzed by Cox proportional-hazard models.
Results: A total of 15,629 MI patients were included, 9,564 (61.2%) of the MI patients received a PCI. Duration of treatment is shown in Fig. 1, demonstrating trend for increasing duration of treatment during the period ($p<0.0001$), as a response to changes in international recommendations. In a multivariable analysis elderly patients (≥ 70 years) had higher risk of discontinuation during the first year (Hazard Ratio (HR) 1.08 (95% CI 1.02-1.13)). Patients with diabetes (HR 0.91 (0.84-0.98)), heart failure (HR 0.91 (0.86-0.97) and MI patients with PCI (HR 0.95 (0.91-0.99)) had a lower risk of discontinuation.

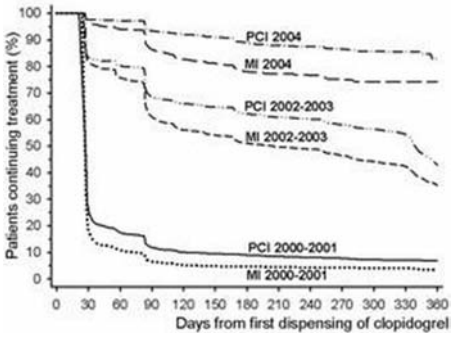


Fig.1:Duration of clopidogrel treatment

Conclusions: Increased duration of clopidogrel treatment indicates increased implementation of clinical guidelines in the treatment of MI patients with and without PCI. However, increased focus on elderly patients is needed.

P1297 Superior effect of eptifibatide added to clopidogrel on biomarker expression detected by fluorokine multi-analyte profiling in patients undergoing elective PCI

P.A. Gurbel, K. Bliden, J. Dichiara, R. Kreutz, M. Hamed, O. Bailon, U.S. Tantry. *Sinai Center For Thrombosis Research, Center For Thrombosis Research, Baltimore, United States of America*

Background: Previous studies demonstrated the synergistic benefit of eptifibatide (E) added to clopidogrel (C) in reducing platelet aggregation, myocardial necrosis and inflammation. Limited information is available on the effect of E on the expression of multiple human cytokines and other biomarkers. The goal was to evaluate the effect of C vs. C+E on the biomarker expression measured by multi-analyte profiling in patients undergoing elective PCI.
Methods: Blood samples from 106 patients treated with either C (n=61) or C+E (n=45) were analyzed by fluorokine multianalyte profiling to compare metallopro-

Biomarker Profile

	C Relative Change	C+E Relative Change	p-value C vs C+E
MMP-9 (ng/mL)	80%	30%	<0.001
vWF (pg/mL)	32%	0%	0.001
Fibrinogen (pg/mL)	13%	-2%	0.007
RANTES (ng/mL)	-39%	-63%	<0.001
MIP-1alpha (pg/mL)	0%	-10%	0.03
TNF-alpha (pg/mL)	15%	-5%	0.002
TNF-beta (pg/mL)	5%	-13%	0.003
CRP (μg/mL)	60%	-10%	<0.001
Fatty Acid Binding Protein (ng/mL)	80%	0%	<0.001
CKMB (ng/mL)	250%	140%	<0.001
Myoglobin (ng/mL)	60%	10%	<0.001
Growth Hormone (ng/mL)	-10%	-35%	0.004
Thrombopoietin (ng/mL)	0%	-18%	0.003

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

teinases, adhesion molecules, growth factors, and procoagulant, inflammation, metabolic, and myocardial ischemia markers between treatment groups at baseline and 24 hours post treatment.
Results: There were multiple profound differences between groups in the biomarker profile. Superior antinflammatory and antinecrosis properties occurred by adding E to C. (Table)
Conclusions: A strategy with C+E consistently produced significant reductions in metalloproteinases, procoagulant markers, inflammation markers, adhesion molecules, growth factors, myocardial ischemia markers, as compared to C alone in patients undergoing stenting. These findings may help to explain the superior clinical outcomes reported from adjunctive use of GPIIb/IIIa inhibitors in PCI.

P1298 Synergistic effect of smoking on platelet responsiveness to clopidogrel

P.A. Gurbel, L. Lawal, A. Singla, O. Bailon, K. Bliden, U.S. Tantry.
Sinai Center For Thrombosis Research, Center For Thrombosis Research, Baltimore, United States of America

Background: Clopidogrel (CLP) is a prodrug that needs metabolic activation by hepatic cytochrome CYP3A4. Recent studies suggested the involvement of CYP1A2 in clopidogrel metabolism and smoking is an inducer of CYP1A2. In this retrospective study, we sought to examine the interaction of smoking and clopidogrel responsiveness.
Methods: Patients undergoing elective coronary stenting (n=152) were studied. Clopidogrel responsiveness was assessed by light transmittance aggregometry (LTA) with 20 uM ADP. Platelet aggregation (PA) was measured in 15 age matched smokers and nonsmokers treated with 75 mg daily CLP. Relative platelet inhibition (RPI): [Pre (PA)-Post(PA)/Pre(PA)] x 100%, was determined in 22 age matched smokers and nonsmokers who were treated with 300mg CLP and 21 smokers and nonsmokers who were treated with 600mg CLP at the time of coronary stenting.
Results: PA was significantly lower ($p<0.05$) in smokers on long term CLP treatment as measured by LTA. RPI was higher in smoking patients treated with either 300 mg or 600mg CLP as compared to non-smokers (Table).

	Smokers	Non-Smokers	p-value
75mg Clopidogrel (PA,%)	n=15	n=15	
LTA-20μM ADP	53±7	61±14	<0.05
300mg Clopidogrel (PA,%)	n=22	n=22	
LTA-20μM ADP	30±19	22±20	0.09
600mg Clopidogrel (PA,%)	n=21	n=21	
LTA-20μM ADP	39±16	28±20	<0.05

Conclusion: Clopidogrel responsiveness is superior in smokers as compared to non-smokers whether measured after bolus dosing or during chronic therapy. Our results suggest that smoking may induce a CYP enzyme important in the generation of the active clopidogrel metabolite.

BIFURCATION AND LEFT MAIN STENTING

P1299 Evaluation of a dedicated bifurcation stent system for the treatment of bifurcation lesions. Results of the NILE registry

T. Lefevre[1], P. Brenot[2], P. Guyon[3], B. Glatt[2], P. Brunel[4], F. Tarragano[5], F. Bedogni[6], T. Royer[2], G. Pavlides[7]. *[1]ICPS, Massy, France; [2]Centre Cardiologique d'Evecquemont, Evecquemont, France; [3]Centre Cardiologique du Nord, Saint-Denis, France; [4]Nouvelles cliniques nantaises, Nantes, France; [5]Hopital Lariboisiere, Paris, France; [6]Instituto Sant Ambrogio, Milan, Italy; [7]Onassis Cardiac Surgery Center, Athens, Greece*

Background: A variety of bifurcation stent delivery systems allowing continuous access to both branches and optimal side branch ostium scaffolding have recently been announced or introduced. However, stent design, crossing profile and flexibility of the device as well as delivery system may influence the rate of technical success. An innovative bifurcation system has been developed by Minvasys (France). It consists of a bare metal stent platform which combines an open-cell design and a 6 French compatible special delivery system with 2 separate balloons, one for stent deployment in the main branch (MB) and one for opening stent strut toward the side branch (SB) and perform final kissing balloon inflation (Kiss) using a strategy of provisional side branch stenting.
Aim and design of the study: A prospective registry involving 10 centers was set up in Europe including 10 centers in order to assess the feasibility and safety of this device. Primary endpoint was stent placement success.
Results: Between November 2004 and October 2005, 75 patients, aged 65±11 years, diabetes 19%, LAD 53%, proximal MB reference diameter 2.99±0.40 mm, SB 2.19±0.39 mm, left anterior descending-diagonal bifurcation in 53% of cases and "true bifurcation" (Medina 111 or 011) lesions 63%, were included. Device placement success was obtained in 95% of cases and device success (correct positioning and Kiss using the NILE delivery system was obtained in 91% of cases. A stent was deployed in the side branch in 15% of cases. Angiographic success was obtained in 95% of cases for both branches and 99% for the MB. Only 1 in-hospital MACE occurred (1 non Q wave MI). At 7 month follow-up, there were no additional AMI, 1 death occurred and TVR was performed in 6.7% of cases (total MACE rate 10.7%).
Conclusions: This study confirms the safety and efficacy of this new dedicated device for treating bifurcation lesions using a strategy of provisional side branch stenting.

P1300 Therapy of bifurcation lesions: main branch stenting + mandatory side branch PCI vs. Main branch stenting with provisional side branch PCI: a randomized study

H. Von Korn[1], M.A. Ohlow[2], J. Yu[1], B. Huegl[1], W. Schulte[1], A. Wagner[1], K. Haberl[1], B. Lauer[1]. *[1]Zentralklinik Bad Berka, Kardiologie Dept., Bad Berka, Germany; [2]Bad Berka, Germany*

Background: The interventional therapy of bifurcation lesions is an unsolved problem.
Methods: We initiated a controlled prospective randomized trial and included all patients (pts) with bifurcation lesions. Pts were randomized into two therapeutic options: Stenting of the main branch (MB, Taxus-stent, PES) + mandatory SB-PCI (kissing-balloons) with provisional side branch (SB) stenting (therapy A) or stenting of the main branch (Taxus-stent) with provisional SB-PCI only when the SB had a TIMI flow < 2 (therapy B).
Results: We included 110 pts. Mean follow up (FU) duration was 6.1 months. Patient and procedural characteristics are shown in tables 1 and 2. Final TIMI flow 3 (MB) was reached in all pts (group A and B), stent diameter or -length (MB) were not different in both groups. Peak troponin I value 24 h after PCI was 4.0 (A) vs. 2.4 ng/ml (B, p= 0.6) Six month - FU See table 3, in group B, no PCI of the SB was done during FU.

Table 1

	Therapy A, n= 56	Therapy B, n= 54	p
Mean age (years)	66.8	65.1	0.4
Men (%)	71.4	77.8	0.5
Diabetics (%)	25.0	25.9	0.9
Mean ejection fraction (%)	62.4	60.1	0.2
MB: LAD (%)	80.4	81.5	0.9
MB: non-LAD (%)	19.6	18.5	0.9

Table 2

	Therapy A	Therapy B	p
Direct stenting (%)	53.6	75.9	<0.05
SB-PCI (%)	78.6	14.8	<0.05
Kissing balloons (%)	73.2	13.0	<0.05
Crossover therapy (%)	16.1	16.7	0.9
Final TIMI 3-Flow SB (%)	96.4	98.1	0.6

Table 3

	Therapy A	Therapy B	p
MACE %	17.9	11.1	0.3
Cardiac death (%)	0	1.9	0.3
Stenosis > 50% MB and/or SB at FU (%)	23.2	22.2	0.9
Late loss MB (mm)	0.24	0.29	0.5

Conclusion: A simple strategy using PES with only provisional SB-PCI is not inferior to a more complex strategy with mandatory SB-PCI.

P1301 Comparison of sirolimus-eluting stents versus paclitaxel-eluting stents in the treatment of bifurcation lesions

M. Ferenc[1], J. Minners[1], H.J. Buettner[1], J. Allgeier[1], K. Werner[1], T. Comberg[1], M. Gick[1], P. Kuebler[2], P. Kienzle[1], F.-J. Neumann[1]. *[1]Heart Center Bad Krozingen, Interventional Cardiology, Bad Krozingen, Germany; [2]Military Hospital, Interventional Cardiology, Wroclaw, Poland*

Drug eluting stents are the most commonly used stents in the percutaneous treatment of coronary bifurcation lesions. Whether sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) have comparable outcomes in this setting is unknown. 692 patients undergoing percutaneous treatment of a de novo coronary bifurcation lesion at our institution with at least one drug eluting stent between 2002 and 2005 were included in the analysis. Data are presented as Kaplan-Meier graphs focussing on target lesion revascularisation (TLR) within one year as a measure of long term procedural success and death or myocardial infarction within one year reflecting safety. 420 patients received SES and 272 PES. Baseline clinical characteristics were comparable between the two groups. TLR within one year was performed in 80 patients (12%), 42 in the SES and 38 in the PES group (p=0.13). In patients receiving stents in both the main and the side branch of the bifurcation lesion ("double stenting") SES had a significantly lower TLR rate (SES 11% vs. PES 21%, p=0.02, figure). There was no difference between the groups with respect to death or myocardial infarction within one year (5% vs. 7%, p=0.41).
Conclusion: SES and PES have similar safety in the treatment of bifurcation lesions. However, SES are associated with a reduced TVR rate when "double stenting" is performed.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1302 Percutaneous treatment of de novo coronary bifurcation lesions with modified T-stenting or stenting of the main branch with kissing balloon of the side branch

M. Ferenc[1], H.J. Buettner[1], P. Kienzle[1], H.P. Bestehorn[1], J. Minners[1], M. Gick[1], T. Comberg[1], O. Morel[2], F.J. Neumann[1], K. Werner[1]. *[1]Heart Center Bad Krozingen, Interventional Cardiology, Bad Krozingen, Germany; [2]University hospital, Interventional Cardiology, Straussbourg, France*

Background: Percutaneous treatment of coronary bifurcation lesions may involve stenting of the main branch including final kissing balloon of the side branch (single stenting) or stenting of both branches. The latter is associated with excellent angiographic results immediately post procedure, but may expose patients to higher long term risks related to metal burden or stent crushing.
Methods: We present 1-year follow-up data from our registry of 1038 consecutive patients undergoing percutaneous catheter intervention for de novo bifurcation lesions at our institution between January 2002 and September 2005. We treated 656 patients with the single stent strategy and 382 patients with stenting of both branches using the modified T-stent technique.
Results: Baseline clinical characteristics were well matched between both groups. Target lesion revascularisation (TLR) after one year was performed in 13% of patients treated with a single stent and 17% of patients who underwent modified T-stenting (p=0.03). Stratifying by stent type demonstrated an increased TLR rate after modified T-stenting for both, bare metal stents (BMS; n=346) and drug eluting stents (DES; n=692) (19% vs. 24%, p=0.04 and 10% vs. 15%, p=0.02, respectively). The combined endpoint of death and myocardial infarction (MI) was reached by 5% of patients in the single stenting and 7% in the modified T-stenting group (p=0.24). There was no significant difference in the 1-year incidence of death and MI between BMS and DES (5.5% vs. 5.9%, p=0.7).
Conclusions: Bifurcation lesions that can be managed with the single stent strategy have a lower restenosis rate than lesions treated with modified T-stenting, regardless of whether BMS or DES are used. Compared with single stenting, modified T-stenting does not increase the 1-year risk of death and MI. DES show lower restenosis rates than BMS and similar 1-year rates of death and MI.

P1303 Treatment of bifurcation lesions with drug eluting stents. One stent or two: is there a difference

H. Routledge[1], T. Lefevre[2], P. Garot[3], P. Dumas[2], T. Unterseeh[3], A. Ohanessian[2], O. Tavolaro[3], Y. Louvard[2], M.C. Morice[2]. *[1]ICPS, Massy, France; [2]Icps, Cardiologie Interventionnelle, Angio/Icps, Massy, France; [3]ICPS, Quincy, France*

Purpose: In PCI of bifurcation lesions with bare metal stents data suggest that a single stent strategy is superior in terms of angiographic success and mid-term results to a more complex two stent approach. In provisional T-stenting (PTS) the threshold for SB stenting varies between operators and studies. We sought to determine whether use of a second stent predicts outcome in PTS of bifurcations with DES.
Methods: The population comprised 290 consecutive patients in whom one or more bifurcation lesion was treated using PTS and one or more DES. LMS bifurcations were excluded. In this single centre prospective registry a second stent was implanted for residual SB stenosis $>$ 50% or TIMI flow $<$ 3. 41% patients had unstable symptoms or acute/recent MI. Clinical outcome was documented by patient contact with clinically driven angiographic follow-up and TVR.
Results:

Table 1

	Single Stent(n-=230)	Side Branch Stent (n=60)	P
LAD/Diag	63%	64%	NS
Lesion Type 1	74%	74%	NS
Lesion Type 2	6%	8%	NS
Lesion Type 3	4%	3%	NS
Lesion Type 4	6%	7%	NS
Lesion Type4a/4b	6%/4%	3%/5%	NS
Final Kissing inflation	93%	98%	NS
Angiographic Success MV/SB	100/98%	100/100%	NS
Procedure time (mins)	58	71	$<$0.01
NQWMI (CK 2 x ULN)	0	1.69%	NS
6 Month TLR	2.4%	3.7%	NS
6 Month TVR	3.8%	3.7%	NS
6 Month MACE inc TVR	5.7%	5.6%	NS
12 Month TLR	4.3%	4.3%	NS
12 Month TVR	6.0%	4.3%	NS
12 Month MACE inc TVR	8.0%	6.3%	NS

Conclusions: In patients treated for bifurcation lesions using DES and a PTS strategy with final kissing inflation, procedural success is high and the 1-year MACE rate is low whether or not a SB stent is deployed

P1304 Midterm results of the "Mini-Crush" stent technique in complex bifurcated lesions

F. Sarnago, E. Garcia, E. Martinez, R. Prieto, M. Abeytua, A. Forns, R. Teijeiro, J. Soriano, M. Cortes, F. Fernandez-Aviles. *Gregorio Maranon, Madrid, Spain*

Background: Crushing Stent technique, as originally described and recommended to treat complex bifurcated lesions, has been lately associated with suboptimal stent deployment and struts overlapping therefore reducing midterm and longterm benefit due to increased thrombosis and restenosis. The mini-crush technique has ben suggested in this type of lesions to minimize stent overlap and facilitate stent deployment and correct apposition.
Methods: This variation of the original technique could be also termed exaggerated T-technique minimally protruding the branch stent in the main vessel independent if the branch stent is implanted first (original) or after the main branch implantation (modified). Since September 2003 we have performed the "Mini-crush" stent technique in 85 patients.
Results: Mean age was 66,32±10,8 years, and 45 (52,9%) were female, 58 (68,2%) had unstable angina and 9 (10,9%) stable angina.All patients had true bifurcation lesions with diffuse disease of the branch artery. Lesion distribution was: 35 (41%) were in the Left Main Coronary Artery, 35 (41,%) in the Left Descendent Artery as the main branch and 15 (18%) in other locations. Balloon pre-dilatation was used in 62 (72,9%), Cutting Balloon pre-dilatation in 35 (41,2%), Rotational Atherectomy in 5 (5,9%). In 81 (95,2%) Paclitaxel Drug Eluting Stents were used and in 4 (5%) Sirolimus stents. Systematic high pressure side branch inflation and final kissing balloon was performed in all cases. Final IVUS evaluation was done in 30 (35,3%) Angiographic success was obtained in 83 (98%). There were 4 cases (4,7%) of complications related to the procedure and one case of subacute stent thrombosis (1,2%). Eighty two (97%) and 75 (88,%) patients were free of any other cardiovascular events at 1 and at 6 month of clinical follow-up, respectively.
Conclusions: Mini-crush Stent Technique with minimal stent overlap. High pressure inflation of the stent brach and systematic final kissing balloon appears like a good approach to treat complex bifurcated coronary lesions, with good results at mid term clinical follow-up and could be a valid alternative to provisional stenting in very complex bifurcated lesions with diffuse brach disease.

P1305 Evaluation of a dedicated coronary bifurcation stent: a matched pair analysis with drug-eluting and bare metal stents

P.W. Radke[1], D. Jain[2], A. Conrad[2], C. Thomsen[2], V. Kurowski[2], H. Schunkert[2], F. Hartmann[2]. *[1]University Hospital Schleswig Holstein, Cardiology Department, Luebeck, Germany; [2]University Hospital Schleswig-Holstein, Luebeck, Germany*

Purpose: The optimal approach for the treatment of coronary bifurcation lesions (CBL) remains under debate. Aim of this study was to evaluate a novel dedicated stent system (FRONTIER stent, FS) and to compare angiographic and clinical results of the FS with drug-eluting (DES) and bare metal stents (BMS) using the provisional stenting (PS) technique.
Methods: 32 CBL lesions were treated with the FRONTIER system. The control group of 64 CBL lesions (32 DES, 32 BMS) was pair matched with the former group stratified by the type of CBL and the main branch (MB) reference diameter. Clincial, procedural and quantitative angiographic data (QCA) were obtained in all patients. A follow-up angiography 6±2 month post index intervention was performed in 70/96 (73%) patients. The rate of major adverse cardiac events (MACE; defined by death, myocardial infarction, target vessel revascularisation) was obtained within the first 6 month post index intervention.
Results: QCA analysis and procedural data are provided in the Table. DES use was associated with the lowest late lumen loss in the MB and the side branch. The MACE rate was 9% (FS), 6% (DES), and 16% (BMS), respectively.

	FS (n=32)	DES (n=32)	BMS (n=32)
MLD MB pre (mm)	0.64±0.44	0.61±0.41	0.56±0.52
MLD MB post (mm)	2.11±0.50	2.05±0.50	2.02±0.51
MLD MB FU (mm)	1.53±0.68	2.00±0.39*	1.59±0.68
MLD SB pre (mm)	0.62±0.53	0.57±0.36	0.46±0.36
MLD SB post (mm)	1.62±0.45	1.44±0.38	1.66±0.57
MLD SB FU (mm)	1.17±0.46	1.41±0.39+	1.28±0.90
Duration (min.)	89±43	77±31	76±30
Contrast agent (ml)	237±108	252±100	256±121
DSP (cGy/cm^2)	5140±3847	6192±5048	6401±4097

DSP: dose surface product, MB: main branch, MLD: minimal lumen diameter, SB: side branch, *: p$<$0.01 compared to FS and BMS, +p$<$0.05 compared to FS.

Conclusions: The FS accomplishes treatment of CBL with excellent acute clinical and angiographic results. Furthermore, patient contrast and radiation exposure is comparable with conventional techniques. PS using DES provides superior clinical and angiographic long-term results as compared to BMS and FS. Next generation CBL systems will combine a dedicated specific CBL design with drug-eluting stent surfaces.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1306 Interventional cardiac three dimensional software (IC3D) for determination the individual optimal projection view in coronary bifurcations

C. Schlundt[1], S. Achenbach[1], M. Schneider[1], J.G. Kreft[2], L. Klinghammer[2], W.G. Daniel[2], J. Ludwig[2]. *[1]University Erlangen-Nuremberg, Medical Clinic Ii, Erlangen, Germany; [2]Siemens Medical Solutions, Forchheim, Germany*

Background: Interventional treatment of coronary bifurcations is technically challenging. Not only anatomic parameters (diameter of the main and the side branch, bifurcation angle) of coronary bifurcations, but also the optimal projection views perpendicular on the bifurcation (without vessel foreshortening or overlapping) are important.
Methods: Online reconstruction of coronary bifurcations with IC3D provides the quantitative parameters of the main and the side branch, the bifurcation angle and the individual optimal projection view, which allows a perpendicular view on the bifurcation. We reconstructed 400 coronary bifurcations (n=100 patients) to determine the optimal projection view and the possibility to reach this position in the cathlab. The limitations of possible positions were defined for cranial/caudal angulation with ±45°, for LAO/RAO with ±125°.
Results: The optimal projection for the left main and for LAD/diagonal was to realize in 59%. In 75% it was possible for the bifurcation CX/obtuse marginal, in 88% for the bifurcation RPLB/PDA (see figure). The case of impossible projection view was always caused by the limitation of cranial/caudal angulation.

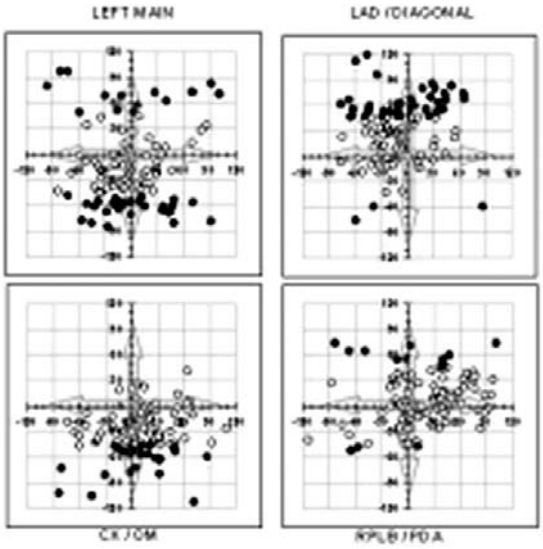


Figure 1. White spots = realizable angulation; black spots = not realizable angulation

Conclusion: The individual optimal projection view for coronary bifurcations in the cathlab is not possible in every patient. However, in case of realizable angulation IC3D could be a useful tool for determining the individual optimal projection view in treatment of coronary bifurcations.

P1307 Ostial versus crossover stenting with sirolimus-eluting stent for the treatment of ostial left anterior descending artery lesions

K. Kishi, H. Chen, S. Miyazaki, K. Mahara, R. Ogura, N. Suzuki, T. Takahashi, S. Hosokawa, R. Otani, Y. Hiasa. *Tokushima Red Cross Hospital, Cardiology, Komatsushima, Japan*

Background: Percutaneous coronary intervention in ostial lesions of left anterior descending artery (LAD) have higher restenosis rates and the risk of plaque shift to left circumflex artery (LCX). The aim of this study was to evaluate the clinical and angiographic outcomes of ostial versus crossover stenting with sirolimus-eluting stent (SES) for ostial LAD lesions.
Methods: From August 2004 to January 2006, 74 consecutive patients (pts) (62 men, mean age 69±9 years) with de novo ostial LAD lesions without ostial LCX narrowing were treated with single SES. Intravascular ultrasound was performed in all pts during the procedure.
Results: Thirty-six pts were treated with SES stenting at the ostial LAD without jeopardizing the ostial LCX, and 38 pts were treated with crossover SES stenting from distal left main trunk across the LCX with final kissing balloon dilatation. Baseline clinical and angiographic characteristics were comparable between the 2 groups. The use of debulking atherectomy prior to stenting was similar between the 2 groups (directional coronary atherectomy: 31% vs. 37%, rotablator: 14% vs. 16%). The mean post-intervention minimal lumen diameter (MLD) and reference diameter (RD) were significantly larger in the crossover group (MLD: 3.03±0.47 mm vs. 3.32±0.66 mm, $p<0.05$, RD: 3.45±0.40 mm vs. 3.72±0.51 mm, $p<0.05$). The mean 9-month follow-up MLD and RD were significantly larger in the crossover group (MLD: 2.56±0.67 mm vs. 2.86±0.55 mm, $p<0.05$, RD: 3.18±0.56 mm vs. 3.53±0.41 mm, $p<0.05$). One acute thrombosis occurred in the crossover group (2.6%). Although the 9-month angiographic restenosis rate was similar between the 2 groups (3% vs. 0%), the ostial LCX stenosis tended to occur more frequently in the ostial group (8% vs. 0%, p=0.07).
Conclusions: SES implantation for ostial LAD lesions, either ostial or crossover stenting, appears safe with low rates of restenosis. However, crossover stenting may be superior to ostial stenting in terms of avoiding the development of ostial LCX stensosis during follow-up period

P1308 Percutaneous treatment of unprotected left main coronary stenoses with paclitaxel-eluting stents. Mid-term results of a french prospective multicenter study: the Friend Registry

D. Carrie[1], H. Eltchaninoff[2], T.H. Lefevre[3], M. Silvestri[4], G. Levy[5], E. Maupas[6], P. Brunel[7], B. Glatt[8], D. Blanchard[9]. *[1]CHU Rangueil, Cardiologie B, Toulouse, France; [2]Hopital Charles Nicolle, Cardiologie, Rouen, France; [3]Hopital Jacques Cartier, Angiologie, Massy, France; [4]Clinique Parc Rambot, Cardiology, Aix En Provence, France; [5]Clinique Clemenville, Cardiology, Montpellier, France; [6]Clinique des Franciscains, Cardiology, Nimes, France; [7]Nouvelles cliniques nantaises, Cardiology, Nantes, France; [8]centre Cardiologique du Nord, Saint-Denis, France; [9]Clinique Saint Gatien, Cardiology, Tours, France*

Purpose of the study: Percutaneous treatment of unprotected left main coronary artery (ULMCA) disease is progressively gaining acceptance in light of the first results from drug-eluting stent registries. In this regard, the majority of data comes from single center studies. We thus assessed early and mid-term results of patients treated for ULMCA disease in the multicenter FRIEND registry.
Methods: After ethical committee approval and informed consent, all consecutive patients with unprotected left main stenoses treated with Taxus stents were included in a multicenter prospective study (23 centers). Major adverse cardiac events (MACE): death, myocardial infarction, target lesion (TLR), target vessel revascularisation (TVR), acute, sub-acute and late stent thrombosis were adjudicated at 1 and 6 months by an independent committee. Immediate and 9-month angiographic results were assessed by a central core lab (Corysis, St-Denis, France). For the distal lesion of ULMCA, a strategy of main branch stenting with provisional T-stenting of the side branch followed by kissing balloon inflation was strongly recomanded.
Results: From December 2005 to July 2006, 154 Pts were included, mean age 68±11 years, 83% male, 31% unstable angina, 25% diabetics, 46% 3-vessel disease. The mean Euroscore was 4.2±2.8 (estimated in-hospital mortality rate after surgery 4.1%). The LM reference diameter was 3.6± 0.5mm. LM lesion was ostial-proximal in 28%, mid shaft 18% and distal 66%. In this group, 72% were located at the bifurcation including LAD, LCX or both ostia affected. All patients were successfully treated on the LM (stent length 15.7+5.2mm) and a final kissing balloon inflation was performed in 90%. Apart from the LM stenosis, a total of 1.2+0.8 lesions were treated during the hospitalisation (total stent length 47±16mm). An intra-aortic balloon pump was used prophylactically in 1.3% and glycoprotein IIbIIIa inhibitors in 10.8%. In-hospital MACE rate was 4.5%: death in 2.6% (3 acute stent thrombosis at day 2, 3 and 5 and 1 before PCI); 2 Pts had asymptomatic non-Q-wave MI, 1 pt Q-wave MI and 1 CABG. At 1-month follow-up (150 pts) there was no death.
Conclusion: ULMCA PCI using the TAXUS stent is feasible and safe in a multicenter study. Preliminary results showed favourable 1-month follow-up with a total death rate of 2.6%. Adjudicated clinical and angiographic follow-up at 9 month will be available at the meeting.

P1309 Long-term outcome in patients with left-main coronary disease treated with drug-eluting stents

J. Suarez De Lezo[1], A. Medina[2], M. Pan[2], M. Romero[2], E. Hernandez[1], C. Amador[1], A. Delgado[1], J. Segura[2], S. Ojeda[2], D.J. Pavlovic[2]. *[1]Reina Sofia Hospital, Cardiology, Cordoba, Spain; [2]Dr. Negrin Hospital, Cardiology, Las Palmas, Spain*

Purpose: The treatment of left main (LM) coronary disease with drug-eluting stents (DES) is becoming a promising alternative to surgery. However, there is little information on long-term safety and efficacy. This study analyzes the long-term evolution of a consecutive series of patients with LM disease treated with DES.
Methods: From May/02 to January/07 269 patients treated with DES for unprotected LM-disease were included in the CORPAL registry. The mean age at treatment was 64±11 years; 202 were male (75%). Clinical presentation was unstable angina in 236 (88%) and stable angina in 33 (12%); 98 patients (36%) were diabetic. At cardiac catheterization, the ejection fraction (EF) was 58±13%. Lesions at the LM were located at the ostium or body in 58 (22%) and at the bifurcation in 211 (78%). In 81 patients (30%), LM treatment was performed under intracoronary ultrasound guidance (IVUS); 155 patients (58%) required additional stent treatment for remote lesions in the coronary tree. In most patients with bifurcational involvement (194; 92%), the LM was treated with a single DES oriented towards the left anterior descending artery; balloon dilation of the circumflex origin was required in 128 (48%) and T-stenting in 17 (6%). The mean final stent diameter at the LM was 3.3±0.4 mm.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Results: Primary success was obtained in 256 patients (95%). Major adverse cardiac event (MACE) were observed at one moth in 13 patients (5%) (6 died, 7 had acute myocardial infarction (AMI)). After a mean follow-up of 2±1 years, late-onset LM-related MACE was recorded in 34/254 patients (13%). Target lesion revascularization was required in 23 patients (9%); 4 patients (2%) had an AMI; 7 patients died (3%). Causes of death were cardiac 7 (3%) (4 sudden death, 1 heart failure and 2 AMI); non-cardiac 8 (3%) (3 cancer) and 1 of unknown cause (0.4%). Factors influencing late MACE were investigated. A smaller LM diameter (3.51±0.4 vs 3.66± 0.4 mm; p< 0.05) and a lower minimal lumen diameter post treatment (3.14 ±0.4 vs 3.30±0.4 mm; p< 0.05) were associated with the appearance of late MACE.
Conclusions: DES for LM-disease is a safe and efficient treatment, with a low rate of late complications.

P1310 Treatment of distal LMS bifurcation lesions with drug eluting stents. One stent or two?

H. Routledge[1], M.C. Morice[1], P. Garot[2], O. Tavolaro[2], Y. Louvard[1], P. Dumas[1], T. Unterseeh[2], T. Lefevre[1]. *[1]Icps, Massy, France; [2]Icps, Quincy, France*

Purpose: In treatment of distal left main (LM) bifurcation lesions, whether a simple single stent strategy is equivalent in terms of angiographic success and mid-term results to a more complex two stent approach remains to be determined. We sought to determine whether use of a second stent predicts outcome in the treatment of LM bifurcation lesions with drug eluting stents (DES).
Methods: The study population comprised 151 consecutive patients in whom a LM bifurcation lesion was treated using one or more DES. In this single centre prospective registry the predominant strategy is provisional T stenting. Decisions regarding SB stenting were those of the individual operator. Clinical outcome was documented by patient contact at 6 and 12 months, with recommended angiographic follow-up and clinically driven TVR.
Results see Table 1:

Table 1

	Single Stent (n-=88)	Stents both branches (n=63)	P value
True Bifurcation*	70%	79%	NS
Provisional T strategy	100%	83%	NS
Final Kissing inflation	97%	97%	NS
Angiographic success	100%	100%	NS
Procedure time (mins)	66	70	NS
NQWMI (CK 2 x ULN)	1.1%	4.8%	NS
6 Month TVR	2.4%	8.2%	NS
6 Month Death	4.5%	4.8%	NS
6 Month MACE	8.2%	19.7%	0.058
12 Month TVR	6.2%	12.1%	NS
12 Month Death	8.0%	6.9%	NS
12 Month MACE	14.5%	25.4%	P=0.13

*Medina types 1,1,1; 0,1,1. **At 6 months data are shown for all patients and at 12 months for 91%. Complete follow-up data will be available for presentation.

Conclusion: In patients treated for LM bifurcation lesions with DES there is a trend towards lower 6-month and 1-year MACE rate with the use of a single stent approach. This requires further investigation in randomised studies.

P1311 Is the stent type an independent predictor of mortality after percutaneous intervention on unprotected left main coronary artery?

A.E. Alahmar[1], E.B. Roberts[2], M. Andron[2], K. Bashir[2], M. Nafatti[2], R. Moore[2], M. Egred[2], J.L. Morris[2], R.H. Stables[2], R.A. Perry[2]. *[1]Liverpool, United Kingdom; [2]Cardiothoracic Centre Liverpool, Liverpool, United Kingdom*

Background: the incidence of cardiac death following percutaneous coronary intervention of de novo lesion in unprotected left main coronary artery (ULMCA) remains relatively high. The safety of drug-eluting stent (DES) use in this group is uncertain. Aim: to assess the impact of stent type (DES vs bare-metal BMS) implantation on cardiac death following percutaneous coronary intervention of ULMCA.
Methods: We analysed all patients (total number 77) who were treated with percutaneous intervention for de novo lesions in ULMCA in our centre between January 2001 and December 2005. The two indications for percutaneous interventions were patients' refusal of surgery, or patients' preference. We have excluded the 7 patients who presented in cardiogenic shock. Out of the 70 patients included in this analysis, 39 were elective and 31 were acute presented with non ST elevation myocardial infarction. There were 33 males and 37 females. 17 patients were diabetics, 39 were hypertensive, and 40 were smokers. Seven patients had left ventricle ejection fraction (LVEF) of <35%. Lesions were located at the ostium of the left main coronary artery in 11(16%) patients, at the body in 13(18%), and at the distal bifurcation in 46 (66%). Median reference vessel diameter was 3.5 (IQR 3.37- 4.0). All patients were treated with stent implantation, 17 with Cypher, 21 with Taxus, and 32 with bare metal stents (BMS). During hospitalisation 2 patients died of myocardial infarctions. Mean follow-up was 605±319 days, during which 10 cardiac deaths occurred. Cox proportional hazards model with the use of the stepwise procedure was used to assess the correlates of cardiac death among multiple clinical (age, sex, presence of diabetes), procedural (acute or elective), and angiographic (lesion location, LVEF, DES or BMS) variables. The two independent predictors of cardiac death were the use of BMS (odds ratio 3.67; 95% CI 1.04-12.69; P=0.043), and LVEF<35% (odds ratio 10.62; 95% CI 2.65-42.54; P=0.001).
Conclusion: In our series, the choice of stent had a significant impact on long-term mortality following percutaneous coronary intervention of ULMCA; BMS implantation was a significant predictor.

PERCUTANEOUS CORONARY INTERVENTION FOR COMPLEX LESIONS

P1312 Prognostic impact of percutaneous coronary intervention for total chronic occlusion of left anterior descending artery in DES era

A. Migliorini, R. Valenti, U. Signorini, R. Vergara, A. Corsini, G. Parodi, N. Carrabba, D. Antoniucci. *Careggi Hospital, Department of Cardiology, Florence, Italy*

Purpose: Registries studies have shown improved survival in patients treated with successful percutaneous coronary intervention (PCI) by balloon angioplasty or bare metal stenting for total chronic occlusion (CTO) as compared to patients with unsuccessful PCI. No data exist about the prognostic impact of successful PCI for left anterior descending artery (LAD) CTO treated with drug-eluting stent (DES).
Methods: The Florence DES Registry started on January 2003. From January 2003 to December 2006, 500 CTO (> 3 months) patients underwent PCI, and 138 patients had LAD CTO. The impact of successful PCI on survival was assessed by Kaplan-Meier log rank test and by forward stepwise multivariate Cox regression analysis.
Results: Successful PCI was achieved in 92 patients (67%). Out of the 138 patients, 55 (40%) patients were admitted for acute coronary syndrome and had multivessel PCI, being the target vessel other than the CTO vessel. In the remaining 83 patients (60%), all with stable clinical presentation, CTO was the culprit lesion. There were no significant differences in baseline clinical and angiographic characteristics between patients with successful and unsuccessful PCI: mean age 70 yrs ±11 yrs vs 70 yrs ±12 yrs; male sex 85% vs 83%; diabetes 26% vs 15%; previous myocardial infarction 54% vs 50%; multivessel disease 76% vs 80%; ejection fraction 41% ±14% vs 41% ±13%. All patients with successful recanalization received DES and most cases needed more than 1 stent (mean stent length 42±20 mm; mean number of total stent 1.8±0.8). Six out of the 46 patients with failed PCI underwent coronary artery by-pass grafting. No procedural death occurred or during hospital stay. Patients with successful PCI were scheduled for 6 month angiographic follow-up. The angiographic follow-up rate was 87%, and the patency rate was 94%. The clinical follow-up rate was 100% (median FU rate = 180 days, IQ range 180-380 days). Mortality rate was 8.7% in patients treated with successful PCI and 19.6% in patients with failed PCI (p=0.067). In the subset of patients aged < 75 yrs survival rate was significantly higher in patients treated with successful PCI (98% ±1% vs 74% ±8%; log rank test p < 0.001) and multivariate Cox analysis showed that successful LAD revascularization for CTO was an independent predictor of mortality in this subset of patients (HR 0.07, p=0.016).
Conclusion: DES provide a high mid-term patency rate in patients treated for LAD CTO. The mantainance of LAD patency may explain the dramatic improvement in survival as compared to patients with permanent LAD occlusion or treated by surgery.

P1313 Immediate and mid-term Outcomes of 100 consecutive chronic total occlusions (CTO) treated with the STAR technique

C. Godino, M. Carlino, A. Latib, A. Palloshi, E. Romagnoli, S. Furuichi, D. Tavano, R. Rogacka, A. Colombo. *San Raffaele Scientific Institute, Invasive Cardiology Unit, Milan, Italy*

Background: CTO remain one of the most challenging lesion subsets in interventional cardiology, despite the development of new medical devices and increasing operator expertise.
Objectives: To evaluate the safety and efficacy of the subintimal tracking and reentry (STAR) technique for CTO recanalisation.
Methods: We included all consecutive patients treated with the STAR technique, following failed attempts with conventional wires and/or devices for CTO during the same and/or prior procedure. The end points analysed were angiographic success (<30% residual stenosis and TIMI grade 3 flow), 6 month angiographic in-segment restenosis (stenosis >50% at QCA), and major adverse cardiac events (MACE), including death, myocardial infarction (MI) and target lesion revascularisation (TLR).
Results: One hundred patients were included, with 36 having had a previous failed attempt to recanalise the CTO. The morphology was blunt in 77, the length of the occlusion >20 mm in 67 and the right coronary artery was the index vessel in 75. Stenting was performed in 89 patients and drug-eluting stents (DES)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

were implanted in 65 of them. Angiographic success was obtained in 83 occlusions. Eighteen patients had an intraprocedural vessel perforation, 10 limiting procedure, 1 tamponade, but none resulting in emergency surgery or death. In-hospital non-Q wave myocardial infarction (MI) occurred in 12 patients. At angiographic follow-up, (6.2±4.1 months, mean ± SD, performed in 70 patients), the in-segment restenosis rate was 54% (38/70) and was significantly lower in DES patients 44% (22/50) vs. bare metal stent (BMS) 80% (16/20), $p<0.006$. The need for TLR was 37% (33/89), and it was significantly lower in DES 29% (19/65) vs. BMS 58% (14/24), $p<0.01$. At 6-month clinical follow-up there were no further MI, cardiac-death, or stent thrombosis.
Conclusion: These results confirm and support previous data of our group regarding this latest approach to recanalise difficult CTO. The STAR technique is feasible and relatively safe with acceptable rates of procedural major complications.

P1314 Angiographic and 3D intravascular ultrasound assessment of overlapping bare metal and drug-eluting stents in patients with diabetes mellitus

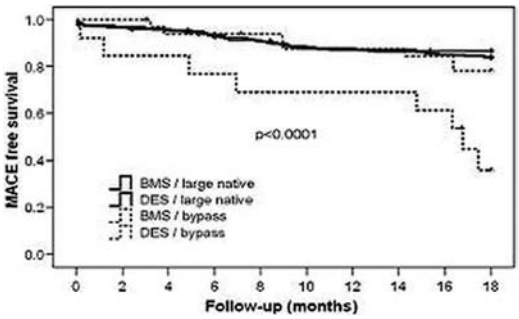
R. Kawaguchi[1], M. Sabate[2], D.J. Angiolollo[2], P. Jimenez-Quevedo[1], C. Corros[1], N. Suzuki[2], F. Alfonso[1], C. Macaya[1], T.A. Bass[2], M.A. Costa[2]. *[1]University of Florida, Cardiology, Jacksonville, United States of America; [2]San Carlos University Hospital, Madrid, Spain*

Purpose: Overlapping drug-eluting stents (DES) have been suggested to induce inflammation and fibrin deposition. Diabetes mellitus (DM) has been linked to enhanced proliferative response after stenting. Thus, we examined the impact of overlapping bare metal stents (BMS) and 3 different DES on vascular response of DM patients using 3D intravascular ultrasound (IVUS).
Methods: DIABETES I, II and III trials enrolled 320 DM patients with de novo lesions treated with BMS, sirolimus-eluting stent (SES), paclitaxel-eluting stent (PES), and tacrolimus-eluting stent (TES). There were 49 lesions with overlap (OL) of the same stent type: 19 BMS and 30 DES (SES: 12, PES: 8, TES: 10). Volumetric IVUS and quantitative coronary angiography (QCA) were performed post procedure (PO) and at 9-month follow-up (FU). The overall stent segment, the OL and non-OL subsegments were analyzed.
Results: The baseline demographics were similar in all stent groups. PO-QCA measurements were similar in all stent groups, and between OL and non-OL subsegments in each individual type of stents. Late loss was significantly higher in BMS group compared with SES and PES groups in both OL segments and non-OL subsegments. Binary restenosis was observed in 40% of BMS group, 0% of SES group, 14.3% of PES group and 50% of TES group ($p<0.05$). Follow up MLD segment was located in non -OL subsegment in 74.3% of the cases overall (BMS=66.7%, SES=77.8%, PES=85.7%, TES=75%). At FU-IVUS, %IH was significantly lower in SES and PES versus BMS in both OL and non-OL subsegments. TES and BMS showed similar %IH at OL and non-OL subsegments. %IH was greater in OL subsegment compared with non-OL in BMS (38.4±21.6 vs 25.2±10.1 $p<0.05$). No differences between %IH in the OL versus non-OL were observed in each DES group (SES= 0.9±1.9 vs 1.7±2.8, PES=18.2±17.9 vs 14.6±11.5, TES =4.2±15.2 vs 27.2±10.2). Mean vessel area in the OL and non-OL subsegments remained unchanged from PO to FU in all stent groups. There were no late malapposition or aneurysm formation developed in either DES or BMS groups. TLR was observed in 36.8% of the BMS group, 0% of the SES group, 10% of the PES group and 25% of the TES group. Stent thrombosis was not observed up to 1-year follow-up in this current study.
Conclusions: Overlapping BMS is associated with enhanced IH response in DM patients, whereas overlapping DES, particularly SES and PES, appear effective to inhibit IH without detectable late vascular adverse effects.

P1315 Drug-eluting stents compared with bare metal stents improve late outcome after saphenous venous bypass graft but not native large vessel interventions

R. Jeger[1], C. Kaiser[2], H.P. Brunner-La Rocca[2], P. Bonetti[3], P. Buser[3], M. Pfisterer[3] on behalf of BASKET Investigators. *[1]Heart Center, Department of Cardiology, Leipzig, Germany; [2]University Hospital, Department of Cardiology, Basel, Switzerland; [3]Kantonsspital Graubuenden, Department of Cardiology, Chur, Switzerland*

Purpose: To assess the impact of drug-eluting stents (DES) vs. bare metal stents (BMS) on long-term outcome in saphenous venous bypass graft (SVG) compared with native large vessel interventions.
Methods: Using the Basel Stent Kosten Effektivitäts Trial (BASKET) database, the efficacy of two different DES vs. a BMS in reducing major adverse cardiac events (MACE), i.e., cardiac death, myocardial infarction (MI), and symptom-driven target-vessel revascularization (TVR) after SVG vs. native large vessel (≥3.0 mm) interventions was assessed after 18 months.
Results: Large vessel interventions were performed in 605 patients, of whom SVG interventions in 47 (8%) and native large vessel interventions in 558 (92%). Patients with SVG interventions were older, had more hypertension, prior MI, prior revascularization, multi-vessel disease, and more chronic angina but less ST-elevation MI as reason for the intervention than patients with native large vessel interventions. Number of stents used and stent length was higher in SVG than native large vessel interventions. Baseline characteristics were not different for DES and BMS within the two groups. In patients with SVG disease, 18 month-outcome was better in DES- than BMS-treated patients (MACE 21% vs. 62%, p=0.007, mainly due to TVR 18% vs. 46%, p=0.045), whereas in patients with native large vessel interventions MACE was similar (16% vs.13%, p=0.40; see Figure).



Conclusions: Among patients with SVG disease, treatment with DES resulted in a better long-term outcome regarding clinical endpoints than treatment with BMS reducing MACE rates to the level of native vessels. In contrast, no DES benefit was found in similarly sized native vessels.

P1316 Intravascular ultrasound analysis for the neoinitmal formation after the overlapping sirolimus eluting stent implantation

A. Miyazawa, K. Kozuma, H. Kyono, G. Endo, K. Yamakawa, Y. Kawamura, N. Shiratori, T. Issiki. *Teikyo University, Division of Cardiology, Tokyo, Japan*

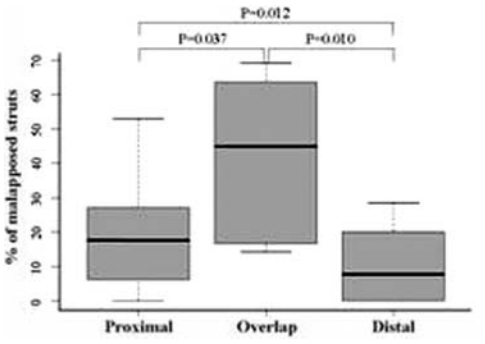
Background and Purpos: Overlapping drug-eluting stents potentially affect the neointimal formation; however their possible effect on the neointima characteristics has not been fully elucidated. The purpose of this study was to investigate the neointimal characteristics after overlapping sirolimus-eluting stents (SES) using intravascular ultrasound (IVUS).
Methods: Twenty-eight patients who received overlapping SES (36 overlapping segments and 64 non-overlapping segments) were available for 8-month follow-up volumetric IVUS analysis. Stent overlap was identified by double layers of stent struts. Using Simpson's method, neoinitma volume was calculated. The volume index was obtained by dividing volume by segment length. In each segment, the length of stent that contains IVUS-detectable neointima was determined to investigate neointimal formation on the overlapping and non-overlapping segment. Ratio of stent length with IVUS-detectable neoinitma to the segment length was calculated.
Result: Mean length of overlapping and non-overlapping segment was 5.78±3.40 and 16.58±7.81mm respectively. The difference of neointima volume index between overlapping and non-overlapping segment was not significant. (overlapping vs. non-overlapping; 0.46±0.61 vs. 0.28±0.41mm^3/mm, P=0.22) However, ratio of stent length with neoinitma was greater within overlapping segment than within non-overlapping segment (overlapping vs. non-overlapping; 30.57±0.61 vs. 51.54±38.71%, $P<0.01$).
Conclusion: the current IVUS study may suggest that overlapping segment might have higher chance of neointima formation compared to non-overlapping segment.

P1317 Strut malapposition in overlapping drug-eluting stents by optical coherence tomography

J. Tanigawa[1], P. Barlis[2], K. Dimopoulos[1], M. Dalby[1], P. Moore[1], C. Di Mario[1]. *[1]Osaka Medical College, First Department of Internal Medicine, Takatsuki, Japan; [2]Royal Brompton Hospital, London, United Kingdom*

Purpose: The technique of overlapping drug-eluting stents (DES) is frequently used to cover long diseased segments or as a bailout for edge dissection or incomplete lesion coverage. It is known that strut malapposition is associated with poor intimal coverage following DES implantation and this may increase the risk of late stent thrombosis. Overlap stenting is rather an empirical technique that raises concerns related to the area with double struts hence also contributing to possible malapposition.
Methods: We investigated stent strut malapposition of 20 DES with 10 overlapping segments in 10 coronary lesions with DES immediately after implantation using Optical coherence tomography (OCT). Stent strut malapposition was defined as a strut with no contact to the intima. A total of 661 struts were evaluated.
Results: Despite aggressive stent optimization using balloons with a final balloon/artery ratio of 1.26±0.18 at a maximum inflation pressure of 18.0±1.9atm, 41.8±21.5% of struts were malapposed at the overlapped segment. This was compared to 20.1±17.6% in the proximal and 9.7±10.6% in the distal stented segment ($p<0.05$).

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020



Percentage of malapposed struts

Conclusions: OCT revealed that almost half the struts at overlapping stent segments were malapposed. This may explain the reason behind delayed endothelialization of overlapping stents. Larger studies are needed to confirm this finding.

P1318 Clinical outcomes of sirolimus-eluting stents (SES) versus paclitaxel-eluting stents (PES) in long lesions

M.A. Sadaka[1], A. Zuffi[2], B. Farah[2], J.C. Laborde[2], J. Fajadet[2]. *[1]Clininque Pasteur, Unit of Interventional Cardiology, Toulouse, France; [2]Clinique Pasteur, Unite de Cardiologie Interventionnelle, Toulouse, France*

Background: Numerous trials have demonstrated that the SES and the PES are much more effective than bare-metal stents in preventing restenosis. In contrast, evidence on the relative performance of the SES and PES has just begun to accrue.Recently, several randomized studies addressed the issue ofthe potential global differences in performance between the 2 drug-elutingstents. In this study, we focus on the different clinical outcomes of the two the stents in the long lesion.AIM:- In the present study, we compared the long term clinical outcome of SES versus PES in long lesions.MEHTODS: The present study included 300 patients with long lesions more than 20 mm. PCI was performed according to standard techniques via femoral or radial approaches using either SES or PES. DES type selection either SES or PES was decided according to the stents availability in the cath lab. While direct stenting or pre-dilatation was dependent on lesion characteristics. The clinical follow-up period was 328 127 days for major adverse cardiac events MACE {death, non-fatal myocardial infarction and target vessel revascularization TVR}.
Results: SES were used in 179 patients (59.67%) while PES were used in 121 patients (40.33%) (p=0.11). The total number of DES utilized was 528 stent, 391 SES (74.05%) and 137 PES (25.95%) (p=0.021). The total number of treated long lesions was 346 lesions, 200 lesions treated with SES (57.8%) versus 146 lesions treated with PES (42.2%) (p=0.46). There was no statistical difference between SES and PES as regard the rate of subacute stent thrombosis (0.56% in SES group vs. 0.83% in PES group; p=0.68). In terms of mid to long term overall MACE, there was no statistical difference between SES group and PES group (13.15% in SES group versus 12.56% in PES group; p=0.82). Also there was no statistical significant difference between the group of SES and the group of PES as regard the mortality (1.71% vs.1.75%; p=0.89), non-fatal myocardial infarction (9.14% vs. 9.65%; p=0.82) and the TVR (1.71% vs. 1.75%; p=0.89).
Conclusion: The present study showed no difference between SES and PES in treatment of long lesions (whether in diabetic or non-diabetic patients) as regard the short and long terms clinical outcomes.

P1319 Long-term follow-up after drug-eluting stents for the treatment of long-diffuse coronary stenoses

F. Mazuelos[1], J. Suarez De Lezo[1], A. Medina[2], M. Pan[2], M. Romero[2], J. Segura[2], F. Esteban[2], A. Delgado[1], A. Rodriguez-Almodovar[2], S. Ojeda[2]. *[1]Reina Sofia Hospital, Cardiology, Cordoba, Spain; [2]Dr. Negrin Hospital, Cardiology, Las Palmas, Spain*

Purpose: Drug-eluting stents (DES) have been shown to reduce restenosis rate. The purpose of this study was to describe the clinical and angiographic follow-up in a large series of patients with long coronary lesions treated with DES
Methods: Between May 2002 and May 2006, 672 consecutive patients (74% male) having 755 diffuse coronary lesions (length >20mm) were treated with DES. The mean age was 65±10,4. Patients presented with previous myocardial infarction (26%), diabetes mellitus (42%) and unstable angina (85%); 58% had a multivessel disease. The mean lesion length was 30.31± 10. Among lesions, 18% were chronic total occlusions, 11% were restenosis and 14% calcified lesions. The mean reference diameter was 3.0±0.3 mm and minimal lumen diameter (MLD) was 0.64±0.5 and the percentage stenosis was 79±14%. MLD post treatment was 2.67±0.4 mm and the percentage stenosis was 10±0.4%. Sirolimus eluting stents were used in 68% of the patients, paclitaxel eluting stents in 25% and tacrolimus eluting stents in 7%. Forty five percent of lesions were treated with a single long stent, 43% with multiple overlapped stents and 12% with multiple nonoverlapped stents.
Results: The procedural success rate was 97.5%. Late angiography was performed in 421 cases (56%), in a mean follow-up time of 7 months. MLD at follow up was 2.04±0.8 mm. Angiographic late loss was 0.63±0.6.The incidence of binary restenosis per lesion was 23%. The major adverse cardiac outcomes are show in the table. The mean follow up time was 26±15 months.
The incidence of angiographic stent thrombosis was 1% (8/755). Four cases (0.5%) occurred in the first month. The late (>1month) incidence of angiographic stent thrombosis was 0.5% (4/755).

Major adverse cardiac outcome

Major adverse cardiac outcome	1 month n=672	1 year follow up n=584	2 year follow up n=512	Cumulative rate
Target lesion revascularization	4 (1%)	49 (8.4%)	19 (3.7%)	72 (15%)
Myocardial infarction	15 (2%)	8 (1.4%)	6 (1.2%)	29 (5.3%)
Cardiac Death	6 (1%)	9 (1.5%)	6 (1.2%)	21 (4%)
Total major adverse cardiac event	17 (3%)	59 (10%)	25 (4.9%)	101 (20%)

Conclusions: DES apperar to provide long-term advantages over historical series of bare stents in long lesions. However, major adverse cardiac event rates are higher than these observed in other types of coronary lesion subsets.

P1320 Factors determining restenosis after drug eluting stents in complex coronary lesions

M. Romero[1], J. Suarez De Lezo[1], A. Medina[2], M. Pan[2], J. Segura[2], S. Ojeda[2], D.J. Pavlovic[2], P. Martin[1], C. Duran[2], A. Delgado[1]. *[1]Reina Sofia Hospital, Cardiology, Cordoba, Spain; [2]Dr. Negrin Hospital, Cardiology, Las Palmas, Spain*

Purpose: Drug eluting stents (DES) have reduced restenosis rate in high risk coronary lesions.This study examines the factors determining restenosis in patients (pts) with complex coronary lesions who were enrolled on the CORPAL trial and treated with DES.
Methods: From May/03 to November/04 we studied 646 pts with 870 coronary lesions randomly treated with Sirolimus (SES; n=446) or Paclitaxel-eluting stents (PES; n=424). At baseline, the complex coronary lesions included: bifurcation (n=298), chronic total occlusion (n=125), small vessel (n=192), in-stent restenosis (n=67) and long-diffuse stenosis (n=312). The mean age was 62±10 years; 496 pts were male (77%) and 230 were diabetic (36%); 490 pts underwent angiographic re-evaluation at 10±6 month follow-up (240 SES and 250 PES). All pts enrolled between May/03 and November/03 were scheduled for six-month angiographic re-evaluation (347 lesions). From December/03 to the end of the study, only pts with clinical recurrence were re-evaluated (143 lesions).
Results: 90 lesions developed restenosis (>50% stenosis) at follow-up (18%); target lesion revascularization was required in 77 lesions (9%). Our univariate analysis identified the following significant factors determining restenosis. Restenotic pts were older (64±11 vs 61± 10 years; p<0.05), with lower ejection fraction (57±13% vs 59± 12%; p< 0.1), lower minimal lumen diameter (MLD) after treatment (2.5 ±0.5 vs 2.7±0.4 mm; p< 0.05) while the percentage of post-procedure stenosis was higher (10±10 vs 8±8%; p<0.05). Stented length was also longer (31±16 vs 27±14 mm; p<0.05). Lastly, restenosis was more frequent in pts treated with PES (22% vs 15%; p<0.1). The table shows the significant independent predictors of restenosis in our multivariate analysis.

Multivariate analysis

	Exp (B)	95% C.I. for Exp (B)	p
Age	0.97	(0.94-0.99)	<0.1
MLD post	2.42	(1.35-4.33)	<0.01
Stented length	0.97	(0.96-0.99)	<0.01
Type of DES	1.8	(1.10-2.98)	<0.05

DES: Drug-eluting stentMLD: minimal lumen diameter.

Conclusions: Restenosis after DES is more frequent in older patients, longer stented segments, lower post-procedure MLD and in pts treated with PES.

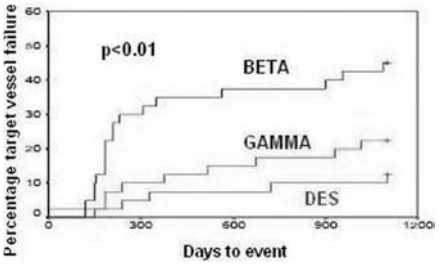
P1321 A randomized comparison of sirolimus eluting stent versus beta brachytherapy versus gamma brachytherapy in high-risk patients

H.M. Nathoe[1], P.R. Stella[2], P. Bouma[2], J. Battermann[2], P.P.T. De Jaegere[3], G. Pasterkamp[3], P.A.F.M. Doevendans[3]. *[1]University Medical Center Utrecht, Cardiology, Utrecht, Netherlands; [2]University Medical Center, Utrecht, Netherlands; [3]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands*

Purpose: PCI is the less invasive coronary revascularization procedure, but is hampered by the need of re-interventions. Drug eluting stents (DES) compared with bare metal stents significantly reduce the need for re-interventions. The benefit of DES over intra-coronary brachytherapy (BT) in high-risk patients, is not elucidated yet.
Methods: a total of 120 patients with re-stenosis after PCI and/or diabetes were randomized to DES (Sirolimis) or beta BT or gamma BT. BT was applied directly after a successful angioplasty procedure using a balloon based intra-coronary delivery system. The primary objective was freedom from target vessel failure at

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

3 years after the index treatment. Secondary objectives were angiographic (QCA) or intracoronary ultrasound (IVUS) outcomes at 6 months.
Results: 40 patients per group aged 60 years on average were included. Baseline characteristics were not different between DES, beta and gamma BT, except for diabetes (35 vs 45 vs 13%, respectively, p=0.06) and re-stenosis (90 vs 63 vs 66%, respectively, p< 0.01). Freedom from target vessel failure at 3 years was 90 vs 55 vs 77.5% in the DES, beta and gamma group (p<0.01). Binary re-stenosis (> 50% stenosis by QCA) was respectively 11 vs 12.5 vs 12.5% in each group. IVUS_derived lumen area in the DES, beta and gamma group was at the proximal treated site 6.4 vs 6.6 vs 5.7 mm^2, at the mid treated site 6.6 vs 7.1 vs 5.6 mm^2 and at the distal treated site 6.4 vs 6.5 vs 5.7 mm^2, respectively.



Conclusions: in high risk patients, the use of sirolimus eluting stents as compared with beta or gamma brachytherapy significantly reduced the need of coronary re-interventions at 3 years. However, no significant differences in angiographic restenosis or IVUS_derived lumen area were observed at 6 months.

P1322 Drug eluting stents reduce major adverse cardiac events in elderly patients in comparison with bare metal stent at long-term follow-up

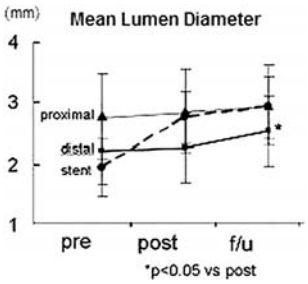
G. Falsini[1], F. Liistro[2], L. Bolognese[2], P. Angioli[2], K. Ducci[2]. *[1]Arezzo, Italy; [2]Ospedale San Donato, Cardiovascular Department, Arezzo, Italy*

Drug Eluting Stents reduce major adverse cardiac events in elderly patients in comparison with Bare Metal Stent at long –term follow-up.
Background: Although elderly patients constitute a fast-growing portion of cardiovascular patients, they are not adequately represented in current clinical trials on drug eluting stents.
Objective: to compare clinical outcomes of elderly patients undergoing percutanepus coronary interventions with drug eluting stents or bare metal stents.
Methods: We analyzed the data of 577 consecutive patients aged ≥ 75 years who underwent percutaneous coronary intervention (PCI) and stent implantation since May 2002. Patients with acute myocardial infarction were excluded. The choice of stent was under operator decision. Periprocedural and follow-up events were compared between patients treated with BMS (n = 427) and DES (n = 150). MACCE were defined as: cardiac death, re-AMI, coronary artery by-pass grafting, repeat coronary revascularization of the culprit lesion (TLR) and cerebrovascular events.
Results: 577 elderly were treated with PTCA and stenting of coronary artery; 427 patients were treated with BMS (BMS group) and 150 with DES (DES group). Average follow-up was 363+280 days for BMS group and 284+140 days for DES group. Basal clinical characteristics were similar between groups with the exception of previous PCI more frequent in DES group (10.4 vs 4.9%, p=0.036) and a trend of major multivessel coronary artery disease and smaller vessel in DES group. Cumulative MACCE, re-AMI and TLR occurred more frequently in BMS group vs DES group (MACCE: 22.0% vs 12.0%, p=0.017; re-AMI: 4.9% vs 0, p=0.011; TLR: 12.2% vs 5.6%, p=0.04). Early stent thrombosis (ST), late ST and very late ST occurred respectively in 7 (1.8%), 4 (1.2%) and 3 (0.9%) patients of BMS group vs 0, 0, 1 (0.8%) patients of DES group (p=ns). There were no difference on rate of stroke between group (0.9% vs 0.8%). At multivariate analysis predictors of MACCE were age (OR 3.1; CI 95% 0.63–4.2; p=0.018) and BMS use (OR 0.21; CI 95% 0.09–0.51; p=0.001); predictor of cardiac death was diabetes (OR 4.5; CI 95% 1.19-18.9; p=0.034) and predictor of TLR was BMS use (OR 0.165; CI 95% 0.37–0.74; p=0.018). Kaplan-Meyer analysis revealed a significant differences in cumulative event free-survival between the two groups (p=0.001).
Conclusions: The use of drug eluting stents to treat atherosclerotic de novo lesions in elderly patients reduce major adverse cardiac events at long term follow-up.

P1323 Impacts of intravascular ultrasound guidance on the accuracy of stent positioning and resultant peri-stent vascular responses: tips for optimal sirolimus-eluting stent implantation

K. Ikeno[1], Y. Morino[2], M. Nagaoka[2], Y. Ikari[2], T. Tanabe[2]. *[1]Tokai University Hachioji Hospital, Department of Cardiology, Hachioji, Japan; [2]Tokai University Hospital, Department of Cardiology, Isehara, Japan*

Purpose: Several studies have indicated that clinical outcomes of sirolimus-eluting stents (SES) are significantly associated with longitudinal positioning of stent relative to underlying plaque distribution. The purpose of this study was to investigate the actual impacts of intravascular ultrasound (IVUS) on the positioning of SES as well as to elucidate serial vascular responses under this meticulous approach.
Methods: Serial quantitative coronary angiography and IVUS assessment (pre-, post- intervention, and 8 month follow-up) were performed for the in-stent and peri-stnt margin segments (5mm outside of stent) of 63 patients implanted with SESs. %Residual plaque area of less than 50% was considered as an optimal target for the stent landing segments during procedure.
Results: %Residual plaque volume at proximal and distal margin was 41.6±10.7% and 38.3±10.5%, respectively. The target was achieved in 80% of proximal and 90% of distal margin. Under this condition, no deleterious lumen changes were observed in the in-stent and proximal margin segment from post-intervention to follow up (Figure). Furthermore, at distal margin, mean lumen diameter was significantly increased from post-intervention to follow-up (2.30±0.53 mm vs 2.57±0.53 mm, p<0.05) (Figure). Serial IVUS analysis indicated that positive remodeling contributed to the distal lumen enlargement.



Figure

Conclusions: 1) IVUS guidance allows accurate interpretation of axial and longitudinal plaque distribution, contributing to adequate stent positioning. 2) Under this condition, negative vascular responses are suppressed at the proximal margins and "positive edge effects" can be expected at the distal margin, mostly ascribable to positive vascular remodeling.

VASCULAR ACCESS FOR PERCUTANEOUS CORONARY INTERVENTION

P1324 Transradial access compared with femoral puncture closure devices in percutaneous coronary interventions: effect on quality of life and complications (the TARANTA study)

A. Sciahbasi[1], D. Fischetti[2], A. Picciolo[2], R. Patrizi[1], G. Colonna[2], F. Summaria[1], A. Montinaro[2], E. Lioy[1]. *[1]Policlinico Casilino, Roma, Italy; [2]Vito Fazzi Hospital, Lecce, Italy*

Purpose: Transradial access (RA) for cardiac catheterization (CC) is associated with lower complications and is often preferred by patients (pts). Vascular closure devices (VCD's) may reduce post-procedural bed rest and improve in-hospital quality of life. Aim of this study was to evaluate quality of life and major complications in pts who underwent CC with radial and femoral approach and with the use of different VCD's.
Methods: Since January 2006 we have enrolled 1,048 consecutive pts submitted to coronary angiography or angioplasty in two different hospitals. The procedures (proc) were performed according to the routine practice of the physician (Ph) using systematic RA (419 proc; 3 Ph), systematic femoral approach with manual compression (MC) (247 proc; 2 Ph), systematic femoral approach with either Angio-seal closure device (195 proc; 2 Ph) or with Starclose closure device (187 proc; 2 Ph). Pts with known vascular disease, ischemic Allen test, or emergency catheterization were excluded. Post-procedural quality of life was assessed in all pts by an ad hoc questionnaire using 0 to 10 visual analog scales. Major complications (vascular death, surgical interventions at the puncture site, major bleeding requiring blood transfusions, stroke or transient ischemic attack) were evaluated during hospitalization.
Results: There were no significant differences between groups for age (Table), sex and body mass index. VCD's and RA were better tolerated than MC (Table) without significant differences between RA and VCD's (Table). However vascular

Table

	MC	Radial	VCD's	P
Age	67,6±10,5	66,83±11,04	66,95±10,3	NS
Discomfort to urinate	1,79±3,3	0,59±1,9	0,74±1,39*	<0,0001
Discomfort to feed	1,46±2,82	0,4±1,6	0,48±1,1*	<0,0001
Pain (vascular compression)	3,5±3,5	1,2±2,4	1,5±1,7*	<0,0001
Global discomfort	2,72±1,9	1±1,2	1,2±1,2*	<0,0001
Complications (n; %)	6 (2,4%)	2 (0,5%)	10 (2,6%)**	<0,02

*p= NS vs RA; **p= NS vs MC.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

complications were significantly reduced by RA. There were no significant differences in complications between MC and VCD's (Table).
Conclusions: VCD's are as well tolerated as RA and both are better accepted than MC. However RA is associated with a significant reduction in vascular complications compared to VCD's and MC.

P1325 Multicenter, randomized clinical trial of the FISH device: a novel closure device and procedure sheath

A.R. Kamdar[1], R. Raymond[1], J. Hermiller[2]. *[1]Cleveland Clinic Foundation, Cleveland, United States of America; [2]St. Vincent Hospital, Cardiovascular Medicine, Indianapolis, United States of America*

Purpose: A number of currently marketed femoral artery closure devices are available to shorten times to hemostasis and ambulation. The Femoral Introducer Sheath and Hemostasis (FISH) device allows closure material to be placed at the vascular access site via initial sheath introduction. This provides femoral arterial access and closure in a single device comprised of a bioresorbable, hemostatic patch pre-mounted on a customized sheath. Sheath removal and closure device deployment can be completed outside the catheterization lab, improving patient flow efficiency. This trial reports the results of a multi-center randomized trial comparing the FISH device to traditional manual compression (MC).
Methods: Eight investigational sites in the US enrolled 297 patients from January 2004 to June 2006 in an open-label, randomized study with a 2:1 ratio of FISH device (n=191) to MC (n=106). Diagnostic (n=206) and interventional (n=91) cases were performed utilizing FISH devices in sizes 5Fr, 6Fr, and 8Fr. Post-procedure, the FISH sheath was removed and hemostatic patch deployed across the arteriotomy. MC was applied as needed for confirmation of hemostasis (defined as absence of any bleeding at the site). Patients were followed for time to hemostasis (1° endpoint), time to ambulation, eligible discharge, and minor and major complications through a 30 day follow-up. Patients also provided a subjective rating on site comfort. Significance level was set at < 0.05.
Results: Median times to hemostasis for the FISH device vs MC were 6 and 17 minutes ($p<0.0001$) and median times to ambulation were 2.0 hours and 4.2 hours, respectively ($p<0.0001$). Median times to eligible discharge for the FISH device versus MC were 2.3 hours and 4.5 hours ($p<0.0001$). Major complications between the FISH and MC groups were not significantly different (0.7% versus 0%). The absolute difference consisted of one episode of bleeding requiring transfusion in the FISH group. Minor complications between the two groups were not significantly different (2.9% vs. 1.5%). There was one death during the course of the trial in the FISH group, unrelated to device use. Subjective patient ratings of site comfort were not significantly different. Four cases of device failure (2.1%) were reported.
Conclusions: These data suggest superior times to hemostasis and ambulation for the FISH device compared to MC with apparent equivalence in minor complications and patient comfort. Need for transfusion was noted in one FISH patient. Further study of this novel combined sheath and closure device compared to other closure devices may be helpful.

P1326 A comparison of collagen plug and suture based femoral closer devices

J. Cosgrave, A. Qasim, A. Latib, T.C. Aranzulla, G. Melzi, F. Airoldi, G.M. Sangiorgi, I. Michev, A. Colombo. *EMO Centro Cuore Columbus, Cardiology Dept, Milano, Italy*

Purpose: To perform a comparison of collagen-plug and suture-based arterial closure devices after percutaneous procedures.
Methods: From November 2004 till September 2005, we analysed patients undergoing diagnostic or interventional procedures with femoral closure devices either Angio-Seal or Closer S (Perclose). A single operator with a large experience with these devices, (utilizing them both more than 1000 times) performed all the femoral artery closure procedures. The end-point was the rate of acute failure of the closure device.
Results: 349 patients were included; 179 Closer S devices were implanted in 166 patients and 189 Angio-seal in 183 patients. 13 patients in the Closer group received bilateral devices compared with 6 in the Angioseal group. More patients in the closer group underwent percutaneous intervention and there was a concomitant higher use of heparin and IIbIIIa inhibitors. The acute failure rate of Closer S was significantly higher 18 cases (10.1%) compared with Angioseal 2 cases (1.1%) (p=0.0001). The overall rate of minor haematomas was similar 7.3% in Closer S and 9.5% in Angioseal p = 0.59. There were 2 major complications all in the Closer S group (2%):1 thrombotic femoral artery occlusion and 1 retroperitoneal haematoma not related to the closure device.
Conclusions: This is the first study, to our knowledge, to compare a collagen plug vs. a suture-based closure device. Of note all the procedures were performed by a single operator with a large experience with both devices, despite this the acute failure rate of Closer S was considerably higher than Angio-seal.

P1327 Protamine to reverse heparin is safe and allows rapid sheath removal after paclitaxel-eluting coronary stenting

M.L. Rossi, D. Zavalloni, G. Gasparini, G. Belli, M. Scatturin, P. Pagnotta, V. Lisignoli, P. Presbitero. *Istituto Clinico Humanitas, Division of Interventional Cardiology, Rozzano-Milano, Italy*

Background: Immediate post-procedural reversal of heparin with protamine can reduce groin complications and shorten bed rest and hospital stay after percutaneous coronary intervention (PCI) with bare-metal stents. No data are available with newer and possibly more thrombogenic paclitaxel-eluting stents (PES).
Aim: To assess safety of post-procedural protamine administration after successful coronary PES implantation.
Methods: A recent consecutive series of 350 patients received 0,5 mg of protamine per 100 units of heparin whenever the post-procedural ACT was > 180 seconds, followed by immediate removal of the sheath. Outcomes were compared to an historic control group comprising 350 consecutive patients in the previous 6 months, also underwent PCI with PES but without reversal of anticoagulation by protamine. The incidence of acute, subacute and late stent thrombosis, as well as in-hospital vascular complication were compared.
Results: The 2 groups were well matched for clinical, angiographic and procedural characteristics. Results are summarised in the Table.

	Protamine Group (350)	Control (350)
Mean age	64±9	65±11
Male	82%	84%
Acute coronary syndromes (UA/AMI)	168 (48%)	161 (46%)
Postprocedural ACT (secs)	275±20	289±18
Stent length (mm)	18,1±7,2	17,8±9
Stent diameter (mm)	3,06±0,4	2,98±0,4
Acute stent thrombosis (<24 h)	0	2 (0,6%)
Subacute stent thrombosis (<30 days)	3 (0,8%)	4 (1%)
Late thrombosis (6 months)	2 (0,6%)	0
Pseudoaneurism/severe hematoma (n)	1/0	4/5
Hospital stay after procedure (min)	820±420	1225±235

Conclusion: Immediate heparin neutralisation by protamine after successful PES implantation does not predispose to stent thrombosis and appears safe and feasible also in ACS, reducing vascular complication, bed resting, delayed discharge and patients discomfort.

P1328 Comparison of operator radiation exposure during coronary angiography and interventions by left radial, right radial and femoral approach

H.-H. Minden, J. Meyhoefer, T. Ali, T. Schau, C. Butter. *Heart Center Bernau, Cardiology, Bernau, Germany*

Purpose: Radiation exposure to laboratory staff has been recognized as a considerable hazard in the cardiac cath-lab. It is determined by the dose-area product (DAP) and the type of procedure [coronary angiography (CA), percutaneous coronary intervention (PCI)]. Controversial data have been published on the amount of radiation exposure during cardiac catheterization via radial and femoral approach, respectively. The aim of the study was to accurately assess the radiation doses received by the operators dependent on the selected access site [left radial (LR); right radial (RR); femoral (F)].
Methods: X-ray exposure data were acquired from a consecutive series of 137 patients undergoing diagnostic and interventional studies (73 LR; 36 RR; 28 F). The procedures were performed by 3 experienced operators. Operator radiation exposure (ORE) was measured with an electronic radiation dosimeter attached to the lead apron. The ORE [Hp7 and Hp10 (μSv)] was determined at the end of each procedure. Moreover the fluoroscopy time and the DAP were recorded. In order to compare the radiation doses of the different approaches absolute values and the doses per minute fluoroscopy time were statistically examined.
Results: The fluoroscopy time and the DAP per minute fluoroscopy time depended on the procedure type, but not on the access site (P = NS). In contrast, the ORE was significantly higher when the procedure was performed from the RR artery (cumulative for all procedure types $p < 0.001$; CA $p < 0.05$; CA + PCI $p < 0.05$) as compared to LR and F access site. For all procedure types, ORE for LR and F approach were not statistically different. In addition it could be shown that the ORE was influenced by patient body mass index, but not by body height.

Operator radiation exposure (ORE): Hp7/m

	Femoral	Left radial	Right radial
CA	8,5±2,6	6,3±1,0	11,4±1,4
CA + PCI	3,4±1,4	3,0±0,6	8,1±0,8
PCI	2,5±0,8	3,7±1,0	6,3±1,4

Conclusion: CA and PCI can safely be performed using LR approach without an increase in radiation exposure to the operator as compared to femoral artery catheterization. The use of RR access site is burdened with a substantially higher ORE. Special devices for radiation protection should be developed for RR coronary procedures.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1329 Operator irradiation is significantly more important using radial route as compared to femoral route during coronary angiograms and ad-hoc percutaneous coronary interventions

C. Brasselet[1], T. Blanpain[1], S. Tassan-Mangina[1], A. Deschildre[1], S. Duval[1], G. Crepin[1], M. Gawron[1], N. Gaillot-Petit[2], J.P. Clement[2], D. Metz[1]. [1]Hopital Robert Debre, Chu, Departement De Cardiologie, Reims, France; [2]Unite de Radioprotection, CHU, Reims, France

Objectives: While underestimated by interventional cardiologists during a long time, irradiation of operators and patients during coronary angiograms (CA) and percutaneous coronary interventions (PCI) is currently a main concern. Femoral and radial routes are routinely used to perform CAs and PCIs. The objective of this operator-blinded registry was to compare related-peripheral arterial route irradiation of operators and patients.
Material and Methods: Four interventional cardiologists were screened during 423 consecutive procedures. Irradiation of operators and patients were assessed using an electronical personal dosimeter with silicon diode located on the left arm and a plate ionisation chamber (diamentor) on the digital apparatus of radiology, respectively. Protection of operator was ensured using lead apron, low leaded flaps and leaded glass (0.5 mm leaded-equivalent for each). Effective doses on electronical dosimeter (μSv), surface-doses delivered to patients (Gycm^2) and durations of procedures and fluoroscopy times (min) were recorded. Exclusion criteria were ACS with ST segment elevation, previous CABG or indication of right catheterism.
Results: Electronical dosimetry and passive dosimetry of operators assessed under the lead apron were insignificant. In contrast, irradiation of operator assessed on the left arm was significantly more important throughout radial route as compared to femoral route for CAs and CAs followed by ad-hoc PCIs: 42.2±42.8 μSv versus 23.1±28.7 μSv; p=0.0001 and 97.7±97.2 μSv versus 70.3±76.8 μSv; p=0.043, respectively. Similarly, irradiation of patients was significantly more important throughout radial route as compared to femoral route for both CAs and CAs followed by ad-hoc PCIs: 72.1±50.6 Gycm^2 versus 43.5±24.2 Gycm^2; p<0.0001 and 147.6±77.5 Gycm^2 versus 115.2±75.7 Gycm^2; p=0.006, respectively. Operator irradiation was related to procedural duration (radial: 17.1±9.6 min versus femoral: 11.1±6.0 min; p<0.0001 and radial: 44.0±18.9 min versus femoral: 38.6±17.0 min; p=0.048 for CAs and CAs followed by ad-hoc PCIs, respectively) and fluoroscopy time (radial: 5.4±4.7 min versus femoral: 2.3±2.0 min; p<0.0001 and radial: 11.1±6.2 min versus femoral: 7.7±4.8 min; p<0.0001 for CAs and CAs followed by ad-hoc PCIs, respectively).
Conclusions: While radial route decreases peripheral arterial complication rate, increased irradiation of operators throughout radial route is currently a growing problem, especially for the interventional cardiologist health concerns. Radial route indication should be promptly reconsidered in the light of the present findings.

PERCUTANEOUS CORONARY INTERVENTION FOR ST-ELEVATION MYOCARDIAL INFARCTION

P1330 Outcome of high risk patients with ST elevation myocardial infarction treated with primary PCI: importance of center experience

S. De Servi[1], R. Zanini[2], A. Politi[3], E. Bramucci[4], F. Barlocco[4], M. Onofri[5], A. Magalini[6], D. Vetturi[1], S. Klugmann[7] on behalf of LOMBARD-IMA Registry. [1]Ospedale Civile di Legnano, Cardiology, Legnano, Italy; [2]Mantova, Italy; [3]Como, Italy; [4]Pavia, Italy; [5]Busto Arsizio, Italy; [6]Brescia, Italy; [7]Milano, Italy

Background: The ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Interventions (PCI) state that PCI should be performed in STEMI pts in institutions that perform >36 primary PCI procedures per year. The TIMI Risk Index (TRI) is a simple metric using age, systolic blood pressure and heart rate to predict early mortality in patients (pts) with ST-elevation myocardial infarction (STEMI).
Methods: In a series of 1575 STEMI pts, stratified by TRI and treated with primary PCI in 30 centers over 1-year period, 30-day mortality was correlated with primary PCI centers volume.
Results: Pts in the top TRI quartile (score >32) had the highest 30-day mortality (11.7%) as compared to the other quartiles (mean 30-day mortality rate: 2,5%). Table 1 shows the 30-day mortality of the 394 pts included in the 4th quartile, using different cut-off numbers of primary PCI procedures performed in the various centers.

Table 1

Center volume (cut-off number of primary PCI procedures)	Mortality in centers performing < cut-off	Mortality in centers performing ≥ cut-off	P
36	14.8%	11.3%	0.20
50	15.6%	10%	0.04
60	15.3%	9.4%	0.02
70	13.8%	10.2%	0.11
80	13.8%	9.6%	0.06
100	13.7%	8.9%	0.04

Conclusions: The most significant difference in 30-day mortality in high risk STEMI pts was observed between centers performing more or less than 60 primary PCI procedures for year. This number should be considered the minimal center volume requirement to achieve an acceptable mortality in high-risk STEMI pts.

P1331 Local hypercoagulability after sirolimus-eluting stent implantation: implication for long-term endothelial dysfunction

K. Yamaguchi[1], T. Wakatsuki[2]. [1]The University of Tokushima Graduate School, Institute of Health Biosciences, Department O, Tokushima, Japan; [2]Tokushima, Japan

Purpose: Endothelial dysfunction is known to cause hypercoagulability. The long-term effects of sirolimus-eluting stent (SES) on endothelial function are not known. We evaluated endothelial function and local hypercoagulability more than six months following SES or bare metal stent (BMS) implantation.
Methods: Twenty-seven patients treated six months earlier with a coronary stenting for isolated proximal left anterior descending (LAD) stenosis, with no evidence of restenosis, were studied. Ten patients had been stented with BMS, and 17 had been with SES. Changes in diameter at distal site of the stented LAD in response to intracoronary acetylcholine infusions (30μg/min) were assessed by quantitative angiography. We also measured plasma levels of prothrombin fragment F1+2 (F1+2) and D-dimer sampled in coronary sinus (CS) and sinus of Valsalva (V).
Results: The mean percent change in the diameter of the stented LAD was significantly more in the SES group than in the BMS group (-34.6±6.7 vs. -20.2±6.2%, p<0.05). The translesional F1+2 gradient [F1+2(CS) minus F1+2(V)] and D-dimer gradient were greater in the SES group than in the BMS group (0.50±0.73 vs. -0.14±0.21 nmol/l, p<0.05 and 0.24±0.42 vs. -0.15±0.32μg/ml, p<0.05, respectively).
Conclusions: An increased local coagulative response and more severe endothelial dysfunction were observed long term after SES implantation as compared to BMS. In the SES group, delay of endothelial regrowth might be associated with our findings.

P1332 Reduction of distal embolization by means of thrombus aspiration prior to PCI in STEMI patients

K. Kozuma[1], K. Tanabe[2], H. Kyono[2], S. Sonoda[3], K. Hibi[4], Y. Shiratori[3], H. Yamamoto[2], A. Miyazawa[3], T. Isshiki[3] on behalf of VAMPIRE study investigators. [1]Teikyo University, Division of Cardiology, Tokyo, Japan; [2]Mitsui Memorial Hospital, Cardiology, Tokyo, Japan; [3]Itabashi Central Hospital, Cardiology, Tokyo, Japan; [4]Yokohama City University Hospital, Cardiology, Kanagawa, Japan

Purpose: It has been demonstrated that distal embolization was an adverse predictor for patients' prognosis after primary PCI in STEMI patients. This study was designed to clarify the timing of occurrence of embolization during primary PCI and to investigate the efficacy of up-front thrombus aspiration in reducing distal embolization as a subanalysis of the Vampire study (VAcuuM asPIration thrombus REmoval).
Methods: Patients were randomly assigned to primary PCI with or without thrombus aspiration. Patients with cardiogenic shock, left main disease, and renal failure were not included in the study. Distal embolization was assessed at each point of the procedure as follows; post GW insertion and/or TVAC crossing (point 1), after balloon dilatation (point 2), after stenting (point 3), and final angiogram (point 4). Cine angiograms were evaluated by independent experienced cardiologists.
Results: A total of 355 patients were enrolled in the study among 23 centers in Japan. Out of these patients, 343 cases had enough quality for the evaluation. There were no differences in clinical and angiographic characteristics between TVAC group (n=189) and the control group (n=180). Procedural success rates were 99% in both groups. Final TIMI-3 flow was not different between the two groups (84.8% in the TVAC group, 80.2% in the control group). Occurrences of distal emboli were significantly reduced in TVAC group (table). Balloon dilatation was the most critical point for the distal embolism in the control group (table).

Incidence of distal embolization

Time point	Th Asp (n=180)	Control (n=175)	P value
GW/TVAC insertion	22 (12.2%)	28 (16.0%)	0.19
POBA	20 (11.1%)	48 (27.4%)	<0.001
Stent	32 (17.8%)	53 (30.3%)	0.021
Final	29 (16.1%)	50 (28.6%)	0.018

Th Asp: Thrombus Aspiration, GW: guide wire, TVAC: Aspiration catheter, POBA: balloon dilatation.

Conclusions: Aspiration therapy prior to primary PCI would reduce the incidence of distal embolization, especially at the timing of balloon dilatation.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1333 Percutaneous treatment of unprotected left main in elderly patients with non ST elevation acute coronary syndrome: 1-year outcome of patients treated with bare metal vs drug eluting stents

F. Barlocco[1], T. Palmerini[2], I. Sheiban[3], G. Guagliumi[4], F. Liistro[5], A. Marzocchi[3], M. D'ubano[5], O. Valsecchi[2], S. De Servi[5]. *[1]Ospedale civile di Legnano, Cardiology, Legnano, Italy; [2]Bologna, Italy; [3]Torino, Italy; [4]Bergamo, Italy; [5]Arezzo, Italy*

Background: Elderly patients with unprotected left main coronary artery (ULMCA) stenosis represent a very high risk subset of patients with non ST elevation acute coronary syndrome (NSTE-ACS), frequently unsuitable for surgical revascularization.
Aims: To assess immediate and long term results in elderly (=> 75 years old) with NSTE-ACS undergoing PCI with drug-eluting stents (DES) or bare metal stents (BMS) for ULMCA disease.
Methods: Over the last 5 years, 167 elderly pts with NSTE-ACS and ULMCA disease were treated with PCI and DES or BMS in 5 centers. PCI was performed with DES or BMS in pts either deemed unsuitablefor surgery or for pts preference.
Results: Mean age was 81.6±4.2 years, 38% of pts were female. Diabetes, chronic renal failure and peripheral vascular disease were present in 27%, 21% and 34% of pts respectively. Multivessel coronary disease was found in 78% of pts and LV dysfunction in 56%. Angiographic success was obtained in 99% of pts. Stenting was performed in all cases, with DES used in 42% of them. Multivessel coronary revascularization was accomplished in 77% of pts. Eight pts died (5%) during the hospitalization. At a mean follow-up of 13.9±10.4 month, 29 pts died (19.8%) and 6 pts (4%) had non-fatal myocardial infarction (MI). Predictors of 30-day MACE (death + MI) in the multivariate forward stepwise logistic analysis and predictors of MACE from 30th day after PCI to end of follow up in the forward stepwise multivariate Cox proportional hazard regression model are show in table 1.

Table 1

Covariate adjusted	p	Hazard ratio (95% CI)
Renal dysfunction	0.018	4.96 (1.32-18.61)
Treatment of bifurcation	0.019	13.63 (1.55-119.9)
Left ventricular ejection fraction< 50%	0.011	15.95 (1.90-133.6)
Male gender	0.013	0.19 (0.05-0.71)
Predictors of MACE from 30th day after PCI to end of follow up		
Renal dysfunction	0.038	2.52 (1.05-6.03)
Non STE-MI	0.002	3.39 (1.56-7.40)
Use of DES	0.026	0.32 (0.12-0.87)

Conclusion: I n high risk elderly patients with NSTE-ACS, PCI of ULMCA disease is feasible with an acceptable mid-term outcome. Outcome after 1 month is improved by the use of DES.

P1334 Direct stenting after thrombus removal before primary angioplasty in acute myocardial infarction: a sub anaysis of the The DEAR-MI study

P.L. Silva Orrego[1], P. Colombo[1], R. Bigi[2], D. Gregori[3], R. Pirola[1], S. Klugmann[1]. *[1]Niguarda Hospital, Cardiology, Milan, Italy; [2]University of Milan, Medicine, Milan, Italy; [3]University of Turin, Public Health, Turin, Italy*

Purpose: To determine whether direct stenting, after thrombus removal during primary angioplasty (PPCI) in patients with ST-elevation acute myocardial infarction (STEMI) improves myocardial reperfusion and prevents distal embolization compared with conventional stent implantation.
Background: Thrombus removal and direct stenting in PPCI may reduce thrombus dislodgment and impaired microcirculatory reperfusion. The impact of direct stenting (DS) after thrombus removal in this clinical setting has not been investigated.
Methods: In the DEAR MI study, one-hundred-forty-eight consecutive STEMI patients, admitted within 12 hours of symptom onset and scheduled for PPCI were randomly assigned to PPCI or manual thrombus aspiration before standard PPCI. In this population, we compared myocardial reperfusion: complete (>70%) ST-segment resolution (STR) and myocardial blush grade (MBG) 3 and the rate of angiographic embolization in patients treated with (group 1) or without (group 2) DS. We also looked for interaction of DS with thrombus removal.
Results: Baseline clinical and angiographic characteristics were similar in the two groups. Comparing group 1 and 2, complete STR was 63% vs. 40% ($p<0.01$), MBG-3 82% vs. 40% ($p<0.0001$), TIMI flow 3 89% vs. 68% ($p<0.05$), corrected TIMI frame count 21.5+12 vs. 17.3+6 ($p<0.01$), no reflow 15% vs. 3% ($p<0.05$), and angiographic embolization 19% vs. 5% ($p<0.05$). The odds ratio of achieving MBG3 in group 1 vs group 2 was 0.25 (95% CI 0.06-1), whilst the odds ratio of distal embolization was 10 (95% CI 1.1-100). After adjusting for confounding factors, thrombus aspiration independently predicted complete STR (p=0.03), whilst both thrombus aspiration ($p<0.001$) and DS ($p<0.05$) independently predicted MBG-3.
Conclusions: Direct stenting in AMI diminished distal embolization and improves myocardial reperfusion. This effect is more significantly better after thrombus aspiration

P1335 The effect of post-dilation of the culprit lesion on the outcomes of patients undergoing primary percutaneous coronary intervention for acute myocardial infarction

D. Brosh, A. Assali, I. Teplitsky, I. Ben-Dor, Z. Iakobishvili, E. Lev, S. Fuchs, D. Hasdai, A. Battler, R. Kornowski. *Rabin Medical Center, Cardiology, Petach-Tikva, Israel*

Background: Percutaneous coronary intervention (PCI) of the culprit vessel is the preferred treatment in acute myocardial infarction (AMI). Because of the frequent presence of high thrombus burden in the culprit lesion in AMI, there is always a concern that post-dilation following stenting of the culprit lesion may cause distal embolization and consequently no-reflow, which may affect the outcomes.
Aim: To assess the effect of post-dilation of the culprit lesion in AMI on procedural success and outcomes.
Method and Results: We used our database of all pts undergoing primary PCI for AMI between 1/2001 and 6/2006. After excluding those with cardiogenic shock and late arrival (>12 hours), patients were allocated into 2 groups: no post-dilation of the culprit lesion (N= 577) and post-dilation of the culprit (N=205). The decision to perform post-dilation of the culprit lesion was left to the operator discretion.Patients clinical and angiographic characteristics are shown in Table 1:

	No Post-dilation (n=577)	Post-dilation (n=205)	P Value
Age (yrs)	60±13	60±13	0.6
Male	81%	82%	0.8
Initial TIMI Flow 0-1	65%	63%	0.2
Thrombus	87%	90%	0.4
Anti GP 2B/3A	80%	80%	1.0
DES use	13%	20%	0.02
Distal embolization	10.9%	12.3%	0.7
No-reflow (incl. Transient)	4.5%	8.4%	0.05
Final TIMI 3 Flow	98%	99%	0.9
6 Months outcomes			
Death	5.0%	3.5%	0.5
TVR/CABG	9.6/6.1%	9.8/4.1%	0.9/0.4
MACE	16.4%	15.9%	0.9

Conclusion: In this cohort of patients undergoing primary PCI for AMI, post-dilation of the culprit lesion did not improve long-term outcomes, but was associated with increased rate of transient no-reflow. It seems that post-dilation of the culprit lesion in AMI may compromise the coronary flow, and therefore it may not be justified if optimal angiographic result was obtained.

P1336 Analysis of intracoronary aspirate in primary coronary angioplasty. Predictors and implications

S. Mingo Santos[1], J. Goicolea[1], I. Sanchez-Vegazo[1], R. Ocaranza[2], J.A. Fernandez Diaz[2], J.R. Dominguez[2], J. Oteo[2], A. Garcia Touchard[2], P. Guemez[2], L. Alonso Pulpon[2]. *[1]Hospital Puerta de Hierro, Cardiology, Madrid, Spain; [2]Hospital Do Meixoeiro, Cardiology, Vigo, Spain*

Thrombus-aspirating devices (TAD) are often used in thrombi rich lesions, especially in primary PCI (PPCI). However there is controversy regarding their clinical utility. We hypothesized that the lack of consistent clinical effect can be due to the heterogeneity of the lesions, since the benefit may be restricted to those patients in which thrombus is obtained. Accordingly we have prospectively analysed the predictors for obtaining aspirated material (AM), as well as the amount, pathological and inmunohystochemical characteristics of AM.
We have performed 253 consecutive primary or rescue PCI in STEMI between January 2005 and December 2006. TAD was used in 200 patients (79%). The device successfully crossed the lesion in 190 (95% of the TAD), and AM was obtained in 136 (71.6% of TAD). The AM was subsequently weighted, analysed and classified as: Fresh (< 1 day), Lytic (1 to 5 days) or Organised (> 5 days), according to different markers (CD31, CD61, CD68, Actyn and Mieloperoxidase). The main predictors for obtaining AM were: Degree of ST elevation, artery diameter, culprit coronary, the presence of angiographic thrombus and the number of aspirations. In multivariate analysis only the presence of angiographic thrombus and the culprit vessel remained as independent predictors. We were able to analyse 72 samples of AM (53% of total), 6 of them were insufficient, and 66 were finally analysed (48.5% of total). The mean weight was 62 mg (SD 80). The amount of AM was greater in the LAD, when initial TIMI flow was 0, and in larger arteries. The main component of AM was categorized as: 35 fresh thrombus (53%), 18 lytic (27.3%), and 13 organised (19.7%), however in 19 cases (28.6%) more than one type of thrombus was found. There was a stepwise increase in mortality with older thrombi: 0% in fresh, 5.6% in lytic and 15.4% in organised (p 0,04). There was no significant correlation between the amount of AM and mortality.
Conclusion: TAD use in PPCI is often successful in obtaining AM. This success is increased in larger arteries, LAD occlusion or when angiographic thrombus is present. Fresh thrombus as the main component of AM is obtained in the majority of cases and this implies a better outcome. These data should help in deciding when to use TAD in PPCI.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1337 Drug eluting versus bare metal stents in acute ST elevation myocardial infarction (DEVINE) - a randomised control trial

J.E. Pitt, M. Reeve, R. Watkin, H. Whitlam, G. Pulikal, J. Ment, N. El Gaylani, J.M. Beattie, G. Murray, M. Pitt. *Heartlands Hospital, Cardiology, Birmingham, United Kingdom*

Introduction: Percutaneous coronary intervention (PCI) using stents is the optimal reperfusion strategy for acute ST elevation myocardial infarction (STEMI). Drug eluting stents (DES) are used extensively with excellent early and long-term clinical results. Whether DES can be used safely to treat acute thrombotic coronary occlusions is unclear.We present preliminary data from a randomised study of DES versus bare metal stents (BMS) in STEMI.
Methods: Primary PCI has been the standard reperfusion method for STEMI in our unit for the last 4 years. From April 2005 consecutive patients presenting with STEMI were recruited to the trial. Prior to coronary angiography, patients were randomised to receive paclitaxel eluting stents (PES) or BMS. The default intervention strategy was to limit revascularisation to the infarct related artery.Abciximab was used unless contraindicated. Study end points were target lesion revascularisation (TLR) <30 days (evaluating early stent thrombosis) and >30 days (evaluating restenosis and late thrombosis). Follow up was scheduled for 30 days, 6 months and 1 year. Surveillance angiography was not undertaken. We aimed to recruit 250 patients.
Results: We present data for the first 163 patients. Patient characteristics were not significantly different between the BMS (n=82) and PES (n=81) patients with regards to age (mean 57 vs 58 years), diabetes mellitus, smoking, hypertension and abciximab use. Table 1 illustrates TLR and mortality for both groups. Eight patients from the BMS group had TLR at >30 days (4 underwent coronary bypass surgery and 4 had DES implantation). One patient randomised to PES required TLR at >30 days. This was due to stent thrombosis at 6 months following discontinuation of antiplatelet medication pending non-cardiac surgery. A single fatality from stent thrombosis occurred 8 days post PCI in the PES group.

Table 1

	BMS	PES	Significance
TLR<30 days, n (%)	2 (2.5)	2 (2.5)	p= ns
TLR>30 days, n (%)	8 (9.9)	1 (1.2)	p<0.05
Mortality at 30 days, n (%)	4 (4.9)	5 (6.1	p=ns

TLR=target lesion revscularisation, BMS=bare metal stent, PES=paclitaxel eluting stent.

Conclusion: This study suggests that PES use in STEMI is safe when compared to BMS and may reduce the requirement for subsequent TLR.

P1338 The presence of a chronic total occlusion in patients with ST-elevation myocardial infarction is responsible for the increase mortality related with multivessel coronary disease

S.B. Baptista, P. Magno, J.R. Loureiro, C. Monteiro, P. Leal, N. Morujo, M. Nedio, P. Farto E Abreu, V.M. Gil. *Hospital Fernando Fonseca, Cardiology Department, Amadora, Portugal*

Purpose: The presence of multivessel coronary disease (MVD) is associated with worse outcome in patients with ST-elevation myocardial infarction (STEMI). It was recently suggested that the impact of MVD on mortality in these patients is due to the presence of a chronic total occlusion (CTO) in a vessel not related to the MI. Our objective was to evaluate the impact on 6-month mortality of a CTO of another vessel in patients with STEMI treated with primary percutaneous coronary intervention (PPCI) and to confirm if this is the main determinant of mortality in patients with multivessel disease.
Methods: 488 consecutive patients with STEMI treated with PPCI between 1998 and 2006 were divided into three groups: single vessel disease (SVD, 226 patients), multivessel disease (MVD, 207 patients) and multivessel disease with CTO of a non-infarct related artery (CTO, 55 patients).
Results: The three groups had significant differences in clinical characteristics associated with worst prognosis. Twelve percent of patient in SVD group presented in cardiogenic shock, compared with 16.0% in the MVD group and 27.8% in the CTO group. Six-month mortality was 11.5%, 17.9% and 27.3%, respectively in the SVD, MVD and CTO groups (p=0.013). After correction for baseline differences, the presence of MVD was an independent predictor of mortality (OR 2.11, 95%CI 1.19-3.74, p=0.011). However, when the presence of a CTO was included in the regression model, MVD was no longer a mortality predictor; instead, the presence of a CTO was a strong predictor of 6-month mortality (OR 3.87, 95%IC 1.74-8.57, p=0.001).
Conclusions: The presence of MVD is associated with a worse outcome in patients with STEMI treated with PPCI. However, the impact of MVD on 6-month mortality in these patients is due to the presence of a CTO in a non-infarct related artery.

P1339 Gender difference after sirolimus-eluting stents for STEMI: women demonstrate less late loss and more negative late loss at 9 months follow-up compared to men. Results from the MISSION intervention S

B.L. Van Der Hoeven, S.S. Liem, H. Putter, J.W. Jukema, D.E. Atsma, E.E. Van Der Wall, M.J. Schalij. *Leiden, Netherlands*

Background: Sirolimus-eluting stents (SES) are effective in preventing in-stent restenosis in STEMI patients. Since STEMI in women is more often caused by plaque erosion compared to plaque rupture (the main cause of STEMI in men), this may influence the outcome after SES implantation. In this substudy of the MISSION! Intervention study the 9 months angiographic outcome after SES (Cypher) implantation in men and women was evaluated.
Methods: Post-procedural and 9-months follow-up QCA analyses was performed in 131 patients after SES implantation. The following angiographic parameters were analysed: reference diameter (RD), minimal luminal diameter (MLD), in-segment late loss (LL), in-stent LL, percentage diameter stenosis (%DS) and binary restenosis (BRS, defined as ≥50% DS) at 9 months. LL was calculated by subtraction of post-procedural MLD with the follow-up MLD. Negative LL was defined as a LL <0 mm.
Results: 131 patients, 35 (37%) women and 96 (73%) men were included. Baseline clinical and angiographic characteristics and the angiographic outcome at 9 months are listed in the table. The presence of negative LL was associated with the increase in RD during follow-up for both women and men (p both <0.001).

	Female	Male	P-value
Age (yrs)	59±14	29±10	NS
Diabetes mellitus (%)	20	10	0.15
Post-procedural results			
– RD	2.71±0.41	3.03±0.51	<0.001
– In-segment MLD	2.18±0.41	2.42±0.51	<0.001
– In-segment %DS	19.6±7.8	20.1±8.4	NS
– In-stent MLD	2.49±0.32	2.73±0.39	0.001
– SSL	20.9±10.2	22.9±0.10	NS
Follow-up results			
– RD	2.77±0.42	3.03±0.50	<0.001
– In-segment MLD	2.21±0.44	2.25±0.58	NS
– In-segment %DS	19.9±10.8	25.9±13.0	0.02
– In-stent MLD	2.35±0.44	2.53±0.54	0.08
– Binary restenosis	2.9	4.2	NS
– In-segment LL	-0.03±0.39	0.18±0.44	0.02
– In-stent LL	0.14±0.22	0.21±0.43	0.38
– Negative in-segment LL	57	32	0.01
– Negative in-stent LL	26	24	NS
– Change in in-segment RD	-0.06±0.43	0.00±0.26	0.31

Conclusion: Despite the smaller post-procedural RD and MLD, women demonstrated less in-segment LL compared to men. Most interestingly, the prevalence of negative in-segment LL was higher in women, compared to men. Negative LL was strongly associated with an increase of the RD at follow-up.

LIPIDS

P1340 Effects of pioglitazone on the kinetics of cholesteryl esters of High Density Lipoproteins (HDL) in vivo

J.E. Carreon-Torres, M. Monter Garrido, O. Perez Mendez. *Instituto Nacional de Cardiologia, Fisiologia, Mexico City, Mexico*

Purpose: We have previously demonstrated that pioglitazone treatment shifts HDL size distribution towards small particles type HDL3c. However, little is known about its effects on HDL remodelling factors and on HDL-cholesteryl esters (CE) turnover. We tested the hypothesis that the pioglitazone treatment results in high proportion of small HDL particles by a coordinate response of LCAT, CETP and PLTP that results in a decreased exchange of CE between HDL and pro-atherogenic lipoproteins, VLDL and LDL.
Methods: New Zealand White rabbits (n=6) received 1.75 mg/kg/day of pioglitazone during 4 weeks. Control group (n=6) received only the vehicle. LCAT plasma activity was measured using apo AI/phosphatidilcholine/[^{3}H]-cholesterol proteoliposomes. CETP activity was estimated by incubating [^{3}H]-CE-labelled HDL3 as donor particles with tested plasma. PLTP activity was determined using [^{3}H]-phosphatidilcholine complexes as donor and HDL as acceptor particles. For the CE kinetics, the animals received HDL containing 1.0 x 10^5 cpm of [^{3}H]-labelled CE by injection into the marginal ear vein. Blood samples were obtained at 5 min after injection and at different intervals up to 5 h. [^{3}H]-labelled CE curves were constructed for HDL and for apo B containing lipoproteins, considering the radioactivity in the 5 min serum sample as 100%.
Results: Our results confirmed that pioglitazone increases the relative proportion of HDL3c from 2.7 to 9.7% (p<0.05). In treated rabbits, plasma LCAT (4.0±0.9% of esterification), CETP (25.6±2.6% transfer) and PLTP (12.1±11.6% of transfer) activities were similar to those of the control group (LCAT, 3.3±0.9% of esterification; CETP, 29.1±4.0% transfer; PLTP, 11.0±3.8% of transfer, p= NS for all), suggesting a little, if any, effect of plasma remodelling factors in the genesis of small HDL particles during pioglitazone treatment. The animals that received pioglita-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

zone showed a lower clearance of HDL-CE than the control group, associated to a reduced CE enrichment of VLDL and LDL fraction in treated animals.
Conclusion: The changes on the HDL size distribution induced by pioglitazone are not realted to modifications of the factors that play key roles in reverse cholesterol transport (LCAT, CETP and PLTP). However, pioglitazone reduces the CE transfer from HDL to proatherogenic lipoproteins. This decreased transfer may contribute to explain the antiatherogenic properties of this drug.

P1341 Baseline LDL is an important predictor of the benefit of intensive statin therapy in PROVE IT-TIMI 22

R. Giraldez, R.P. Giugliano, J. Qie, S.A. Murphy, C.P. Cannon, E. Braunwald on behalf of PROVE IT-TIMI 22 Investigators. *TIMI Study Group/Brigham and Women's Hospital, Cardiology, Boston, United States of America*

Purpose: Intensive (vs moderate) statin therapy reduced the odds of the primary endpoint (death, MI, UA leading to hospitalization, revascularization after 30 days, or stroke) by 16% in the PROVE IT-TIMI 22 trial. However, it is unknown whether this difference depends on baseline LDL.
Methods: We analyzed the RR of the primary and secondary (CHD death, MI, or revascularization after 30 days) endpoints in 3,976 ACS pts treated with atorvastatin 80mg (A80) or pravastatin 40mg (P40) in the PROVE IT-TIMI 22 trial, stratified by quintiles of baseline LDL. Interaction terms were used to assess whether there was a difference in relative benefit between treatments dependent upon quintiles of baseline LDL, adjusted for differences in baseline characteristics.
Results: A progressive increase in the relative benefit of A80 over P40 was seen across baseline LDL quintiles (Fig 1). After adjustment for baseline characteristics (patients with higher baseline LDLs had fewer high-risk features), the benefit of A80 in quintile 5 was significantly higher than quintile 1 (interaction p = 0.04). No difference in the primary endpoint was apparent for baseline LDLs <82 mg/dL (Fig 2). Consistent results were seen for the secondary endpoint (interaction p = 0.03), and in analyses that excluded pts with prior statin therapy, although the benefit of A80 emerged at even lower LDLs (~ 66 mg/dL) in the statin-naïve subgroup.

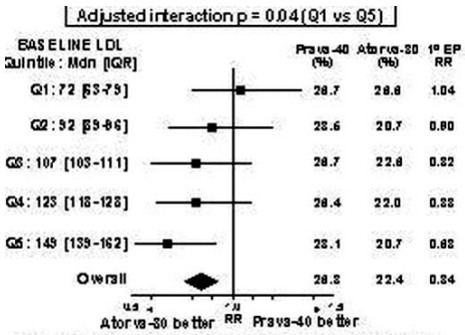


Fig 1. RR of the Primary Endpoint by Baseline LDL Quintiles

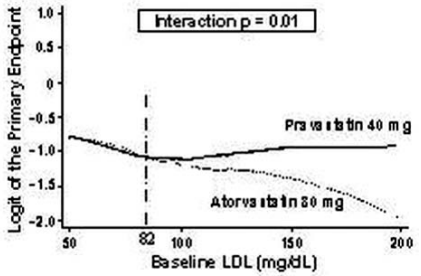


Fig 2. Probability of the Primary Endpoint by Baseline LDL

Conclusion: A graded incremental benefit of intensive statin therapy with atorvastatin 80mg (vs pravastatin 40mg) is seen in pts post-ACS with baseline LDL > 82 mg/dL. Statin-naïve patients with even lower baseline LDLs (> 66 mg/dL) appear to benefit from intensive statin therapy.

P1342 The lipoprotein subfraction profile: heritability and identification of quantitative trait loci

B. Kaess[1], A. Baessler[1], K. Stark[1], F. Huber[2], H.-R. Kalbitzer[2], H. Schunkert[3], C. Hengstenberg[1], M. Fischer[1]. *[1]University Hospital Regensburg, Innere Medizin 2, Regensburg, Germany; [2]University of Regensburg, Regensburg, Germany; [3]University of Schleswig-Holstein, Medizinische Klinik 2, Luebeck, Germany*

LDL and HDL cholesterol are routine parameters in assessing cardiovascular risk. However, over the last years there has been growing evidence that distinct lipoprotein particle features, i.e. particle concentration, mean size and subclass distribution, provide much more prognostic information than the assessment of their cholesterol content. Yet, the biological and genetic mechanisms controlling the lipoprotein subclass distribution are unclear. Therefore, we aimed [1] to determine the heritability of the entire spectrum of LDL and HDL subclass features in siblings and [2] to identify gene loci influencing the lipoprotein subfraction pattern.
Methods: We used NMR spectroscopy to analyze the lipoprotein subclass distribution in 1.275 CAD patients derived from the Regensburg myocardial infarction family study. We calculated heritability estimates, performed a microsatellite genome scan and calculated linkage for all subfractions.
Results: HDL and LDL subclass profiles showed heritabilities ranging from 31-67% (all $p<10^{-5}$) for HDL and 23-48% (all p<10-3) for LDL traits using univariate calculation. After multivariate adjustment, we found heritability estimates of 27-48% (all p<0.05) and 21-44%, respectively. The linkage scan revealed a significant LOD score of 3.3 for HDL particle concentration on chromosome 18 as well as a highly suggestive signal for HDL size on chromosome 12 (2.9). After multivariate adjustment, we found a maximum LOD score of 3.7 for HDL size.
Conclusion: Our study is the first to analyze heritability and linkage for the entire spectrum of LDL and HDL subclass features. Our findings may lead to the identification of genes controlling the lipoprotein subclass distribution and may allow the development of new therapeutic strategies.

P1343 Lipid management and LDL-C goal attainment in Asian clinical practice

R. Zambahari[1], H.S. Kim[2], C. Deerochanawong[3], Y. Wu[4], S.J. Lin[5], L. Zhao[6], Q. Zhang[7], P. Yan[8] on behalf of REALITY ASIA Study Group. *[1]National Heart Institute, Cardiology, Kuala Lumpur, Malaysia; [2]Seoul Nat'l University Hospital, Seoul, Korea, Democratic People's Republic Of; [3]Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand; [4]Peking University School of Public Health, Epidemiology, Bejing, China, People's Republic of; [5]Taipei Veterans General Hospital, Cardiology, Taipei, Taiwan; [6]Fu Wai Hospital, Cardiology, Beijing, China, People's Republic of; [7]Merck & Co., Inc, Outcomes Research, Whitehouse Station, United States of America; [8]Gleneagles Medical Centre, Cardiology, Singapore City, Singapore*

Background: NCEP ATP-III guidelines are used by most countries in Asia to prevent CVD events. However, there is limited data on LDL-C goal attainment rates based on ATP-III in Asia.
Objective: Evaluate NCEP ATP III goal attainment and lipid management in clinical practice in 6 major Asia countries
Methods: Retrospective chart review of patients from China, Korea, Malaysia, Singapore, Taiwan and Thailand. Four hundred and thirty seven randomly selected centers (except China) recruited patients based upon prespecified randomization criteria. Patients aged 18-75 yrs that were newly initiated on statin monotherapy and met study inclusion criteria were included in the current analysis. Physicians reviewed patient's charts to provide data on statin therapy, cholesterol levels and CVD events. Data on cardiovascular risk factors, lipid measurements, and co-morbid conditions were collected from up to six months prior to initial statin use (baseline) and data on lipid measures and statin prescriptions were collected up to a minimum 1 year following the initial statin (follow-up).
Results: Of the 2622 patients included 66% were CHD/CHD equivalent, 24% non-CHD with 2+ risk factors and 10% non-CHD <2 factors. Mean age of patients was 57 yrs (SD 10.1), 54% were males and 40% were diabetics. Average lipid profiles at baseline were: LDL-C 149 mg/dl (SD 41.0), TC 236 mg/dl (SD 46.6), HDL-C 48.9 mg/dl (SD 14.6). There were significant ($p < 0.05$) difference in lipid levels across countries with China having the lowest and Korea the highest average LDL-C levels. Overall there were significant ($p < 0.05$) difference in type of statin prescribed by countries. In terms of equipotency the most common (84%) lipid therapy was simvastatin 10mg and 20mg or equipotent statins. Discontinuation rate during follow-up was low at 7% and only 11% of patients switched to another statin. Overall 48% attained goal, highest goal attainment rate was in China (57%) and lowest in Taiwan (24%). In CHD/diabetes group the goal attainment rate was 38%. Besides country significant predictors of goal attainment in the multiple logistic regression were age, risk category, baseline LDL-C and initial statin potency.
Conclusions: Though there were some difference in lipid management across the 6 countries studied the overall NCEP ATP-III goal attainment rate across the region is low, particularly in the CHD/CHD equivalent. More efficacious and well tolerated treatments alternatives are required to enable more patients attain guideline recommended goals.

P1344 The trends in clinical management of hypercholesterolemia in China: goal attainment from 2000 to 2004-06

L. Zhao[1], Z. Chen[1], L. Liang[1], X. Tian[1], Y. Wu[2]. *[1]Cardiovascular Institute and Fu Wai Hospital, Epidemiology, Beijing, China, People's Republic of; [2]School of Public Health, Peking University, Epidemiology, Beijing, China, People's Republic of*

Background: Studies have shown that treatment of hypercholesterolemia can

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

greatly reduce the risk of CVD events and deaths among these patients. Our previous study showed a very low goal attainment rate (26%) among hypercholesterolemia patients in China tertiary hospitals. However, there is no data on trends in cholesterol goal attainment in Chinese patients since after. Objective: To assess the secular trends in clinical management of hypercholesterolemia in China with respect to the cholesterol goal attainment in the recent years.
Method: Data from 2 retrospective surveys of clinical management of cholesterolemia in China (the First and Second Multi-center Survey of Clinical Management of Dyslipidemia in China) was compared to understand the trends of goal attainment in past 5 yrs. We recruited 2136 patients from 25 tertiary hospitals from 12 metropolitan cities in the 1st survey in 2000 and 512 patients from 21 tertiary hospitals from 12 metropolitan cities in the 2nd survey in 2004-06, who suffered from hypercholesterolaemia and had been receiving the lipid-lowering treatment (the same medication and same dosage) for at least 2 months at the time of survey. Serum lipids level was determined for each patient at the time of enrollment, to assess whether the patient's serum lipid level reached the goal for treatment. The goal attainment rate defined as the proportion of patients whose lipid level, both of low density lipoprotein cholesterol (LDL-C) and total cholesterol (TC), achieved the goal for treatment according to the Chinese National Recommendations for Prevention and Treatment of Dislipidaemia published in 1997.
Results: Patients in the 1st and 2nd survey had similar clinical profile in terms of age (60.9 and 59.8 yrs), sex (47.2% and 48.8% were men), type of lipid disorder (37.5% and 33.4% had combined hypercholesterolaemia), and risk (36.5% and 31.4% had atherosclerotic diseases, ASD). The percent of statins use was higher in the 2nd survey (78.5%) than in the 1st (70.0%), P value$<$0.01. The goal attainment rate was much higher in the 2nd survey than in the 1st survey (39.3% vs 26.6% for overall patients, 39.3% vs 25.0% for combined hypercholesterolaemia, 26.7% vs 16.6% for high risk patients with established ASD, and 41.5% vs 31.7% for patients using statins, all P value$<$0.01).
Conclusions: Although the goal attainment rate has been much improved for hypercholesterolaemia patients over recent 5 yrs in China, it is still far from the goals set by the recommendations. Further effort should be made to improve the goal attainment rate, which is critical to the prevention of CVD.

P1345 Influence of achieved lipid levels on progression of coronary atherosclerosis in response to the ACAT inhibitor pactimibe

S.R. Kalidindi, S.E. Nissen, K.-W. Moon, E.M. Tuzcu, I. Sipahi, P. Schoenhagen, S.J. Nicholls. *The Cleveland Clinic Foundation, Department of Cardiovascular Medicine, Cleveland, United States of America*

Purpose: Clinical studies have suggested that the acyl-coenzyme A:cholesterol acyltransferase (ACAT) inhibitor pactimibe may promote progression of coronary atherosclerosis. This study investigated the impact of achieved lipid levels on the potential proatherogenicity of ACAT inhibition.
Methods: 408 subjects with angiographically documented coronary artery disease were randomized to either pactimibe or placebo in the ACTIVATE study. Intravascular ultrasound was performed at baseline and after 18 months. Subjects were stratified according to achieved quartiles of low-density lipoprotein (LDL-C) and high-density lipoprotein (HDL-C) cholesterol and compared with regard to changes in percent atheroma volume (PAV) and total atheroma volume (TAV).
Results: Subjects (mean age of 59$\pm$10 years, 71% males, BMI of 31$\pm$6 kg/m^2, 74% hypertension, 85.5% hyperlipidemia, 26.5% diabetes mellitus, 50% metabolic syndrome and 21% smokers) had mean LDL-C levels of 86 v 91 mg/dL (p=0.11) and mean HDL levels of 43 v 44 mg/dL (p=0.22) with placebo and pactimibe respectively. There was no difference between pactimibe and placebo with regard to the change in PAV in either the lowest (0.2 v 1.2%, p=0.22) or the highest LDL-C quartiles (1.6 v 0.9%, p=0.28). In contrast, pactimibe resulted in a greater increase in TAV compared to placebo in patients with the highest (4.8 v –4.1 mm^3, p=0.01), but not the lowest achieved LDL-C quartile (–2.9 v –2.5 mm^3, p=0.84). There was no difference between pactimibe and placebo in either the change in PAV within the lowest (1.5 v 0.8%, p=0.31) and highest (–0.3 v 0.2%, p=0.45) HDL-C quartiles or the change in TAV within the lowest (–2.3 v –7.1 mm^3, p=0.37) and highest (0.8 v –6.6 mm^3, p=0.1) HDL-C quartiles. A significant interaction (p=0.002) between treatment and achieved LDL-C was found on multivariate analysis.
Conclusion: A detrimental effect of pactimibe on plaque progression was only observed in patients with higher levels of LDL-C. This may reflect an increase in intracellular levels of cytotoxic free cholesterol as a potential mechanism for the proatherogenecity of ACAT inhibition in humans.

P1346 Mixed dyslipidemia is associated with higher rate of cardiovascular/cerebrovascular events among statin-treated patients

V. Sazonov[1], J. Beetsch[1], C. Wentworth[2], H. Phatak[2]. *[1]Merck & Co., Inc., Global Outcomes Research (GORHTA), Whitehouse Station, United States of America; [2]Analytic Consulting Solutions, Inc., Wakefield, United States of America*

Purpose: Despite statin therapy, many patients remain above goal for low density lipoprotein (LDL-C). In addition, other lipid abnormalities may also increase the risk of cardiovascular (CV) and/or cerebrovascular (CB) events in those patients.This studyevaluated the association between presence of other lipid abnormalities and CV/CB events among statin-treated patients not at goal for LDL-C.
Methods: A retrospective cohort study using UK General Practice Research Database included patients who were: $>$35 years of age; had first-ever statin prescription between Jan-2000 and Dec-2004; a CV/CB event (myocardial infarction (MI), stroke, angina, or revascularization) during follow-up; statin therapy $\geq$6 weeks; $>$2 years pre- and complete post-statin history with laboratory data; no concomitant other lipid lowering drugs; and $\geq$1 complete lipid profile (CLP) pre- and post-statin initiation. CLP was defined as total cholesterol (TC), LDL-C, high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) recorded on the same day. Goal was defined as LDL-C$\geq$2.5 mmol/L in patients with diabetes and/or prior CV/CB events, and LDL-C $\geq$3.0 mmol/L in others. Multivariate Cox proportional hazards model assessed the relationship between CV/CB events and low HDL-C and/or elevated TG, controlling for risk factors including diabetes, hypertension, prior CV event, Framingham risk score $>$30%, baseline TC, age, gender, year of statin initiation, smoking, BMI, and treatment (mean statin dose, medication possession ratio).
Results: Out of 19,843 statin-treated patients with CLP, our study cohort included 6,823 (34.4%) statin-treated patients not at goal for LDL-C. Among those, 10.5% (n=715) experienced a CV/CB event during follow-up (mean=2years). Patients with CV/CB events were older, more likely male, more had CV disease, worse managed HDL-C but better managed LDL-C and were less likely smokers, obese or diabetics compared to those without CV/CB events. CV/CB event distribution was as follows: 8.7% of patients experienced MI, 60.8% angina, 10.9% revascularization and 19.6% stroke. Likelihood of CV/CB event increased significantly with presence of low HDL-C and/or elevated TG: hazard ratio=1.24; 95% Confidence Interval [1.06-1.46], in patients with elevated LDL-C despite statin use.
Conclusions: In this UK general practice based cohort not at goal for LDL-C, 10.5% of patients experienced MI, stroke, angina or revascularization despite statin therapy. Low HDL-C and/or elevated TG increased the likelihood of experiencing a CV/CB event by additional 24%.

P1347 The use of fibrates instead of statins in patients with hypercholesterolaemia is related to increased cardiovascular risk

P. Jankowski, D. Czarnecka, K. Styczkiewicz, M. Brzozowska-Kiszka, M. Loster, B. Kiec-Wilk, M. Kloch, J. Wilinski, L. Bryniarski, K. Kawecka-Jaszcz. *Jagiellonian University Medical College, I Dept of Cardiology and Hypertension, Cracow, Poland*

Background: Recent evidence from randomized trials suggests that fibrates may not provide as big benefit as it was believed before. However, patients studied in large trials vary significantly from population treated in every day clinical practice. Therefore the aim of the present analysis was to evaluate the relationship between fibrates prescription and the cardiovascular (CV) complication rate in every day clinical practice.
Methods: We followed 940 coronary patients (mean age 57.5$\pm$9.9 years; 249 women and 691 men) with hypercholesterolaemia (defined as total cholesterol $\geq$ 5.0 mmol/l and/or lipid lowering agent; patients prescribed simultaneously a statin and a fibrate were excluded from the analysis) for 51.9$\pm$19.8 months. Thirty seven (3.9%) patients were prescribed a fibrate and 522 (55.6%) a statin. The Cox proportional hazard regression analysis was used to assess the relation between fibrates prescription and long-term event-free survival.
Results: Comparing the fibrate group to those not prescribed a fibrate total mortality was 16.2% (6 deaths) vs 8.5% (77 deaths), p=NS; CV mortality was 16.2% (6 deaths) vs 6.8% (61 deaths) p$<$0.05; CV death or myocardial infarction or stroke occurred in 27.0% (10 events) vs 13.2% (119 events), p$<$0.05; respectively. When compared with statin group fibrate group had higher total mortality (16.2% vs 7.3%, p=0.05), CV mortality (16.2% vs 5.7%, p$<$0.05) and the risk of CV death or myocardial infarction or stroke (27.0% vs 12.1%, p$<$0.01). As shown in the table the fibrate prescription was independently related to the risk of major CV complications.

The results of Cox regression analysis

	Univariate HR 95% CI	Multivariate HR 95% CI
Total mortality	2.02 (0.81 – 5.03)	3.06 (1.09 – 8.05)
Cardiovascular mortality	2.73 (1.08 – 6.86)	4.43 (1.48 – 13.20)
Cardiovascular death or myocardial infarction or stroke	2.29 (1.16 – 4.54)	2.58 (1.19 – 5.61)

Adjustments were made for age, gender, ejection fraction, extent of coronary atherosclerosis, NYHA class, heart rate, risk factors and treatment.

Conclusion: The use of fibrates instead of statins in coronary patients is related to increased cardiovascular risk. These results should be taken into account in decision making in clinical practice.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1348 Determinants of intensive statin therapy in acute myocardial infarction in clinical practice

J. Ferrieres[1], J. Puel[1], J.E. Wolff[2], B. Ritz[3], G. Kirkorian[4], E. Aliot[5], B. Charbonnier[6], N. Danchin[7] on behalf of the FAST-MI investigators. *[1]CHU Rangueil, Department of Cardiology B, Toulouse, France; [2]Centre Hospitalo-Universitaire de Dijon, Department of Cardiology, Dijon, France; [3]Centre Hospitalier Saint Joseph Saint Luc, Exploration fonctionnelle cardio-vasculaire, Lyon, France; [4]Hopital Louis Pradel, Department of Cardiology, Lyon, France; [5]CHU de Brabois, Department of Cardiology, Vandoeuvre Les Nancy, France; [6]CHRU de Tours, Department of Cardiology D, USCI, Tours, France; [7]Georges Pompidou European Hospital, Department of Cardiology, Paris, France*

Background: Intensive statin therapy (IST) reduces major adverse cardiovascular events in randomized controlled trials. The benefits of IST appear to be consistent in various subgroups. However, cardiologists are often reluctant to use IST at discharge in acute myocardial infarction (AMI). The aim of our study was to assess the determinants of IST at discharge in a registry of AMI.
Methods: FAST-MI is a nation-wide registry carried out over a 1-month period in the fall 2005 which included consecutive pts with AMI admitted to coronary care units at the 223 participating centers. We analyzed the prescription of statins at discharge in 2894 AMI patients. IST was defined as the use of simvastatin 80 mg/d, atorvastatin 80 mg/d or rosuvastatin 20-40 mg/d. Multiple logistic regression analysis was used to evaluate the determinants of IST in comparison with standard dosages of statin therapy at discharge.
Results: Among 2894 patients alive at discharge, 375 (13.0%) used IST. Nearly all the FAST-MI patients on IST were on atorvastatin 80 mg/d (98.4%). After multivariate adjustment, in-hospital coronary angioplasty (p=0.004), anterior AMI (p=0.005), admission in a university hospital (p=0.001), and specific geographical areas (p=0.001) were positively associated with IST. In the same model, female sex (p=0.002), older age (p=0.0001), diabetes (p=0.032), previous AMI (p=0.008), and the use of statins before AMI (p=0.04) were negatively associated with IST.
Conclusions: Despite trials showing that IST is a safe and efficient therapy in AMI, there is a large variation of the use of IST in the "real world". Qualitative studies are needed in order to disentangle factors associated with local practice, the fear of side effects or the constraint of the health system.

P1349 The impact of individual apolipoproteins on endothelial function and thrombosis/fibrinolysis system in young subjects

K. Marinou, D. Tousoulis, C. Antoniades, C. Vasiliadou, N. Alexandropoulos, N. Papageorgiou, S. Brilli, C. Pitsavos, C. Stefanadis. *Athens, Greece*

The role of lipids in atherogenesis is now well established. However, the exact mechanisms by which different lipoproteins affect endothelial function and induce atherothrombosis still not well understood.
Aim: We examined the effect of lipid profile on endothelial function and thrombosis/fibrinolysis systems, in a cohort of young low-risk individuals.
Methods: The study population consisted of 201 healthy subjects (aged 34.2±3.3 years old) with no risk factors for atherosclerosis. The effect of total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), tryglycerides, apo-AI, apo-B and apo-E on endothelial function (as determined by calculating endothelium-dependent dilation (EDD) using gauge-strain plethysmography) was examined. Plasma levels of plasminogen activator inhibitor-1 (PAI-1) and tissue plasminogen activator (tPA) were determined by ELISA.
Results: EDD was correlated with HDL (r=0.267, p=0.001), LDL (r=-0.355, p=0.0001), triglycerides (rho=-0.366, p=0.0001), apo-AI (r=0.240, p=0.004) and apo-B (r=-0.277, p=0.005). Similarly, PAI-1 levels were correlated with cholesterol (r=0.294, p=0.03), triglycerides (r=0.395, p=0.001) and ApoA1 (r=-0.314, p=0.020). tPA was correlated with triglycerides (r=0.539, p=0.0001), HDL (r=-0.357, p=0.012), ApoA1 (r=-0.415, p=0.0001), ApoB (r=0.344, p=0.012) and PAI-1 (r=0.467, p=0.001). In multivariate linear regression, LDL (β=-0.217(SE:0.098), p=0.028), apo-AI (β=0.277(SE:0.124), p=0.027) and age (β=-916(SE:0.369), p=0.015) were independent predictors for EDD in this population. Similarly, PAI-1 was independently associated with ApoB (β=0.098(SE:0.047), p=0.042), ApoE (β=-1.7(SE:0.804), p=0.037), HDL (β=-0.151(SE:0.07), p=0.032) and total cholesterol (β=0.062(SE:0.026), p=0.019). ApoB was the only independent predictor of tPA (β=0.037(SE:0.009), p=0.0001) in these subjects.
Conclusions: Elevated lipid levels, within the normal range, affect endothelial function and modify thrombosis/fibrinolysis system in young individuals. Apolipoproteins and especially apo-AI are important determinants of endothelial function in these subjects, independently of other lipids. Apo-B, apo-E and HDL are independent predictors of the release of PAI-1. These findings suggest that full measurement of the lipid profile including individual apolipoprotein levels, may be of great importance in risk stratification of young individuals.

P1350 Treating patients with a prior history of statin related muscle side effects to LDL-C goals using fluvastatin XL alone, or in combination with ezetimibe: A randomized, double blind multicentre study

E.A. Stein[1], C.M. Ballantyne[2], M. Engelhardt[3], C.R. Gimpelewicz[3], S. Ghani[3] on behalf of Lescol XL Myalgia Study Group. *[1]Metabolic & Atherosclerosis Research Center, Cincinnati, Oh, United States of America; [2]Baylor College of Medicine, Center for CV Disease Prevention, Houston, Tx, United States of America; [3]Novartis Pharma AG, GM SMP CD&MA, Basel, Switzerland*

Purpose: Statin intolerance due to myalgias and other non-serious muscle related side effects (MRSE) is a significant problem in clinical practice limiting the ability for effective therapy to treat patients at risk for CVD. Approximately 40,000,000 pts are prescribed statins and studies suggest 5-10% experience MRSE resulting in 2-4 million being denied the most effective class of lipid lowering. Extended release fluvastatin (FXL) may have a lower propensity for MRSE. This randomized, double-blind, double-dummy international multicenter study was carried out in patients with a documented history of prior MRSE on statin therapy. A non-statin, ezetimibe (EZE), was used as a positive control.
Methods: Patients who had discontinued statins due to MRSE on current statin treatment were randomized to FXL (n=69), FXL plus EZE 10 mg (n=64) or EZE monotherapy (n=66) for 12 weeks. Primary objective was the comparison of percent reduction in LDL-C between FXL or FXL-EZE vs. EZE alone (ANCOVA). Patients achieving LDL-C thresholds recommended by guidelines of the ESC, EASD and NCEP were examined through odds ratios (Cochran-Mantel-Haenszel test). MRSE and tolerability were assessed by the MRSE recurrence and study discontinuations (Cox's proportional hazard model).
Results: Mean baseline LDL-C for all groups was ~175 mg/dL. Mean LDL-C reduction at week 12 was 16% for EZE, 33% for FXL and 46% for FXL+EZE (p<0.001). 84% of pts on FXL based treatment remained free of any MRSE and only 4% on FXL, 3% on FXL-EZE and 8% on EZE discontinued due to MRSE.

Table 1

Various LDL-C-goals	Guideline	EZE	FXL	FXL+EZE
< 3.4 mmol/l (130 mg/dl)	NCEP	33.3	69.6*	87.5*
< 3.0 mmol/l (115 mg/dl)	ESC	16.7	43.5*	78.1*
< 2.6 mmol/l (100 mg/dl)	ESC, NCEP	1.5	33.3*	67.2*
< 2.0 mmol/l (77 mg/dl)	ESC/EASD	0.0	14.5*	31.9*
< 1.8 mmol/l (70 mg/dl)	ESC/EASD, NCEP	0.0	8.7*	26.6*

* p < 0.01 vs. EZE.

Conclusion: Inability to utilize a statin results in very few patients achieving even moderate LDL-C goals, however FXL alone or in combination with EZE resulted in effective LDL-C reduction and significantly greater achievement of LDL-C thresholds, with good tolerability, in pts with documented prior MRSE on statin therapy. More than 80% of patients on a FXL based treatment remained free of muscle pain.

P1351 Genotype C/T for Rs35767 polymorphism of the promoter P1 of IGF-1 gene correlates with serum HDL and Lp(a) levels in stable angina patients

P. Burchardt[1], A. Gozdzicka-Jozefiak[2], W. Nowak[2], T. Grotowski[3], R. Link[1], T. Siminiak[2]. *[1]Poznan University School of Medical Sciences, Poznan, Kowanowko, Poland; [2]University of A.Mickiewicz, Dept. of Biology, Poznan, Poland; [3]Kowanowko Cardiac and Rehabilitation Hospital, Kowanowko, Poland*

Bacground: The role of IGF-1 in the development of coronary arteriosclerosis has been intensively studied, but the possible effect of polymorphism in promoter region of IGF-1 gene remains unclear.
Aim: The purpose of our study was to analyze and identify polymorphism in promoter P1 region (between -1277 to -977bp) of IGF-1 gene, as well as to associate the polymorphisms with serum lipoprotein levels and with medical history data.
Methods: Blood samples were collected from 101 patients with stable angina for plasma isolation and for isolation of genomic DNA with salt-extraction approach. Using polymerase chain reaction (PCR), analyses of sequences of the promoter P1 IGF-1 gene (between -1277 to -977bp) were performed for each patient. The products were verified with electrophoresis on agarose gel and analyzed using single strand conformation polymorphism (SSCP) evaluate IGF-1 promoter gene polymorphism. DNA fragments were separated by electrophoresis and underwent further silver staining. Beckman-Coulter Genetic Analysis System CEQ 2000XL was used for automated sequencing, allowing more accurate determination of nucleotide sequence changes essential for the identification of gene promoter structure It was made throughout pts with different SSCP result to confirm probability of polymorphism. Lipid profile was evaluates by routine spectrophotometric methods.
Results: 101 consecutive pts were included (67 males and 44 females). Positive history for MI had 38 pts(24M, 14F), family history of CAD had 36pts (20M 16F) and history of stroke was positive in 5 pts.
We observed 29 subject of genotype C/T and 1 of T/T for polymorphism Rs35767 at –1245bp (28,7% and 0,99% of pts studied, respectively). Genotype C/T was found in 14 women (31,82%) and in 15 men (26,32%). We observed a positive

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

correlation between lower serum HDL and lipoprotein a (Lpa) levels (p=0,046 and p=0,029) among patients with the presence of genotype C/T and T/T, respectively.
Conclusion: In patients presenting with stable angina pectoris, the C/T genotype for Rs35767 polymorphism of the P1 of IGF-1 gene correlates with lower serum HDL and higher Lp(a) levels. The confirmation of the role of this polymorphism in the predisposition to dyslipidemias requires large scale clinical trials.

P1352 Too moderate first treatment decisions result in mostly ineffective treatment of patients with dyslipidaemia in both primary and secondary CVD prevention

Z. Fras[1], M.F. Kenda[2]. [1]*University Medical Center, Dept. For Vascular Medicine, Ljubljana, Slovenia;* [2]*Slovenian Society of Cardiology, Cardiovascular Research Centre, Ljubljana, Slovenia*

Aims: To elaborate the possibilities on how to improve effectiveness and efficiency of current treatment practice of dyslipidemia in Slovenia. Subjects and methods. Altogether the data on 6,209 pts collected from 211 physicians – 141 (66,8%) in primary care (mostly GP's) (4,228 cases) and 70 (33,2%) from specialist practice (1,981 cases) – were analysed by the recent nationwide retrospective trial. Every physician provided the data on risk factors as well as lipid values (1) at start, (2) upon the first control after the start of treatment, and (3) current/last available values for their 30 consecutive pts. Besides, all treatment actions already taken as well as those foreseen for the future were reported.
Results: The study population was at very high risk for either first or repeated CVD events. In pts with manifest CVD 61.2% had coronary, 16% cerebrovascular, and 11.4% peripheral artery disease, while 11.3% a kind of polyvascular atherosclerotic disease. Initial values for total (LDL) cholesterol were 6.91±1.33 (4.33±1.16) mmol/L in pts treated as primary, while 6.46±1.36 (3.98±1.20) mmol/L in those treated as secondary prevention. Both diet and drugs were prescribed as a first treatment step in 52.6%/68.4% of pts in primary/secondary prevention arm. The vast majority of pts (96.8%) received statins, where 51.6%/51.2% in primary/secondary prevention started with simva (average doses were 20.9/17.59 mg in primary/secondary prevention), followed with 23.3%/31.2% pts on atorva (15.6/18.6 mg), 8.5%/6.2% rosuva (11.5/10.5 mg), 8.5%/7.5% fluva (46.7/47.3 mg) and 5.7%/3.9% lovastatin (15.6/18.5 mg). This resulted in initial only 13.3% (16.2%) drop of total (LDL) cholesterol in primary, and 13.8% (17.3%) in secondary prevention arm (all $p<0.01$). Current (final) levels of total (LDL) cholesterol differed from the initial ones by 21.2% (26.1%) in primary and 22.8% (27.1%) in secondary prevention. Target LDL values were reached by only 24.9% in primary and 21.5% in secondary prevention arm (which increased to 37.7% with the <3.0 mmol/L target value), while treating physicians in both cases believed that the target values were achieved in over 50% of treated pts.
Conclusions: Our data confirmed that the current treatment of dyslipidemia is far away from being satisfactory, and mainly the first treatment decision in most cases (especially in secondary prevention) is not adequate. Here we found both more aggressive treatment with statins from the beginning as well as the use of combination treatment for LDL lowering as the most important currently underused possibilities.

P1353 Alternate day therapy in patients with combined hiperlipidemia

K. Ozdemir, M.A. Duzenli, N. Aygul, M. Gurbilek, T. Karabag. *Selcuk University Meram Faculty of Medicine, Cardiology Depaertment, Konya, Turkey*

Objectives: In combined hyperlipidemia, the combination of statins and fibrates is more likely to be accompanied by myopathy and hepatotoxicity than would either drug alone. We examined atorvastatin and fenofibrate on alternate days, and compared with standard fenofibrate and atorvastatin therapy.
Method: 300 patients completed the 12-month follow-up period. In patients with coronary heart disease (CHD) or risk equivalents; If LDL-C>100 mg/dl and TG<200 mg/dl atorvastatin therapy was started; if LDL-C<100 mg/dl and TG>200 mg/dl or TG>500 mg/dl fenofibrate was started, and if LDL-C>100 mg/dl and TG>200 mg/dl statin and fenofibrate alternate day was started. In patients without CHD or risk equivalents; If LDL-C>130 mg/dl and TG<200 mg/dl atorvastatin therapy was started; if LDL-C<130 mg/dl and TG>200 mg/dl, or TG>500 mg/dl fenofibrate was started and if LDL-C>130 mg/dl and TG>200 mg/dl alternate day statin and fenofibrate was started. Follow-up visits were scheduled on the last days of treatment months 1, 3 and 12.
Results: Mean changes at the 12th month versus baseline are demonstrated in figure. In contrast to atorvastatin, alternate day therapy produced considerably less LDL-C lowering(p=0.003) but ordinarily greater reductions in TG and increases in HDL-C(p<0.001,p=0.008, respectively). However, the percentage of change in TC, nonHDL-C and TC/HDLC ratio were similar to that achieved with atorvastatin alone. In contrast to fenofibrat, alternate day therapy resulted in greater reductions in TC (p<0.0001), LDL-C (p<0.0001), nonHDL-C (p<0.0001) and TC/HDL-C ratio (p=0.001) but less TG lowering(p=0.026). The change in HDL-C was similar in both groups.
Conclusion: The alternate-day therapy may be an alternative in combined hyperlypemia managemet.

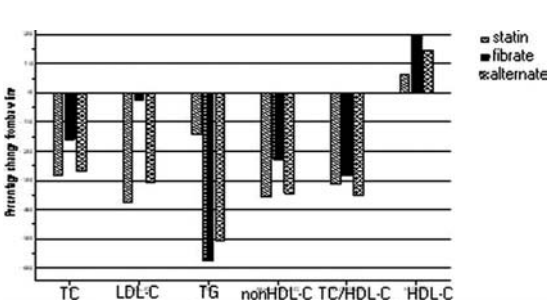


Figure 1

P1355 Cholesterol metabolism and long-term mortality among men with high cardiovascular risk

T. Strandberg[1], T.A. Miettinen[2], H. Gylling[3]. [1]*University of Oulu, Public Helath Science and General Practice, Oulu, Finland;* [2]*University of Helsinki, Helsinki, Finland;* [3]*University of Kuopio, Kuopio, Finland*

Purpose: Serum cholesterol levels are affected by both synthesis and absorption of cholesterol, but there are scarce studies of their prognostic significance. We assessed cholesterol absorption and synthesis with serum markers (noncholesterol sterols) and related them to long-term mortality in middle-aged men.
Methods: This was a prospective cohort study of 236 men (mean age 60 years) at high risk of cardiovascular diseases in 1985-1986. Most of the men were hypercholesterolemic (median cholesterol 6.7 mmol/L, interquartile range 6.0-7.4). Of them, 29 (12%) had a history of cardiovascular disease or cancer, 6 (3%) had diabetes, and 46 (20%) were defined to have metabolic syndrome. At baseline, weight gain from age 25 and traditional risk factors were assessed together with noncholesterol sterols, which are expressed as a ratio to serum cholesterol to standardize for variations in cholesterol concentrations. These noncholesterol sterols included lathosterol (reflect cholesterol synthesis), and plant sterols (campesterol and sitosterol) and cholestanol (reflect cholesterol absorption). Cholestanol ratio was used in the analyses, because it is not influenced by diet. Main outcome measure was 19-year mortality. Cox regression was used for multivariate analyses.
Results: During the follow-up 85 men (36%) died. At baseline, non-survivors had had significantly higher age-adjusted weight gain, and blood glucose, but lower LDL cholesterol than survivors. Serum triglyceride and HDL-cholesterol levels were similar. There were more smokers among non-survivors. Of the noncholesterol sterols, cholestanol to cholesterol ratio was significantly lower in non-survivors than survivors (p=0.03), while lathosterol to cholesterol ratio was not significantly different. In multivariate analysis, the level of the baseline cholestanol ratio was significantly dictated (inverse association) by the lathosterol ratio and the presence of the metabolic syndrome. In Cox analyses with age, smoking, and baseline diseases as covariates, higher cholestanol ratio per SD predicted lower mortality risk (RR 0.77, 95% CI 0.60-0.98, p=0.03), but the association was no more significant when glucose was added to the model.
Conclusions: Higher cholesterol absorption was associated with a lower 19-year mortality among hypercholesterolemic, high-risk men. This may be explained by an inverse association between cholesterol absorption and glucose metabolism.

P1356 Implications of guidelines for statin treatment for primary prevention of cardiovascular disease - risk factor analysis of the Scottish Health Survey 2003

I.U. Haq[1], J. Hill[2], J. Craig[3], L.D. Ritchie[4]. [1]*Royal Victoria Infirmary, Newcastle, United Kingdom;* [2]*Quality Improvement Scotland, Edinburgh, United Kingdom;* [3]*Quality Improvement Scotland, Glasgow, United Kingdom;* [4]*University of Aberdeen, Aberdeen, United Kingdom*

Purpose: To determine the proportion of the population aged ≥40 years who do not have symptomatic coronary heart disease (CHD) or cardiovascular disease (CVD) who might benefit from statin treatment according to British guidelines.
Methods: CHD and CVD risk was calculated for adults from data from the Scottish Health Survey 2003 using the Framingham risk equations. Left ventricular hypertrophy was assumed to be absent. Those with diabetes were counted separately as guidelines recommend statin treatment for all diabetics ≥ 40 years. The prevalence of risk was calculated for those with CHD risk ≥15% or CVD risk ≥20%. The prevalence of individuals with total cholesterol (TC) ≥ 7.5 mmol/l or BP ≥ 160/100 mmHg or those taking drugs for hypertension was also calculated if they were not already included in attaining the prespecified CVD risk threshold.
Results: Moving from a CHD risk of 15% over 10 years to CVD risk of 20% increased the eligible population from 23.9% to 32.7%. Adding in individuals not already included with TC ≥ 7.5mmol/l, and those with high BP, increased the numbers to treat by a further 6%, and 8% respectively. The cumulative percentage of the population was 46.9% comprising 54.1% of men and 41.1% of women. Including only those with TC ≥ 4.0 mmol/l and ≥ 5.0 mmol/l decreased the percentage to treat to 46.1% and 41.7% respectively.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Table 1. Prevalence of CVD risk in people aged 40 years or over who had a total cholesterol measurement in the Scottish Health Survey and no overt CVD disease, n(%)

Age (years)	Number sampled	DM	DM + CHD risk ≥15%	DM + CVD risk ≥20%	DM + CVD risk ≥20% or TC ≥7.5	DM + CVD risk ≥20% or TC ≥7.5 or BP ≥160/100 or BP Rx
40-49	747	11 (1.5)	22 (2.9)	26 (3.5)	67 (9.0)	102 (13.7)
50-59	777	32 (4.1)	127 (16.3)	155 (19.9)	218 (28.1)	300 (38.6)
60-69	561	57 (10.2)	230 (41.0)	298 (53.1)	331 (59.0)	401 (71.5)
70-79	326	41 (12.6)	175 (53.7)	249 (76.4)	259 (79.4)	279 (85.6)
80+	112	10 (8.9)	50 (44.6)	98 (87.5)	98 (87.5)	102 (91.1)
Total 80+	2523	151 (6.0)	604 (23.9)	826 (32.7)	973 (38.6)	1184 (46.9)

DM - diabetes mellitus; TC - total cholesterol (mmol/l); BP - blood pressure; Rx - treated with drug therapy.

Conclusions: Almost 1 in 2 people with no symptoms of cardiovascular disease could be treated with drugs if global risk, targeted at 10 year CVD ≥20% and individual risk factors were each treated. This should be added to the considerable number of people eligible for treatment for secondary prevention

P1357 Associations of circulating malondialdehyde-modified low-density lipoprotein with lipoprotein subclasses in healthy men

R. Takahashi[1], K. Okumura[2], M. Yoshikane[1], N. Ikeda[1], T. Murohara[3]. *[1]Chunichi Hospital, Department of Cardiology, Nagoya, Japan; [2]Nagoya University School of Medicine, Cardiovascular Research Medicine, Nagoya, Japan; [3]Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan*

Purpose: Oxidized low-density lipoprotein (LDL) and small LDL particles are both regarded as atherogenic lipoproteins. In vitro studies have demonstrated that small LDL particles have increased susceptibility to oxidation. The aim of this study was to investigate the relationship of circulating malondialdehyde-modified (MDA)-LDL, an oxidized form of LDL, and lipoprotein subclasses as well as other atherogenic factors in healthy men.
Methods: The study group consisted of a total of 170 apparently healthy Japanese men (55±9 years), who did not have any history of cardiovascular disease and who were not taking any medication. MDA-LDL was measured by a sandwich enzyme-linked immunosorbent assay. Plasma cholesterol concentrations in major lipoproteins and their subclasses were determined by high-performance liquid chromatography with gel permeation columns. Plasma levels of fasting insulin and adiponectin were also determined.
Results: In univariate analysis, body mass index, waist circumference, systolic blood pressure (BP), diastolic BP, white blood cell count, C-reactive protein, uric acid, fasting insulin, homeostasis model assessment of insulin resistance, total cholesterol, very-low-density lipoprotein (VLDL) cholesterol, LDL cholesterol, triglycerides, large VLDL cholesterol, medium VLDL cholesterol, small VLDL cholesterol, large LDL cholesterol, medium LDL cholesterol, small LDL cholesterol, very small LDL cholesterol, small high-density lipoprotein (HDL) cholesterol, and very small HDL cholesterol were positively correlated with MDA-LDL, whereas adiponectin and large HDL cholesterol were negatively correlated with MDA-LDL. In stepwise multiple regression analysis, very small LDL cholesterol (β=0.725, F=136.78), medium VLDL cholesterol (β=0.265, F=25.65), very small HDL cholesterol (β=-0.279, F=21.69), small HDL cholesterol (β=0.134, F=6.86), and systolic BP (β=0.110, F=6.84) were identified as independent determinants of MDA-LDL (R^2=0.714, $p<0.0001$).
Conclusion: Circulating MDA-LDL levels are strongly associated with very small LDL cholesterol levels in healthy men. MDA-LDL is more associated with lipoprotein subclasses than other atherogenic factors.

P1358 Subclinical atherosclerosis imaging as a new tool to evaluate the appropriateness of guidelines for the primary prevention of cardiovascular disease among young adults

I. Stauffer[1], M. Depairon[2], R. Darioli[2]. *[1]University Hospital, Angiology Unit, 1011 Lausanne, Switzerland; [2]University Hospital, Angiology Unit, 1011-Lausanne, Switzerland*

The detection of subclinical atherosclerosis by B-mode ultrasounds was developed to assist physicians in cardiovascular (CV) risk assessment. The purpose of this prospective study was to evaluate how the guidelines are appropriate to identify high risk subjects requiring clinical interventions in primary prevention. The study population included all patients (P) aged from 20 to 60 years, who were consecutively referred to our Lipid Clinic. Their estimated 10-year cardiovascular risk assessment and their eligibility for a lipid-lowering drug therapy (LLDT) was assessed by using the 3 th JES-ESC (ESC) and NCEP-ATP-3 (ATP-3) guidelines (GL). B-mode ultrasounds on carotid and femoral arteries was performed to detect atherosclerotic plaques (focal thickening of intima-media > 1.2 mm). P with plaques on > 2 carotid and/or femoral sites were considered as having the highest risk to be a victim of a future CV event (HRP). GL were considered as appropriated when LLDT was recommended in HRP and respectively if it was not required for non HRP.
Among these 734 P, 296 (40%) were classified as HRP, and 10% vs 49% of all P ($p<0.001$) were qualified for LLDT according to the ESC and ATP-3 GL. Appropriateness of ESC and ATP-3 GL was obtained in 62% vs 57% of cases ($p<0.06$). However, underuse of LLDT was more frequent with ESC than with ATP-3 GL (34% vs. 17%, $p<0.001$). On the other hand, overuse was more common with ATP-3 than with ESC GL (26% vs. 4%, $p<0.001$).
In conclusion, these results suggest that, among young adults, subclinical atherosclerosis imaging could be more relevant than risk-scoring algorithms based on CV risk factors to detect high risk P and improve the performance of primary prevention.

P1359(W) Alcohol dehydrogenase type 1C (ADH1C) variants, alcohol consumption traits, HDL cholesterol and risk of coronary heart disease in women and men

S.B.J. Ebrahim[1], D.A. Lawlor[2], Y. Ben Shlomo[2], R. Harbord[2], N. Timpson[2], T. Gaunt[3], I. Day[3]. *[1]London School of Hygiene & Tropical Medicine, Dept of Epidemiology & Population Health, London, United Kingdom; [2]University of Bristol, Soical Medicine, Bristol, United Kingdom; [3]University of Southampton, Human Genetics, Southampton, United Kingdom*

Purpose: The alcohol dehydrogenase 1C gene (ADH1C) $\gamma2\gamma2$ variant reportedly interacts with moderate alcohol consumption to increase HDL cholesterol levels and reduce coronary heart disease (CHD). We undertook replication studies in two large population cohorts of women and men.
Methods: 3234 women and 1313 men with relevant genotypic and phenotypic data from two prospective population cohorts were genotyped for ADH1C variants.
Results: No association was found between ADH1C variants and HDL cholesterol, blood pressure or CHD risk, although ADH1C was associated with alcohol consumption. There was no evidence of interactions between ADH1C variants and alcohol intake on HDL cholesterol, blood pressure or CHD risk. Life-long abstainers were at particularly high CHD risk and had adverse risk factor profiles.
Conclusion: Our findings do not support the hypothesis that ADH1C variants are associated with HDL cholesterol and CHD risk in people who drink regularly. The high risk among abstainers merits further exploration.

P1360 Evidence of myocardial adrenergic innervation abnormalities in hyperlipidaemic subjects: the beneficial effect of statins

E.A. Zacharis, M. Marketou, S.I. Koukouraki, V.K. Prassopoulos, I. Karalis, G.F. Diakakis, F.I. Parthenakis, N.S. Karkavitsas, P.E. Vardas. *Heraklion University Hospital, Cardiology, Heraklion, Greece*

Purpose: Hyperlipidaemia results in endothelial dysfunction and myocardial perfusion abnormalities even in the absence of any organic heart disease. We investigated the association of dyslipidaemia with myocardial adrenergic innervation disturbances using I 123 -meta-iodobenzylguanidine (I 123 -MIBG) and assessed the effect of statin therapy thereupon.
Methods: We included 28 hyperlipidaemic subjects (20 men, aged 57±10 years, total cholesterol>240 mg/dl, LDL-C>160mg/dl), while 17 healthy volunteers served as a control group. None had any disease that may have affected myocardial adrenergic innervation. All subjects underwent a planar and a SPECT myocardial imaging of the heart after an intravenous infusion of 5mCi I 123 -MIBG. Heart to mediastinum ratio (H/M) was used for quantitative assessment of adrenergic innervation, 10 minutes and 4 hours after drug infusion, while SPECT scintigraphy evaluated the regional distribution of adrenergic activity. Fifteen of the hyperlipidaemic subjects received 40 mg/day atorvastatin for 6 months, while the remaining ten received placebo. An I 123 –MIBG study was repeated at six months.
Results: Total cholesterol and LDL-C levels were significantly reduced (from 310±135 mg/dl and 182±79 mg/dl to 190±72 mg/dl and 96±37 mg/dl respectively, $p<0.05$). The H/M ratio at 10 min and 4 hours in hyperlipidaemics was 1.81±0.22 and 1.75±0.26 respectively; significantly lower than normals (2.31±0.9 and 2.15±0.10 respectively, $p<0.05$ for both) and was improved under atorvastatin treatment (1.99± 0.8 and 1.96±0.25 respectively, $p<0.05$). During SPECT scintigraphy, 19 hyperlipidaemic subjects (68%) showed defects in the inferior wall, nine (32%) displayed additional regional disturbances in myocardial adrenergic activity in the anterior wall and ten subjects (36%) in the apex. These defects were ameliorated mostly in the inferior and anterior wall on re-evaluation, but only in those receiving atorvastatin. No regional disturbances were detected in healthy subjects.
Conclusions: This is the first study to show a high prevalence of myocardial adrenergic innervation disturbances in hyperlipidaemic subjects, while the atorvastatin further intensifies the cardioprotective effect of statins.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1361 Correlation between circulating levels of IGF-1, its binding proteins and lipid profile in patients with stable angina

P. Burchardt[1], A. Gozdzicka-Jozefiak[2], W. Nowak[2], R. Link[3], T. Grotowski[1], M. Woloszyn[1], T. Siminiak[2]. [1]*Poznan University School of Medical Sciences, Poznan, Kowanowko, Poland;* [2]*University of A.Mickiewicz, Dept. of Biology, Poznan, Poland;* [3]*Kowanowko Cardiac and Rehabilitation Hospital, Kowanowko, Poland*

Background: Insulin-like Growth Factor (IGF-1) has been suggested to be involved in the development of atherosclerosis. Macrophage concentration within atherosclerotic plaque is known to be modulated by binding IGF-1 to their surface receptor. On the other hand, IGF-1 stimulates LDL uptake and its degradation by activated leucocytes.
Purpose: The aim of the study was to investigate the association between serum levels of IGF-1 as well as IGF Binging Protein-3 (IGFBP3) and lipid profile in patients with stable angina undergoing coronary angiography.
Methods: 101 consecutive patients scheduled for diagnostic coronary angiography were enrolled into the study. IGF-1 and IGFBP3 serum levels were measured by RIA and IRMA techniques. Lipids fractions were evaluated by routine assays. 65% of were previously diagnosed with dyslipidaemia and were on use statins at the time of evaluation
Results: Mean IGF-1 levels were 197.5±57.1 ng/ml, whereas mean lipid values for the groups studied were: total cholesterol (TC) 194.6±51.0 mg/ml; HDL 48.7±15.3 mg/ml; LDL 118.1±44.4 mg/ml; triglycerides (TG) 144.2±71.5 mg/ml; LP (a) 0.16±0.2; apoB 1.0±0.33 and apoAI 1.5±0.25, respectively. Significant correlations were found between IGF-1 and total cholesterol (R=0.238, p=0.02), LDL cholesterol (R=0.204, p=0.04) and TG (R=0.250, p=0.01), but not with lipoprotein levels. This findings were independent on patients' body mass index (BMI): IGF-1/BMI index correlated with TC (R=0.25, p=0.01) and LDL (R=0.23, p=0.02), but also with lipoprotein a (R=0.21, p=0.03) and apoB (R=0.2, p=0.05) Conclusion: A strong positive correlation was observed between IGF-1 and lipid profile in patients with stable angina, despite wide statin use in hypercholesterolaemia. Future studies on the role of IGF-1 in the pathogenesis of atherosclerosis have to consider the reciprocal interactions between IGF-1 and lipid metabolism.

P1362 Association between class B vitamines and lipid metabolism

P. Penz[1], A. Vachulova[1], M. Caprnda[1], P. Blazicek[2], O. Hanninen[3], J. Lietava[2] on behalf of Homocystein Slovakia. [1]*Teaching Hospital, Internal Departement, Bratislava, Slovak Republic;* [2]*Hospital of Ministry of Defence, Clinical Biochemy, Bratislava, Slovak Republic;* [3]*University of Kuopio, Physiology, Kuopio, Finland*

Introduction: Hyperhomocysteinemia (HHcy), an independent risk factor of coronary artery disease (CAD), is associated with increased atherosclerosis and decreased plasma high-density lipoprotein cholesterol (HDL-C) in mice. In group of patients with CAD plasma homocysteine (Hcy) concentrations negatively correlated with HDL-C and apolipoprotein A1 (apoA-I) Association of vitamin B6, B12, folic acid with metabolism of cholesterol was not appropriate studied.
Methods: We analysed subjects (N=445) from general population. After exclusion patients on hypolipidemic therapy we analyzed plasma level of vitamins B6, B12 a folic acid, homocysteine. Hyperhomocysteinemia was stated as level of Hcy above 11,4 μmol/L for women and above 12.6 μmol/L for men. From parameters of lipoproteins metabolism we analyzed total cholesterol (Chol), LDL-C, HDL-C, triglycerides (Tg), Apoliprotein A1 (apoA1) and Apolipoprotein B 100 (apoB).
Results: We observed positive correlation between Hcy and waist (r = 0,159; p = 0,002), negative between Hcy and apoA1 (r = -0,13; p = 0,013). Group with decreased level of vitamin B12 have significantly decreased apoA1 (1,07±0,137 vs. 1,13±0,185 [mg/l]; p = 0,011) a non significantly decreased HDL-CH (1,26±0,29 vs. 1,34±0,36 [mmol/l]; p = 0,13). Vitamin B12 positively correlated with cholesterol (r = 0,154; p = 0,003), HDL-cholesterol (r = 0,138; p = 0,008), LDL-cholesterol (r = 0,158; p = 0,003), ApoA1 (r = 0,193; p < 0,0005). Level o folate negatively correlated with circumference of waist (r = -0,119; 0,023). There was also strong positive correlation between vitamin B6 and level of triglycerides (r = 0,269; p = 0,001). Patients with hyperhomocysteinemia have also elevated systolic (157,03 ±29,57 vs. 147,03±27,63; p = 0,01) and diastolic (95,03± 13,08 vs. 90,03±13,75; p = 0,013) pressures (in mmHg). Risk of cardiovascular event in 10 years period calculated according to ESC-SCORE was elevated in HHcy group (5,87±5,03 vs. 3,73±3,86 [%]; p < 0,0005) also in patients with decreased level of vitamin B12 (6,2±5,5 vs. 3,9± 3,9[%]; p = 0,004).
Conclusion: Our results suggest that hyperhomocysteinemia may increase risk of atherosclerosis by decreasing level of ApoA-I. Association between vitamin B12 and metabolism of cholesterol was even stronger and its influence on parameters of lipid metabolism may be not all be mediated through homocysteine.

P1363 Plasma Phospholipid Transfer Protein (PLTP) activity after a high fat meal in patients with coronary heart disease, insulin dependent diabetes, and healthy controls

A. Schlitt[1], X.C. Jiang[2], K. Fingscheidt[3], J. Carter[2], U. Mueller-Werdan[2], M. Russ[2], H. Schmidt[2], K. Werdan[2], M. Buerke[2], B. Schwaab[1]. [1]*Martin Luther-University Halle-Wittenberg, Department of Medicine Iii, Halle (Saale), Germany;* [2]*SUNY Downstate Medical Center Brooklyn, Department of Anatomy and Cell Biology, New York, United States of America;* [3]*Curschmann-Clinic, Department of Anatomy and Cell Biology, Timmendorfer Strand, Germany*

Background: Plasma phospholipid transfer protein (PLTP) mediates both net transfer and exchange of phospholipids between different lipoproteins. Animal studies have shown that it is closely related to the development of atherosclerosis. We have shown in a previous study that serum PLTP-activity is significantly increased in patients with coronary heart disease (CHD). The role of PLTP in diabetes remains unclear.
Materials and Methods: To evaluate the influence of a high fat meal on serum PLTP activity, 50 non-diabetic patients with coronary heart disease (CHD), 50 insulin dependent Typ 2 diabetics (T2DM) with CHD, and 50 healthy controls were recruited in the Curschmann clinic for rehabilitation, Timmendorfer Strand. We determined serum PLTP activity and other markers before, and 4 and 8 hours after a high-fat meal (consisting of a total of 1,265 kcal/m^2 body surface area: 105 g of fat, consisting of 52 g saturated fat and 300 mg cholesterol, with 48 g carbohydrates and 32 g protein).
Results: As expected, serum PLTP activity was significantly increased in CHD patients in comparison to healthy controls (mean±standard deviation: 71.0±46.2 pmol/μl/h in CHD-patients versus 54.0±33.8 pmol/μl/h in controls, p=0.032) at baseline. Surprisingly, PLTP activity was decreased in insulin dependent Typ 2 diabetics (T2DM) at baseline (46.6±35.2 pmol/μl/h, thus, T2DM versus controls p=0.339 and T2DM versus CHD p=0.002). Moreover, we found that serum PLTP activity was increased to its maximum 4 hours after fat loading, and then decreased to nearly basal levels after 8 hours both in controls and CHD patients. In T2DM PLTP activity slightly increased from 4 to its maximum at 8 hours.
Conclusion: The results of this study add another piece to the PLTP jigsaw. We hypothesize that the increased risk in diabetic patients for severe coronary and other atherosclerotic events is partly related to an abnormal postprandial metabolism of PLTP, which has pro-oxidative and pro-inflammatory properties.

P1364 Impact of a compliance program on cholesterol control: results of the randomized ORBITAL Study in 8,108 patients treated with Rosuvastatin in Germany

S.N. Willich[1], J. Mueller-Nordhorn[1], F. Sonntag[2], H. Voeller[3], N. Van Den Boom[4], W. Meyer-Sabellek[1], K. Wegscheider[5], E. Windler[5], H. Katus[6]. [1]*Charite University Medical Center, Social Medicine, Epidemiology And Health Econ, Berlin, Germany;* [2]*Cardiology Practice, Henstedt-Ulzburg, Germany;* [3]*Rehabilitation Center, Ruedersdorf, Germany;* [4]*AstraZeneca, Wedel, Germany;* [5]*University of Hamburg, Hamburg, Germany;* [6]*University of Heidelberg, Heidelberg, Germany*

Background: Compliance with statin therapy is closely related to achievement of low-density lipoprotein (LDL-C) goals in patients with dyslipidemia. In the present study we determined whether a compliance-enhancing program could increase the level of lipid control in patients treated with rosuvastatin.
Methods: A total of 8,108 patients (56% men, mean age 59 years and 44% women, 63 years) with LDL-C ≥115 mg/dL (3.0 mmol/L) if statin-naïve or else ≥125 mg/dL (3.2 mmol/L) were randomized to receive rosuvastatin 10 mg daily either with or without a compliance-enhancing program for 12 months. Patients not achieving goal after 3 months were to be up-titrated to rosuvastatin 20 mg daily thereafter.
Results: At 3, 6, and 12 months, rosuvastatin plus compliance initiatives was similarly effective to rosuvastatin alone in terms of 1998 European LDL-C goal (<115 mg/dL [3.0 mmol/L]) achievement (72% vs 70%; 71% vs 69%; 68% vs 68%, respectively) and changes in the lipid profile. Significant differences were observed in the subgroup of statin-naïve patients (at 3 and 6 months, 80% vs 76%, P<0.01 and 78 vs 73%, P<0.001, respectively). The frequency of adverse events and clinically important changes in laboratory data were consistent with the known safety profile of rosuvastatin.
Conclusions: Rosuvastatin 10/20 mg daily enables the majority of patients to achieve LDL-C <115 mg/dL within 3 months and provides a sustained improvement of their lipid profile. The compliance-enhancing program was only effective in statin-naïve patients at early timepoints, but had no overall effect over 12 months.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1365 Dietary intervention prevents dyslipidemia associated with highly active antiretroviral therapy in HIV-1-infected individuals: a randomized trial

J.P. Ribeiro, R.K. Lazzaretti, R. Kuhmmer, C.A. Polanczyk, E. Sprinz. *Hospital De Clinicas De Porto Alegre, Cardiology Division, Porto Alegre, Brazil*

Background: Treatment of HIV-1-infected individuals with highly active antiretroviral therapy (HAART) is associated with dyslipidemia, which is characterized by hypertriglyceridemia and hypercholesterolemia. Current guidelines recommend diet and exercise as first step intervention for HIV-1-infected individuals with HAART-related dyslipidemia, but there is no evidence from randomized trials to support this recommendation.
Objetive: To evaluate the effects of dietary intervention on the development of dyslipidemia in HIV-1 infected individuals who are started on HAART.
Methods: Eighty HIV-1- infected patients naive from previous treatment were randomized to receive HAART with dietary intervention (n = 42) or HAART without dietary intervention (controls, n = 38) for 12 months. Dietary intervention, according to the National Cholesterol Education Program, was given every 3 months. Before and after intervention, 24 h food records, body mass index, weight/hip ratio, and lipid profile were obtained. Data were analyzed by intention to treat, using mixed-effects models.
Results: After randomization, groups had similar characteristics. Dietary intervention resulted in reduction in total caloric intake (mean ± SD: from 2,655±619 to 2,289±516 Kcal/day) and percentage of fat intake (from 31±7 to 21±3% of calories), while controls increased caloric intake (from 2,600±569 to 2,814±669 Kcal/day), with no change in percentage of fat intake. Body mass index (from 23±3 to 26±4 kg/m^2) and waist/hip ratio (from 0.86±0.05 to 0.91±0.06) increased in the controls and were unchanged by dietary intervention. Plasma cholesterol (from 150±29 to 189±34 mg/dL) and LDL-cholesterol (from 85±25 to 106±31 mg/dL) increased in the controls and were unchanged in the dietary intervention group. Plasma triglycerides were reduced by dietary intervention (from 134±67 to 101±42 mg/dL) and increased in controls (from 134±70 to 158±77 mg/dL). After one year follow-up, 17% of patients who received dietary intervention had lipid profile compatible with dyslipidemia, while 50% ($p < 0.05$) of controls had dyslipidemia.
Conclusion: This randomized trial demonstrates that dietary intervention prevents dyslipidemia associated with HAART in HIV-1-infected individuals.

P1366 Physicians perception of guideline recommended LDL-target values. Characteristics of misclassified patients

B. Mayer[1], P. Linsel-Nitschke[1], W. Lieb[1], B. Franzel[2], U. Elsasser[3], H. Schunkert[3]. *[1]UK S-H, Campus Luebeck, Medizinische Klinik II, Luebeck, Germany; [2]essex Pharma, Muenchen, Germany; [3]MedPharmTec, Muenchen, Germany*

Aims: Guideline-based treatment of hyperlipidemia requires that physicians perceive the conditions that define LDL-cholesterol target levels in individual patients. The objective of the present study was to investigate the awareness of primary care physicians for patient characteristics relevant for designation of LDL target values.
Methods and Results: The Manage Lipids Study investigated 25.250 patients who were considered by their 907 primary care physicians to require either dietary or pharmacological treatment for hyperlipidemia. The physicians were asked to estimate the guideline-recommended LDL target value for each of their patients. In parallel, the corresponding NCEP ATP-III guideline LDL target values were determined centrally. The appropriate utilization of risk factors, co-morbidities, risk scores and preexisting atherosclerotic diseases for the assignment of LDL target values to individual patients was analyzed by logistic regression. By guideline criteria, LDL targets of 20% based on calculated risk scores (OR: 2.69, CI: 2.40-3.02; $p<0.001$). Interestingly, female MI patients received incorrect assignments more frequently than male patients (OR: 1.32, CI: 1.12-1.55; $p<0.001$).
Conclusion: In the primary care setting, physicians give correct assignment of guideline-recommended LDL targets only to about half of their high risk patients. Perception of correct LDL target values varies largely between male and female patients as well as the conditions defining the high risk in such patients. Identification of high-risk characteristics in patients requiring low LDL target values needs improvement in order to enhance guideline-based therapy of hyperlipidemia.

P1367 Vytorin on carotid intima-media thickness and overall rigidity

A.M.M. Meaney, W.Z.R. Zuniga, G.S.O. Solache, A.V.H. Vela, H.V.M. Velazquez, E.M.C. Mendoza, E.-M. Meaney. *Hospital 1o de Octubre, ISSSTE, Cardiovascular Unit, Mexico City, Mexico*

Purpose: To assess the effect of three lipid-lowering therapies on the reduction of the carotid intima-media thickness (IMT) in high risk coronary Mexican patients.
Methods: The study is a randomised, comparative, open clinical trial, which includes 90 high risk coronary patients (ATP III types C and D). Patients were randomly allocated to three different therapy groups: group 1: pravastatin 40mg, group 2: simvastatin 40mg, and group 3 simvastatin 20mg plus ezetimib 10mg initially, If therapeutic goals were not attained (<100mg/dl of LDL cholesterol [LDL-C] for type C and < 70mg of LDL-C for type D), patients in group 1 received pravastatin 40mg plus ezetimib 10mg, group 2 simvastatin 80mg and group 3 simvastatin 40mg plus ezetimib 10mg. The primary end point was the change of the carotid IMT, measured by quantitative B-mode ultrasound over one year. The secondary end points were the change in the level of LDL-C and the change in high sensitive C-reactive protein (CRPhs) over one year follow-up.
Results: Group 1 included 30 patients (43% women, 56% with diabetes mellitus type 2 [DM2]), aged 59±8 years. All patients in this group received pravastatin plus ezetimib at the end of the study, since they did not attain the therapy goal. Group 2 included 30 patients (35% women, 61% with DM2), 1 aged 57±8 years. 80% of the patients received 80mg of simvastatin. Group 3 with 30 patients (30% women, 46% with DM2), aged 57±9 years. 80% of the patients received 40mg of simvastatin plus ezetimib 10mg. The overall baseline IMT combining four measurements in the internal carotid artery were: 1.21±0.24mm, 1.08±0.24mm and 1.09±0.2mm for groups 1, 2 and 3 respectively (p=>0.05). After treatment for one year the IMT were 0.73±0.03mm, 0.76±0.04mm and 0.71±0.04mm for groups 1, 2 and 3 respectively, with the greatest reduction observed in groups 1 and 3 compared with group 2 (p=<0.05). Baseline LDL-C levels were 128±30 mg/dl in group 1, 130±33 mg/dl in group 2 and 131±39 in group 3, at the end of the study. LDL-C levels were 48±41, 45±37 and 48±31 in groups 1,2 and 3. No significantly differences were observed in CRPhs, HDL cholesterol, triglycerides, blood pressure and body mass index, among groups.
Conclusions: Reduction in LDL-C below 50mg/dl were observed in the three therapeutic groups. It was also observed a reduction of the carotid IMT in all the three groups being significantly lower in the groups that had combined therapy (statins plus ezetimib). Our study is the first evidence that dual therapy has a beneficial effect on a surrogate marker of atherosclerosis (IMT).

P1368 Implementation of guidelines for lipid lowering treatment in high risk patients in the outpatient setting: results of the 2L-Outpatient Registry

F. Towae[1], C. Juenger[1], K. Bestehorn[2], H. Wienbergen[1], D. Bock[1], J. Senges[1], A.K. Gitt[1] on behalf of 2L-Outpatient Registry. *[1]IHF Ludwigshafen an der Uni Heidelberg, Cardiology, Ludwigshafen, Germany; [2]University, Institut fuer klinische Pharmakologie, Dresden, Germany*

Background: Lipid lowering treatment has proven to decrease cardiovascular complications in secondary as well as in primary prevention. Guidelines recommend LDL-cholesterol levels <100 mg/dl (2.6 mmol/l) in high risk patients. Little is known if these treatment goals are achieved high risk patients in the outpatient setting.
Methods: From May 2006 to December 2006, 6711 consecutive patients with known coronary artery disease (CAD) or CAD risk equivalent (CAD-RE) such as diabetes mellitus or peripheral arterial disease (PAD), all on chronic statin treatment, were enrolled into the 2L-Outpatient-Registry in Germany (295 outpatient centres) to document current LDL-cholesterol and adaptation of lipid-lowering treatment. We compared patients with known CAD (n=6054) with patients with CAD-RE (n=657).
Results: Under chronic statin treatment 38.2% of patients with known CAD and 27.2% of patients with CAD-RE already had reached LDL-chol <100mg/dl. In those patients with LDL >100mg/dl, lipid lowering therapy was altered by increasing statin dose or/and adding ezetimibe in 55.6% for CAD and in 51.3% for CAD-RE patients respectively.

Results

	CAD (n=6054)	CAD risk equivalent (n=657)	p- value*
Age (years)	65.8	63.8	< 0.01
Female gender [%]	27.2	50.2	< 0.01
Diabetes [%]	30.6	90.5	< 0.01
PAD [%]	8.6	17.2	< 0.01
Prior Stroke [%]	4.1	4.4	n.s.
Mean LDL Chol [mg/dl]	110	124	< 0.01
LDL < 100 mg/dl [%]	38.2	27.2	< 0.01
Increase of statin dose	23.9	20.9	ns
Adding ezetimibe	21.1	18.9	ns
Increase of statin dose +ezetimibe	10.5	11.5	ns

Conclusion: About only one third of high risk patients reached LDL<100mg/dl in the outpatient setting. Due to the awareness of guidelines, in 55.1% of patients who had not reached LDL treatment goal of <100mg/dl lipid lowering treatment was adapted by increasing statin dose or/and adding ezetimibe

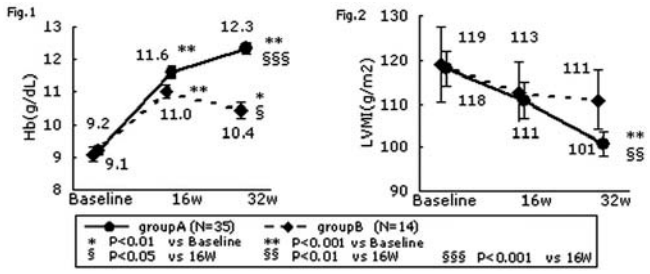
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

DRUG THERAPY

P1369 The favorable effect of continuous adequate treatment of anemia on left ventricular mass in patients with chronic kidney disease in Japan

M. Akaishi[1], M. Suzuki[2], Y. Hada[3], M. Hiroe[4], K. Aonuma[5], Y. Tsubakihara[6], T. Akizawa[7]. *[1]Kitasato Institute Hospital, Tokyo, Japan; [2]Toho University Ohashi Medical Center, Tokyo, Japan; [3]Sakakibara Memorial Clinic, Tokyo, Japan; [4]International Medical Center of Japan, Tokyo, Japan; [5]Tsukuba University Hospital, Ibaraki, Japan; [6]Osaka General Medical Center, Osaka, Japan; [7]Showa University Hospital, Tokyo, Japan*

Purpose: We previously reported that Left ventricular mass index (LVMI) decreased after 16-weeks adequate anemia treatment in patients with chronic kidney disease (CKD). The purpose of this study was to clarify the effect of continuing the adequate treatment on further decrease in LVMI.
Methods: One hundred seventy one patients with CKD not on dialysis with serum creatinine levels >2mg/dL and hemoglobin <10g/dL were assigned randomly (at 3:1 ratio) to receive either darbepoetin alfa (group A) or epoetin alfa (group B). In first 16 weeks, all patients of both groups underwent adequate anemia treatment of which target hemoglobin (Hb) level was 12.0. For the next 16 weeks, the target level of Hb was kept at 12.0-13.0g/dL in group A (continuous adequate treatment), while the target level of Hb was set at 10.0-12.0g/dL in group B. Two-dimensional echo-guided M-mode echocardiograms were obtained before, after 16 weeks, and after 32 weeks treatment. Three cardiologists reviewed the quality of records and measured the left ventricular dimensions independently without knowledge of clinical profiles of patients.
Results: Of 171 patients, 127 patients were qualified to assess echocardiograms, and finally 49 triads of satisfactory echocardiograms were obtained. The change in Hb and LVMI (Mean±SEM)are shown in Fig.1 and 2. Group A (N=35)showed incremental improvement of anemia and progressive decrease in LVMI, whereas group B (N=14)did not show regression of left ventricular hypertrophy (LVH). Additionally, there was significant association between the regression of LVH and Hb values at 32 weeks across the groups(p=0.004)



The change in Hb and LVMI

Conclusions: Continuous and adequate treatment of anemia in CKD patients results in progressive and persistent regression of LVH.

P1370 The cardioprotective effects of ACE-inhibition by perindopril not modified by renal function in patients with stable coronary artery disease

J.J. Brugts[1], E. Boersma[1], M. Chonchol[2], J.W. Deckers[1], M. Bertrand[3], W.J. Remme[4], R. Ferrari[5], K. Fox[6], M.L. Simoons[2] on behalf of EUROPA-investigators. *[1]Erasmus MC, Cardiology, Rotterdam, Netherlands; [2]University of Colorado HSC, Renal Disease and Hypertension, Denver, United States of America; [3]Lille Heart Institute, Cardiology, Lille, France; [4]Sticares Cardiovascular Research Foundation, Cardiology, Rotterdam, Netherlands; [5]Azienda Ospedalier and University di Ferrara, Cardiology, Ferrara, Italy; [6]Royal Brompton and National Heart hospital, Cardiology, London, United Kingdom*

Background: A recent study reported that an impaired renal function identified a subgroup of patients with coronary artery disease most likely to benefit of ACE-inhibition therapy. In light of the growing interest in tailored-therapy for targeting medications to specific subgroups, remarks on the consistency of the treatment effect by ACE-inhibitors are highly important. Therefore, we examined whether the level of renal function modifies the cardio-protective effects of ACE-inhibitor therapy by perindopril in patients with stable coronary artery disease.
Methods and results: The present study involved 12056 patients with stable coronary heart disease without heart failure randomized to perindopril or placebo. Estimated glomerular filtration rate (eGFR) was calculated using the abbreviated MDRD-equation. Cox regression analysis was used to estimate multivariable-adjusted hazard ratios. During follow-up, 454 events (7.9%) occurred in patients with eGFR≥75 and 631 events (10.0%) with eGFR<75 ml/min per 1.73 m^2. Treatment benefits of perindopril were apparent in both patient groups with eGFR≥75 (HR 0.77; 95%CI 0.64-0.93) and eGFR<75 (HR 0.84; 95%CI 0.72-0.98) for the primary endpoint. We observed no significant interaction between renal function and treatment benefit (Pv=0.47). Furthermore, the absolute risk reduction by perindopril was comparable between both groups at longer follow-up. Using different eGFR cut-off points resulted in similar trends.

Treatment effect by perindopril and eGFR

	eGFR 60 HR 95% CI	Testing interaction	eGFR 75 HR 95% CI	Testing interaction	eGFR 90 HR 95% CI	Testing interaction
Primary endpoint	0.77 (0.68-0.89)	0.19 ns.	0.77 (0.64-0.93)	0.47 ns.	0.76 (0.56-1.04)	0.71 ns.
	0.96 (0.74-1.24)		0.84 (0.72-0.98)		0.82 (0.72-0.93)	
Total mortality, AMI, UAP or cardiac arrest	0.84 (0.76-0.93)	0.48 ns.	0.83 (0.76-0.93)	0.44 ns.	0.76 (0.61-0.96)	0.30 ns.
	0.92 (0.76-1.13)		0.89 (0.79-1.00)		0.88 (0.80-0.97)	
Cardiovascular mortality, AMI and UAP	0.84 (0.75-0.93)	0.76 ns.	0.83 (0.72-0.97)	0.81 ns.	0.76 (0.59-0.97)	0.41 ns.
	0.88 (0.71-1.09)		0.86 (0.75-0.97)		0.86 (0.77-0.95)	

Upper and lower line correspond to the levels of eGFR (dichotomous) above and below the mentioned cut-off level. (*) P-value for interaction.

Conclusion: Treatment with perindopril reduced cardiovascular endpoints irrespective of renal function. Therefore our data suggest that, in contrast to recent literature, renal function does not modify treatment effect of ACE-inhibition and cannot be used to identify subgroups of patients more likely to benefit of ACE-inhibition.

P1371 Beta-blockers in patients with chronic obstructive pulmonary disease and atherosclerosis; from contraindication to indication?

Y.R.B.M. Van Gestel, S.E. Hoeks, G.M.J.M. Welten, O. Schouten, H. Stam, F.W. Mertens, R.T. Van Domburg, M.R.H.M. Van Sambeek, D. Goei, D. Poldermans. *Erasmus Medical Center, Rotterdam, Netherlands*

Aim: Beta-blocker use in patients undergoing abdominal aortic (AAA) surgery is associated with improved survival. However, there is a general reluctance to prescribe beta-blockers in patients with chronic obstructive pulmonary disease (COPD) as it is considered to worsen symptoms. We evaluated the influence of beta-blockers on perioperative and long-term outcome in patients with moderate and severe COPD undergoing AAA surgery.
Methods: All 769 consecutive patients scheduled for AAA surgery underwent a preoperative pulmonary function test. COPD was defined as FEV1/FVC<0.70 and FEV1<80% of the predicted value corrected for age, gender and length. Cardiac history, ECG and beta-blocker use was noted in all patients. Cardiac imaging tests at rest and during stress were performed and scored for the presence of rest wall motion abnormalities and myocardial ischemia. Study endpoint was perioperative and long-term mortality. The mean follow-up was 4 years, range 0-15. Multivariate regression analysis was used to examine the effect of beta-blockers on perioperative and long-term outcome.
Results: Of the total 769 patients, 300 patients (42%) had moderate or severe COPD. The mean age of these patients was 71 (±8) years and 89% were male. Whithin 30 days after surgery 25 patients (8%) died. During long-term follow-up 176 patients (59%) died. Beta-blockers were used in 43%. Univariate analysis showed that beta-blockers were associated with an improved postoperative outcome (OR: 0.31; 95%CI: 0.11-0.84). After adjusting for clinical baseline characteristics and test results, beta-blockers remained significantly associated with an improved postoperative outcome (OR: 0.35; 95%CI: 0.12-0.99). In addition, beta-blockers were independently associated with significant improved long-term survival (HR: 0.65; 95%CI: 0.46-0.93).
Conclusion: Beta-blocker use is associated with improved postoperative outcome in COPD patients undergoing AAA surgery. In addition, the use of beta-blockers was associated with an improved long-term survival.

P1372 The PREDICT (Residual Platelet Aggregation after Deployment of Intracoronary Stent)-score

T. Geisler, D. Grass, M. Paterok, C.H. Zuern, B. Bigalke, C.H. Doesch, K. Goehring-Frischholz, K. Dietz, C.H. Herdeg, M. Gawaz. *University Hospital Tuebingen, Cardiology Department, Tuebingen, Germany*

Purpose: The purpose of the study was to develop a score to characterize relevant clinical variables that influence residual platelet aggregation after clopidogrel loading dose (LD).
Methods: 1092 patients treated with coronary stenting for stable angina and acute coronary syndromes (ACS) were enrolled. Clopidogrel-dependent platelet inhibition was assessed by residual ADP (20μMol/L)-induced platelet aggregation ≥6h after LD. Primary endpoints wereincreased RPA as defined by platelet aggregation in the upper tertial of the study cohort (>46.9%). Secondary endpoints were the occurrence of a major adverse event (death, myocardial infarction, ischemic stroke) within 30 days.
Results: Eleven clinical factors were included in the primary analysis. In multivariate logistic regression analysis increased RPA was significantly influenced by ACS, reduced left ventricular function, type II diabetes mellitus, renal failure

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(serum creatinine >1.5 mg/dl), and age > 65 years. In a model including these factors, the risk to show high RPA increased by stepwise cumulation of score variables (Odds ratio for patients presenting with 4 factors 2.91, 95% confidence interval (CI) 1.58-5.36 and with 5 factors 4.02, 95% CI 1.78-9.05, p=0.001). In 30-day follow-up the incidence of major adverse events was higher in patients with RPA in the upper tertial (3.3 vs 2.3 in the second and 1.3 in the first tertial).
Conclusions: The PREDICT-Score offers a good tool to estimate residual platelet activity after clopidogrel LD by easily available patient details. Additionally, we could demonstrate its association with 30-day outcome. Thus, patients with a high risk score may benefit from intensified antiplatelet therapy in terms of improved platelet inhibition and risk reduction for short-term thromboischemic events.

P1373 Clozapine-induced myocarditis: role of catecholamines in the murine model

J.F. Wang[1], J.Y. Min[1], T.G. Hampton[1], I. Amende[1], S. Malek[1], W.H. Abelmann[1], A.I. Green[2], J.P. Morgan[1]. *[1]Beth Israel Deaconess Medical Center, Cardiology, Boston, United States of America; [2]Dartmouth Medical School, Department of Psychiatry, Lebanon, United States of America*

The atypical antipsychotic drug clozapine is an effective agent to treat psychosis. Cardiotoxicity of clozapine, however, has raised concerns, especially for the treatment of patients with schizophrenia. Increased catecholamines have been postulated to trigger an inflammatory response resulting in myocarditis. Here, we used a mouse model of clozapine to study whether the drug could cause adverse cardiac effects associated with an increase in catecholamines.
Methods: Male BalbC male mice, age ~ 6 weeks, were administered 5, 10 or 25 mg/kg clozapine for 7 and 14 days; and one group 2 mg/kg propranolol and 25 mg/kg clozapine for 14 days (n=8 for all groups). Saline-treated mice served as controls (n=8). Catecholamines were measured by HPLC. TNF-alpha was determined by ELISA. H & E-stained heart sections were examined for histopathology.
Results: Clozapine-treated mice showed a significant dose-related increase in myocardial inflammation and necrosis compared to saline-treated mice. The cardiac lesions consisted of eosinophilic contraction bands, lymphocytic infiltrate and coagulative necrosis. Norepinephrine and epinephrine levels were significantly increased on day 7 after all clozapine doses: 4.01±0.67 ng/ml and 4.41±0.34 ng/ml (5 mg/kg); 7.96±0.53 ng/ml and 14.02±1.63 ng/ml (10 mg/kg); 8.75±0.58 ng/ml and 10.05±1.59 ng/ml (25 mg/kg) compared to controls 1.50±0.21 ng/ml and 0.21±0.01 ng/ml. On day 14 both levels were increased, as follows: 3.85±0.42 ng/ml and 3.89±0.58 ng/ml (5 mg/kg); 8.51±0.42 ng/ml and 17.83±1.46 ng/ml (10mg/kg); 8.67±0.41 ng/ml and 12.51±1.02 ng/ml (25 mg/kg) compared to controls 1.12±0.18 ng/ml and 0.97±0.02 ng/ml ($P<0.05$). Propranolol (2 mg/kg) significantly decreased clozapine-induced (25 mg/kg) norepinephrine and epinephrine levels on day 14: 4.28±0.64 ng/ml and 2.21±0.31 ng/ml compared to clozapine (25 mg/kg) only ($P<0.05$). Administration of 5 mg/kg clozapine slightly increased TNF-alpha to 127±9% (NS), 10 mg/kg significantly to 153±10% and 25 mg/kg significantly to 250±8% after 14 days compared to controls ($P<0.05$, n=4). Propranolol (2 mg/kg) attenuated clozapine-induced (25 mg/kg) TNF-alpha release to 185±9% compared to clozapine (25 mg/kg) only ($P<0.05$).
Conclusion: Our study indicates that clozapine-induced myocarditis is modulated by the beta-adrenergic system and its interactions with cytokines. Our data further suggest that a beta-blocker may be effective in reducing the incidence and severity of myocarditis. This mouse model, therefore, may be helpful to study etiology, treatment and prevention of clozapine's cardiac toxicity in man.

P1374 High clopidogrel loading dose is superior to a standard 300 mg regimen in patients undergoing percutaneous coronary intervention: evidence from a meta-analysis

G. Biondi-Zoccai[1], C. Moretti[2], P. Agostoni[3], M. Valgimigli[4], A. Abbate[5], D. Angiolillo[6], G. Montalescot[7], G. Sangiorgi[8], G. Trevi[7], I. Sheiban[7]. *[1]University of Turin, Interventional Cardiology, Turin, Italy; [2]Turin, Italy; [3]Antwerp, Belgium; [4]Ferrara, Italy; [5]Richmond, United States of America; [6]Jacksonville, United States of America; [7]Paris, France; [8]Milan, Italy*

Purpose: Combined antiplatelet treatment with aspirin and clopidogrel is pivotal to minimize peri-procedural adverse events in patients undergoing percutaneous coronary intervention (PCI). There is however debate on the best clopidogrel loading dose. We performed a systematic review and meta-analysis on the optimal clopidogrel loading dose.
Methods: Pertinent trials comparing a high (>300 mg) vs a standard (300 mg) clopidogrel loading dose in patients scheduled for PCI were systematically searched in several databases (December 2006). The primary end-point was the 1-month rate of death or myocardial infarction. Secondary end-points included other ischemic and bleeding adverse effects. Peto fixed effect odds ratios (OR) were computed with pertinent 95% confidence intervals and p values.
Results: A total of 10 studies (7 randomized and 3 non-randomized) were included, enrolling 1567 patients (712 treated with a 300 mg loading dose, 790 with a 600 mg dose, 54 with a 900 mg dose, and the remaining 11 with other regimens). Overall, a high loading dose proved significantly superior to a standard loading in preventing cardiac death or non-fatal myocardial infarction (OR=0.59 [0.30-0.84], p=0.009), without any statistically significant increase in major or minor bleedings (respectively p=0.55 and p=0.98). Sensitivity analysis restricted to randomized trials confirmed the statistically significant superiority superiority of high loading dose (p=0.001) in preventing death or myocardial infarction. Moreover, meta-regression disclosed a significant interaction between event rate and benefits of high loading dose (p=0.005), suggesting that the higher the underlying risk, the greater the favorable impact of high loading.
Conclusions: A high clopidogrel loading dose appears significantly superior to a standard one in patients scheduled for PCI, especially among those at higher risk of peri-procedural ischemic events.

P1375 Prevention of stroke in elderly patients with atrial fibrillation: effectiveness of low-intensity anticoagulant treatment

U. Cucchini, C. Pegoraro, E. Osto, F. Marzot, S. Iliceto, V. Pengo. *Padova, Italy*

Background: Atrial fibrillation (AF) is the most common sustained arrhythmia with a rate as high as 13-15% in elderly subjects. It is now clear that AF is the most frequent cause of severe ischemic stroke and vitamin K antagonists (VKAs) are beneficial reducing stroke by 68%. Widespread use of VKAs in this population is limited by the substantial risk of severe or fatal bleeding.
Methods: As hemorrhagic events occur more frequently at higher INR values, the purpose of this study was to evaluate if lower intensity anticoagulation (target INR 1.8) was able to reduce major and fatal bleeding retaining its ability to prevent ischemic stroke in elderly patients (75 years or more) with nonvalvular AF. This was an open label randomized trial with cumulative primary end-points consisting of ischemic stroke, systemic or visceral embolism and major haemorrhage.
Results: 401 subjects were randomized to low intensity anticoagulation (n=198) or standard anticoagulation (n=203). Mean age was 80 years and all of them were at low-medium risk for stroke ($CHADS_2$ -score $\leq$ 4). Mean follow up was 4.1 years. According to intention to treat analysis there were 18 primary events (2,21 per 100 pts/y) in the low-intensity group and 28 (3,31 per 100pts/y) in the standard intensity group (p=0,17). Less ischemic stroke occurred in the low intensity group (6; 0,71 per 100Pts/y) in comparison to standard group (15; 1,77 per 100Pts/y; p=0,06). In the latter group 6 ischemic stroke occurred in patients who discontinued anticoagulation. Twelve and 13 major haemorrhages (0,15 per 100 pts/y) occurred during the same study period in the low-intensity and control group (p=0,91). Bleeding-related death were 3 (0,37 per 100Pts/y) in the low intensity and 6 (0,71 per 100 pts/y) in the standard group (p=0,33). Mean intervals between INR controls was 26 days in low intensity and 24 days in standard intensity group.
Conclusions: A low-intensity anticoagulant treatment in elderly patients is at least as effective and safe as standard treatment and reduced the frequency of INR controls.

P1376 Assement of angiopoietin 1 and angiopoietin 2 gene expression in peripheral monocytes after angiotensin converting enzyme inhibition treatment in hypertensive patients

M. Marketou, J.E. Kontaraki, E.A. Zacharis, G.E. Kochiadakis, D.A. Arfanakis, A.N. Giaouzaki, P.E. Vardas. *Heraklion University Hospital, Cardiology Dept., Heraklion, Greece*

Purpose: Angiopoietins (Ang) are significant angiogenic and endothelial cell growth factors and are related with an increased risk of atherogenesis and target organ damage in hypertension. We investigated the effect of perindopril – a long-acting angiotensin-converting enzyme inhibitor (ACE-i) - on Ang1 and Ang2 gene expression in peripheral monocytes in hypertensive patients.
Methods: We recruited 30 previously untreated patients with mild or moderate hypertension (19 male, aged 63±10 years) who were randomly assigned to receive treatment with either perindopril (n= 16) or atenolol (n= 14), achieving a mean blood pressure below 140/80 mmHg. Blood samples were taken before and 3 months after therapy initiation. Mononuclear cells were isolated using anti-CD14+ antibodies and mRNAs were estimated by real-time quantitative reverse transcription-PCR and expressed as fold induction.
Results: Both treatments reduced all blood pressure components significantly ($p < 0.001$). In contrast with atenolol group, Ang1 gene expression was significantly downregulated after treatment with perindopril (fold induction in perindopril group 0.7±0.59 versus 1.51±1.68 in the atenolol group, p= 0.02). Ang2 gene expression did not show any significant difference between the two groups (fold induction in perindopril group 10.68±12.4 versus 12.4±15.9 in the atenolol group, p= 0.19).
Conclusions: Treatment with perindopril results in a significant attenuation in Ang1 expression in hypertension patients. Our findings may provide new insights into the benefits and cardiovascular protection of ACE-i in hypertensive patients.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1377 Safety, tolerance and pharmacokinetics of biolimus A9 in healthy subjects in a single ascending dose study

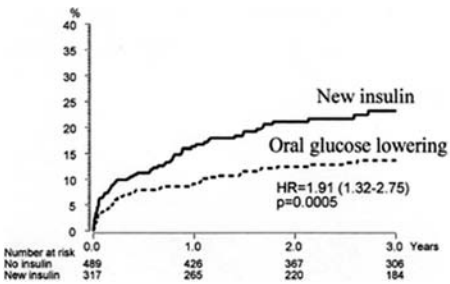
U. Christians[1], C. Dingmann[2], B. Bucher-Bartelson[3], W. Steudel[2] on behalf of Biolimus A9 Single Ascending Dose Study Group. [1]*University of Colorado Health Sciences Center, Anesthesiology, Denver, Co, United States of America;* [2]*University of Colorado Health Sciences Center, Department of Anesthesiology, Denver, Co, United States of America;* [3]*Colorado Prevention Center, Denver, Co, United States of America*

Background: Biolimus A9 (BA9) was developed for coating coronary stents to prevent smooth muscle cell proliferation and restenosis. The primary goal of this study was to identify the highest safe IV dose of BA9 that is tolerated in healthy humans. Secondary goals included: characterizing clinical symptoms of BA9 toxicity and evaluating the dose-dependent pharmacokinetics of BA9 and its metabolites after IV administration.
Methods: This Phase 1 trial in healthy subjects was designed as a double-blind, placebo-controlled, randomized, ascending single-dose safety trial. BA9 was administered intravenously over 30 min to a total of 28 enrolled subjects between the ages of 21 - 45. The subjects were assigned to 4 cohorts: cohort 1: 0.0075 mg/kg BA9 IV, n=6; 2 subjects received placebo (vehicle alone); cohort 2: 0.025 mg/kg BA9 IV, n=6; 2 subjects received placebo; cohort 3: 0.075 mg/kg BA9 IV, n=5; 1 subject received placebo; cohort 4: 0.25 mg/kg BA9 IV, n=4; 2 subjects received placebo. BA9 and metabolite concentrations were measured using a validated, sensitive, automated LC-MS/MS assay. Pharmacokinetic parameters were calculated using a non-compartmental model.
Results: Single IV BA9 doses up to 0.075 mg/kg were well tolerated. The highest dose of 0.25 mg/kg produced reversible adverse events and still can be considered safe. The most frequent adverse events related to high BA9 exposure were headache, nausea and mouth ulcers due to immunosuppression. Exposure to the highest BA9 dose of 0.25 mg/kg did not result in QTcB prolongation. Measurable Biolimus A9 exposure (>10 pg/mL) could be documented for at least 2 weeks. The BA9 metabolites 46-hdroxy, 25-hydroxy, 24 hydroxy, 12-hydroxy, 14-hydroxy, 11-hydroxy, piperidine hydroxyl, 49-hydroxy, and 16-O-desmethyl BA9 as well as sirolimus, everolimus, 16-O-desmethyl and 27-O-desmethyl everolimus were detected in blood of healthy subjects after a single BA9 IV dose.
Conclusions: All BA9-related adverse events at the highest single dose were reversible. Exposure to single BA9 doses (0.075 mg/kg) exceeding those coated on drug-eluting stents (BioMatrix II) up to 22-fold were tolerated without BA9-related adverse events.

P1378 May post myocardial infarction treatment with insulin provoke cardiovascular events in patients with type 2 diabetes?

L.G. Mellbin[1], K. Malmberg[1], A. Norhammar[1], H. Wedel[2], L. Ryden[1] on behalf of For the DIGAMI 2 investigators. [1]*Karolinska Institute, Medicine, Stockholm, Sweden;* [2]*Nordic School of Public Health, Gothenburg, Sweden*

Aims: Patients (pat) with type 2 diabetes (DM) and acute myocardial infarction (MI) have a serious prognosis. We explored the impact of glucose lowering treatment (GLT) on long-term prognosis.
Methods: 1181 MI pat (mean age 68 years; 67% males) with type 2 DM, discharged alive, were followed for a median of 2.1 years. The impact of GLT on cardiovascular (CV) events (death, MI and stroke) was analyzed by an updated Cox proportional hazard regression model, correcting for age, sex, smoking, DM duration, previous MI or heart failure, renal function and coronary interventions during hospitalisation and updated mean fasting glucose. At discharge 23, 17 and 59% of the pat were on sulphonylureas (SU), metformin (MET) and insulin (INS). Results are presented as Hazard Ratio (HR) and 95% Confidence Intervals (CI).
Results: Total mortality was not influenced by MET (HR 0.91, CI 0.61-1.34), SU (HR 1.08, CI 0.78–1.50) or INS (HR 1.12, CI 0.83-1.51). The risk for nonfatal MI and stroke decreased in pat on MET (HR 0.63, CI 0.42-0.95; p=0.03), was not influenced by SU (HR 0.81, CI 0.57-1.14; p=0.23) but increased on INS (HR 1.73, CI 1.26-2.37; p<0.0001). The result remained the same when comparing pat who at randomisation were assigned to newly instituted INS or to continue oral GLT (figure).



New MI or stroke during followup(Adj HR)

Conclusions: In patients with type 2 DM and MI, controlling for confounders including updated blood glucose, there was no significant difference in mortality between SU, MET and INS. The risk for nonfatal MI and stroke increased significantly by chronic INS while MET was protective.

P1379 Diabetic patients without baseline renal impairment are at increased risk of developing contrast induced nephropathy post percutaneous coronary intervention

E. Chong[1], L. Shen[2], H.C. Tan[1]. [1]*National University Hospital, The Heart Institute, Singapore, Singapore;* [2]*National University of Singapore, Biostatistics Department, Singapore, Singapore*

Purpose: We hypothesized that diabetic patients without baseline renal impairment (defined as serum creatinine < 1.5mg/dL) are also at increased risk of developing contrast induced nephropathy (CIN), defined as >25% increase in serum creatinine level within 48 hours post percutaneous coronary intervention (PCI), compared with non diabetics.
Methods: We retrospective studied 1158 patients who underwent elective or emergency PCI between July 2004 and April 2006 and divided them into 3 groups (Gps): Gp A: Diabetics with normal renal function (n= 304) Gp B: Non diabetic with normal renal function (n=465) Gp C: Patients with impaired baseline renal function (n=70). Oral N-acetylcysteine (NAC) 1.2g bid for 48 to 72 hours was routinely given to Gp C patients but not to the other 2 Gps.
Results: Median age for Gp A B C were 58, 56, 64 years respectively. Gp C was significantly elder than the other Gps ($p < 0.001$). Prevalence of hypertension in Gp A B C was 76.3%, 56% and 85.7% respectively. Gp A and C had significantly higher proportion of hypertensive patient than Gp B ($p < 0.001$). Baseline demographics were comparable among the 3 Gps with regard to gender, left ventricular systolic function (median value for Gp A B C were 51.5%, 55%, 50% respectively) and volume of contrast use (mean value for Gp A B C were 223±89 ml, 222±86ml, 194±51ml respectively). The baseline serum creatinine levels in Gp A B C were 0.95 mg/dL, 0.99 mg/dL and 1.67 mg/dL respectively. The incidence of CIN in the 3 Gps were: Gp A 8.9%, Gp B 4.3% and Gp C 4.5%, p=0.042. There was no difference in the incidence of CIN in the renal impaired group (Gp C) with NAC prophylaxis compared to the normal renal function group (Gp B) (4.5% vs 4.3%, p = 0.789). The incidence of CIN in the normal renal function diabetic group (Gp A) without NAC prophylaxis was significantly higher than the other 2 Gps (p< 0.001).
Conclusions: Our findings suggest that diabetic patients with normal renal function are also at increased risk of developing CIN and that prophylaxis with NAC prior to PCI should be considered.

P1380 Antrodia camphorata modulates smooth muscle cell proliferation and migration and decreases neointima formation after arterial injury

Y.-H. Li[1], H.-C. Chung[1], T.-H. Chao[1], S.-L. Liu[1], J.-C. Chen[2]. [1]*National Cheng Kung University Medical Center, Div.Of Cardiology, Dept.Of Internal Medicine, Tainan, Taiwan;* [2]*Southern Taiwan University of Technology, Tainan, Taiwan*

Background: Antrodia camphorata (AC) is a well-known traditional Chinese medicine. It has been shown to interfere with matrix metalloproteinase expression and inhibit migration of cancer cells. We examined whether AC could inhibit rat aortic smooth muscle cell (RASMC) proliferation and migration and evaluated its effect on neointima formation in mouse carotid artery after injury.
Methods: In MTT cell proliferation assay, RASMCs were pretreated with AC or saline and stimulated with 10 ng/mL platelet-derived growth factor (PDGF). The proliferation was expressed as MTT absorbance ratio of AC-treated to saline-treated cells. In Transwell migration chamber assay, RASMCs were treated with AC or saline. PDGF (10 ng/mL) was added to the lower compartment. Migrated cells on the lower side were fixed and counted. The migration ability was expressed by the cell number ratio of AC-treated to saline-treated cells. In wound scratch assay, RASMCs were pretreated with AC or saline and were seeded into confluent cell monolayers. They were wounded with pipette tips and stimulated with 10 ng/mL PDGF. The migration ability was expressed by the migration distance ratio of AC-treated to saline-treated cells. The left common carotid arteries of C57BL/6 mice were ligated near the carotid bifurcation. Then, the mice were fed with water or AC for 4 weeks and the severity of neointima formation was measured and expressed as intima/media (I/M) ratio.
Results: AC treatment reduced the PDGF-induced RASMCs proliferation (saline vs 50 vs 100 vs 500 μ g/mL AC, 100% vs 43±8% vs 31± 7% vs 15±2%, p<0.05). In Transwell migration chamber assay, AC treatment inhibited PDGF-induced RASMC migration in a dose dependent fashion (saline vs 50 vs 100 vs 500 μ g/mL AC, 100% vs 66±17% vs 52± 10% vs 35±10%, p<0.05). The inhibitory effect of AC on RASMC migration was also proved in wound scratch assay (saline vs 50 vs 100 vs 500 μ g/mL AC, 100% vs 98±5% vs 85±3% vs 69±12%, p<0.05). The AC-treated mice demonstrated significantly less neointima formation at 4 weeks after carotid ligation (I/M ratio, water, n=14 vs 250, n=15 vs 1250 mg/kg AC, n=15; 1.51±0.26 vs 0.48±0.15 vs 0.41±0.12, p<0.05).
Conclusion: Our data indicated that AC is an effective inhibitor of PDGF-induced

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

RASMC proliferation and migration. AC treatment significantly reduced neointima formation in the mouse carotid ligation model.

P1381 Simvastatin attenuates cardiac hypertrophy, but not myocardial fibrosis, in spontaneously hypertensive rats with and without large blood pressure variability

N. Takayama[1], H. Kai[2], H. Kudo[2], T. Mori[2], D. Fukui[2], K. Takemiya[2], A. Ikeda[2], T. Imaizumi[2]. *[1]Kurme University School of Medicine, Cardiology Department, Kurume, Japan; [2]kurume University school of medicine, Kurume, Japan*

Purpose: In hypertensives, large blood pressure (BP) variability aggravates organ damages. Recently, we have shown that acute BP elevation induces perivascular inflammation and cardiac remodeling. Statin has an anti-inflammatory effect. We assessed the hypothesis that large BP variability exaggerates cardiac remodeling in spontaneously hypertensive rats (SHR) and statin attenuates it with or without large BP variability.
Method: A new model of chronic hypertension with large BP variability was created by performing bilateral sino-aortic denervation (SAD) in SHR. After operation, simvastatin (Simva, 0.2 mg/kg/day) or the vehicle was administered in SHR+sham+vehicle (control SHR), SHR+sham+Simva, SHR+SAD+vehicle, and SHR+SAD+Simva. 6 weeks after operation, 24-hour BP was monitored telemetrically. Thereafter, the left ventricle (LV) was weighed and subjected to histological analysis.
Results: The mean BP did not differ among the 4 groups. SAD had significantly increased BP variability. Simva did not affect BP variability. SAD remarkably aggravated LV and myocayte hypertrophy and perivascular fibrosis and induced massive reparative fibrosis. In sham-operated SHR and SAD, Simva significantly reduced by LV weight over body weight ratio [LVW/BW] and myocyte diameter, but not the perivascular fibrosis.
Conclusions: Large BP variability aggravated hypertensive cardiac remodeling such as LV and myocyte hypertrophy and the perivascular and reparative fibrosis. Statin attenuated cardiac hypertrophy, but not myocardial fibrosis, in SHR with and without large BP variability.

P1382 Safety of biolimus A9 in a double-blinded, placebo-controlled multiple ascending dose trial

U. Christians[1], B. Bucher-Bartelson[2], M. Gonzalez[3], S. Reilley[4] on behalf of Biolimus A9 Multiple Ascending Dose Study Group. *[1]University of Colorado Health Sciences Center, Anesthesiology, Denver, Co, United States of America; [2]Colorado Prevention Center, Denver, Co, United States of America; [3]P'Kinetics, Pembroke Pines, Fl, United States of America; [4]Northwest Kinetics, Tacoma, Wa, United States of America*

Background: Biolimus A9 (BA9) was developed for coating coronary artery stents to prevent smooth muscle cell proliferation and restenosis. It was the goal of this study to establish safety of BA9 IV administration by infusion in healthy subjects: (A) to establish a significant safety margin of BA9 exposure after BioMatrix II drug eluting stent implantation, (B) to establish tolerability of BA9 exposure during multiple dosing, and (C) to characterize the pharmacokinetics of BA9 and its major metabolites after multiple doses.
Methods: This Phase 1 trial in healthy subjects was designed as a single center, double-blind, placebo-controlled, randomized, multiple ascending IV dose safety and tolerability trial. BA9 or placebo was administered intravenously to a total of 19 enrolled subjects between the ages of 21-65 years. Fifteen subjects were randomized to receive BA9. Subjects randomized to receiving BA9 were dosed (0.00625 mg/kg dose infused IV over 30 minutes) every 12 hours for a total of 7 days, and those randomized to placebo received an equivalent volume of formulation without BA9. Once safety was established, the doses were doubled to 0.0125 mg/kg/12 hours for the following 7 days. BA9 was quantified in blood using a highly sensitive, validated LC-MS/MS assay.
Results: During this multiple ascending dose trial, 7.8-10.0-fold higher exposure to BA9 than after implantation of up to two BA9-eluting stents (BioMatrix II) was achieved over 42 days. There was no accumulation of BA9 during the first week of dosing and accumulation by an average of 1.7-fold between study day 8 and 14 after the dose was doubled. All treatment-related adverse events were of mild (61/68 events) and moderate (7/68) intensity and of transient nature. The major likely Biolimus A9-related adverse events during the exposures achieved over the study period were transient headaches, anemia and liver enzyme elevations. There was no clinically relevant immunosuppression as assessed using a PHA-stimulated lymphocyte proliferation assay.
Conclusions: Our study established an at least 7.8-10.0-fold safety margin over the exposure typically observed after implantation of up to two BioMatrix II stents.

P1383 Relationship between blood pressure variability and left ventricular function as defined by pre-ejection period and ejection time in treated hypertensive subjects

G. Bilo[1], A. Giglio[2], K. Styczkiewicz[1], D. Czarnecka[3], L. Lonati[2], G. Branzi[2], G. Mancia[4], K. Kawecka-Jaszcz[5], G. Parati[5]. *[1]Ist Aux Italiano and Jagiellonian Univ, II Cardiology Unit-I Dept Cardiology-Hypert, Milan And Crakow, Italy; [2]S.Luca Hospital, Ist Auxologico Italiano, II Cardiology Unit, Milan, Italy; [3]Jagiellonian Univ, I Dept Cardiology-Hypert, Crakow, Poland; [4]University Milano-Bicocca-Ist Aux Italiano, Clinical Medicine, Milan, Italy; [5]Jagiellonian University, I Dept Cardiology and Hypertension, Crakow, Poland*

Purpose: Blood pressure variability (BPV) correlates with target organ damage and cardiovascular events. Little is known on its relation with left ventricular (LV) function. Aim of this study was to assess the relationship between (BPV) and LV function as defined by pre-ejection period (PEP) and ejection time (ET).
Methods: Forty-nine treated hypertensive subjects (age 61.5±10.1 years, BMI 26.6±4.1 kg/m^2) underwent 24 h ambulatory BP monitoring (ABPM; A&D TM2430). Mean 24 h, day and night systolic (S) and diastolic (D)BP and heart rate (HR) values were computed. BPV was quantified by 24h standard deviations (SD) and by weighted 24 h SD (wSD) of BP as previously described. PEP and ET were measured from simultaneous registration of ECG and phonocardiogram (Colin VP-1000 device). ET/PEP ratio was also computed.
Results: Age was related to ET (r=0.39, $p<0.005$) and ET/PEP (r=0.44, $p<0.002$) and BMI was related to PEP (r= -0.36, $p<0.02$). 24 h HR was strongly related to ET (r=-0.74, $p<0.001$) and to ET/PEP (r=-0.57, $p<0.001$). Pearson's correlation coefficients of BP and BPV parameters with PEP, ET and ET/PEP are presented in Table. * $p<0.05$, ** $p<0.01$, ° $p<0.005$, °°$p<0.001$. In multivariate analysis (adjusted for age, BMI, 24h HR and 24h SBP) SBP wSD (but not 24h SD) remained significantly related to PEP (β=-0.31), while 24h SBP SD (β=0.26), 24h SBP wSD (β=0.34) and daytime SBP SD (β=0.31) were related to ET/PEP.

	PEP			ET			ET/PEP		
24 h	Day	Night	24 h	Day	Night	24 h	Day	Night	
SBP	-0.23	-0.20	-0.21	0.12	0.06	0.18	0.23	0.16	0.26
DBP	0.23	0.21	0.21	-0.33*	-0.32*	-0.29*	-0.38**	-0.36*	-0.33*
SBP SD	-0.39**	-0.39°	-0.31*	0.32*	0.31*	0.31*	0.45°	0.47°°	0.40°
DBP SD	-0.28	-0.33*	-0.11	0.11	0.18	0.01	0.25	0.34*	0.06
SBP wSD	-0.43°	NA	NA	0.36*	NA	NA	0.51°°	NA	NA
DBP wSD	-0.30*	NA	NA	0.15	NA	NA	0.29*	NA	NA

Conclusions: BPV is an independent predictor of cardiac cycle subperiods indirectly defining LV function. The factors involved in this relationship may include sympathetic activation (through increased myocardial contractility and increased peripheral resistance) and arterial compliance. Our results further support wSD as a more reliable index of 24 h BPV.

P1384 F 15845: a potent persistent sodium current blocker abolishes ischemia-induced ST-segment elevation

C. Pignier, R. Letienne, B. Vacher, A. Delhon, B. Le Grand. *Centre de Recherche Pierre Fabre, Maladies Cardiovasculaires II, Castres, France*

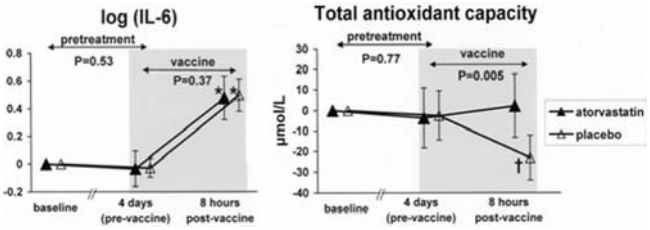
The effects of F 15845, a new compound targeting cardiac sodium channel operating in "persistent" mode, have been investigated in different models of cardiac ischemia. Investigation of its mechanism of action was performed on human cardiac wild type (hNav1.5) and mutated (DeltaKPQ) sodium channels transfected in HEK 293 cells by means of patch clamp technique in whole cell configuration. F 15845 inhibited veratridine-induced persistent sodium current (INap) in a concentration-dependent manner. When elicited at –30 mV from a holding potential of –110 mV, F 15845 reduced persistent INa with IC50 of 6 μM, and with IC50 of 3 μM when INap was elicited from –90 mV. This suggested that action of F 15845 on INap could be voltage-dependent. Whereas voltage activation parameters were not affected, F 15845 (10 μM) shifted steady-state inactivation V0.5 mean values from –80.7±2.3 mV to –89.7 mV (n=7, $P<0.05$). Similar results were obtained on INa-DeltaKPQ with 50±9% inhibition (n=6,$P<0.05$) and a leftward shift of –3.8 mV (n=6, $P<0.001$) of the steady-state inactivation V0.5 at 10 μM F 15845. As a comparison, ranolazine reduced veratridne-induced INap by 11.4 ±7.1% (n=5) and 15.2±7.6% (n=4), at 10 and 32 μM, respectively. The potential antianginal activity of F 15845 was evaluated in two models of myocardial ischaemia-induced ST segment changes, a supply ischaemia model in anesthetized rabbits subjected to a transient coronary occlusion and a demand ischaemia model in anesthetized dogs with coronary stenosis subjected to left atrial pacing. In the rabbit model, F 15845 produced highly effective, dose-dependent inhibition of ischaemia-induced ST segment elevation following i.v. (ED50 0.05 mg/kg) or oral (ED50 0.13 mg/kg) administration, without hemodynamic effects. The oral anti-ischemic activity remained significant 4 hours after a single administration of F 15845. In the canine model of demand ischaemia-evoked ST segment changes, F 15845 (0.16-0.63 mg/kg) inhibited ischaemia-induced ST segment elevation from 0.16 mg/kg i.v. in the absence of cardiac hemodynamic and electrocardiographic effects. In conclusion, F 15845, a novel persistent sodium channel blocker, exerts potent antianginal activities without any hemodynamic cardiac effects.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1385 Beneficial effect of atorvastatin on the oxidant stress response induced by acute inflammation

A. Dagre, C. Vlachopoulos, C. Masoura, C. Vasiliadou, K. Aznaouridis, J. Skoumas, E. Stefanadi, C. Pitsavos, C. Stefanadis. *Athens Medical School, Hippokration Hospital, Athens, Greece*

Purpose: Acute inflammation is associated with increased oxidant stress and a transient increased cardiovascular risk. It is currently unknown whether atorvastatin influences the potential adverse effect of acute inflammation on oxidant state.
Methods: In this randomized, double blind, placebo-controlled study, we generated an acute, mild inflammation by Salmonella Typhi vaccination in 50 volunteers with mild hypercholesterolemia (mean age 41 years), after a 4-day period of treatment with atorvastatin 40 mg or placebo at bedtime. Interleukin-6 (IL-6, a major cytokine that initiates the inflammatory cascade) and lasma total antioxidant capacity (TAC, a measure of antioxidant reserve) were measured 3 times: at baseline and 4 days later (before and 8 hours after vaccination). Values of IL-6 were log-transformed prior to analysis because of skewed distribution.
Results: In the pretreatment period, a torvastatin did not affect the level of IL-6 and TAC. In the placebo group, vaccination caused a significant increase of IL-6 (by 3.36 pg/mL, *P<0.001, shaded area of left figure) and a decrease of TAC (by 20.6 μ mol/L, † P=0.001, shaded area of right figure) at 8 hours. Pretreatment with atorvastatin fully abrogated the vaccination-induced reduction of TAC (P=0.005 compared to placebo by ANCOVA, right figure), although it did not prevent the prominent rise of IL-6 (P=NS compared to placebo, left figure).



Changes from baseline

Conclusions: In dyslipidemic patients, atorvastatin may fully abrogate the deterioration of oxidant state caused by acute inflammation, although this drug does not blunt the initiation of the acute inflammatory response. The potential clinical significance and the mechanisms that underlie this divergent effect of atorvastatin warrant further investigation.

P1386 Prasugrel 60 mg versus Clopidogrel 600 mg: greater platelet inhibition with Prasugrel is explained by higher concentrations of the active metabolite

K.J. Winters[1], C.D. Payne[2], C.S. Ernest[1], G.Y. Li[1], N.A. Farid[1], J.A. Jakubowski[1], D.E. Salazar[3], D.S. Small[2]. *[1]Eli Lilly and Company, Indianapolis, United States of America; [2]Eli Lilly and Company, Windlesham, United Kingdom; [3]Daiichi Sankyo, Inc., Edison, United States of America*

Background: The thienopyridine prodrugs prasugrel (Pras) and clopidogrel (Clop) are each metabolized to an active metabolite (AM) that irreversibly inhibits ADP-induced platelet aggregation with comparable potency; the metabolic pathways differ. The approved Clop regimen is a 300 mg loading dose (LD) followed by daily 75 mg maintenance doses (MD). Due to "Clop resistance" in 20-30% of patients given a 300 mg LD, some physicians use a Clop 600 mg LD. Pras 60 mg and Clop 600 mg reduce maximum platelet aggregation (MPA) more than Clop 300 mg, but Pras 60 mg and Clop 600 mg have not been compared.
Methods: In a randomized crossover study, 41 healthy subjects received each of the following treatments (LD/MD for 7 days, in mg): Pras 60/10, Clop 300/75, and Clop 600/75, each separated by ≥14 day washouts. Plasma AM concentrations were measured using a validated LC/MS/MS assay. MPA to 20 μM ADP was assessed by light transmittance aggregometry.
Results: The rank order of AM C_{max} and AUC was Pras 60 mg > Clop 600 mg > Clop 300 mg after the LD and Pras 10 mg > Clop 75 mg during MD, indicating that lower MPA can be explained by higher exposure to the AM. Exposure to Clop's AM increased less than proportionally to dose from 75 mg to 300 mg to 600 mg, suggesting dose-limited Clop absorption and/or metabolism.
Conclusions: These results support our hypothesis and the results of studies that find little additional MPA reduction from a Clop 600 mg LD compared to 300 mg.

Dose group, treatment phase	Pharmacokinetic parameter estimate for active metabolite (N=31-33)[a]			MPA (%) to 20 μMADP (N-41)[b]	
	C_{max}[c] (nM)	$AUC_{(0\text{-}tlast)}$[c] (nM × hr)	T_{max}[d] (hr)	30 min	24 hr
60 mg Pras, LD	1460(42%)	1700(32%)	0.5(0.5-2.0)	38.6(33.7, 43.4)	11.6(6.8, 16.5)
10 mg Pras, MD	250(47%)	237(35%)	1.0(0.25-2.0)	NM[e]	19.8(14.9, 24.7)
600 mg Clop, LD	458(61%)	750(47%)	1.0(0.5-1.5)	75.6[f](70.6, 80.6)	31.7[f](26.7, 36.8)
75 mg Clop, MD	162(68%)	171(58%)	1.0(0.5-1.5)	NM[e]	39.9[f](34.8, 45.0)
300 mg Clop, LD	396(57%)	520(55%)	1.0(0.5-1.1)	77.7[f](72.6, 82.7)	42.7[f](37.7, 47.7)
75 mg Clop, MD	181(62%)	186(55%)	0.5(0.5-2.0)	NM[e]	35.4[f](30.3, 40.5)

a) Does not include 8-10 subjects whose blood samples were mishandled during processing or shipping; 3 subjects not included because Cmax < 1ng/mL. b) Least squares mean (90% confidence interval). c) Geometric mean (coefficient of variation). d) Median (range). e) Not measured during maintenance dosing. f) p < 0.001 vs. prasugrel at same time in same treatment phase.

P1387 Similar association between age and outcomes in high-risk ACS patients treated with enoxaparin or unfractionated heparin

R.D. Lopes[1], G. Marcucci[1], H.D. White[2], S.A. Spinler[3], J. Col[4], D.C. Gulba[5], P.E. Aylward[6], R.M. Califf[2], J.J. Ferguson[7], K.W. Mahaffey[2]. *[1]Duke Clinical Research Institute, Durham, United States of America; [2]Green Lane Cardiovascular Service, Auckland, New Zealand; [3]University of the Sciences in Philadelphia, Philadelphia, United States of America; [4]Clinique Universitaire St. Luc, Brussels, Belgium; [5]Krankenhaus Dueren, Dueren, Germany; [6]Flinders Medical Centre, Adelaide, Australia; [7]Texas Heart Institute, Houston, United States of America*

Background: Using SYNERGY data, we studied the effect of age on outcomes and the association of age and outcomes with the use of enoxaparin or UFH.
Methods: Enrollment required ≥2 of the following: + biomarkers, ECG changes, or age ≥60. Baseline traits were analyzed. To adjust for differences, baseline covariates, age, and random treatment assignment were analyzed using multivariable models. Logistic models were used for 30d death/MI and in-hospital bleeding. Cox proportional hazards models were used for 30d and 1y death. Risk odds ratios are for increase in 10 yrs of age. Potential differential effect of treatment on age was evaluated using interaction terms. Age was described as <75 and ≥75 and analyzed as a continuous variable.
Results: 9977 pts had age data; 7437 (74.5%) <75 and 2540 (24.5%) ≥75. Patients ≥75 had more CV risk factors, including hypertension (75 vs 66%), prior MI (31 vs 27%), TIA (7 vs 3%), CHF (14 vs 8%), PVD (13 vs 9%), stroke (8 vs 4%), Killip class ≥3 (4 vs 2%), and higher systolic BP (median 134 vs 130 mm Hg).

Event of interest, p value for interaction of age & treatment	Treatment group	Risk OR	95% CI
Death or MI to 30 days, p=0.857	UFH	1.15	1.04, 1.27
	Enoxaparin	1.13	1.02, 1.26
Death to 1 year, p=0.520	UFH	1.41	1.23, 1.62
	Enoxaparin	1.49	1.30, 1.70
TIMI bleed,* p=0.174			
Age <75	UFH	1.20	1.03, 1.39
	Enoxaparin	1.23	1.07, 1.42
Age ≥75	UFH	0.62	0.41, 0.93
	Enoxaparin	0.96	0.70, 1.32
GUSTO bleed, p=0.085	UFH	1.06	0.84, 1.32
	Enoxaparin	1.33	1.07, 1.65
Transfusion, p=0.214	UFH	1.00	0.92, 1.10
	Enoxaparin	1.07	0.98, 1.18

*Association b/t age and TIMI bleed changed at about 75 yrs. Data are presented for pts =75 for that endpoint.

Conclusion: Patients ≥75 have more high-risk characteristics and worse long-term outcomes. The association of age with outcomes is similar in patients treated with enoxaparin or UFH.

P1388 Oral contraceptive use as a major cause of C-reactive protein rise in the female general population

E.R. Rietzschel[1], M.L. De Buyzere[1], D. De Bacquer[2], M. Langlois[3], S. Bekaert[2], P. Segers[3], P. Van Damme[4], P. Verdonck[4], G.G. De Backer[3], T.C. Gillebert[4] on behalf of the ASKLEPIOS investigators. *[1]University Hospital Ghent, Department of Cardiovascular Diseases, Ghent, Belgium; [2]Ghent University, Department of Public Health, Ghent, Belgium; [3]AZ St-Jan AV Hospital, Department of Clinical Chemistry, Bruges, Belgium; [4]Asklepios Primary Care Physicians VOF, Erpe-Mere/Nieuwerkerken, Belgium*

Purpose: High-sensitive C-reactive protein (hs-CRP) is promoted as a marker of low-grade inflammation, identifying individuals with increased cardiovascular risk. Hormonal therapy with estrogen (E) alone or combined with progestins (P) are among the most frequently used drugs in the world. Recent reports consistently link hormone replacement therapy (HRT) to elevated levels of hs-CRP, venous and arterial thrombosis and adverse outcome. Oral contraception (OC) is a drug therapy using 10 to 100 fold higher levels of estrogen than HRT, yet its effects on inflammation (hs-CRP) at the population level are less documented.
Methods: The Asklepios study is a blinded sample of 2524 M/F volunteers (median age 45.9 y), representative of the Belgian population between 35-55 years, free from overt cardiovascular disease. The subjects were extensively screened (biochemistry, questionnaire data, cardiac and vascular echography). hs-CRP was assayed by particle-enhanced immuno-turbidimetry on fasting subjects, free from clinical inflammation.
Results: Of 1301 women, 803 (NoH; 62.6%) were taking neither OC/HRT, 352 women (OC; 27.4%) were taking OC and 128 (HRT; 10.0%) were taking HRT. Crude hs-CRP levels were (in mg/l; median [IQR]): NoH 1.0 [0.5-2.1]; HRT 1.3 [0.7-2.6] and OC 3.5 [1.5–5.9]. After multivariate adjustment for confounders:

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

age, season, smoking, blood pressure, total & HDL-cholesterol, body size, diabetes, physical activity, fruit, vegetable and alcohol intake, educational achievement and drug therapy (lipid-lowering, antihypertensive, aspirin), the hs-CRP levels were (adjusted geometric mean [95% CI]): NoH 1.0 [0.9–1.1]; HRT 1.2 [1.1–1.5] and OC 3.3 [3.3–3.6]; (OC vs NoH: $p<0.001$; HRT vs NoH: $p<0.05$). Effects on other inflammatory markers (interleukin-6, ox-LDL-cholesterol, ...) was far less pronounced.
Conclusions: Contraceptive hormone therapy is a major cause of hs-CRP rise in the general population. The magnitude of CRP-rise (3-fold) by far exceeds other population-prevalent non-infectious stimuli and is much larger than the hs-CRP rise for HRT (+20%). More than 50% of apparently healthy women taking OC have hs-CRP levels > 3 mg/l, considered to indicate "high-risk". Future research should take into account this effect when reporting CRP data in women potentially taking OC, aim to qualify the biological significance of the reported effect and assess the potential of hs-CRP as a tool to select those women at high thrombotic risk under hormonal therapy.

P1389 Effects of N-3 PUVA supplementation on mortality in cardiovascular disease

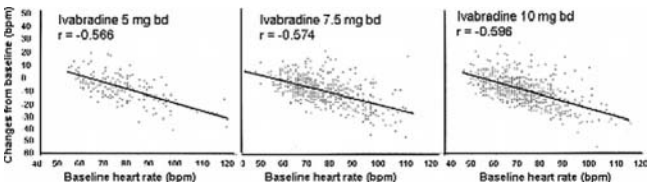
A. De Waha, D. Moertl, B. Meyer, G. Sodeck, M. Huelsmann, R. Pacher, R. Berger. *Vienna, Austria*

Purpose: The effects of N-3 polyunsaturated fatty acids (PUVA) on total mortality and various cardiovascular endpoints on patients with cardiovascular disease is unclear. We performed a meta-analysis of randomized, double-blind, controlled trials (RCT) investigating the supplemental intake of N-3 PUVA in patients with cardiovascular disease.
Methods: In a comprehensive literature search, RCTs comparing fish oil supplementation with placebo in patients with cardiovascular disease were analysed for relevant outcome data. Two investigators independently extracted trial data, applied inclusion criteria and performed quality assessment.
Results: A total of 19 trials, published between 1966 and 2006, included 2442 patients in the intervention and 2383 patients in the placebo group. The pooled estimate showed a significant reduction of the total mortality by N-3 PUVA intake compared to placebo (relative risk 0.69, 95% confidence interval 0.52 to 0.92). This was also true when excluding studies in which patients with recent myocardial infarction were involved (RR 0.60, 95% CI 0.36-1.00). No significant risk reduction could be detected concerning the endpoints restenosis rate after percutaneous transluminal coronary angioplasty (PTCA; RR 0.96, 95% CI 0.83-1.11); myocardial infarction (RR 0.87, 95% CI 0.64-1.18), occurrence of implantable cardioverter defibrillator (ICD) shocks (RR 0.94, 95% CI 0.71-1.26); sudden death (RR 0.50, 95% CI 0.20-1.25), episode of cardiac decompensation (RR 1.16, 95% CI 0.71-1.90), and heart failure death (RR).
Conclusions: This meta-analysis of RCTs suggests a significant reduction of total mortality by N-3 PUVA supplementation in patients with cardiovascular disease. Data on various cardiovascular endpoints are inconclusive.

P1390 Low incidence of severe bradycardia during therapy with ivabradine: the heart lowering effect is limited by baseline heart rate

I. Savelieva[1], J.S. Borer[2], A.J. Camm[1] on behalf of Ivabradine Programme Investigators. [1]*St George's University of London, Cardiac And Vascular Sciences, London, United Kingdom;* [2]*Weill Medical College, Cornell University, New York, United States of America*

The use of heart rate (HR)-lowering drugs in patients with heart disease may be associated with the risk of excessive bradycardia leading to hypotension, exacerbation of angina and arrhythmias. Ivabradine is a novel pure HR-lowering agent for treatment of stable angina that acts specifically on the sinus node by selectively inhibiting the I_f current. In experiments, ivabradine produced a plateau dose-response, use-dependent effect on HR reduction. Objectives. To investigate (1) whether HR reduction by ivabradine correlates with baseline HR in the clinical setting; and (2) whether this property of ivabradine translates into fewer adverse event reports of bradycardia compared with conventional HR-lowering drugs.
Methods: A total of 1328 patients with documented coronary artery disease and stable angina had their resting ECGs recorded at baseline and after 3 to 4 months of treatment with ivabradine 5, 7.5, or 10 mg bd. ECGs were read centrally by cardiologists blinded to treatment assignment.
Results: Inverse linear correlations between baseline HR and changes in HR on treatment were observed for all 3 doses of ivabradine (Figure). Thus, the magnitude of the HR-lowering effect of ivabradine was the highest in patients with sinus tachycardia at baseline and the least in those with the lowest baseline HR, which is consistent with the known effect of HCN4 channel function modulation by the autonomic nervous system. The incidence of bradycardia < 40 bpm was 0% and 0.5% in patients receiving 2 recommended treatment doses of 5 and 7.5 mg bd, respectively.
Conclusion: The HR-lowering effect of ivabradine is determined by HR at baseline. This property accounts for a low incidence of severe bradycardia during therapy with ivabradine.



P1391 The effect of N-acetylcysteine on oxidative stress after PCI for acute myocardial infarction

K. Iltumur[1], S. Gulsum[2]. [1]*Dicle University Faculty of Medicine, Cardiology Department, Diyarbakir, Turkey;* [2]*Dicle University, Cardiology, Diyarbakir, Turkey*

The prognostic value of oxidative stressin patients with acute myocardial infarction is known. As an antioxidant and anti-inflammatory agent the protective effects of N-acetylcysteine (NAC) are documented in several studies. This study was designed to determine the effect of NAC treatment on the oxidative stress after primary percutaneous intervention (PCI) for acute myocardial infarction (AMI).
Fifty patients (mean age 54.72±8.2 years) presenting with AMI who underwent reperfusion therapy (PCI) were randomized into a NAC (+) group (n = 25) and NAC (-) group (n = 25). Twenty-five control subjects were also enrolled in the present study. Malondialdehyde (MDA), oxide low-density lipoprotein (ox-LDL) and total antioxdant capacity were analyzed for investigation of oxidative stress. Blood samples were obtained just following PCI and 2 hours following procedure. Malondialdehyde and ox-LDL levels were significantly higher in AMI group than controls (MDA; 0.47±0.046 vs 0.26±0.055 mmol/L $p<0,001$, ox-LDL; 0.68±0.07 vs 0.27±0.03 U/L $p<0,0001$). However, at admission, total antioxidant activity were not different between the groups (2.02±0,27 vs 2.024±0.15, $p>0.05$). MDA levels prior and following the procedure were not significant difference in NAC (+) group (0.47±0.046 vs 0.51±0.056, $p>0,05$), whereas these levels were significantly higher in NAC (-) group (0.47±0.048 vs 0.54±0.056 $p<0.05$). Similarly, total antioxidant activity levels prior and following procedure were not significant difference in NAC (+) group (2.02±0.18 vs 2,01±0,34, $p>0,05$), whereas these levels were significantly reduced in without NAC group (2.01±1.03 vs 1.86±0.23, $p<0.05$).
Conclusion: The antioxidant N-acetylcysteine significantly diminishes oxidative stress after primary PCI for ST elevation AMI.

P1392 An endoscopic control of buccal and enteric-coated aspirin effect in coronary artery disease patients with gastrointestinal diseases: 12-month follow-up

N. Kucheriavaya[1], E. Kokurina[2], O. Ermakova[1], E. Bochkareva[1]. [1]*Russian Center For Preventive Medicine, Metabolic Disorders Department, Moscow, Russian Federation;* [2]*Russian Center For Prevent Med, Metabolic Disorders, Moscow, Russian Federation*

Purpose: To investigate the gastroduodenal mucosal tolerability to acetylsalicylic acid (ASA) buccal form (B-ASA) compared to enteric-coated ASA (EC-ASA) in coronary artery disease (CAD) patients with gastrointestinal diseases, in a randomized cross-over comparative study.
Methods: 51 pts (36 male, 15 female) aged 51-75 years with known CAD and clinically diagnosed remission of gastrointestinal diseases before the enrollment (gastric or duodenal ulcer, erosions, chronic gastritis) were included. All patients were randomized into 2 groups: I - received B-ASA 12,5 mg/day for 6 months, then EC-ASA 100 mg/day for 6 months; II – had the reverse order of treatment courses. Endoscopy was performed on entry and at the end of every 6-month treatment period. A 0-4 grade Lanza scale for evaluation of mucosa damage was used. Increase of a Lanza score by 1 or more after 6-month treatment was considered as a negative effect. Decrease of a score by 1 or the absence of any mucosa lesions were regarded as positive effect. Every 2 month all patients underwent usual clinical examination. Before the enrollment the Lahza score grade 3-4 were revealed endoscopically despite of clinically remission in 3 pts who required antiulcerous therapy and excluded from the study.
Results: After 6 month the negative effects was noted at 23 (61%) patients in EC-ASA group and only at 3 (8%) pts in B-ASA group ($p < 0,01$). In opposite in B-ASA group the positive dynamic of gastroduodenal mucosa was observed at 20 (53%) pts and there were no patients (0%) with the same effect in EC-ASA group ($p < 0,001$). No Lanza score dynamic was found at 15 (39%) and 15 (39%) patients in B-ASA and EC-ASA group ($p > 0,05$). We also reported 2 (4%) patients refused B-ASA due to local irritant action on the gum mucosa. 9 (19%) patients on EC-ASA were withdrawn according to dyspeptic symptoms and negative endoscopic data appeared.
Conclusions: The results of this study indicate that EC-ASA caused considerably more frequent duodenal and gastric damage without noticeable clinical symptoms than did B-ASA. In contrast, the administration of B-ASA led to reliable improvement of mucosa state. We assume that this feature of B-ASA is associated with the visceral microcirculation improvement caused by significant antiaggregation action had been demonstrated in early study and the absence of direct damage of gastroduodenal mucosa. We conclude that buccal ASA therapy appears to be safe in CAD patients with chronic gastric and duodenal erosions.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1393 Levosimendan improves quality of life and reduces emotional stress scores in patients with advanced heart failure

K. Papadopoulos[1], J.T. Parissis[2], M. Nikolaou[2], V. Bistola[2], D. Farmakis[2], V. Gogas[2], G. Filippatos[2], D. Kremastinos[2]. [1]*Attikon University Hospital, Athens, Greece;* [2]*Athens, Greece*

Aim: Levosimendan improves central hemodynamics and symptoms in acutely decompensated chronic heart failure (CHF) patients. However, its effects on quality of life, emotional stress and functional capacity of patients with advanced CHF have not been properly investigated.
Methods: Sixty-three advanced CHF patients (NYHA III-IV, Left Ventricular Ejection Fraction<30%) were randomized (2:1) to receive either a 24-hour levosimendan infusion of 0.1 μg/kg/min or placebo. Questionnaires addressing quality of life [Kansas City Cardiomyopathy Questionnaire (KCCQ), functional and overall, Duke's Activity Status Index (DASI)] and emotional stress [Zung self-rating depression scale (SDS), Beck Depression Inventory (BDI)], as well as plasma BNP and 6-min walking distance (6MWT as a marker of exercise capacity) were assessed before treatment and at hospital discharge.
Results: A significant improvement in NYHA class (2.1±0.7 from 3.3±0.7, $p<0.01$), 6MWT (305±152 from 215±142 meters, $p<0.01$) and plasma BNP (598±398 from 1078±756 pg/ml, $p<0.01$) was observed post-treatment only in levosimendan-treated group. KCCQ functional (45±19 from 35±17%, $p<0.05$) and overall (34±13 from 28±11%, $p<0.05$), DASI (26±13 from 22±12, $p<0.05$), Zung SDS (38±12 from 42±13, $p<0.01$) and BDI (11±6 from 14±8, $p<0.05$) scores also improved in levosimendan-treated patients, while remained unchanged in the placebo group. The hospital length stay was shorter in levosimendan group compared to placebo (3.2±1.7 versus 5.8±2.1 days, $p<0.01$). Levosimendan-induced BNP reduction was significantly correlated with concomitant increase in 6MWT ($r=0.643$, $p<0.001$) as well as with the decrease of BDI ($r=0.30$, $p<0.05$) and Zung SDS ($r=0.25$, $p=0.05$).
Conclusion: Levosimendan seems to have a beneficial effect on quality of life, physical activity and emotional stress in advanced CHF patients, reducing concurrently hospitalization length.

P1394 Isoeugenodilol inhibits smooth muscle cell proliferation and neointimal thickening after balloon injury via inactivating ERK1/2 pathway

J.R. Wu[1], J. Wu[2], J. Yeh[3], S.-F. Liou[4], Z.-K. Dai[5], I.-J. Chen[2], B.-N. Wu[2], Y.-P. Chang[2]. [1]*Kaohsiung Medical University Hospital, Pediatrics, Kaohsiung, Taiwan;* [2]*Kaohsiung Minucipal Hsiao-Kang Hospital, Pediatrics, Kaohsiung, Taiwan;* [3]*Kaohsiung Minicipal Hospital, Pharmacology, Kaohsiung, Taiwan;* [4]*Chia-Nan University of Pharmacy, Pharmacology, Tainan, Taiwan;* [5]*Kaohosiung Medical University, Pediatrics, Kaohsiung, Taiwan*

Purpose: To determine the efficacy and the possible mechanism of a synthesized drug, isoeugenodilol (a new third generation α-/β - adrenoceptor blocker) on the proliferation of cultured rat vascular smooth muscle cells (VSMCs) and neointimal formation in a rat carotid arterial balloon-injury model.
Methods: VSMCs were isolated from the thoracic aorta of Wistar rats, then incubated with or without drugs (isoeugenodilol, isoeugenolol, or labetalol). The final cell numbers were measured by incorporation of BrdU using a cell proliferation ELISA. The immunoreactive bands of primary antibodies of anti-MAP kinase 1/2 (ERK1/2), anti-phospho MAP kinase (ERK1/2), was detected by chemiluminescence reagents. The extent of neointimal formation was quantified by computed planimetry of histologically stained sections.
Results: Isoeugenodilol significantly inhibited both 10% fetal bovine serum (FBS)-and 20ng/ml platelet-derived growth factor (PDGF)-BB-induced proliferation. Neointimal formation, measured 14 days after injury, was reduced by the oral administration of isoeugenodilol in a dose-dependent fashion (5 and 10 mg/kg/day). The ratio of intima-to-media cross-sectional areas (I/M ratio) was calculated blindly using an imaging analysis system. Treatment with isoeugenodilol (10 mg/kg) resulted significantly (from 1.77±0.52 to 0.42±0.12; $P<0.01$; n=8) in inhibition of neointimal formation in rats at 2 weeks post-balloon injury In an in vitro assay, isoeugenodilol inhibited the migration of VSMCs stimulated by PDGF-BB.
Conclusions: These findings indicate that isoeugenodilol shows an inhibitory potency on neointimal formation due to inhibition of both migration and proliferation of VSMCs. The levels of phosphorylated MEK1/2 and Pyk2 as well as those of proliferative cell nuclear antigen (PCNA) were concentration-dependently reduced by isoeugenodilol. These results indicate that i soeugenodilol suppresses mitogen-stimulated proliferation of VSMCs in vitro and significantly attenuates neointimal formation in rats.

P1395 European post-marketing surveillance study on Niaspan in patients with high CV risk

J. Kastelein[1], D. Poldermans[2], U. Hostalek[3] on behalf of The NEMO Study Group. [1]*Academic Medical Center, Dept of Vascular Medicine, Amsterdam, Netherlands;* [2]*Academisch Ziekenhuis Rotterdam, Rotterdam, Netherlands;* [3]*Merck KGaA, Darmstadt, Germany*

Purpose: The main objective was to evaluate the safety and tolerability of prolonged-release nicotinic acid (Niaspan) up to 2000 mg/day for 6 months on top of a statin in a usual care setting in dyslipidemic patients at high cardiovascular risk.
Methods: This was a multicentre, open-label, observational study. Included were outpatients treated with Niaspan and a statin, who were considered at high cardiovascular risk (CHD with at least one previous cardiovascular event or with proven (CABG, PTCA) coronary artery disease or with significant stenosis documented by angiography, and/or diabetes mellitus type 2, and/or PROCAM Score > 20% in 10 years) and who had HDL-C values <1.3 mmol/l (50mg/dl) and/or triglycerides >1.7 mmol/l (150mg/dl). At each visit (after 2-3 months and after 6 months), the incidence of adverse events (AE) and of serious AE was evaluated. Lipid parameters were recorded at baseline and at each visit, if available.
Results: A total of 1053 patients were recruited, thereof 82.4% with CHD, 53.1% with metabolic syndrome, and 42.1% with diabetes. Flushing was the most common side effect (40.1%), but led only in 11.1% to withdrawal. Other drug-related AE occurred at low frequency (11.9%), and were cause of withdrawal in 8.5%. Serious drug-related AE were reported in 6 patients (0.6%); all resolved following stop of treatment. There was no hepatotoxicity (elevation of AST (GOT) or ALT (GPT) on the level of individual patients) or serious muscle AE (CPK >10 x ULN). TC (mean percent change -4.2%), LDL-C (mean percent change -4.1%), HDL-C (mean percent change +22.9%), and triglycerides (mean percent change -15.2%) improved markedly after 6 months of therapy compared to baseline.
Conclusions: This observational study confirms the safety and tolerability profile of Niaspan known from previous studies. Furthermore, the positive treatment effects of Niaspan could be shown under the conditions of daily practice.

P1396 Endothelial Protection, AT1 blockade and Cholesterol-Dependent Oxidative Stress: the EPAS trial

H. Morawietz[1], S. Erbs[2], J. Holtz[3], A. Schubert[2], W. Goettsch[4], V. Adams[2], F.W. Mohr[2], G. Schuler[2], R. Hambrecht[2]. [1]*University of Technology Dresden, Dept. Vasc. Endothelium And Microcirculation, Dresden, Germany;* [2]*University of Leipzig, Cardiology, Leipzig, Germany;* [3]*Martin Luther University Halle-Wittenberg, Institute of Pathophysiology, Halle, Germany;* [4]*University of Technology Dresden, Dept. Vasc. Endothelium And Microcirculation, Dresden, Germany*

Statins and angiotensin type 1 (AT_1) receptor blockers reduce cardiovascular mortality and morbidity. In the Endothelial Protection, AT_1 blockade and Cholesterol-Dependent Oxidative Stress (EPAS) trial, we tested in a clinical trial in PROBE (Prospective Randomized Open Label and Blinded Evaluation) design whether statin and AT_1 receptor blocker therapies independently or in combination influence endothelial expression of anti- and proatherosclerotic genes and endothelial function in arteries of patients with coronary artery disease. Sixty patients with stable coronary artery disease undergoing elective coronary artery bypass grafting (CABG) surgery were randomized 4 weeks before surgery to: A) without inhibition of renin-angiotensin system or statin, B) statin (pravastatin 40 mg/d) without inhibition of renin-angiotensin system, C) AT_1 blockade (irbesartan 150 mg/d) without statin, or D) combination of statin and AT_1 blocker in same dosages. 49 patients completed the study. Groups did not differ in clinical characteristics. Primary endpoint was therapy-dependent regulation of an antiatherosclerotic endothelial expression quotient Q including mRNA expression (in arbitrary units measured by real-time PCR) of eNOS and CNP, divided by expression of oxLDL receptor LOX-1 and NAD(P)H oxidase subunit gp91phox in left internal mammary arteries biopsies obtained by CABG surgery (*$P<0.05$ vs. A). Statin therapy increased Q from 3.2±0.4 (A) to 4.4±0.4* (B). AT_1 blockade showed a trend to increase Q to 4.2±0.5 (C). Combination of statin and AT_1 blocker further increased Q to 5.1±0.6* (D), but a putative interaction of both therapies in Q was not significant. Furthermore, preoperative therapy with statin, AT_1 blocker and their combination improved endothelial function in rings of internal mammary arteries. Maximal dilatation in response to 10^{-6} M acetylcholine was in A) 51.5±3.2%, B) 68.8±6.0%*, C) 78.6±11.4%*, and D) 86.1±7.7%*.
In the EPAS trial, statin and AT_1 blocker therapy independently and in combination improved endothelial expression quotient of anti- and pro-atherosclerotic genes and endothelial function, but a potentiation by interaction of both therapies was not observed.
Our data support beneficial effects of both therapies in the treatment of coronary artery disease.

P1397 Contrast induced nephropathy using sodium bicarbonate or sodium chloride and isosmolar Iodixanol

E. Adolph, T. Chatterjee, S. Kische, H. Ince, P. Schuff-Werner, C. Nienaber. *University Hospital Rostock, Cardiology, Rostock, Germany*

Background: For prevention of contrast induced nephropathy (CIN) after coronary angiography, hydration with sodium chloride solution is recommended. A recent study showed a benefit of sodium bicarbonate hydration versus sodium chloride when using the non-ionic monomeric low-osmolar contrast medium iopamidol (Merten GJ. et al, JAMA 2004). The aim of this study was to determine the effects of sodium bicarbonate versus sodium chloride on CIN rates in a cohort with chron-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

ical nephropathy using the non-ionic dimeric isosmolar contrast medium iodixanol.
Methods: The study was a prospective, randomized, single-center, double-blind trial including 135 patients (age: 71,4+7,6 yrs, 30f/105m) with elevated baseline serum creatinine levels (SCr) (mean SCr 138,06+38,9 μmol/l). Eligible patients were randomized to receive either a 154-mEq/l infusion of sodium bicarbonate (n=66, group A) or one of sodium chloride (n=69, group B) as a bolus of 2 ml/kg per hour for 2 hour before and as an infusion of 1 ml/kg per hour for 6 hours between and after the angiography with administration of iodixanol. The primary end point of this study was a SCr increase of 25% or 44 μmol/l on the first or second day following diagnostic contrast medium application. SCr, serum cystatine C (CysC), plasma viscosity (PV) and urinary enzymes (alaninaminopeptidase (AAP), N-acetyl-β-D-glucosaminidase (NAG) and α1-microglobuline (α1M)as indicators of early tubular impairment were measured at baseline and day 1 and 2 after contrast medium administration.
Results: The total CIN rate was 4,4% (n=5) and similar in both groups (group A: 4,5%, n=3, group B: 2,9%, n=2). All patients with CIM showed a decline of their SCr values 10 to 14 days after angiography. No patient required any additional therapy. First day after application of iodixanol there was a significant increased of SCr, Cyst C, AAP, NAG, α1M and PV in both groups. On the second day after contrast medium application Cyst C, AAP, NAG and PV were still significantly increased compared with the initial values. Comparing the treatment groups we observed a significant higher increase of AAP, NAG and α1M at the first day after application of iodixanol in the sodium bicarbonate group.
Conclusion: There is a low incidence of CIN after administration of contrast medium iodixanol in patients with chronic nephropathy when combined with a sufficient sodium chloride hydration. The control measurements 10 to 14 days after the diagnostic procedure showed prediagnostic values in all CIN patients. No additional benefit by using sodium bicarbonate was found in this study.

P1398 Complex interrelationships between urine albumin excretion, metabolic syndrome and essential hypertension. Insights from Hippokration Hellenic Hypertension Study (3H Study)

C. Tsioufis, D. Tsiachris, K. Dimitriadis, M. Selima, C. Thomopoulos, A. Kakkavas, C. Mihas, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: Microalbuminuria, apart from being an early marker of intrarenal vascular dysfunction, could be considered as a separate component of the metabolic syndrome (MS). The aim of our study was to investigate the effect of MS on urine albumin excretion in a large hypertensive population.
Methods: A total of 1049 consecutive subjects with essential hypertension (age 55.5±12 years, 524 males) that were included in the Hippokration Hellenic Hypertension Study (3H Study) (an ongoing registry of hypertension related target organ damage) were considered for analysis. Microalbuminuria (MA) was determined as albumin to creatinine ratio (ACR) > or = 22mg/g in men and > or = 31mg/g in women in morning spot urine samples.
Results: The prevalence of MS, based on ATP III criteria, was 37.8%. Hypertensives with MS compared to those without had increased body mass index (31.3 vs. 27.7 kg/m^2, $p<0.001$), office systolic blood pressure (147.4 vs. 144.8 mmHg, $p<0.05$), pulse pressure (56 vs. 54 mmHg, $p<0.05$) and uric acid levels (5.7 vs. 5.1 mg/dl, $p<0.001$). Moreover, subjects with MS exhibited significantly increased ACR values (19.3 vs. 13.2 mg/g, $p<0.001$), as well as a higher prevalence of microalbuminuria (16.4% vs. 8%, $p<0.001$), even after controlling for age, sex and office blood pressure (adjusted $p<0.001$). Multiple linear regression analysis showed that, apart from age and office blood pressure levels, MS was the strongest independent predictor of ACR (β =0.112, p=0.002). Additionally, m ultiple logistic regression analysis revealed that the risk of microalbuminuria increased more than twofold with the presence of MS (OR=2.178, p=0.001), while examining each component of MS separately, impaired fasting glucose (OR=1.747, p=0.018) and low HDL levels (OR=1.745, p=0.024) increased significantly the risk of microalbuminuria.
Conclusions: There is a strong association between MS and increased urine albumin excretion in essential hypertension, exceeding what could be attributed to each individual component of the syndrome. The MS-associated renal impairment at the glomerulus level could partly explain the higher cardiovascular risk in this setting.

P1399 N-terminal pro-B-type natriuretic peptide and C-reactive protein predict death irrespective of atorvastatin treatment in type 2 diabetic dialysis patients

K. Winkler[1], V. Krane[2], C. Drechsler[2], J. Lilienthal[3], W. Maerz[4], C. Wanner[4] on behalf of The German Diabetes and Dialysis Study Investigators. *[1]University of Freiburg, Clinical Chemistry, Freiburg, Germany; [2]University of Wuerzburg, Nephrology, Wuerzburg, Germany; [3]DATAMAP GmbH, Freiburg, Germany; [4]Synlab Center of Laboratory Diagnostics, Heidelberg, Germany*

Patients with type 2 diabetes (T2DM) are at increased risk for cardiovascular (cv) events which was shown to be reduced by statin therapy. Despite 4 years of atorvastatin (A) treatment diabetic dialysis patients showed no reduction in cv events and death in the German Diabetes and Dialysis (4D) Study. We now evaluate the association of risk markers with cv endpoints and death in this population.
Methods: The 4D study was conducted as a double-blind, prospective study of 1255 patients suffering from T2DM receiving hemodialysis who were randomly assigned to 20 mg A per day or matching placebo (P). C-reactive protein (sCRP), N-terminal pro-B-type natriuretic peptide (NT-pro-BNP), troponin T, and the activity of platelet activating factor acetylhydrolase (PAF-AH) were analyzed in samples drawn at baseline and at 6 months after randomization. Hazard ratios (HR) of risk markers for death and a composite of death from cardiac causes, nonfatal myocardial infarction, and stroke were calculated by binary logistic regression adjusted for covariates.
Results: During the initial 6 months of treatment PAF-AH activity decreased by 24% in the A group and increased by 3.1% in the P group ($p<0.001$ between groups) and sCRP (median) decreased by 4% (A) and increased by 7% (P) (p=0.012 between groups). NT-pro-BNP increased by 39% (A) and by 40% (P), whereas troponin T increased by 7% in the A group only. However, there were no significant differences in the changes between groups with regard to NT-pro-BNP and troponin T. HRs at baseline of the 3rd vs. 1st tertile adjusted for treatment, age, sex, BMI, smoking, hypertension, diabetes duration, triglycerides, LDL- and HDL cholesterol, and the respective remaining risk markers tested were 2.95 (95%CI 2.11-4.12, $p<0.001$), 2.72 (95%CI 1.96-3.76, $p<0.001$), 2.50 (95%CI 1.79-3.48, $p<0.001$), and 1.01 (95%CI 0.71-1.44, p=0.947) for NT-pro-BNP, sCRP, troponin T, and PAF-A activity, respectively, for death, and 2.37 (95%CI 1.7-3.3, $p<0.001$), 1.0 (95%CI 7.3-1.37, p=1.0), 1.91 (95%CI 1.38-2.65, $p<0.001$), and 1.21 (95%CI 0.86-1.72, p=0.28) for NT-pro-BNP, sCRP, troponin T, and PAF-A activity, respectively, for the composite primary endpoint.
Conclusions: Treatment with A significantly reduced LDL but did not affect clinical endpoints in this study population. The same is true for PAF-AH activity which is associated with lipoproteins, especially LDL. However, NT-pro-BNP, sCRP and troponin T were not affected by A but predicted clinical endpoints. Thus, these risk markers may be closer associated with clinical outcome than those affected by statin treatment.

P1400 Is impact on sleep among all beta blockers same? third generation nebivolol versus second generation metoprolol

M.B. Yilmaz[1], A. Erdem[1], K. Yalta[2], O. Turgut[1], A. Yilmaz[1], I. Tandogan[1]. *[1]Cumhuriyet University School of Medicine, CARDIOLOGY, Sivas, Turkey; [2]Cumhuriyet University School of Medicine, Cardiology Dept., Sivas, Turkey*

Background: Sleep is a basic physiologic process, inevitable for life. Various parameters of quality of sleep were shown to be affected negatively by beta blockers. Nebivolol has been classified as a third generation beta blocker with vasodilating properties. This study was devised to compare the effects of Metoprolol succinate (extended release) and Nebivolol on sleep quality among patients with mild hypertension.
Methods: This was a prospective, randomised, open-label, parallel group study. Eligible patients underwent Pittsburg Sleep Quality Index (PSQI) by a blinded author, and were randomized to receive first dose of Metoprolol or Nebivolol before leaving the clinic. Visits were scheduled for 1, 2, 4, and 6 weeks after the initiation of active drug administration. After median of 6 weeks, patients underwent repeat PSQI test by the same author, blinded to study drugs.
Results: There were 23 patients in the Nebivolol group and 20 patients in the Metoprolol group (mean age:41±6 vs. 39±5 years, p=0.209), completing the follow up. At the initial phase, systolic blood pressure (BP), diastolic BP, PSQI scores were not different between the two groups. After the follow up, both systolic and diastolic BPs normalized in both groups. PSQI total score was significantly improved (5.78±2.56 vs. 4.48±1.78, p=0.002), by Nebivolol therapy, whereas; PSQI total score was worsened (4.75±1.41 vs. 6.40±1.50, $p<0.001$ by Metoprolol therapy.
Conclusion: Nebivolol was associated with improved sleep quality in terms of PSQI scores, whereas, Metoprolol was not, in relatively young hypertensive patients with mild hypertension.
Key words: Nebivolol, Metoprolol, sleep quality, Pittsburg sleep quality index

P1401 Hypertriglycerydemia predicts platelet resistance to acetylsalicylic acid in patients with stable coronary artery disease

T. Wcislo, M. Dominak, L. Figiel, M. Krzeminska-Pakula, J.D. Kasprzak. *Medical University of Lodz, II Chair and Department of Cardiology, Lodz, Poland*

Background and purpose: Acetylsalicylic acid resistance (ASAr) used in a standard daily dose 75mg is reported to occur in 5-42% of patients with stable coronary artery disease (CAD). The aim of the study was to define clinical and biochemical predictors of suboptimal response to acetylsalicylic acid (ASA) in patients (pts) with stable coronary disease.
Methods: 299 Caucasian pts with stable coronary artery disease undergoing elective coronary angiography were included in the study (105 woman, 194 man, mean age 60,5±10,5 years, mean height 1,73±0,1m, mean weight 80,6±9kg,

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

mean BMI 27,1±3,8 kg/m^2),. All patients have been receiving daily dose of 75 mg ASA for at least 7 days before admission and were divided into two groups: I - resistant group (n=55), II - respondent group (n=244) to the treatment according to the result of turbidimetric measurement of blood platelet aggregation. The resistance criterion was set at value of ARU (Aspirin Resistance Units)>550.
Results: Among the patients treated with a daily dose of 75mg of ASA, 55 were resistant (mean age 59, 8±10,6 years, ARU=608±32,4), and 244 were responsive (mean age 60,6±10,5 years, ARU=454±49). In the assessment of classic risk factors in resistant group vs. responsive group no significant differences were detected, including smoking status: diabetes was present in 29,1%(of responders) vs. 25,4%(of non-responders);p=0,57, hypertension 60% vs. 58,2%;p=0,8, respectively – differences statistically not significant. According to the results of logistic regression of risk factors of the coronary artery disease statistically significant difference between the groups of resistant vs. responsive patients was found in triglycerides concentration (TG): 161±89 vs. 128±64mg/dl; p=0,0047, but not for other lipid or inflammatory parameters. In patients with the value of TG>122mg/dl the risk of ASA resistance increased 2,4x-fold (95% CI: 1,28;4,31;p=0,005). Moreover, a trend toward higher values of HDL in responsive group was found – (51,3 vs. 47,4 mg/dl; p=0,06). The differences in other parameters between the both groups did not reach statistical significance (p<0,05).
Conclusion: The prevalence of ASA resistance in the population of patients with stable coronary disease treated with a daily dose of 75mg of ASA is 18,4% and cannot be predicted by medical history or clinical/demographic variables. The only independent factor prognostic to ASA resistance in patients with stable coronary disease is serum triglyceride concentration. Further investigations in large-scale populations are needed to confirm this association.

P1402 Detection of early cardiovascular disease: intervention with valsartan - results from the DETECTIV trial

D. Duprez[1], N. Florea[2], K. Jones[1], J.N. Cohn[1]. [1]*University of Minnesota, Cardiovascular Division -Vcrc Room 270, Minneapolis, United States of America;* [2]*University of Minnesota, Cardiology, Minneapolis, United States of America*

Purpose: Early cardiovascular (CV) disease can be identified in asymptomatic individuals by noninvasive evaluation of functional and structural abnormalities of the vasculature and heart. Angiotensin II plays a key role in the progression of CV disease. This study aimed to examine the effect of angiotensin II receptor blockade on functional and structural CV abnormalities in patients with early disease.
Methods: Subjects underwent screening with 10 tests of CV function and structure (large and small artery elasticity, resting and treadmill exercise BP, carotid IMT, retinal vascular photography, micro-albuminuria, ECG, echocardiography and plasma BNP). Each test result was scored as normal 0, borderline 1 or abnormal 2 and a total CV disease score was the sum of all scores. Subjects with CV disease score of 6 or higher were randomized in a double-blind study; they received for the first 6 months either placebo (P) (n = 38, mean age 54±11 yrs) or valsartan (V) 160 mg od (n = 38, mean age 57±19 yrs), followed by 6 months valsartan 160 mg od in both groups (P/V and V/V).
Results: CV disease score fell at 6 months from 9.0±2.1 to 6.8±2.6 in the placebo (P) group (regression to mean (R-M) + P + life style recommendation effect) but fell further (P<0.03) in the valsartan (V) arm from 8.6±2.4 to 5.5±2.5. In the P group V from 6 tot 12 months (R - M, P effects eliminated) further reduced CV disease score to 5.1±2.7 (P<0.001). In the V group after 12 months V the CV disease score further decreased to 5.0±2.5 (P<0.01). Changes in CV disease score were accompanied by improved small artery elasticity, in the V group from 4.19±2.37 to 6.58±3.57 after 6 months V and to 7.43± 4.18 ml/mmHgx100 (P<0.001) after 12 months V. In the P group small artery elasticity did not change during the first 6 months. In the P group V from 6 to 12 months increased the small artery elasticity from 5.60±3.20 to 6.56±3.06 ml/mmHgx100 (P<0.001). Changes in the CV disease score were also accompanied by reduced blood pressure (P<0.01) and after 12 months a reduction in LV mass (P=0.03). No drug-induced side-effects were observed.
Conclusions: These data indicate that angiotensin II receptor blocker therapy can slow progression and/or reverse early CV disease in asymptomatic non-hypertensive patients.

P1403 Aspirin-triggered lipoxin in patients treated with aspirin and selective vs. non-selective COX-2 inhibitors

G. Renda, M. Zurro, F. Santarelli, D. Sacchetta, S. Tacconelli, M. Zimarino, P. Patrignani, M. Romano, R. De Caterina. *G. d'Annunzio University, Institute of Cardiology, Chieti, Italy*

Introduction: COX-2 inhibition has been described to suppress the synthesis of a lipid mediator through the lipoxygenase pathway, "aspirin-triggered lipoxin" (ATL), reported to cause the slow-onset adaptation of the gastric mucosa to aspirin. The aim of this study was to test the hypothesis that the co-administration of aspirin and celecoxib abolishes the synthesis of ATL, and that this effect is not different from what obtained by the co-administration of aspirin with ibuprofen, in patient with stable ischemic heart disease and osteoarthritis.
Methods: 24 patients chronically treated with aspirin (100 mg daily) were co-administered celecoxib 200 mg BID, ibuprofen 600 mg TID, or placebo for 7 days. We measured the urinary excretion of ATL and of 11-dehydro-TXB2 (TXM, an index of systemic TX biosynthesis), and serum thromboxane(TX)B2 and lipopolysaccharide(LPS)-stimulated prostaglandin(PG)E2 generation as indices of COX-1 and COX-2 inhibition, respectively.
Results: At baseline, neither serum TXB2, nor LPS-stimulated PGE2 significantly differed in the 3 groups. Urinary excretion of TXM and ATL was also not significantly different (ATL= 0.38±0.21 ng/mg creatinine in the celecoxib group; 0.27±0.20 in the ibuprofen group; 0.28±0.15 in the placebo group). On day 1 and 7, after 4h from the co-administration of both celecoxib and ibuprofen, but not placebo, a comparable inhibition of LPS-stimulated PGE2 generation was observed (P<0.0001 vs. baseline for both), indicating an inhibition of COX-2. In addition, the co-administration of celecoxib or placebo did not undermine ASA-related inhibition of TXB2 generation. Differently, the co-administration of ibuprofen with ASA was associated with a significant increase of serum TXB2 on day 7, before drug administration (P<0.01 vs. baseline). In parallel, however, the urinary excretion of ATL after 4h from the co-administration of celecoxib or ibuprofen or placebo on day 1 (0.24±0.33, 0.26±0.21 and 0.37±0.22 ng/mg creatinine, respectively), and 7 (0.36±0.41, 0.35±0.15 and 0.23±0.18 ng/mg creatinine, respectively), as well as the urinary excretion of TXM, were not significantly different among the 3 groups of patients, and they were not significantly different from those detected at baseline.
Conclusions: In this patient population, neither the non-selective COX inhibition with ibuprofen nor the selective COX-2 inhibition with celecoxib appreciably interfere with the synthesis of ATL, suggesting that this mediator is unlikely to be involved in the exacerbation of gastrotoxicity determined by the association of aspirin with coxibs vs. aspirin alone in this setting.

DEVELOPMENTAL BIOLOGY AND CARDIOMYOCYTE DIFFERENTIATION

P1404 Tbx1 is required for coronary artery patterning

R. Kelly, M. Dandonneau, L. Miquerol, M. Theveniau-Ruissy. *Developmental Biology Institute of Marseilles, Marseille Cedex 9, France*

TBX1, encoding a T-box containing transcription factor, is the major candidate gene for DiGeorge or del22q11.2 syndrome, characterised by craniofacial and cardiovascular defects including tetralogy of Fallot and common arterial trunk. Mice lacking Tbx1 provide a model for DiGeorge syndrome and have severe defects in the development of pharyngeal derivatives including cardiac progenitor cells of the second heart field which contribute to the arterial pole of the heart. During normal development the embryonic ventricular outflow tract is divided to generate the ascending aorta and pulmonary trunk concomitant with ventricular septation; counterclockwise rotation of the outflow tract ensures alignment of the aorta and pulmonary trunk with the left and right ventricles. The outflow tract of Tbx1 mutant embryos is short and narrow compared to that of wild-type littermates and fails to divide; as a result Tbx1 mutant embryos die at birth with a common arterial trunk. We have carried out a series of genetic crosses using transgene markers of the second heart field and coronary artery endothelial cells to further investigate the Tbx1 mutant outflow tract. Our results suggest that the Tbx1 mutant heart forms in the absence or severe reduction of a specific subpopulation of second heart field cells normally giving rise to subpulmonary myocardium. In addition, mutant hearts display incomplete rotation of the myocardial wall of the outflow tract and severe coronary artery patterning defects. During normal development left and right proximal coronary arteries connect with the left and right coronary sinuses at the base of the ascending aorta, avoiding subpulmonary myocardium. In Tbx1 mutant hearts, coronary arteries course aberrantly across the normally coronary refractory ventral region of the heart, the predominant phenotype being connection of the left coronary artery to the right coronary sinus. These results suggest that Tbx1 directly or indirectly regulates coronary artery patterning and provide the first insights into the genetic basis of coronary artery patterning defects.

P1405 Protein related to DAN and Cerberus is critical for heart looping in Danio rerio

I.I. Mueller[1], E.W. Knapik[2], A.K. Hatzopoulos[2]. [1]*Eberhard-Karls-Universitaet Tuebingen, Medizinische Klinik Iii, Kardiologie, Tuebingen, Germany;* [2]*Vanderbilt University, Medicine, Devision of Genetic Medicine, Nashville, Tn, United States of America*

The Protein related to DAN and Cerberus (PRDC) belongs to the DAN protein family, a subgroup of the cystine knot superfamily. DAN proteins inhibit the Bone Morphogenetic Proteins (BMP) signaling pathway by forming heterodimers with BMP family members. The mouse PRDC binds and blocks activity of BMP2 and BMP4 in vitro. However, the function of PRDC during development is unknown. We cloned the zebrafish prdc gene and studied its expression and role during embryonic development. Prdc gene expression starts at 17 hpf in the lateral plate mesoderm and the optic lobe. Prdc expression in the lateral plate mesoderm persists until the pharyngeal arches form. Later, prdc is restricted to the mes-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

enchymal core of the arches until 60 hpf. In the eye, prdc expression is present between 17 and 72 hpf. The expression starts in the optic lob at the time of invagination. At 21 hpf, prdc expression is confined to the anterior region of the optic cup, but around 23 hpf it extends to the lens placode. Prdc transcripts mark the retinal neuroepithelium and the lens epithelium until 42 hpf. After this time point, prdc expression is localized to the marginal zone of the retinal epithelium. The premordium of the swim bladder expresses prdc throughout its embryonic development (30 to 72 hpf), whereas intestinal bulb, liver and pancreas show no prdc expression. In addition, we detected low levels of prdc in the intersomitic space (21 to 36 hpf), and in the epithelium of the foregut (72 hpf). Knock down of Prdc function, by injecting morpholino antisense oligonucleotides into wild type embryos, causes severe heart defects. The heart forms, but fails to loop properly in most (95%) of the injected embryos. We also observed that heart jogging is affected in about 20% of the prdc morphants as the straight heart tube remains closer to the embryonic midline. In summary, our analysis indicates that: 1) prdc has characteristic temporal and spatial expression domains during development in zebrafish; 2) Prdc might be required to block BMP activity locally and in a well-timed manner during development of the eyes, pharyngeal arches, swim bladder and somites; and, 3) Prdc function is critical for heart development.

P1406 Natural tissue engineering

H. Moellmann[1], H.M. Nef[1], C. Troidl[2], S. Voss[2], S. Kostin[2], M. Klement[2], M. Weber[1], C. Hamm[1], A. Elsasser[1]. *[1]Kerckhoff Heart Centre, Dept of Cardiology, Bad Nauheim, Germany; [2]Max-Planck-Institute, Bad Nauheim, Germany*

Purpose: We could recently demonstrate a fully differentiated tissue formation including vascular structures inside a ventricular septum defect occluder in man. However, the extent and the mechanism of this tissue formation are yet not fully understood.
Methods: In order to further investigate the potential tissue formation we developed a pig model with minimal invasive placement of a polyurethane scaffold in the left ventricle and in the infrarenal aorta serving as control. The polyurethane scaffolds had no direct contact to ventricular or aortic structures. These foreign bodies were analyzed using immunohistochemistry, western blot, and quantitative real-time PCR (RT-PCR).
Results: The tissue formation on the foreign bodies could be confirmed in both, the intraventricular and aortal scaffold. The newly formed tissue was mainly defined by smooth muscle cells. Numerous fibroblasts, myofibroblasts and vascular structures including vascular endothelial cells could be identified by immunohistochemistry. We found strong evidence, that the tissue formation is promoted by homing stem cells given the high degree of CD34, c-kit, CD133, and sca-1 positive cells as evidenced by immunohistochemistry and RT-PCR. Interestingly, early cardiomyocyte markers (GATA-4, Nkx2.5) were found in the intraventricular foreign body, whereas in the scaffold placed in the infrarenal aorta no cardiomyocyte formation could be demonstrated.
Conclusion: Since the foreign bodies had no direct contact to ventricular or vascular structures, it has to be assumed that the differentiated cells had not migrated per continuitatem but rather had been derived from circulating stem cells. The fact that a cardiomyocyte-like transdifferentiation occurred only in the intraventricular but not in the aortal foreign body suggests that the intraventricular milieu and potential paracrine action play a crucial role.

P1407 MicroRNA-1 is involved in cardiomyocyte differentiation of human-derived cardiomyocyte progenitor cells

J.P.G. Sluijter, A. Van Mil, T.H. Korfage, C.H.G. Metz, P.A.F.M. Doevendans, M.J. Goumans. *University Medical Centre Utrecht, Experimental Cardiology Laboratory, Utrecht, Netherlands*

Background: Myocardial regeneration can occur in humans, albeit with very low efficiency. To improve regeneration of the injured myocardium, one can improve the intrinsic capacity of the heart to regenerate itself and/or replace the damaged tissue by cell transplantation. Recently, we have isolated cardiomyocyte progenitor cells (CMPCs) from human fetal hearts and from adult human biopsies that can be expanded in culture and efficiently differentiated into beating cardiomyocytes. In the past few years, several studies have demonstrated that microRNAs (miRNAs) are important during angiogenesis, heart development, and maintenance of stem cell populations. MiRNAs regulate the transcription of target genes by translational repression. Although extensively studied in invertebrates, little is known regarding miRNA function in mammalian tissues. We hypothesize that, since miRNAs regulate stem cell maintenance, miRNAs are involved in proliferation/differentiation of the human cardiomyocytes progenitor cells in vitro.
Methods and results: Human fetal CMPCs were isolated, cultured and efficiently differentiated into beating cardiomyocytes. Total RNA was isolated and after miRNA enrichment a temporal miRNA expression profile is determined by micro-array analysis (μParaflo™microfluidic chip, Lcsciences). From all human targeted miRNAs (total 453), 188 miRNAs (42%) were expressed in proliferating human CMPCs and 195 (43%) in differentiated CMPC. Among the highly up- and down- regulated miRNAs, we identified, miRNA-1, known to control myogenic differentiation, as one of the highly up-regulated miRNA. It's increased 1000 fold upon cardiomyocyte differentiation of the CMPC. To unravel it's function in CMPC behavior, we transfected miRNA-1 into proliferating CMPCs. MiRNA-1 over-expression resulted in reduced cell proliferation, as assessed by MTT-assay and cell-cycle analysis by flow cytometry, and enhanced differentiation into cardiomyocytes.
Conclusion: Our results demonstrate a strong regulatory role of miRNAs in human CMPC proliferation and differentiation into cardiomyocytes. miRNA-1 functions as a key regulator, and is involved in the onset of human CMPC differentiation into cardiomyocytes.

P1408 Epithelial-mesenchymal transition of the epicardial cells requires specific signals from microenvironment and constitutes the source of cardiac primitive cells in the adult human heart

C. Castaldo[1], D. Nurzynska[1], F. Di Meglio[1], R. Miraglia[1], C. Bancone[2], G. Romano[1], S. Montagnani[2]. *[1]Universita' degli Studi "Federico II", Scienze Biomorfologiche e Funzionali, Naples, Italy; [2]Monaldi Hospital, Naples, Italy*

During heart morphogenesis a subset of epicardial cells undergoes an epithelial-mesenchymal transition and invades myocardium contributing to the formation of myofibroblasts, vascular endothelium and smooth muscle cells. Recently, the presence of resident stem cells able to give rise to the cells of cardiac lineages was observed in the adult human heart, raising questions concerning their origin and biology. The scope of the present study was to investigate whether the epithelial-mesenchymal transition takes place in the adult human heart, generating the population of cardiac stem cells, and which molecular factors are involved in its initiation and progression.
Since the subepicardial space is rich in extracellular matrix components and cytokines, constituting the specific environment for epicardially derived cells, cardiac fibroblasts obtained from the subepicardium layer of adult human atrium were cultured to create the most appropriate conditions for the in vitro study. After the non-enzymatic removal of cells, the presence of extracellular matrix proteins - fibronectin, collagen III and IV, tenascin and laminin - was confirmed by immunofluorescence. This substrate was used to obtain and culture the sheets of epithelial cells from the epicardium of normal adult human atria. The epithelial phenotype of the cells was confirmed by the positive immunolabeling of E-cadherin and β-catenin at the intercellular junctions and cytokeratin in the cytoplasm. While in the presence of basic fibroblast growth factor (10 ng/ml) or platelet-derived growth factor-BB (40 ng/ml) the epithelial sheets remained intact, the addition of epidermal growth factor (40 ng/ml), hepatocyte growth factor (40 ng/ml) or transforming growth factor beta (0,5 ng/ml) resulted in the change of cell characteristics. The intercellular contacts were lost and the cells acquired spindle-like shape and vimentin expression. When induced to differentiate into endothelial, smooth muscle cells or cardiomyocytes, these cells expressed factor VIII, smooth muscle actin or myosin heavy chain α/β, respectively.
The results of our study indicate that in the specific conditions epithelial-mesenchymal transition takes place in the adult human epicardial cells. We suggest that epicardially derived cells enrich the pool of cardiac primitive cells and contribute to the regenerative properties of the heart. A better understanding of complex interactions of the extracellular matrix proteins and growth factors with their specific receptors on the cell surface will be pivotal for progressing therapeutic cardiac regeneration.

ELECTROPHYSIOLOGY AND EXITATION-CONTRACTION COMPLICATION

P1409 Upregulation of HERG potassium channel function by phosphatidylinositol-4-phosphate 5-kinase

T. Kubo[1], W.G. Ding[1], F. Toyoda[1], Y. Fujii[1], M. Omatsu-Kanbe[1], Y. Miura[2], T. Mino[1], H. Matsuura[2]. *[1]Shiga University of Medical Science, Physiology, Otsu, Japan; [2]Dainippon Sumitomo Pharma Co.,Ltd., Pharmacology, Suita, Japan*

The human ether-a-go-go related gene (HERG) potassium channel plays an important role in the repolarization of human cardiac action potentials, and mutation or drug block of HERG potassium channel leads to long QT syndrome associated with lethal ventricular arrhythmias. There is some evidence that HERG potassium current (I_{HERG}) is decreased in amplitude by stimulation of Gq-phospholipase C (PLC)-coupled receptors, such as α_1 -adrenergic and M_1 -muscarinic receptors (α_1 -R and M_1 -R, respectively), at least partly through the reduction of membrane phosphatidylinositol 4,5-bisphosphate ($PI(4,5)P_2$). The present study was undertaken to examine the effect of phosphatidylinositol-4-phosphate 5-kinase (PI(4)P5-K), the synthetic enzyme of $PI(4,5)P_2$, on I_{HERG} using the whole-cell patch-clamp method. Chinese hamster ovary (CHO) cells were transiently transfected with α_1 -R, M_1 -R and/or PI(4)P5-K, together with HERG potassium channel constructs. I_{HERG} was activated by depolarizing steps (2 s in duration) to various test potentials (-50 through +40 mV) applied from a holding potential of -80 mV, and the degree of I_{HERG} activation was evaluated by the amplitude of tail current elicited on repolarization to -60 mV. The density of I_{HERG} (+10 mV) in cells expressing α_1 -R or M_1 -R alone averaged 23.1±4.8 pA/pF (n = 16) and 24.1±2.2 pA/pF (n = 77), respectively, and was significantly increased to 38.1±4.7 pA/pF

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

(n = 22) and 36.1±4.6 pA/pF (n = 29) by coexpression of PI(4)P5-K. The stimulation of α_1 -R and M_1 -R by phenylephrine and acetylcholine, respectively, decreased the amplitude of I_{HERG} by 25.8±6.1% (n = 10) and 19.0 ±2.7% (n = 12), which was accompanied by a significant acceleration of deactivation kinetics. The Ca^2+ chelator BAPTA or protein kinase C inhibitor bisindolylmaleimide-I did not affect the inhibitory action of α_1 -R and M_1 -R. However, this inhibitory effect of α_1 -R and M_1 -R stimulation on I_{HERG} was significantly attenuated in cells expressing PI(4)P5-K (9.4±2.2% reduction, n = 19 and 7.4±1.7% reduction, n = 11, respectively). These results suggest that HERG potassium channel function is closely dependent upon changes in membrane $PI(4,5)P_2$ level that is regulated by PI(4)P5-K as well as Gq-PLC-coupled receptors and that replenishment of $PI(4,5)P_2$ by PI(4)P5-K is accompanied by the upregulation of HERG potassium channel.

P1410 Coexistence of HERG current block and protein trafficking defect in the drug-induced acquired long QT syndrome

H. Takemasa, T. Nagatomo, H. Abe, R. Kohno, K. Kawakami, T. Tsurugi, Y. Otsuji. *Univ. of Occup. and Environ. Health, 2nd Dept. of Int. Med., Cardiology, Kitakyushu, Japan*

Purpose: Many drugs associated with acquired long QT syndrome (LQTS) directly block human ether-a-go-go-related gene (HERG) K^+ channels. Recently, trafficking defect of the HERG channel protein has been reported as a new mechanism of the acquired long QT syndrome (LQT). However, it is unclear whether trafficking defect and HERG current block coexist in the acquired LQT. We evaluated the trafficking defect of HERG channels by ketoconazole which known as a direct HERG current inhibitor.
Methods: HERG channels (wild-type, F656C or Y652A mutation) were heterologously expressed in HEK-293 cells and whole-cell currents were recorded using a path-clamp technique (23°C). Trafficking defect was evaluated by western blot analysis, and the surface expression of HERG channels was analyzed by immunocytochemistry and flowcytometry.
Results: Ketoconazole inhibited HERG peak tail current in a concentration-dependent manner (0.04 - 40 μM) with an IC50 of 1.9 μM (n = 3 - 5 cells at each concentration, Hill coefficient 0.7). The effect of ketoconazole on HERG required channel activation. Fully-glycosylated mature 155-kDa HERG proteins were reduced in a concentration-dependent manner (0.1 - 10 μM) after 48 hours exposure to ketoconazole. Normalized image density were 0.80 ±0.21, 0.59±0.29 and 0.52±0.15 at 0.1, 1 and 10 μM, respectively ($P < 0.05$ vs. control). Relative fluorescence intensity of antibody labeled HERG channels in the cell membrane, which calculated by flowcytometry, was reduced in a similar way. Confocal fluorescence imaging analysis demonstrated that ketoconazole reduced surface membrane expression of the HERG channels. These disruptions of protein trafficking were gradually recovered up to 48 hours after washout of ketoconazole. Current density of the HERG channels was also reduced but acute direct effect of ketoconazole on HERG current was preserved. Although HERG current blocks were significantly attenuated in F656C and Y652A mutant channels, disruption of protein trafficking was not significantly different compared with wild-type. Ketoconazole had no effect on the trafficking of SCN5A sodium channels.
Conclusions: Our findings indicate that ketoconazole inhibits HERG channel protein trafficking as well as HERG current in therapeutic concentrations. We must pay attention not only to direct HERG block, but also to HERG protein trafficking when evaluating new drugs.

P1411 Distinct modulation of electrophysiological properties of HCN isoforms by KCNE2

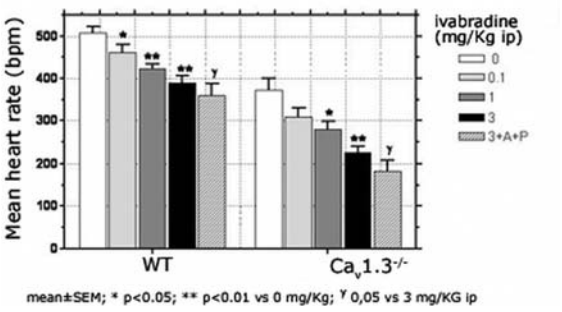
N. Zagidullin, M.C. Brandt, L. Motloch, Q. She, I. Khan, G. Michels, U.C. Hoppe. *University of Cologne, Cologne, Germany*

Background: KCNE2 was found to modulate several voltage-gated potassium alpha-subunits including HERG, KCNQ1/2, and Kv4.x. Moreover, it has been proposed that KCNE2 might serve as a β-subunit of HCN channels which are critical for heart rate regulation. However, available data about KCNE2 modulation of different HCN isoforms remain contradictory.
Methods: Chinese hamster ovarian cells were cotransfected with plasmid DNA encoding one of the cardiac HCN isoforms (HCN1, HCN2 or HCN4) and KCNE2 or an unrelated control plasmid to investigate the effect of KCNE2 on HCN whole-cell currents and, more importantly, single-channel properties to possibly obtain direct evidence for a functional interaction of both subunits in channel complexes.
Results: KCNE2 significantly increased whole-cell current density of HCN2 (-142.9±24.4 pA/pF, n=14 vs. control -72.8±15.8 pA/pF, n=11; at -140mV, $p<0.05$) and of HCN4 (-72.7±11.7 pA/pF, n=6 vs. -29.7±4.2 pA/pF, n=9; $p<0.05$), while not affecting HCN1 current size (-86.8±16.5 pA/pF, n=10 vs. control -83.8±14.1 pA/pF, n=17; p=n.s.). Moreover, in the physiological voltage range between -70 to -90 mV KCNE2 accelerated the activation kinetic of HCN1 (tau 196±37 ms vs. control 343±52 ms; at -80 mV, $p<0.05$) and HCN2 (tau 421.1±43.4 ms vs. control 813.5±198.1 ms; at -80 mV, $p<0.05$), and accelerated activation of HCN4 at more negative potentials between -110 to -150 mV (499±81.3 ms vs. control 1315±268.8 ms; at -140 mV, $p<0.05$). Increased whole-cell current amplitude might be due to elevated HCN membrane protein levels upon coexpression with KCNE2 (previously suggested for HCN2) and/or increased single-channel activity. However, surprisingly KCNE2 significantly reduced the availability of HCN1 (79.2±7.5% vs. control 97.5±2.3%; n=12, at -90mV, $p<0.05$) and HCN2 (72.7±7.4% vs. control 95.5±0.4%; n=18, $p<0.05$), and decreased the open probability of HCN2 (41.0±5.7% vs. control 66.6±2.9%; $p<0.05$) and HCN4 (11.8±2.4% vs. control 28.9±5.8%,; n=15; $p<0.05$) resulting in a reduction of the single-channel average current of all HCN isoforms. KCNE2 did not alter single-channel amplitude of any HCN subunit.
Conclusion: KCNE2-mediated increase of whole-cell HCN current size is due to elevated membrane protein levels rather than increased single-channel activity. However, KCNE2 differentially modifies single-channel properties of all HCN isoforms indicating a distinct direct functional interaction in the individual channel complexes.

P1412 Physiological effects of I(f) inhibition by ivabradine in mice lacking L-type Cav1.3 calcium channels: a differential role for for HCN and Cav1.3 channels in the genesis and regulation of heart rate

L. Marger[1], M. Bouly[2], F. Mahlberg-Gaudin[2], A. Cohen-Solal[1], A.L. Leoni[3], E. Kupfer[1], J. Striessnig[4], J. Nargeot[1], M.E. Mangoni[1]. *[1]Institut de Genomique Fonctionnelle, Herault, Montpellier, France; [2]Institut de Recherche Internationales Servier, Courbevoie, France; [3]L'Institut du Thorax, Nantes, France; [4]Universitat Innsbruck, Innsbruck, Austria*

The I_f and Ca_v 1.3-mediated L-type calcium currents play important roles in heart rate (HR) and automaticity. The differential role of HCN- and Ca_v 1.3-channels in pacemaking is not completely elucidated and it is not known if automaticity can persist after inhibition and/or inactivation of both HCN and Ca_v 1.3 channels. The effects of I_f inhibition by ivabradine (IVA), the first specific and selective I_f sinus node inhibitor, were investigated by ECG using telemetry in wild-type (WT; n=7) and Ca_v 1.3 KO (Ca_v 1.3-/-; n=7) mice, spontaneously bradycardic.
IVA was administrated once intra-peritoneally (ip bolus) from 0.1 up to 3 mg/kg. In WT and Ca_v 1.3-/- mice, iva dose-dependently reduced the mean HR (Fig.) without changing the QRS complex. At 3 mg/kg, mean HR reduction was –23 and –39% in WT and Ca_v 1.3-/- ($p<0.01$), respectively. In Ca_v 1.3-/- mice, intrinsic HR measurement after injection of atropine (0.5 mg/kg ip) and propranolol (1 mg/kg ip)(A+P) to block autonomic input, showed that I_f inhibition by IVA at 3 mg/kg ip did not stop pacemaking but only lowered intrinsic HR from 226± 34 bpm at 3 mg/kg to 184±24 bpm with A+P at the same dose ($p<0.05$).



Relationship between ivabradine and HR

In conclusion, HCN and Ca_v 1.3 channels control the mean HR. I_f inhibition lowered both the mean and maximal HR. Contrary to HCN, Ca_v 1.3 channels do not reduce the maximal HR, but stabilize HR. Most importantly, normal and intrinsic pacemaker activity can persist in the absence of Ca_v 1.3 channels even after partial inhibition of HCN channels. These observations indicate that multiple mechanisms contribute to cardiac automaticity and, thus to the safety of HR reducing agents such as ivabradine.

P1413 Potassium channel subunits expression in dilated cardiomyopathy demonstrates a shift into a fetal gene expression programme

M.P. De Castro[1], F. Hernandez[1], A. Aranega[1], D. Franco Jaime[2]. *[1]University of Jaen, Experimental Biology, Jaen, Spain; [2]University of Jaen, Experimental Biology, Jaen, Spain*

Over the last years there has been increasing evidence that regulation of the potassium current in the adult heart is dependent on a wide range of interaction between distinct alpha and beta subunits. The modulation of the Ik current has been documented to be generated by the protein products derived form the Kcnq1 and Kcnh2 genes, in interplay with Kcne1 to Kcne5 beta subunits. In vitro experiments have demonstrated that each beta subunit is able to modulate the current properties generated the by Kcnq1 and Kcnh2 pore-forming subunits in distinct manners. Interestingly, recent data have revealed that all of these beta subunits are transcriptionally expressed in the adult human heart. However, it is unclear how these distinct beta subunits are expressed in the myocytes, and whether there are variations on their expression profiles during distinct developmental and/or physiopathological conditions. We have assessed by quantitative RT-PCR

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

the developmental profiles of the alpha and beta subunits during normal cardiogenesis and in a murine model of dilated cardiomyopathy. We have observed that kcnq1 and kcnh2 display a similar expression profile during atrial and ventricular myocardial development. In contrast, beta subunits display a similar profile during atrial development, being kcne3 the most represented subunit, whereas kcne3 is replaced by kcne2 in the ventricular in adult stages. Dilated cardiomyopathy results in moderate increase of both alpha subunits in the atrial chambers but a significant downregulation in the ventricles. Expression of all beta subunits, except kcne5, is significantly downregulated in the atrial chambers, whereas kcne1 and kcne4 are downregulated and kcne2,kcne3 and kcne5 are upregulated in the ventricular myocardium. Interestingly, the most represent beta subunit is not altered in the atrial myocardium whereas there is a shift in the ventricular myocardium in the dilated cardiomyopathic hearts. These data demonstrate for the first time that dilated cardiomyopathy reprogrammes electrical circuitry towards the embryonic gene expression programme.

P1414 Adrenergic beta-3 receptors positively regulate aquaporin-1 water channels via protein kinase C and cyclic nucleotides

W. Zhang, E. Zitron, D. Scherer, D. Thomas, C. Morath, L. Kihm, M. Zeier, V. Schwenger, C. Karle. *Medical University Hospital Heidelberg, Cardiology and Angiology, Heidelberg, Germany*

Background: In human myocardium, aquaporin-1 (AQP1) is likely to be the predominant water channel to maintain osmotic homeostasis in the T-tubular system of cardiomyocytes. Under adrenergic stimulation, ionic fluxes in the T-tubular system increase rapidly. The mechanisms of osmotic compensation of those increased fluxes are unknown. Thus, we hypothesised that AQP1 function may also be modulated by adrenergic stimulation.
Methods: Human AQP1 channels and human β_3 adrenoreceptors were studied in the Xenopus oocyte expression system. Water permeability was assessed by digital evaluation of cell swelling during hypotonic challenge. Currents were recorded with double- microelectrode voltage- clamp.
Results: After co-expression of β_3 adrenoreceptors and AQP1 channels, activation of the receptors by isoproterenol induced an increase of membrane water permeability. In parallel, AQP1- mediated cationic currents were markedly increased. Regulation of AQP1 by β_3 adrenoreceptors was strongly attenuated in mutated AQP1 channels lacking protein kinase C (PKC) phosphorylation sites, demonstrating the role of PKC. Additionally, pharmacological inhibition of cGMP synthesis by application of ODQ also attenuated the effect.
Conclusions: This is the first study to show that aquaporin-1 channels are regulated by β- adrenergic signalling. In line with previous studies of cardiac β_3 -adrenoreceptors, both cyclic nucleotides and protein kinase C dependent pathways are involved. This regulation may contribute to the maintenance of osmotic stability under adrenergic stimulation in cardiomyocytes.

P1415 Reduced activity of the cardiac sodium calcium exchanger during chronic beta1-adrenergic stimulation in mice

F.R. Heinzel[1], S. Khan[1], S. Sedej[1], P. Gronau[1], B. Korff[1], S. Engelhardt[2], B. Pieske[2]. *[1]Herzzentrum, Cardiology, Goettingen, Germany; [2]DFG-Forschungszentrum f. Exp. Biomedizin, Uni Wuerzburg, Wuerzburg, Germany*

Chronic beta-adrenergic stimulation results in myocardial remodeling with contractile dysfunction and increased morbidity and mortality. In young (2-4 months) beta1-adrenoceptor transgenic mice (beta1TG), elevated diastolic [Ca^{2+}] levels in cardiomyocytes precede and promote the development of heart failure (Circulation, 2004;109:1154). The pathomechanisms of impaired intracellular Ca^{2+} homeostasis early in myocardial remodeling, however, are not yet understood. We examined Ca^{2+} transients in young beta1TG and wild-type (WT) mice (Fluo 4AM, 0.5 Hz field stimulation, room temp.).
Results: Peak systolic cytosolic [Ca^{2+}]i was increased (585±77 vs. 363±45 nmol/L) and delayed (143±4 vs. 122±4 ms) in beta1TG vs. WT (both $p<0.05$; $n>15$ cells/genotype). Diastolic cytosolic Ca^{2+} removal during 0.5 Hz stimulation was slower in beta1TG (time constant 224±19 vs. 180±12 ms in WT) and sarcoplasmic reticulum (SR) Ca^{2+}-content (caffeine) was increased (154±6 vs. 70±15 μmol/L cytosol in WT, $p<0.05$). Ca^{2+} removal during caffeine application (TAUcaff, 20 mmol/L) occurs mainly through the sarcolemmal Na^+/Ca^{2+} exchanger (NCX). TAUcaff was significantly increased in beta1TG (3506±308 vs. 2221±257 ms;$n>8$/genotype;$p<0.01$), reflecting decreased NCX forward mode activity. Application of the NCX inhibitor Ni^+ confirmed a reduced Ni^+-sensitive component of cytosolic Ca^{2+} removal in beta1TG (69±5% vs. 84±4% in WT;n=6 and 5 resp.; p=0.059). In conclusion, reduced NCX activity contributes to a slowed diastolic Ca^{2+} removal and increased cellular Ca^{2+} load during chronic beta1-adrenergic stimulation in mice. Reduced NCX activity may play an important role early in the development of heart failure.

P1416 Histidine-rich calcium binding protein as novel mediator between sarcoplasmic reticulum Ca uptake and release

D.A. Arvanitis[1], E. Vafiadaki[1], B. Mitton[2], K.N. Gregory[2], F. Del Monte[3], A. Kontrogianni-Konstantopoulos[4], D. Sanoudou[1], E.G. Kranias[3]. *[1]FBR Academy of Athens, Molecular Biology, Athens, Greece; [2]University of Cincinnati, Pharmacology and Cell Biophysics, Cincinnati, United States of America; [3]Harvard Medical School, Cardiology, Boston, United States of America; [4]University of Maryland, Physiology, Baltimore, United States of America*

Depressed cardiac Ca cycling by the sarcoplasmic reticulum (SR) has been associated with attenuated contractility which can progress to heart failure. The histidine-rich calcium binding protein (HRC) is a SR component that binds to triadin and may affect the ryanodine receptor. HRC overexpression in transgenic mouse hearts was associated with decreased rates of SR Ca uptake. We found that HRC may mediate part of its regulatory effects in cardiac muscle by binding directly to SERCA2. This interaction involves the amino acid residues 320-460 of HRC and part of the N-terminal cation transporter domain of SERCA2 (74-90 aa), which projects into the SR lumen. The triadin binding domain of HRC is located downstream at 609-699 aa. Specific binding between HRC and SERCA was verified in vivo by co-immunoprecipitation and pull-downs using human and mouse cardiac homogenates, as well as in vitro by blot overlays with GST and MBP recombinant proteins. Ca-titration studies indicated that the binding of HRC to SERCA2 is Ca-dependent. The effect of Ca on the HRC/SERCA2 interaction is opposite to this of HRC/triadin. Thus, HRC may mediate a fine cross-talk between SR Ca uptake and release by its direct interaction with SERCA2 and triadin, which may be affected by local Ca changes.

P1417 Evidence of connexin 43 connexons in heart mitochondria

E. Miro-Casas[1], M. Ruiz-Meana[1], E. Agullo[1], I. Torre[1], A. Cabestrero[1], A. Rodriguez-Sinovas[1], M. Morente[1], K. Boengler[2], G. Heusch[2], D. Garcia-Dorado[1]. *[1]Institut de Recerca Vall d'Hebron, Cardiology, Barcelona, Spain; [2]Institut fur Pathophysiologie, Cardiology, Essen, Germany*

We have previously shown the presence of connexin 43 (Cx43) at the inner mitochondrial membrane of cardiomyocytes. The purpose of this study was to test the hypothesis that Cx43 forms connexons (hemichannels formed by 6 Cx43 molecules) at this localization. To this purpose, we first examined the oligomeric state of Cx43 using a membrane-permeant cross-linking agent (DMS) applied to rat heart isolated mitochondria. This resulted in the appearance of new immunoreactive bands for Cx43 with mobility corresponding to the molecular weights of Cx43 monomers and oligomers (dimers, trimers) in immunoblotting analysis. Second, we analyzed mitochondrial uptake of the Cx43 hemichannel-permeant dye Lucifer Yellow (LY) in isolated mitochondria incubated (30min) in substrate-containing buffer with LY 1uM. LY fluorescence measured after washing was not modified by CsA, but was markedly reduced ($p<0.001$) by heptanol (up to 10uM) or carbenoxolone (up to 1uM), two chemically unrelated blockers of Cx43 hemichannels. Finally, we analyzed the potential influence of Cx43 in mitochondrial matrix volume regulation induced by changes of K^+ concentration in isolated mitochondria obtained from HL-1 cardiomyocytes stably transfected with either a retrovirus containing the coding sequence of Cx43 (resulting in an about 2 fold overexpression) or an empty vector. Matrix swelling (light-scattering at 520nm) was markedly attenuated ($p<0.001$) in vehicle transfected as compared to Cx43 overexpressing cells. These results are consistent with the hypothesis that Cx43 forms connexons in the inner mitochondrial membrane of cardiomyocytes, and suggest that these connexons may contribute to regulation of mitochondrial volume and function.

P1418 An obligatory role for beta-dystroglycan in formation of contraction bands in the heart produced by calcium paradox

H. Mani, H. Tanaka, T. Takamatsu. *Kyoto Prefectural University of Medicine, Pathology and Cell Regulation, Kyoto, Japan*

Contraction-band necrosis, an important morphological hallmark of ischemia-reperfusion injury of the heart, is caused by irreversible intracellular calcium (Ca(i)) overload and the resultant contracture. Of various experimental models for ischemia-reperfusion injury, Ca paradox has been widely used to produce severe Ca(i) overload and contraction bands because of its simple experimental procedure: perfusion of the heart with Ca-free solution (Ca depletion) and subsequent reperfusion with Ca (Ca repletion) produce a large uncontrolled gain of Ca(i) leading to contracture. However, despite such a simple procedure no definitive mechanism has been determined for the Ca paradox-induced Ca(i) overload and contracture. To clarify the culprit mechanism for contraction bands, we conducted realtime confocal imaging of both the structure and Ca(i) dynamics of the ventricular myocytes in Langendorff-perfused rat hearts loaded with a membrane indicator RH237 and a Ca(i) indicator fluo3/AM. Immunohistochemical analyses were also performed. While Ca depletion abolished Ca(i) transients, Ca repletion produced oscillatory Ca(i) waves (123±21/min/cell, n=23) and asynchronous lo-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

cal contractions in individual myocytes with progressive contracture within 10min. While pretreatment of the heart with neither 1μM ryanodine plus 0.5μM thapsigargin (n=4) nor 3μM verapamil (n=5) precluded the progressive contracture by Ca repletion, 5mM nickel completely abolished both Ca(i) waves and contracture (n=5), indicating that influx of Ca via either Na-Ca exchanger (NCX) or nonspecific Ca leak contributes to these changes. However, NCX was not prerequisite for contracture because Ca(i) overload via reverse mode of NCX by Na-free perfusion failed to develop contracture in spite of the high-frequency Ca(i) waves (n=3). Mechanical arrest of the heart by 30mM 2,3-butanedione monoxime (BDM) also precluded the development of contracture by Ca repletion (n=5), indicating that the connection of the cell membrane with contractile filaments and extracellular matrix is essential to prevent the Ca(i) overload and contracture. Immunohistochemical analyses revealed that Ca depletion resulted in significant depletion of beta-dystroglycan on the cell membrane, which was precluded by either nickel or BDM. Laminin-2, beta1-integrin and dystrophin were preserved by Ca depletion. In conclusion, irreversible Ca(i) overload and subsequent contracture by Ca paradox are mediated by nonspecific influx of Ca through the cell membrane as a result of derangement of beta-dystroglycan-mediated mechanical connection between the myofilaments and extracellular matrix.

STEM CELLS AND CARDIAC REMODELING-BENCH TO BEDSIDE

P1419 Functional improvement after bone marrow-derived mononuclear vs mesenchymal stem cell therapy in chronic myocardial infarction

M. Mathieu[1], L. Ray[1], B. El Oumeiri[1], K. Touhiri[1], N. Mazouz[2], P. Willemsen[1], S. Brimioulle[2], G. Heyndrickx[3], J. Bartunek[3], K. Mc Entee[2]. [1]*Free University of Brussels, Physiology Dept., Brussels, Belgium;* [2]*Cardio3, Braine-L'alleud, Belgium;* [3]*OLV, Cardiovascular Center, Aalst, Belgium*

Background: Cardiac stem cell therapy with bone marrow-derived stem cells is a promising approach to facilitate myocardial repair after myocardial injury. However, the effectiveness of such a therapy in chronic postinfarction stage and optimal cell type are still debated. Therefore, we conducted a randomized, double-blind and placebo-controlled study with head-to-head comparison of bone marrow mononuclear cells (BMNC) and non-modified mesenchymal stem cells (BMSC) therapy in a large animal model of chronic myocardial infarction.
Methods: Eight weeks after coronary ligation, 24 dogs were randomized into 3 groups receiving myocardial injections of placebo, BMNC (227.106± 32.106 cells) or culture expanded non-modified BMSC (232.106±40.106 cells) directly into the infarcted region. Animals underwent echocardiography at baseline (BL), 8 weeks (8 wks) and 16 weeks (16 wks). Left ventricular wall motion score index (WMSI) was assessed using the 16 segments model. Pressure-volume loops under progressive preload reduction were recorded by the conductance method to obtain the end-systolic elastance (Ees) at BL and 8 weeks after the treatment.
Results: BMNC transplantation induced a progressive decrease in the WMSI at 8 and 16 weeks as compared to baseline. In contrast, injection of the BMSC was associated with only a moderate decrease at 16 wks vs BL. Furthermore, Ees increased after injection of BMNC but not after injection of BMSC.

	WMSI			Ees, mmHg/ml	
	BL	8 wks	16 wks	BL	8 wks
Placebo	1.8±0.09	1.7±0.13	1.7±0.14	2.69±0.19	2.94±0.49
BMNC	1.8±0.11	1.6±0.07**	1.5±0.07**	2.23±0.25	4.31±0.56**
BMSC	1.9±0.08	1.8±0.12	1.7±0.11*	2.10±0.65	2.93±0.5

Values in table are expressed as mean ± SE. (*p<0.05 vs BL, **p<0.01 vs BL).

Conclusions: In a large animal model of chronic myocardial infarction, direct myocardial injection of BMNC results in more improvement of LV function and contractility as compared to BMSC.

P1420 Human foetal cardiomyocyte progenitor cells improve LV systolic function after myocardial infarction in NOD/scid mice

R.W. Grauss[1], M.J. Goumans[2], E.M. Winter[1], A.M. Smits[2], P. Steendijk[1], A.C. Gittenberger-De Groot[1], A. Van Der Laarse[1], M.J. Schalij[1], P.A. Doevendans[2], D.E. Atsma[1]. [1]*Leiden University Medical Center, Cardiology, Leiden, Netherlands;* [2]*University Medical Center Utrecht, Cardiology, Utrecht, Netherlands*

Introduction: Recently, the existence of cardiomyocyte progenitor cells (CMPCs) that reside in the heart became appreciated. We isolated CMPCs from human foetal hearts and showed that these human CMPCs (hCMPCs) can differentiate into functional cardiomyocytes in vitro. In the present study we investigated whether these cells are able to engraft in the ischemic myocardium and improve left ventricular function in an immune-compromised mouse myocardial infarction model.
Methods: hCMPCs were isolated from human fetal hearts by magnetic cell sorting based on expression of SCA-1. Myocardial infarction (MI) was induced in immune-compromised NOD/scid mice. Twenty minutes after MI, hCMPCs labelled with eGFP (hCMPC group, 2.0 x 10^5 cells in 20μl, n=11) or vehicle only (MI+Medium group, n=12) were injected into the infarcted area. Sham operated mice (Sham) were used as baseline (n=10). Two and 14 days after MI, cardiac function was serially assessed using a vertical 9.4T animal MRI. Mice were then sacrificed and the engraftment and differentiation of injected cells was assessed by immunohistochemistry.
Results: At day 2, LV volumes were higher and EF was lower in both MI groups as compared to Sham, with no difference between the MI groups (Fig 1.). However at day 14, EF was higher and ESV was lower in the hCMPC group as compared to the MI+Medium group (P=0.001 and P=0.048 respectively). Although there was a trend towards a reduced EDV, this did not reach significance (P=0.14). hCMPCs engrafted in the infarcted myocardium and expressed also alpha-actinin.

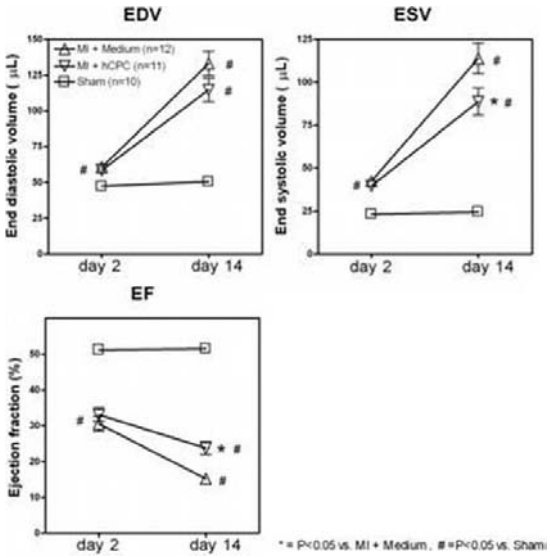


Figure 1.

Conclusions: Foetal hCMPC engraft in the acutely infarcted myocardium, express alpha-actinin and improve LV systolic function. These results indicate the potential of hCMPC to be used in cell-based therapy for the treatment of IHD.

P1421 Early exercise training after myocardial infarction improves cardiomyocyte function

V. Bito[1], S. Ozdemir[1], L. Biesmans[1], M. De Waard[2], J. Van Der Velden[3], D. Duncker[2], K.R. Sipido[1]. [1]*KULeuven, Laboratory of Experimental Cardiology, Leuven, Belgium;* [2]*University Medical Center Rotterdam, Division of Experimental Cardiology, Rotterdam, Netherlands;* [3]*VU University Medical Center Amsterdam, Laboratory of Physiology, Amsterdam, Netherlands*

Background: Recent work has shown that exercise started early after myocardial infarction (MI) improves in vivo cardiac function and remodeling. We investigated whether these effects of early exercise could be related to changes in cardiomyocyte contractile function and calcium (Ca^{2+}) handling.
Methods: Mice with MI following left anterior descending ligation were given free access to a running wheel (MIexe, 5.9±0.2 km/day, N=8) or were housed sedentary (MIsed, N=10) for 8 weeks. Intact single cardiomyocytes were enzymatically isolated from the non-infarcted LV, excluding the border zone. Contraction was measured during electrical field stimulation; membrane currents and [Ca^{2+}] were measured under whole-cell patch clamp, with fluo-3 as Ca^{2+} indicator, all at 30°C.
Results: Myocytes from MIexe were significantly longer than MIsed (164±6 μm in MIexe vs. 143±3 μm in MIsed; P<0.05) but not wider (25±1 μm in MIexe vs. 23±1 μm in MIsed). When stimulated at 1, 2 and 4 Hz, unloaded cell shortening was significantly larger in the MIexe group compared to MIsed (at 1 Hz, L/L0= 6.5±0.7% in MIexe, ncells=27 vs. 4.3±0.5%, ncells=21 in MIsed; P<0.05); time to peak and half-time of relaxation were not different between the 2 groups. [Ca^{2+}]i transients under current clamp had however similar amplitude (at 1 Hz, [Ca^{2+}]i transient amplitude=277±48 nM in MIexe, ncells=12 vs. 371±39 in MIsed, ncells=13). Diastolic Ca^{2+} levels increased at higher frequency of stimulation in both groups but to a lesser extent in MIexe (at 4 Hz, [Ca^{2+}]rest = 133±23 nM in MIexe, ncells= 12 vs. 199±27 in MIsed, ncells=13; P<0.05). Ca^{2+} influx via Ca^{2+} channels, measured as the current density, ICaL, under voltage clamp, was not different between MIexe and MIsed (at +10 mV, peak ICaL = -6.8±1.2 pA/pF, ncells=10 in MIsed vs. -6.7±0.7 pA/pF, ncells=20 in MIexe) and [Ca^{2+}]i transient amplitude under voltage clamp was also not different. In skinned cardiac myocytes, maximal force development during direct Ca^{2+} activation of the myofilaments was significantly larger in MIexe (18.3±0.8 kN/m^2 in MIexe vs. 14.2±0.7 kN/m^2 in MIsed, ncells=15 in each group, P<0.05).
Conclusions: Early exercise training after myocardial infarction induces remodeling of cardiac myocytes. Contractile function improves without significant changes

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

in [Ca^{2+}]i transient amplitude, consistent with adaptive changes in myofilament Ca^{2+} response.

P1422 Angiotensin AT2 receptors are expressed in cardiac c-kit+ cells and mediate cell survival after myocardial infarction in rats

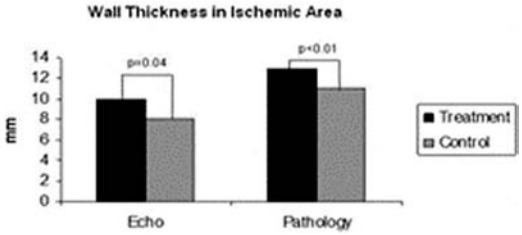
J. Li, C. Birka, E. Kaschina, A. Grzesiak, C. Curato, M. Brinckmann, M. Timm, T. Unger. *Center For Cardiovascular Research, Charite, University Medicine Berlin, Berlin, Germany*

The expression pattern of angiotensin AT2 receptors with predominance during fetal life and upregulation under pathological conditions during tissue injury/repair points towards the fact that AT2 receptors may exert an important action in injury/repair adaptive mechanisms, which may be entirely different from the known effects of angiotensin II mediated through the AT1 receptor. In contrast to the well-studied AT1 receptor, less is known about AT2 receptors in acute ischemia-induced heart injury. We aimed here to elucidate the role of AT2 receptors in response to acute myocardial infarction. The regulation of AT2 receptors on cardiac cellular level was first analyzed in rats with acute myocardial infarction. Double immunofluorescence staining showed that increased AT2 receptor immunostaining was mainly detected in clusters of small c-kit+ cells accumulating in the peri-infarct zone. Further, we isolated and purified the c-kit+ cell population from rat infarcted hearts by modified MACS technology and FACS sorting. These ex vivo cardiac c-kit+ cells, which are characterized by both sca-1 and AT2 receptor expression, continue to proliferate slowly and maintain a stable phenotype under in vitro conditions for more than 16 months after their isolation. Moreover, in these ex vivo cardiac c-kit+ cells, exogenous angiotensin II (10 nM, for 24 hours) supported cell survival but AT2 receptor antagonist, PD123319 (200 nM), abolished the effect of angiotensin II. Together, these data demonstrate that angiotensin AT2 receptors may support cardiac c-kit+ cell survival in response to cardiac ischemic injury in rats.

P1423 Catheter based delivery of adipose-derived stem cells in a large animal chronic ischemia model improves myocardial healing

C.O. Cardoso[1], G.V. Silva[1], M. Fernandes[1], R. Schreiber[2], E.M. Oliveira[2], P.J. Quevedo[2], R.S. Ruiz[2], F.S. Angeli[2], K. Pinkernell[1], E.C. Perin[2]. *[1]Texas Heart Institute, Cardiology Research, Houston, United States of America; [2]Cytori Therapeutics, San Diego, United States of America*

Background: Adipose tissue is a potential source of stem cells for cardiac cell therapy. We sought to determine safety and feasibility of transendocardial injections (TEI) of adipose-derived stem cells (ADSC) in a translational model of chronic ischemia in pigs.
Methods: In a randomized blinded study, 18 pigs (ADSC n=10; control n=8) underwent placement of ameroid constrictors to the LCx artery at baseline. At 30 days, 13 TEI of freshly isolated autologous ADSC (66.6±12.6 x106 cells with 96% of viability) vs. plasmalyte were performed. Four animals received DAPI labeled cells for tracking purposes. Delivery was guided by electromechanical mapping targeting ischemic/viable tissue. At 60 days, animals were euthanized and histopathology analysis performed. At baseline, 30 and 60 days LVEF and wall thickness were assessed by transesophageal echocardiography. Cardiac rhythm was monitored by ECG and implantable loop recorders.ANOVA and t-test were used to compare the two groups.
Results: There were no procedural complications or arrhythmias. Both groups had similar changes in LVEF from baseline to 60 days (64.20± 5.71 to 59.10±7.96% in ADSC vs. 60.85±5.20 to 54.71±7.25% in controls, p=0.24).Interestingly, in the cell treated group LV wall thickness was preserved in the ischemic area as assessed by echo and pathology (figure). DAPI labeled cells were seen in all animals 30 days after injections.



Wall thickness of ischemic myocardium

Conclusions: Catheter based delivery of freshly-isolated ADSC is safe and feasible in a large animal model. This alternative source of stem cells might favorably influence the healing process in the setting of chronic myocardial ischemia.

P1424 Pretreatment of mesenchymal stem cells with TNF-a enhances the cardiac function recovery after experimental ischemia-reperfusion injury

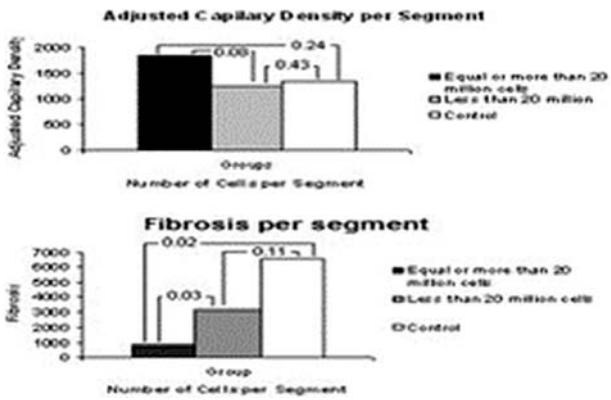
Y. Ahn, Y.S. Kim, H.J. Park, K.H. Kim, J.H. Kim, H.W. Park, M.H. Jeong, J.G. Cho, J.C. Park, J.C. Kang. *Chonnam National University Hospital, Cardiology Dept, Gwangju, Korea, Republic of*

Background: Mesenchymal stem cells (MSCs) have therapeutic potential after myocardial infarction. We hypothesized that cytokines released from infarcted myocardium accelerates MSCs recruitment to damaged region. We elucidated whether TNF-a, one of cytokine released from infarcted myocardium, modulate the behavior of rat bone marrow-MSCs in vivo and in vitro system.
Methods: Allogeneic MSCs were isolated from the femoral bone of Sprague-Dawley rats, characterized, cultured, and labeled with DAPI. TNF-a itself did not show any cytotoxicity to MSCs. MSCs were pre-treated with TNF-a (10ng/mL) for 24 hours before injection into infarcted myocardium of rats. Myocardial infarction was induced by left anterior descending coronary artery ligation for 30 minutes followed by release. Two weeks later, the number of DAPI-labelled MSCs on myocardium of rat was counted, and cardiac function was assessed by using pressure-volume catheter.
Results: The expression of BMP-2 was increased by TNF-a in mRNA (2.7-fold of control, $p<0.05$) and protein level (3.23±0.43 ng/mL in MSC vs. 5.81±0.75 ng/mL in TNF-a-treated MSC, $p<0.05$). The activation of signal transducer and activator of transcription (STAT)-3 and NF-kB were also increased in TNF-a treated MSCs. Adhesion assay showed that the adhesiveness of TNF-a-stimulated MSCs on cardiomyocytes was 1.74-fold increased ($p<0.05$). The number of engrafted TNF-a-stimulated MSCs on rat myocardium was larger than non-treated MSCs (1.82-fold, $p<0.05$). Left ventricular ejection fraction was increased in MSC-injected rats (48.3% vs 24.7%), and more recovered in TNF-MSC-injected rats (61.6% vs. 24.7%).
Conclusion: Our results demonstrated that TNF-a improved the engraftment of MSCs on infarcted myocardium through increase its adhesiveness and BMP-2 probably acted as a putative mediator.

P1425 Transendocardial delivery of bone marrow mononuclear cells in chronic ischemic heart disease: insights from a cell dosing study

G.V. Silva, M.R. Fernandes, C.O. Cardoso, E.M. Oliveira, R.S. Ruiz, P.J. Quevedo, F.S. Angeli, Y.I. Zheng, J.T. Willerson, E.C. Perin. *Texas Heart Institute, Cardiology Research, Houston, United States of America*

Background: Transendocardial injections (TEI) of bone marrow mononuclear stem cells (BMNSCs) have proven to be safe and potentially efficacious as treatment for chronic ischemic heart disease. However, the ideal BMNSCs dose remains unknown.
Methods: At baseline 16 pigs underwent chronic ischemia by placement of ameroid constrictor on the left circumflex artery. Animals were randomized to receive 13 TEI guided by NOGA mapping30 days after ameroid implant. The animals were allocated into 4 groups: control (saline injection), and doses of 50, 100 and 200 million of BMMNSCs. Thirty days after injection animals were sacrificed, and hearts sent to histopathology for fibrosis and capillary density (CD) assessment ($\mu m^2/mm^2$). Hearts were sliced following 17 AHA segmentation, and concentration of cells per segment correlated with amount of fibrosis and CD. An implantable loop recorder monitored for possible arrhythmias due to cell transplantation during the entire study.
Results: There were no adverse events or arrhythmias associated with cell therapy. Overall, cell treated animals had less fibrosis but similar CD when compared to the controls. No differences were seen between the different cell doses in regards to fibrosis and CD. However, a segmental dose of a greater than 20 million cells per segment was associated with a significant reduction in fibrosis and a trend towards increased CD (figure). Also,there was a significant correlation between segmental cell concentration and segmental capillary density adjusted by the amount of fibrosis (r=0.35, p=0.01).



Capilary density and fibrosis

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusions: A cell concentration greater than 20 million BMNSCs per segment correlated with capillary density improvement and reduction in fibrosis A segmental dosing approach should be further evaluated in stem cell trials.

P1426 Cardiac stem cell ablation worsens cardiac remodeling and increases mortality after diffuse myocardial damage in rats

D. Torella[1], G.M. Ellison[2], C. Gasparri[2], A. Leone[2], A.L. Cavaliere[2], D. Boncompagni[2], A. Curcio[2], C. Indolfi[2], D.F. Goldspink[1], B. Nadal-Ginard[3]. *[1]Magna Graecia University, Cardiology, Catanzaro, Italy; [2]Liverpool J. Moores University, Liverpool, United Kingdom; [3]Mount Sinai School of Medicine, New York, United States of America*

Purpose: Under normal physiological conditions the adult heart is an extremely slow-proliferative organ. C-kitpos cardiac stem cells (CSCs) are present in the adult myocardium where most of them are quiescent(>95%). CSCs are involved in maintaining normal cardiac cell homeostasis duing adulthood but their functional role during pathologic cardiac stress is still unkown. We have previously shown that following diffuse myocardial damage, the myocardium responds with rapid CSC activation, proliferation and differentiation into immature small myocytes with a fetal phenotype. These regenerating myocytes can undergo a few rounds of replication before withdrawing from the cell cycle. These cellular events directly correlate with recovery from acute cardiac decompensation and restoration of normal LV function in less than 2 weeks. To establish a cause-effect relationship between these two events, here we sought to evaluate the functional contribution of CSC activation and their myocyte generation following myocardial injury.
Methods: Four days after a single injection of isoproterenol to male Wistar rats (ISO, 5 mg kg^{-1}; which kills ~8% ventricular myocytes in a diffuse pattern), most of the CSCs have re-entered the cell cycle. To ablate the CSC myocardial pool, the antimitotic agent 5-fluorouracil (5-FU, 40mg/kg die), was administered in 1 cycle of 5 days/week starting at the 4th day post ISO injection. This 5-FU dose kills >90% proliferating cells in vivo but has no measurable deleterious effects on non-cycling cells. Animals were sacrificed 7, 14 and 28 days later. LV function was measured by echocardiography.
Results: The increase in CSC number normally found after ISO was completely abolished by 5-FU treatment. As a direct consequence, new myocyte formation (Ki67pos/BrdU labeled) was significantly reduced and was associated with lack of LV functional recovery, as compared to the non 5-FU-treated animals. The lack of CSC activation and consequent new myocyte generation resulted in a disproportionate maladaptative hypertrophy of the spared myocytes followed by their progressive drop-out by necrosis and apoptotis after ISO in 5-FU-treated rats. This resulted in progressive worsening of LV function and increased mortality at 28 days. The myocyte death and LV dysfunction was not a toxic effect of 5-FU because it was not seen in the 5-FU treated control animals.
Conclusions: These results identify CSC activation and new myocyte formation as an integral and essential component of the endogenous myocardial response to diffuse myocardial injury.

P1427 ACE-inhibitors improve myocardial capillarization, EPC migration and attenuate intracardiac cellular proliferation in myocardial hypertrophy

P. Mueller, A. Kazakov, M. Boehm, U. Laufs. *Univ. -Kliniken des Saarlandes, Kardiologie, Homburg, Germany*

Purpose: Endothelial progenitor cells (EPC) from the bone marrow contribute to endothelial homeostasis, repair and to neovascularisation, effects that are potentially important during cardiac remodelling. We hypothesized that ACE-inhibitors may exert beneficial effects during pressure induced myocardial hypertrophy by regulating progenitor cell function.
Methods and results: Increased afterload was induced in C57/Bl6 mice by transaortic constriction (TAC, 360 μm for 35 days; Sham n=12, TAC n=23). TAC-mice were randomized to receive ramipril (R-TAC 5 mg/kg; n=11) or vehicle. Ramipril reduced the development of cardiac hypertrophy. The ratio of heart weight/tibia length was Sham 0.008±0.0003 g/mm vs TAC 0.012±0.001 g/mm, $p<0.01$, and R-TAC 0.009±0.001 g/mm, $p<0.05$. Cardiomyocyte diameter changes (Sham 10.5±0.39 μm; TAC 15.53±1.2 μm; $p<0.000001$; R-TAC 12.18±0.89 μm, $p<0.0001$) were consistent with these data. Ramipril attenuated the extent of cardiac fibrosis (Sham 0.47±0.15%; TAC 2.34±0.86%; $p<0.05$; R-TAC 0.54±0.35%; $p<0.05$). Proliferating cells were identified by immunostaining for Ki67. In Sham, no Ki67pos cardiomyocytes were found. In TAC animals, Ki67pos cardiomyocytes were detected (1±0.2‰; $p<0.001$) and this effect was reduced by ramipril (0.05±0.04‰; $p<0.05$). Similar results were observed for Ki67pos non-cardiomyocytes in the heart (Sham 1.7±0.2‰; TAC 5.7±1‰; $p<0.01$; R-TAC 0.3±0.1‰; $p<0.0001$). Cardiac capillary density was measured by immunostaining for the endothelial marker CD31. The number of CD31pos cells per mm 2 decreased in TAC (Sham 376±27/mm^2; TAC 395±16/mm^2; $p<0.05$), but was significantly enhanced by ramipril (664±17/mm^2; $p<0.00000001$). TAC did not change significantly the ratios of CD31pos cells to total cell number or to cardiomyocytes (Sham 0.15±0.01; TAC 0.12±0.01, respectively Sham 0.75±0.04; TAC 0.78±0.09), but application of ramipril led to a significant increase of both ratios (R-TAC 0.24±0.01; $p<0.00000001$, respectively R-TAC 1±0.03; $p<0.05$). TAC had no significant influence on the migratory capacity of DiLDL/Lectinpos EPC (Sham 114±19; TAC 149±33), but the ACE-inhibitor improved EPC migration in the Boyden chamber (R-TAC 239±20, $p<0.05$).
Conclusions: The reduction of afterload-induced myocardial hypertrophy by treatment with ramipril was associated with enhanced cardiac capillarization, improved EPC migration and reduction of proliferating cardiomyocytes and non-cardiomyocytes in the myocardium. The regulation of progenitor cells from the bone marrow could represent a relevant effect of ACE-inhibitors during cardiac remodelling.

P1428 Cellular cardiomyoplasty with bioartificial matrix

J.L. Barisani[1], A.I. Christen[1], N. Lago[1], O. Masoli[1], J. Bordone[1], J. Mouras[1], J. De Paz[1], S. Chada[1], J. Chachques[2], J. Trainini[2]. *[1]President Peron Hospital, Cardiac Surgery, Buenos Aires, Argentina; [2]European G. Pompidou Hospital, Paris, France*

Purpose: The aim of cellular cardiomyoplasty is to regenerate the myocardium by implantation of living cells. However, in ischemic heart disease the extracellular myocardial matrix is modified. Therefore, it becomes important to associate the implanted cells to an extracellular bioartificial matrix. The aim of this clinical study was to evaluate the performance of a biodegradable collagen matrix.
Methods: In 5 consecutive patients (pts), aged 52±7.6 yrs, presenting left ventricular (LV) post ischemic myocardial scars and candidates for a single coronary artery by-pass graft on a remote area, autologous mononuclear bone marrow cells (BMC) were implanted over the scar (1.25±0.67 x 10 E+08 cells, CD 34+ 5.2%, AC 133+ 2.8%) during surgery. All pts were also implanted a 3D collagen type I matrix (size: 7 x 5 x 0.6 cm) seeded with the same number of BMC on top of the necrotic area.
Results: Neither mortality nor related adverse events were registered at a follow-up of 281±108 days. Blind echocardiography and radioisotopic analysis showed that cell-implanted segments kinetics improved 52%. LV end diastolic diameter decreased from 57.4±2 mm to 52.4±3 mm (p=0.02). Radionuclide LV ejection fraction improved from 37.6±13% to 45.8±13% (p=0.05).
Conclusions: In these pts with ischemic heart disease, treatment with combined BMC and bioartificial matrix implant and a single CABG in a remote area showed functional and hemodynamic improvements. The association of a cell seeded matrix appears to reinforce the infarct scar with viable bioartificial tissues, thus limiting ventricular remodelling. This tissue engineered approach seems to be safe and to improve the efficiency of cellular cardiomyoplasty.

P1429 Percutaneous endocardial cell delivery in patients with acute myocardial infarction. A feasibility study

K. Krause[1], K. Jaquet[2], C. Schneider[2], D. Hausmann[2], S. Geidel[2], K.H. Kuck[2]. *[1]Hamburg, Germany; [2]St. Georg Hospital, Cardiology, Hamburg, Germany*

Background: First clinical studies on intracoronary stem cell infusion in patients with acute myocardial infarction (AMI) revealed promising results with regard on left ventricular ejection fraction (LVEF) improvement. Endocardial cell injection has shown to be superior to the intracoronary approach in preclinical studies, but percutaneous endocardial cell injection has only been reported in patients with chronic ischemic heart disease, so far. This study is the first-in-man report on the safety and feasibility of percutaneous endocardial cell delivery in patients with AMI.
Methods: On day 9±4 after AMI and PCI with stent implantation (culprit lesion: 8 LAD, 2 CX), ten patients (mean 56±14 years) received bone marrow derived mononuclear cells in the border zone of the infarction area using left ventricular mapping-guided percutaneous endocardial injection. At the 6 month follow-up echocardiography, laboratory data (BNP, IL-6, CRP, blood count), LV mapping and clinical assessment were performed.
Results: None of the patients showed periprocedural complications or major adverse events during the 6 month follow up. We injected 2,2x10(8) cells including 1,1x10(6) CD45-/CD34+ (median) stem cells in each patient. Initial unipolar voltage mapping showed a 44±16% reduction of the unipolar voltage in the area at risk and raised to 56±21% at th 6 month follow up.Left ventricular ejection fraction improved from 43±6,8% to 49,3 ±9,3% at the 6 month follow-up. The echocardiographic wallscore was 1.53 (±0,32) at baseline and 1,34 (±0,28) at 6 months.
Conclusion: Percutaneous endocardial injection of mononuclear bone marrow derived cells in patients with AMI was shown to be a safe procedure and may improve left ventricular function.

P1430 Autologous bone marrow mononuclear cells transplantation in patients with idiopathic dilated cardiomyopathy: 12 months follow-up

R. Huang, K. Yao, J.B. Ge, Y.Z. Zou, J.Y. Qian, L.E.I. Ge, A.J. Sun. *Zhongshan Hospital, Fudan University, Cardiology Department, Shanghai, China, People's Republic of*

Objective: The aim of this study is to identify long-term result of cell transplantation in idiopathic dilated cardiomyopathy(IDC)patients who were treated by intra-

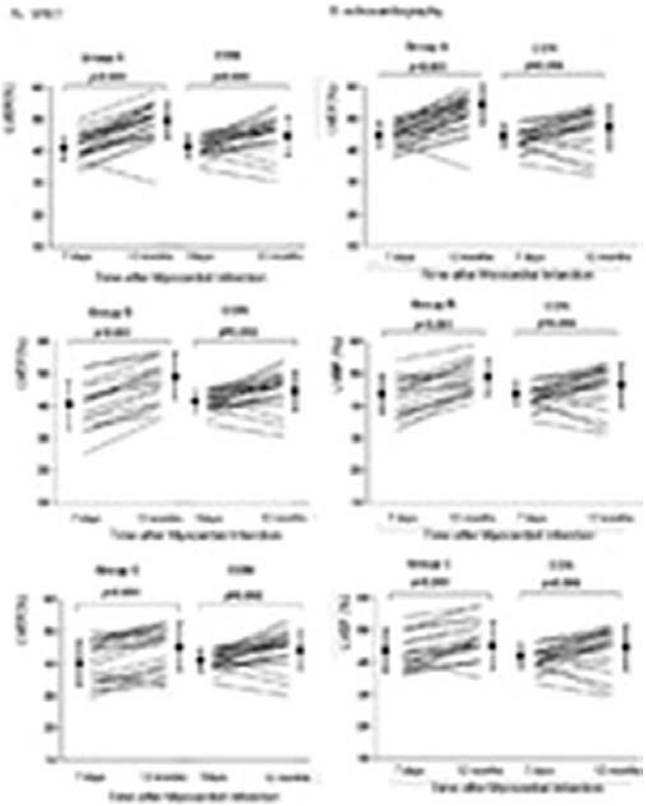
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

coronary transplantation of autologous bone marrow mononuclear cells(BMCs)in addition to standard therapy.
Method: Based on given standard therapy, eighteen patients with idiopathic dilated cardiomyopathy were enrolled and divided into transplantation group and control group. The clinical characteristics of two groups were comparable. Among these patients, 10 patients were performed percutaneous coronary autologous BMCs transplantation. Blood routine test, hepatic function, renal function, glucose, triglyeride(TG), cholesterol, low density cholesterol(LDL), high density cholesterol(HDL), uric acid(UA), and high sensitive C-reactive protein(hsCRP)were measured at the time point of pre-operation and some time after transplantation. All patients were monitored under ultrasonic cardiography, Holter, six-minute-walk test and magnetic resonance imaging over a period of at least 12 months. Annual hospital days were recorded during two-year follow-up.
Results: Six-minute-walk distance elevated significantly 12 months after BMCs transplantation compared with pre- transplantation. The change of left ventricular ejection fraction(LVEF)between pre- transplantation and 12 months later and the sizes of LVEDd had significant changes compared with that of control. But the left ventricular ejection fraction had no significant changes compared with that of control. No malignant arrhythmias and severe side effects could be observed around transplantation and during 12 months follow-up. Survival was similar between the two groups during 12 months follow-up.
Conclusion: Autologous bone marrow mononuclear cells transplantation can prolong six-minute-walk, decrease the sizes of LVEDd. In addition, it was demonstrated that cell transplantation is safe.

P1431 Timing and therapeutic response of Intracoronary Bone Marrow Mononuclear Cells administration in Acute ST-elevation Myocardial Infarction patients

R. Huang, K. Yao, J.B. Ge, Y.Z. Zou, J.Y. Qian, L.E.I. Ge, A.J. Sun. *Zhongshan Hospital, Fudan University, Cardiology Department, Shanghai, China, People's Republic of*

Background: Intracoronary bone marrow monocular cells (BMCs) administration 3-7 days after myocardial reperfusion in acute myocardial infarction (AMI) patients has been shown to be feasible and safe in the short and mid-term. Few studies have directly addressed the optimal timing of cell injections. Here, we evaluate whether the timing of intracoronary BMCs therapy affects the therapeutic response in AMI patients.
Methods: A total of 104 patients with a first ST-AMI who had undergone percutaneous coronary intervention (PCI) of the infarct-related artery were randomly assigned to the groups that underwent intracoronary infusion of BMCs immediately (Group A, n=26), 3 to 7 days (Group B, n=26), 7 to 30 days after PCI (Group C, n=27) or to the control group (CON, n=25), in which saline infusion performed immediately after emergency PCI.



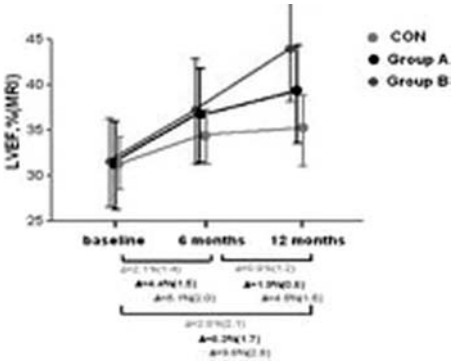
LVEF at baseline and 12 months FU

Results: Compared with CON and group C, the absolute increase from baseline to 12 months in left ventricular ejection fraction (LVEF), decrease in left ventricular endsystolic diameters (LVESd) and myocardial perfusion in Group A and Group B was both significantly higher. The patients of Group A and B derived similar benefits on cardiac function (p=0.578 by SPECT) and LV geometry (LVEDd: p=0.901; LVESDd: p=0.452 by echocardiography), while Group C got no additional benefits compared with CON. Notably, group B delivered more expensive care ($p<0.001$) and had longer hospital days ($p<0.001$) than group A for the similar improvement due to re-PCI after emergent PCI.
Conclusions: The probable optimal timing of cell therapy in AMI patients is immediately after the primary PCI and it seems to be more practicable and cost-effectiveness.

P1432 Repeated autologous Bone Marrow Mononuclear Cell transplantation in patients with large Acute Myocardial Infarction

K. Yao[1], R. Huang[2], J. Ge[2], Y.Z. Zou[2], J.Y. Qian[3], L.E.I. Ge[3], A.J. Sun[3]. *[1]Shanghai, China, People's Republic of; [2]Zhongshan Hospital, Fudan University, Cardiology Department, Shanghai, China, People's Republic of; [3]Zhongshan Hospital,Fudan University, Cardiology, Shanghai, China, People's Republic of*

Background: Intracoronary delivery of autologous bone marrow mononuclear cells (BMC) has been shown to enhance the left ventricular functions in patients with acute myocardial infarction (AMI), but the enhancement was generally small due to the limited numbers and survival time of the deliveried BMC by a single administration. We thus evaluated the effect of repeated BMC application in patients with large acute myocardial infarction.
Methods and Results: Thirty AMI patients with a significantly decreased left ventricular ejection fraction (LVEF 20%-40%), after successful percutaneous coronary intervention (PCI), were randomly assigned to three groups: one-time transplantation group (A, n=10) that received intracoronary infusion of BMC at 3 to 7 days, twice cell transplantation group (B, n=10) that received BMC administration at 3 to 7 days and repeated at 3 to 6 months, and the control group (CON, n=10). We noted no complications associated with repeated BMC transfer. The change in LVEF evaluated by MRI at 12 months was 2.8±2.1% in the CON, 6.3±1.7% in the group A, and 9.6±2.8% in group B ($p<0.001$ vs CON and p=0.005 vs group A). Also, MRI-derived myocardial infarct size decreased significantly in group B than in group A (9.1±3.0% vs 6.1±1.7%, p=0.016). Furthermore, repeated BMC implantation significantly improved myocardial perfusion determined by 201Tl-SPECT compared with one-time transplantation, suggesting LV remodeling process was further attenuated.



LVEF by MRI among three groups

Conclusions: Repeated BMC administration is a safe and effective therapeutic strategy for large AMI patients. Of course, our initial outcomes should be further investigated with a larger cohort and a longer follow-up period. Key Words: myocardial infarction, cell, transplantation, magentic resonance imaging

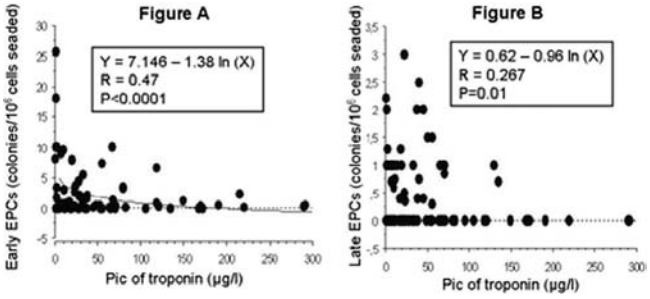
P1433 Relationship between circulating endothelial progenitors and troponin levels in patients with acute coronary syndrome

N. Meneveau, F. Deschaseaux, S. Davani, J.P. Kantelip, F. Schiele, J.P. Bassand. *Cardiology, Besancon, France*

Purpose: The presence of endothelial progenitor cells (EPCs) in the peripheral blood in response to myocardial ischemia has been advocated as a marker of tissue regeneration. Early EPCs have a limited proliferation capacity whereas late EPCs have a strong outgrowth. We aimed to show the magnitude and type of EPCs mobilization according to infarct size as assessed by peak troponin I (TnI) levels in patients with acute coronary syndrome (ACS including ST and non ST MI).
Methods: 85 patients < 75 years old, admitted with a first ACS within 12 hours of onset of symptoms were enrolled. Patients with previous cardiovascular or pul-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

monary diseases, history of renal or hematologic-coagulative disorders, acute-chronic inflammatory diseases, malignancies, or cardiogenic shock were excluded. Peripheral blood samples were drawn at day 0 and day 7. Peak TnI levels was determined from blood samples over the first 72 hours. At day 0 and 7, the type of endothelial colonies (early and late EPC) was determined and quantified. The endothelial origin of colonies-derived cells was confirmed using immunophenotypic analysis.
Results: At day 0, cloning efficiencies of early and late EPCs are shown in the figures A and B, respectively. There was a significant inverse relationship between the magnitude of circulating EPCs and the release of TnI. At day 7, a non significant 20% increase of the early EPCs-derived colonies (p=0.53) and a significant 75% decrease of the late EPCs-derived colonies (p<0.0001) were observed.



Conclusions: The mobilization of both early and late EPCs after ACS inversely correlated with infarct size. These results do not support the role of EPCs as an organism's regenerative capacity in ACS. There is a relationship between the number and the type of EPC and the injury subsequent to the ACS.

P1434 Three-, 6-, and 12-month results of autologous transplantation of mononuclear bone marrow cells in patients with acute myocardial infarction

J. Meluzin[1], S. Janousek[2], J. Mayer[1], L. Groch[2], I. Hornacek[2], O. Hlinomaz[2], R. Panovsky[2], M. Kaminek[3], P. Kala[1], M. Klabusay[1]. *[1]St. Anna Hospital, 1St Department of Internal Medicine, Brno, Czech Republic; [2]FH Brno, Dept. of Internal Med/Cardiology, Brno, Czech Republic; [3]UH Olomouc, Dept. of Nucelar Medicine, Olomouc, Czech Republic*

Purpose: There are only few data on long-term effectiveness of the stem cell therapy. We studied the course of changes in global and regional left ventricular (LV) function in patients with acute myocardial infarction (MI) within 1 year after the autologous mononuclear bone marrow cell transplantation.
Methods: Sixty patients with a first acute MI were randomized into 3 groups and completed a 12-month protocol. Two groups were intracoronarily given bone marrow cells in either higher (100,000,000 cells, HD group, n=20) or lower (10,000,000 cells, LD group, n=20) doses. Twenty patients without cell transplantation served as a control (C) group. Doppler tissue imaging and the gated technetium-99m sestamibi single photon emission computed tomography were performed before cell transplantation and at 3, 6, and 12 months later.
Results: The baseline peak systolic velocities of longitudinal contraction of the infarcted wall (Sinfarct) of 5.2 cm/s, 4.6 cm/s, and 4.4 cm/s in C, LD, and HD groups increased by 0.0 cm/s, 0.3 cm/s (p=NS vs C group), and by 0.7 cm/s (p<0.05 vs C group), respectively, at 3 months. At 12 months, however, the corresponding changes from baseline values of 0.1 cm/s, 0.2 cm/s, and 0.6 cm/s did not differ significantly (all p=NS). In contrast, the post-transplant improvement in global LV systolic function (mean 6-size S, LV ejection fraction) in HD group patients was preserved during the 12-month follow-up and remained significantly better as compared to controls.
Conclusion: In our study, the autologous mononuclear bone marrow cell transplantation provided sustained improvement in global LV systolic function in patients with acute MI. However, when evaluating regional systolic function of the infarcted wall, the short-term benefit was partially lost during the 12-month follow-up.

P1435 Increased circulating erythropoietin and CD34+ progenitor cells in patients with coronary artery disease. Role of anaemia

F. Marzo, S. Cecchetti, A. Lavorgna, G. Coluzzi, C. Rumi, A. Paglia, F. Andreotti, F. Crea. *Catholic University Medical School, Cardiology, Rome, Italy*

Purpose: A reduced circulating number of CD34+ progenitor cells and the presence of anaemia are emerging as strong predictors of cardiovascular events. Erythropoietin (Epo) acts not only on the red cell line, but also on progenitor cell proliferation and mobilization; it is also emerging as a cardiovascular protective factor. We investigated the relation between serum Epo, circulating CD34+, and haemoglobin concentrations [Hb] in patients with coronary artery disease and in controls.
Methods: A consecutive series of 52 patients admitted for unstable (n=39) or stable (n=13) disease and 19 age- and sex-matched controls were enrolled. Patients older than 80 yrs, with left ventricular ejection fraction <30%, active bleeding, iron deficiency, receiving recombinant human Epo, or on haemodialysis were excluded. All patients had angiographic documentation of significant disease (≥75% stenosis). CD34+ cells were measured by double monoclonal antibody flow cytometry. Epo was determined by enzyme-linked immunoassay. Anaemia was defined as [Hb]<14 g/dL in males and <12 g/dL in females; renal dysfunction was defined as glomerular filtration rate (GFR) <60 ml/min/1.73 m^2.
Results: [Hb] did not differ significantly between patients and controls (mean±SEM: 13.9±1.7 vs 14.4±1.3 g/dL, p=0.18). In contrast, circulating CD34+ cells (9.7±2.3 vs 2.6±0.4 cells/µL, p=0.003) and Epo concentrations (19.5±2.4 vs 4.0±0.9 mIU/ml, p<0.001) were markedly higher in patients vs controls, but did not differ significantly in acute vs stable patients (p=0.67 and p=0.11, respectively) or in those with (n=10) or without renal dysfunction (p=0.19 and p=0.3). Anaemia was detected in 22 patients. The number of CD34+ was strikingly higher in the non anaemic vs anaemic group (14.0±3.7 vs 4.0±0.8 cells/µL, p=0.04). Moreover, among patients, [Hb] were significantly associated with CD34+ (p=0.02, r=0.32), GFR (p=0.002, r=0.39) and, inversely, with Epo (p=0.03, r= -0.29).
Conclusions: In light of the expected cardiovascular protective effects of CD34+ and Epo, the increased levels of CD34+ and Epo inpatients with coronary artery disease vs controls suggest a compensatory response to ischaemia, rather than a causal role. Reduced CD34+, lower GFR, and higher Epo concentrations likely represent integrated markers of cardiovascular risk, given the relation with anaemia-in itself a powerful predictor of adverse outcome.

STEM CELL BIOLOGY AND DELIVERY METHODS

P1436 Transcriptional activity of bone marrow-derived very small embryonic-like cells undergoing cardiogenic differentiation

W. Wojakowski[1], M. Kucia[2], E. Zuba-Surma[2], J. Ratajczak[2], B. Machalinski[3], M.Z. Ratajczak[3], M. Tendera[2]. *[1]Silesian School of Medicine, 3Rd Division of Cardiology, Katowice, Poland; [2]University of Louisville, Stem Cell Biology Program, Louisville, United States of America; [3]Pomeranian Medical University, General Pathology, Szczecin, Poland*

Background: Adult bone marrow contains the population of very small embryonic-like cells (VSEL) which can be expanded in vitro, form embryoid bodies and express markers of pluripotent stem cells (Oct-4, Nanog, SSEA-1). These cells can differentiate into endo-, ecto- and mesoderm including neurons and cardiomyocytes. The gene-expression profile of VSELs on different stages of cardiogenic differentiation is unknown.
Methods: VSELs were isolated from bone marrow-derived mononuclear cells of C57BL mice. Lin-/Sca-1+/CD45- (non-hematopoietic) and Lin-/Sca-1+/CD45+ (hematopoietic) cells were isolated by multiparameter, live cell sorting (MoFlo, Dako). VSELs were examined by transmission electron microscopy. To generate embryoid bodies VSELs were co-cultured with murine rhabdomyosarcoma cell line C2C12 where ~5-10% of VSELs at day 5-7 form spheres (VSEL-DS) that are composed of several hundreds of primitive cells. To obtain single cell suspension VSEL-DS werel trypsinized. Cardiomyocytes differentiation: 5x10^2 GFP+ VSEL-DS cells plated in DMEM with 4 mM L-glutamine, 4.5 g/l glucose, 10% heat-inactivated FBS and 10ng/ml bFGF, 10ng/ml VEGF, 10ng/ml TGF. VSEL-DS-derived cardiomyocytes were stained with antibodies to Oct-4, SSEA-1, Nanog, Troponin I, α - sarcomeric actinin, Actn2, Actn3. Expression of embryonic and cardiomyogenic markers was assessed by real time RT-PCR. Transcriptional activity was assessed by microarrays (Miltenyi) comparing the gene expression in VSEL, VSEL-DS and at days 4, 6, 9, 12 and 16 of cardiogenic differentiation. Genes that are >1.7-fold up- or downregulated represent putative candidate genes. Discriminatory gene and pathway analysis were performed.
Results: VSEL were enriched in cardiac markers Nkx2.5/Csx and GATA-4 and during differentiation of VSEL-DS expressed mRNA for troponin I, Mybpc3, a-sarcomeric actinin 2 and 3 genes. Presence of cardiac markers was confirmed by fluorescent staining. Microarray analysis showed 257 genes with significant changes of expression. Up-regulated genes: connexins 31, 37, 40, 45, CD34, VEGF and suppression of genes coding cytokines and receptors (IL-1, 4, 6, VEGFR, TNF, CXCR4, HGF, SDF-1, c-met, c-kit, PDGF) and metaloproteinases.
Conclusions: Adult murine bone marrow contains expandable population of non-hematopoietic very small embrionic-like cells positive for markers of pluripotent stem cells which ungergo differentiation into cardiomyocytes expressing cardiac markers and connexins.

P1437 Bone morphogenetic protein-4 enhances cardiomyocyte differentiation of cynomolgus monkey ES cells in Knockout Serum Replacement medium

M. Hosseinkhani[1], H. Hosseinkhani[2]. *[1]Kyoto University, Cardiovascular Medicine, Kyoto, Japan; [2]International Center for Young scientists, National Institute for Materials Science, Tsukuba, Japan*

Despite extensive research in the differentiation of rodent embryonic stem (ES) cells into cardiomyocytes, there have been few studies of this process in primates.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

In this study we examined the role of bone morphogenic protein-4 (BMP-4) to induce cardiomyocyte differentiation of cynomolgus monkey ES cells. To study the role of BMP-4, embryonic bodies (EBs) were formed and cultured in Knockout Serum Replacement (KSR) medium containing BMP-4 for 8 days and subsequently seeded in gelatin-coated dishes for 20 days. It was found that ES cells differentiated into cardiomyocytes upon stimulation with BMP-4 in KSR medium, which resulted in a large fraction of beating EBs (~16%) and the up-regulation of cardiac-specific proteins in a dose and time-dependent manner. In contrast, the addition of BMP-4 in FBS containing medium resulted in a lower fraction of beating EBs (~6%). BMP-4 acted principally between mesendodermal and mesoderm progenitors and subsequently enhanced their expression. Ultrastructural observation revealed that beating EBs contained mature cardiomyocytes with sarcomeric structures. In addition, immunostaining, RT-PCR and western blotting for cardiac markers confirmed the increased differentiation of cardiomyocytes in these cultures. Moreover, electrophysiological studies demonstrated that the differentiated cardiomyocytes were electrically activated. These findings may be useful in developing effective culture conditions to differentiate cynomolgus monkey ES cells into cardiomyocytes for studying developmental biology and for regenerative medicine.

P1438(W) Amniotic fluid derived stem cells for regenerative therapy of chronic heart disease

S. Neshat Vahid[1], A. Milanesi[2], G. Christ[1], A. Atala[1], S. Soker[1] on behalf of Wake Forest Institute for Regenerative Medicine.
[1]Wake Forest Institutte For Regenerative Med, Winston- Salem, United States of America; [2]Winston-Salem, United States of America

Cell transplantation has been proposed as a promising treatment modality for regeneration of damaged heart muscle. Our approach is to use cell-based tissue engineering techniques to form ex vivo engineered heart muscle with a contractile capability. Because of their multipotential nature, amniotic fluid stem cells (AFS) are a good cell source for treating heart failure. The objectives of the study are to seed AFS cells onto type I collagen sponge scaffolds and induce cardiac differentiation. We will determine the effects of mechanical stimulation on the biomechanics and anatomy of the cardiac-like tissue.
We utilized 5-aza-2-deoxycytidine to induce cardiogenic differentiation. RT-PCR and immunostaining were used to analyze the cells for expression of myogenic and cardiogenic markers. Mouse AFS cell-derived cardiomyocytes were infected with VEGF-165 expressing adenovirus, seeded on collagen sponges and preconditioned in a bioreactor system with cyclic strain stimulation. Functional assessment of the engineered tissue was performed using "organ bath" system. In vitro biomechanical evaluation was performed to assess the linear stiffness, maximum force and maximum stress. To examine tissue formation of the constructs in vivo, the constructs were implanted in C57BL6 mice for 4 weeks. Lastly, we performed echo guided injection of differentiated mAFS cells in the left ventricular wall of hypertrophic mice. MRI analysis was carried 15 and 30 days after injection.
10 to 20 days after induction of differentiation, AFS cells stained positively for cardiomyocyte markers such as troponin I, troponin T, α-actinin. RT-PCR analysis revealed expression of cardiomyocyte markers including GATA-4 and MEF2C. AFS cell-derived cardiomyocytes preconditioned under uniaxial stretching showed muscle tissue organization and contraction in the organ chamber. Mechanically stimulated constructs had higher linear stiffness than nonstimulated-constructs. In addition, the mAFS cells could produce VEGF. The implanted constructs showed integration and extensive capillary network formation and 10 fold higher contactility in organ bath chamber. MRI analysis revealed cell survival in the left ventricular wall for 30 days.
The results demonstrate that multipotent stem cells derived from mouse amniotic fluid can differentiate into cardiac phenotype and form cardiac muscle like tissue. The cells can be genetically modified to express angiogenic growth factors that would enhance cardiac tissue perfusion and regeneration. Taken together, AFS cells represent a promising novel source of cells for regenerative therapies in cardiac diseases.

P1439 Subepicardium of the adult human heart hosts CD117 positive cells that undergo activation in the presence of laminin-1

D. Nurzynska[1], C. Castaldo[1], F. Di Meglio[1], P. Muller[2], L. De Santo[3], C. Bancone[1], C. Amarelli[1], S. Montagnani[2]. *[1]Universita' degli Studi "Federico II", Scienze Biomorfologiche e Funzionali, Naples, Italy; [2]Universitat des Saarlandes, Hamburg, Germany; [3]Monaldi Hospital, Naples, Italy*

The precise spatial and temporal expression of extracellular matrix proteins and their receptors, integrins, is critical for proper heart structure and cardiac cell function. We have analyzed and compared the distribution of CD117 positive cells in the human adult normal (n=6) and pathological hearts with chronic ischemic cardiomyopathy (n=10), in relation to the expression and localization of laminin and integrin isoforms. Examination of tissue sections by immunofluorescence revealed that the left atrium contained the highest number of CD117 (+) cells. Moreover, their number in the diseased hearts was significantly higher than in the normal hearts (about 10-fold higher in the mid section of the left ventricle and 6-fold higher in the apex). Within the same heart, CD117 (+) cells were up to 57-fold more numerous in the subepicardium than in the myocardium. The presence of laminin α1 chain, typical for developing myocardium, was observed in the subepicardium and interstitial spaces of the normal hearts and in the subepicardium and endomysium in the pathological hearts, where the branches of laminin-1 were also spread between the subepicardial space and the main myocardium, co-localizing with CD117 (+) α6 integrin (+) cells. While most of the cells in the subepicardium expressed also α6 integrin subunit, within the myocardium α6 integrin was detected on about 50% of CD117 (+) cells in the diseased hearts. In the normal hearts, the percentage of α6 integrin (+) cells was always much lower than in the pathological conditions and identical between the subepicardium and myocardium.
The expression of laminin α1β1 chains detected by immunoprecipitation and western blot in the extracts of atria was always higher in the normal hearts, while within the mid-section of the left ventricle it was higher in the pathological hearts. In vitro, laminin-1 coating of the culture dish stimulated migration and proliferation of the cardiac CD117 (+) cells and their migration was inhibited in the presence of the antibodies blocking α6 integrin function.
We conclude that chronic post-ischemic remodeling of the heart involves the mechanisms aiming at the regeneration of the myocardium and affecting all: cardiac CD117 (+) cells, extracellular matrix proteins and their receptors. Our observations support the hypothesis that the regeneration process follows the mechanisms operative in the early heart development, during which the epicardium-derived cells give rise to the cells of cardiac lineages and laminin-1 guides primitive cells in their migration from the subepicardial space into the myocardium.

P1440 Studies on the retention of cells delivered to the rat heart

B. Wentworth[1], J. Stewart[1], J. Westrich[1], C. He[1], A. Blaksvedt[2], G. Akita[1], M. O'callaghan[1], G. Molnar[1], M. Donovan[2], P. Yaeger[1]. *[1]MG Biotherapeutics, Cardiovascular Research, Framingham, United States of America; [2]MG Biotherapeutics, Cardiovascular Research, Minneapolis, United States of America*

The studies presented herein were designed to investigate the retention of syngeneic cultured cells (skeletal myoblasts, SM, and bone marrow stromal cells, BMSC) after transplantation into the normal beating Lewis rat heart. The acute retention of 4 million Europium (Eu) labeled SM was quantitatively analyzed after direct injection into LV cardiac muscle and the harvest of likely organs of dissemination. Approximately 80-85% of Eu labeled SM were lost from the heart within 1 minute of injection, a value that was stable for 1 hour. Analysis of distal organs indicated that SM were rapidly disseminated, presumably via the coronary venous circulation, principally to the lung, and then to a lesser extent to the liver by the systemic circulation. In separate studies we examined the longer-term survival of cells injected into the heart. SM or BMSC were labeled with BrdU, directly injected into cardiac muscle and the animals sacrificed 5 days and 3 weeks later. Transplanted cell quantity was estimated by direct counting in representative sections of cardiac tissue after histochemical identification of labeled nuclei. Five days after direct cell delivery there were an estimated 1.4% of the SM nuclei remaining in the injected hearts, and that quantum remained similar after 3 weeks. The identity of the injected SM was confirmed by immunohistochemical staining for fast skeletal myosin heavy chain expressed as a consequence of their differentiation into skeletal muscle fiber cells. There were 0.4% BMSC nuclei remaining in injected hearts 5 days post administration, and that number declined further to 0.1% after three weeks. These data suggest that the majority of either SM or BMSC injected were acutely lost from the heart and that SM ultimately survived and engrafted in the heart to a greater extent than BMSC.

P1441 Negative selection of apoptotic cells improves the efficiency of bone marrow mononuclear cell therapy in a rabbit model of myocardial infarction

G. Lemesle, F. Mouquet, S. Susen, D. Corseaux, A. Ung, M. Richardson, C. Charbonnel, R. Neviere, B. Jude, E. Van Belle.
Inserm Eri-9, CHU Lille, Cardiology, Lille, France

Purpose: Although associated with interesting preliminary results, the efficiency of cardiac cell therapy is limited by a high rate of early death of engrafted cells. We hypothesized that the presence of apoptotic cells could play a role in this issue. The aim of this study was to quantify the number of apoptotic cells among bone marrow mononuclear cells (BMMC) and to analyse their impact on left ventricular (LV) function and remodelling in a rabbit model of cell therapy for myocardial infarction (MI).
Methods: The rate of apoptotic cells among BMMC was measured by flow cytometry after labelling with Annexin V. Negative selection of apoptotic BMMC was performed using Annexin V labelled microbeads. MI was induced by 1 hour ischemia-reperfusion. Seven days later, injection of placebo (n=4), unselected BMMC (ApoHigh n=4) or low apoptotic BMMC (ApoLow n=4) was performed in the infarct area. Two months later, MI scar size was analysed by histology, while LV remodelling and LVEF were analyzed by echocardiography.
Results: The rate of apoptotic cells among BMMC was 33.85% ([27.31%-39.47%] =ApoHigh). After negative selection, this rate decreased by 50% (17.25% [12.45%-24.44%] =ApoLow, $p<0,001$). The impact of negative selection

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

of apoptotic BMMC is presented in the table below. Injection of ApoHigh BMMC decreased scar size by 17.9%, LV dilatation by 7.2% and increased LVEF by 5.8% as compared to placebo. Injection of ApoLow BMMC further decreased scar size by 20.3%, LV dilatation by 13% and further increased LVEF by 16% as compared to ApoHigh BMMC.

Impact of low apoptotic BMMC injection

Treatment group	Placebo	ApoHigh	ApoLow
Scar size (%)	31.2	25.6	20.4 *
LV End Diastolic Diameter (mm)	19.4	18	15.6 §
LVEF (%)	32.7	34.6	41.4 §

* p= 0.057; § p= 0.034 vs placebo.

Conclusion: Rabbit BMMC contain about one third of apoptotic cells. Negative selection of apoptotic cells significantly improves BMMC therapy efficiency. It remains to be seen whether similar results are observed in humans.

P1442 Mobilization of bone marrow-derived stem cells with parathyroid hormone does not deplete bone marrow compared to G-CSF

S. Brunner, E. Deindl, M.M. Zaruba, B. Huber, W.M. Franz. *LMU Munich, Klinikum Grosshadern, Medical Department I - Cardiology, Munich, Germany*

Objective: Cytokine-mediated mobilization of hematopoietic stem cells has become an established method in the field of autologous and allogenic stem cell transplantation from peripheral blood. Furthermore, it presents a new concept in tissue repair and regenerative medicine. We aimed to define the potency of parathyroid hormone (PTH) for stem cell mobilization.
Methods: Healthy wildtype mice were treated with parathyroid hormone (80 μg per kg body weight) for either 6 or 14 days and were compared with granulocyte-colony stimulating factor (G-CSF) and saline treated mice. Hematological parameters were analyzed using a conventional hematological cell analyzer. Subpopulations of CD45+/CD34+ and CD45+/CD34- cells were measured by flow cytometry. Immunohistology was utilized to determine the composition of bone marrow. Serum levels of a distinct cytokine pattern (G-CSF, VEGF, SDF-1) as possible effectors of PTH were determined by ELISA.
Results: Our results showed a significant increase of all characterized subpopulations (CD31+, c-kit+, Sca-1+) of bone marrow derived cells in the peripheral blood after stimulation with PTH (1.5- to 9.8-fold) in a similar manner like G-CSF. In bone marrow the CD45+/CD34+ subpopulations remained constant and resulted in enhanced cell proliferation (1.9-fold), whereas G-CSF treatment showed a depletion of all determined cell populations. Serum levels of G-CSF showed significantly increased values (2.8-fold) after PTH treatment, whereas SDF-1 was downregulated and VEGF remained unchanged both in PTH and G-CSF treated mice.
Conclusion: PTH induces effectively mobilization of bone marrow-derived stem cells and is associated with a change in a serum cytokine pattern. Compared with G-CSF, PTH does not deplete bone marrow. This described new function of parathyroid hormone might be considered as a therapeutic option in the field of bone marrow and stem cell transplantation as well as in ischemic diseases, in which mobilization of bone marrow derived cells by other cytokines could demonstrate positive effects.

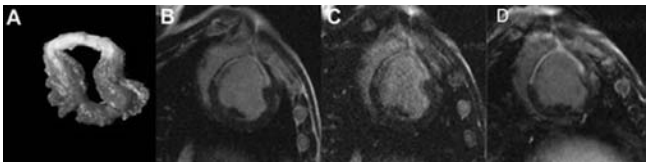
MYOCARDIAL INFARCTION: QUANTIFICATION AND RISK STRATIFICATION BY CARDIOVASCULAR MAGNETIC RESONANCE

P1443 Quantification of infarct size with novel MRI delayed enhancement sequences. Histopathological validation

S. Prat Gonzalez[1], B. Ibanez[1], W. Speidl[1], G. Vilahur[2], G. Cimmino[2], G. Falaschi[2], V. Fuster[2], M.J. Garcia[2], J. Badimon[2], J. Sanz[2]. *[1]Mount Sinai Medical School, Cardiovascular Institute, New York, United States of America; [2]Cardiovascular Research Center, CSIC-ICCC, Cardiovascular Research Center, Barcelona, Spain*

Purpose: To compare two novel MRI sequences for delayed enhancement (DE) imaging for myocardial infarction (MI) with standard, inversion-recovery fast gradient echo (IR-FGRE). In addition, validation with histopathology was performed.
Methods: MI was induced by balloon occlusion of the mid-LAD in 15 pigs. DE imaging was started 10 minutes after 0.2 mmol/kg of Gd-DTPA using: 1) Multislice, IR-FGRE, in multiple breathholds, 2) Multislice, single-shot, 2D IR steady state free precession (SS-SSFP), in one breathhold; and 3) 3D IR-SSFP, in one breathhold. DE was defined as those areas with signal intensity >3 SD above the mean signal of normal myocardium, and quantified as percentage of the left ventricle. Histological staining was performed in 8 pigs.
Results: There were no significant differences in MI size among the sequences (Table). In comparion with histology, all sequences showed excellent correlation and agreement for MI size quantification (Table and Figure: A- histology, B- IR-FGRE, C- SS-SSFP, D- 3D IR-SSFP).

	IR-FGRE	SS-SSFP	3D IR-SSFP	p
MI size (% LV; n=15)	17.5±7.7	15.6±6.9	17.2±7.5	0.74
Correlation (histology; n=8)	0.90	0.93	0.91	<0.01 (all)
Bland-Altman (%LV, histology; n=8)	1.4 (9/-6.4)	1.6 (7.7/-4.5)	2.1 (9/-4.8)	



Conclusions: This study provides a validation of MI size quantification with novel, faster DE sequences in comparison with standard imaging and histology. This can be particularly useful in patients that require short examination times.

P1444 Risk stratification after reperfused acute myocardial infarction using contrast-enhanced cardiovascular magnetic resonance: comparison of first-pass and delayed enhancement imaging

M. Regenfus[1], C. Stingl[1], C. Schlundt[1], J. Von Erffa[1], M. Schmidt[2], W. Adler[1], W.G. Daniel[1]. *[1]FAU Erlangen-Nuernberg, Medical Clinic II, Erlangen, Germany; [2]Siemens Medical Solutions, Medical Clinic II, Erlangen, Germany*

The established parameter for risk stratification after reperfused acute myocardial infarction (MI) is left ventricular (LV) ejection fraction (EF). With the use of contrast-enhanced cardiovascular magnetic resonance (CMR) further parameters for characterization of MI can be determined. We investigated which of the CMR perfusion techniques, first-pass perfusion (FP) or delayed enhancement (DE) would show the best relation to the occurence of major adverse cardiac events (MACE).
Methods: 148 patients (pts) with left ventricular (LV) dysfunction (EF 39±8%) were examined on a 1.5T scanner within 3±2 (2-6) days of an reperfused acute MI. Cine, FP perfusion and DE CMR was acquired. LV EF, infarct size (IS) (from DE imaging) and the extent of microvascular obstruction (MO) (from FP imaging) were quantified. Serial clinical follow-up was obtained in all patients (mean follow-up 4.3±1.8 years) regarding occurrence of MACE. Patient-related and CMR data were analyzed by Cox proportional hazard regression.
Results: Among the 148 patients, there were 34 cardiac deaths and reinfarctions in the follow-up period, additionally there were 32 patients with further myocardial revascularization or hospitalization due to unstable angina or congestive heart failure. Patients with events at follow-up showed significantly lower EF (32±10% vs. 46±10%, $p < 0.001$), larger extent of IS (21±11% vs. 13±13%, $p = 0.008$), and larger extent of MO (10±9% vs. 2±8%, $p < 0.001$) than patients without events. By univariate analysis, EF, extent of MO, and, infarct size by CMR were related to occurence of MACE (table 1). By multivariable analysis, extent of MO remained the strongest predictor after adjustement for LV EF.

	Hazard ratio	Lower limit 95% CI	Upper limit 95% CI	p
EF	3.2	1.5	5.0	< 0.0001
Extent of MO	3.7	1.6	5.1	< 0.0001
Infarct size	1.9	0.9	3.3	0.03

Conclusions: In patients after reperfused acute MI, contrast-enhanced CMR can be used to predict major adverse cardiac events. Next to the established parameter for risk stratification - ejection fraction -, the extent of MO determined from FP imaging prooved highly predictive.

P1445 Quantification of salvaged myocardium early post-MI by cardiac magnetic resonance

B. Ibanez[1], S. Prat-Gonzalez[1], W.S. Speidl[1], G. Vilahur[2], G. Cimmino[2], A. Pinero[2], V. Fuster[2], M.J. Garcia[3], J. Sanz[3], J.J. Badimon[2]. *[1]Mount Sinai School of Medicine, Cardiovascular Institute, New York, United States of America; [2]CSIC-ICCC, Cardiovascular Research Center, Barcelona, Spain; [3]Mount Sinai Chool of Medicine, Cariovascular Institute, New York, United States of America*

Tools assessing the cardioprotective effect of interventions in acute myocardial infarction (MI) are strongly needed. Current endpoints for this purpose include MI size, regional and global functional parameters. However all these are dependent on the coronary anatomy and location of coronary occlusion, not focusing on salvaged myocardium (variable actually evidencing cardioprotection)
Cardiac magnetic resonance (CMR) can visualize area at risk (T2W hyperenhanced areas early post-MI) being conceivable to quantify the extent of salvaged myocardium (area at risk-MI size)
Aim: Using a known cardioprotective agent, we sought to assess the effectiveness of CMR as a tool to quantify salvaged myocardium
Methods: Yorkshire pigs (12) underwent a 90min LAD coronary occlusion followed by reperfusion. They were randomized to metoprolol (7.5mg before reperfusion) or placebo. MI size (positive delayed enhancement 15min after Gadolin-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

ium), area at risk (hyperintense areas on T2W) and salvaged myocardium (area at risk-MI area) were assessed 4 and 22 days post-MI
Results: Despite similar area at risk in both arms (30.6% of LV vs 30.9%), MI size was 27% larger in placebo (28.7% vs. 20.9%, p=0.02).
Salvage myocardium was 5 fold larger in metoprolol (4% vs. 21%, p=0.03).
At 22 days, ejection fraction (EF) increased 15% in metoprolol (p=0.04 vs. day 4), while remained unchanged in placebo
The extent of salvaged myocardium as visualized by CMR at day 4 was a strong predictor of EF improvement (p=0.03)

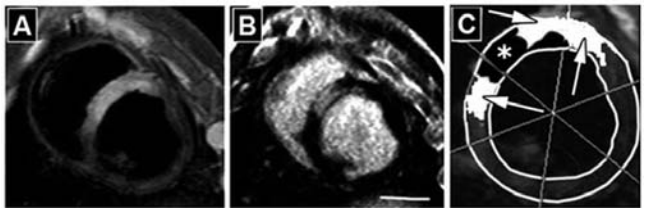


Figure 1. Raw (A-B) and composite (C) CMR images. A: area at risk (T2W); B: MI size (post-Gadolinium); C: composite of A&B (arrows point to salvaged myocardium; *represent the MI size)

Conclusions: Salvaged myocardium can be precisely quantified early post-MI by CMR, and may represent the best endpoint in trials assessing the efficacy of cardioprotective interventions.

P1446 Effect of GPIIbIIIa inhibitors on microvascular function after successfully reperfused myocardial infarction. Myocardial first pass perfusion studied by cardiovascular magnetic resonance

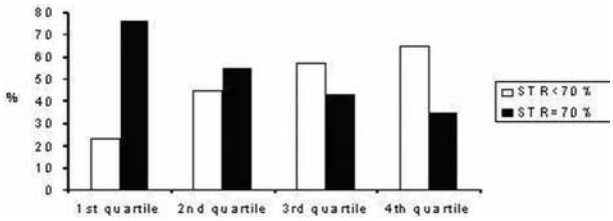
A. Rolf[1], S. Moellmann[1], G. Conradi[1], J. Rixe[1], A. Deetjen[2], C. Hamm[2], T. Dill[2]. *[1]Kerckhoff-Heart-Center, Department of Cardiology - Cardiac Imaging, Bad Nauheim, Germany; [2]Katharinen Hospital, Department of Cardiology - Cardiac Imaging, Stuttgart, Germany*

Purpose: Several recently published studies demonstrated impaired microvascular function despite patency of the infarct related artery and TIMI III flow. Microvascular dysfunction is associated with poorer clinical outcome, decreased left ventricular ejection fractions and adverse left ventricular remodelling. One of the underlying mechanisms compromising microvasculature is caused by microemboli showering downstream during PCI. We therefore examined the effect of periinterventional infusion of GPIIbIIIa inhibitors on prevention of microvascular dysfunction.
Methods: We retrospectively analysed 49 patients, who were referred for cardiac MRI between 4 and 11 days after successfull PCI of the infarct related artery. Adenosine stress- and restperfusion were performed using turboFLASH GRE sequences in three short axis slices. Myocardial Perfusion Reserve Indices (MPRI) were calculated using signal intensity upslope parameters normalized for the ventricular input function. MPRIs of the patient groups were compared in a segment by segement analysis according to the AHA 17 segment modell (omitting segment 17). Statistical testing was based on ANOVA, post hoc analysis was performed using Scheffé's test.
Results: A total of 714 segments was available for statistical testing, some basal segments had to be excluded because there was overlap with the left ventricular outflow tract during stress perfusion. 141 MPRIs/segments were calculated for patients not receiving GPIIbIIIa inhibitors, 405 MPRIs/segments were calculated for patients receiving high dose tirofiban, 168 MPRIs/segments for patients, treated with abciximab. Mean MPRI was 0.86±0.7 for patients without treatment, 1.23±2.1 for abciximab treated patients and 1.64 ±4.6 for tirofiban treated patients respectively ($p < 0.047$). Post hoc analysis showed a significant benefit only for tirofiban treated patients (Δ 0.78, $p < 0.05$).
Conclusion: Mean MPRIs were still reduced in all groups upto 11 days after successfull reperfusion, which confirms results of other studies. MPRIs of patients, who did not receive therapy are on the level of MPRIs reported for stenosed vessels.
Infusion of Tirofiban on the other hand significantly improved microvscular function, yielding MPRIs close to normal values.

P1447 Association between ST-segment elevation resolution and myocardial damage assessed by cardiac magnetic resonance imaging, in patients undergoing successful primary angioplasty

A. Cochet[1], M. Zeller[2], A. Lalande[2], P.M. Walker[2], C. Touzery[2], J.E. Wolf[3], F. Brunotte[3], Y. Cottin[1]. *[1]Unite d IRM CHU, Hopital d enfants, Dijon, France; [2]LPPCE IFR sante STIC, RICO, Dijon, France; [3]Cardiology department, CHU, Dijon, France*

Background: ST-segment elevation resolution (STR) after acute reperfusion for ST-segment elevation myocardial infarction (STEMI) has a major prognostic impact, and is thought to be linked to microvascular perfusion. We investigated the association between STR and myocardial perfusion, as assessed by Cardiac Magnetic Resonance (CMR) imaging in patients after primary percutaneous intervention (PCI).
Methods: STR from the maximal ST-elevation measured on the single worst ECG lead 60 minutes after successful (TIMI 3) primary PCI was measured in 82 consecutive STEMI patients. CMR was performed within 7 days after PCI, after injection of gadolinium-DTPA. First-pass images (FP) were visually analyzed, and the extent of transmural damage was determined by a visual score (FP score), providing an assessment of microvascular perfusion. Patients were classified according to FP score quartiles.
Results: Baseline risk factors, clinical and biological data and either current or acute treatments were similar across the FP score quartiles. Peak CK markedly increased with FP score (p=0.002). LVEF showed a trend toward a decrease with increasing FP scores quartiles. STR significantly increased with increasing FP score quartiles (100(75-100, 74(58-100, 58(33-88), and 58(36-72) %, p=0.009). Moreover, STR correlated negatively with the FP score (r=-0.34, p=0.002). Strikingly, more than one third of patients with severe microvascular obstruction on CMR (higher FP score quartile) had complete STR (≥70%) on the ECG (Figure).



FP score quartiles

Conclusion: Our study confirmed the relationship between STR and microvascular damage in STEMI patients after successful primary PCI. Moreover, we showed that CMR is a more efficient tool when compared to ECG analysis to assess myocardial damage.

P1448 Acute edema in the evaluation of microvascular reperfusion and myocardial salvage in reperfused myocardial infarction with cardiac magnetic resonance imaging

A. Phrommintikul[1], H. Abdel-Aty[2], J. Schulz-Menger[2], M.G. Friedrich[2], A.J. Taylor[1]. *[1]Baker Heart Research Institute, Melbourne, Australia; [2]Franz-Volhard-Klinik, Helios-Klinikum Berlin, Berlin, Germany*

Background: In acute myocardial infarction, acute oedema within the area at risk has been postulated to impair microvascular reperfusion, limiting myocardial salvage. We evaluated acute oedema by cardiac magnetic resonance imaging (CMR) to examine its relationship with microvascular reperfusion and myocardial salvage.
Methods: We performed CMR on 15 patients with acute myocardial infarction (AMI), within 24 hours of successful percutaneous coronary intervention (PCI). CMR identified the area at risk by myocardial oedema and myocardial necrosis using delayed contrast enhancement. Left ventricular (LV) systolic dysfunction was defined by a systolic thickening < 40% (severe< 20%). Microvascular reperfusion was evaluated during acute contrast wash-in. CMR 3 months post-PCI evaluated recovery of LV function and final infarct size. Myocardial salvage was defined as the percentage of the area at risk that was not infarcted on follow up CMR.
Results: There was a significant correlation between impaired microvascular reperfusion and the extent of segmental oedema ($R=0.363$, $P < 0.01$), but not myocardial necrosis ($R = 0.110$, $P > 0.5$) There was also a significant correlation between the extent of myocardial salvage and recovery of systolic function when acute oedema was used to define the area at risk ($R = 0.241$, $P < 0.05$), which was strongest in LV segments with severely reduced systolic function ($R = 0.422$, $P < 0.01$).
Conclusions: In acutely reperfused AMI, acute oedema can be used to identify the area at risk for the purpose of calculating myocardial salvage. The correlation between myocardial oedema and reperfusion status suggests a pathological role of acute oedema in the impairment of microvascular reperfusion.

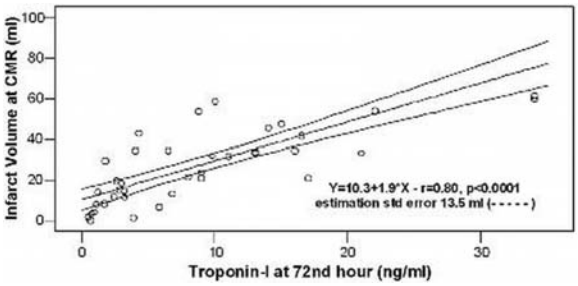
P1449 Cardiac troponin-I assessed at 72 Hours from symptoms onset estimates predischarge infarct size measured by cardiac magnetic resonance

A. Di Chiara, E. Dall' Armellina, F. Meduri, N. Pezzuto, V. Bonasia, P.M. Fioretti. *Az. Ospedaliero-Universitaria, Cardiopulmonary Sciences, Udine, Italy*

Background: Infarct size has prognostic impact in patients (pts) with acute myocardial infarction (AMI). The relationship between Troponin I (TnI) during AMI and infarct size assessed by cardiac magnetic resonance (CMR) is unknown.
Methods: We studied 39 pts (30 males, age 61±11yrs) with a first acute MI (STEMI =34, NSTEMI=5). Mean pre-hospital delay was 4,8±9,3 hrs. In 32 STEMI,

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

23 primary PCI, 5 rescue PCI, 4 thrombolysis were performed. TnI (Beckman Coulter Access) was assessed at admission, 6, 12, 24, 48, 72, 96 hours (±1hr). Time were aligned according to symptoms onset. TnI peak value, TnI area under the curve (AUC) up to 72 hrs were computed. CMR (Siemens Sonata 1,5 T) was performed before discharge in all pts. Infarct size was determined by manual tracing of areas of delayed enhancement in short axes images. Infarct volume was calculated as the sum of each slice infarct area multiplied slice thickness.
Results: Mean peak TnI value was 50±49 ng/ml, TnI AUC 1858±1671 ng/ml. The volume of MI was 28,5±22,1 ml (range 0-109). Univariate linear coefficients (R 2) among TnI values at 24, 48, 72, 96 hours, peak TnI, TnI AUC and predischarge infarct volume were respectively 0.362, 0.527, 0.634, 0.569, 0.426, 0.566 ($p<.0001$). At multivariate regression analysis TnI 72h resulted the strongest predictor of predischarge infarct volume (figure).



Conclusion: Troponin I value assessed at 72 hours from symptom onset is a strong independent predictor of predischarge infarct volume assessed by delayed enhancement CMR.

P1450 Rapid determination of relative infarct size in humans using contrast-enhanced magnetic resonance imaging: validation against FDG-positron emission tomography

M. Neizel[1], W.M. Schaefer[2], E. Schade[1], A. Krombach[3], T. Rassaf[1], R.W. Guenther[3], M. Kelm[1], H.P. Kuehl[1]. [1]*Department of Cardiology, Internal Medicine, University Hospital Aachen, Germany;* [2]*Department of Nuclear Medicine, Nuclear Medicine, University Hospital Aachen, Germany;* [3]*Department of Radiology, Radiology, University Hospital Aachen, Germany*

Background: Determination of the extent of left ventricular (LV) scarring using 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging conveys important prognostic information in patients with ischemic cardiomyopathy (ICM). The method, however, is time-consuming, costly and associated with radiation exposure. Contrast-enhanced cardiovascular magnetic resonance (ce-CMR) imaging may be an attractive alternative. The aim of the study was 1) to validate ce-CMR with FDG-PET for the assessment of relative infarct size (rIS) in patients with ICM and 2) to quantify rIS with ce-CMR using semi-automatic quantitation techniques.
Methods: 46 patients (66±9 years) with ICM (mean ejection fraction 24±8%) and clinical indication for viability testing were investigated with both imaging modalities. For ce-CMR an inversion-recovery sequence was used 15 minutes after i.v. administration of 0.2 mmol/kg gadolinium (TR 2 RR intervals, TE 5,2 ms, FA 25°, TI 250 to 300 ms; Intera, Philips). Each cross-section was divided into 100 cords. Relative infarct size was calculated from the number of cords with ≥50% transmural late enhancement in relation to the total number of cords. In each patient relative IS was also assessed by using semi-automatic thresholding based on 1) visual definition of a signal-intensity cutoff value and 2) the full-width-at-half-maximum technique (FWHM). FDG administration (350 MBq) was performed 2 hours after administration of 200 mg acipimox. PET images (ECAT-EXACT, Siemens) were quantified fully automatically (4D-MSPECT) and displayed in polar plots. Myocardial infarction was defined as area of FDG uptake ≤50%.
Results: Relative infarct size measured 16±11% with ce-CMR and 18±12% with FDG-PET showing a strong correlation between the two imaging modalities (r=0.93). A slightly larger mean rIS was observed with FDG-PET relative to ce-CMR (2%; $p<0.005$). Comparing semi-automatic techniques, visual thresholding showed better agreement with FDG-PET determining rIS (r=0.80; limits of agreement ±14%,) compared to the FWHM technique (r=0.65, limits of agreement ±17%).
Conclusions: Ce-CMR and FDG-PET closely agree in the assessment of rIS and may be used interchangeably. When using semi-automatic thresholding techniques visual estimation of signal intensity cutoff values allows rapid and accurate determination of rIS and is superior to the FWHM technique. The slightly larger mean rIS with FDG-PET may partly be explained with underestimation of FDG-uptake in segments with thin myocardial wall demonstrating no transmural late enhancement.

P1451 Right ventricular envolvment in inferior ST-elevation myocardial infarction: assessment using contrast-enhanced cardiovascular magnetic resonance as compared to electrocardiogram and echocardiography

M. Regenfus[1], M. Schmid[1], A. Hagel[1], C. Schlundt[1], M. Schmidt[2], J. Ludwig[1], W. Bautz[1], W.G. Daniel[1], A. Schmid[1]. [1]*FAU Erlangen-Nuernberg, Internal Medicine, Erlangen, Germany;* [2]*Siemens Medical Solutions, Erlangen, Germany*

Right ventricular infarction (RVI) occurs according to pathological specimen nearly in about one-half of patients with inferior myocardial infarction (MI) and, however, is underdiagnosed by established diagnostic techniques. Delayed contrast-enhanced cardiovascular magnetic resonance (DE-CMR) is a highly sensitive tool for detection of myocardial necrosis. We investigated the role of DE-CMR for the diagnosis of RVI as compared to the right precordial electrocardiogram (ECG) and echocardiography.
Methods: 24 patients (pts) with acute inferior MI were enrolled. They underwent an ECG including the right precordial leads and echocardiography. After catheter-based acute reperfusion therapy, contrast-enhanced CMR was performed for assessing presence and extent of right ventricular delayed enhancement (DE). ECG was rated positive for RVI with ST-segment elevation in the V_4 r right precordial lead, echocardiography with wall motion abnormalities or right ventricular dilation. Agreement between DE-CMR and the other diagnostic methods was determined using Kappa statistics.
Results: DE-CMR detected RVI in 13/24 (54%) pts with an average extent of 8.5±12.4% of right ventricular mass. V_4 r ECG was positive for RVI in 9/24 (38%) pts, and echocardiography in 5/24 (21%) pts. DE-CMR results for presence of RVI exhibited only moderate agreement with results for RVI on V_4 r ECG (kappa 0.43), and echocardiography (kappa 0.35).
Conclusions: DE-CMR detects right ventricular envolment in acute inferior MI more frequently than established diagnostic techniques. Hereby, agreement between DE-CMR and right precordial ECG and echocardiography is only moderate.

P1452 Contrast-enhanced MRI in acute myocardial infarction: predictive value of infarct size and microvascular obstruction for LV wall motion recovery

M. Sirol, P. Malzy, F. Beauvais, P. Henry, G. Sideris, D. Logeart, A. Leenhardt, R. Rymer, A. Cohen-Solal. *Hopital Lariboisiere, Cardiologie Dept., Paris, France*

Background: Cardiovascular magnetic resonance (CMR) has been recently recognized as one of the major imaging technique for the evaluation of left ventricular function, myocardial perfusion, infarct size and myocardial viability. It may also be an optimal imaging modality to predict left ventricular wall motion recovery (LVR) after acute myocardial infarction.The relative contribution of microvascular obstruction (MO) in addition to infarct transmurality is unknown. Therefore, the aim of our study was to study the ability of CMR to predict LVR in patients presenting with first acute ST elevation myocardial infarction (AMI).
Methods: Twenty eight patients (mean age 56±8 years, 76% males) presenting with first episode of AMI and treated by primary PCI were studied. CMR was performed within the first week of ST elevation AMI and repeated at a mean time of 6±1.4 months later. Steady state free precession cines, first pass perfusion (FP), delayed hyper-enhancement (DHE) images were obtained on a 1.5-T MR system (Avanto, Siemens). Segmental LV function was assessed using a semi-quantitative scale and AHA 17-segment model as follow: 0 = normal; 1 = mild hypokinesis; 2 = severe hypokinesis; 3 = akinesis; 4 = dyskinesis. Similarly, infarct transmural extent was separately assessed using a 5-grade scale as follow: 0 = no transmural DHE; 1= 1-25% transmural DHE; 2 =26-50% transmural DHE; 3 = 51-75% transmural DHE; 4= 76-100% transmural DHE. Two blinded observers analyzed data from both CMR examination at baseline (initial scan) and at follow up for ventricular volumes, ejection fraction (EF), LV mass, and FP perfusion defects. MO was defined as presence of areas of hypo-enhancement in delayed contrast-enhanced images.
Results: A total of 476 segments were evaluated of which 204 (43%) demonstrated areas of delayed hyper-enhancement (DHE). Only 49 segments with DHE presented MO (24%). Among segments with DHE, 133 (65%) demonstrated improved regional LV function, while 47 (35%) demonstrated the same or worsening of LV function at follow up. When evaluating segments with MO, the presence of MO was associated with a reduced likelihood of LVR in particular in segments with 50% to 100% transmural DHE. There was a good correlation between the area of perfusion defect on FP perfusion imaging and the area of MO as defined by DHE images ($r = 0.68$; $p < 0.0001$).
Conclusion: CMR demonstrated the ability of predicting LV wall motion recovery within the first week of ST elevation MI. Infarct size as well as MO are a good predictors of regional LV function recovery.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1453 Prediction of myocardial recovery by dobutamine magnetic resonance imaging and delayed enhancement early after reperfused acute myocardial infarction

A. Barmeyer, A. Stork, K. Muellerleile, M. Bansmann, M. Bavastro, M. Heuer, G. Adam, T. Meinertz, G. Lund. *Hamburg, Germany*

Purpose: To study the value of early dobutamine magnetic resonance imaging (DOB) and delayed myocardial contrast enhancement (DE) to predict segmental myocardial recovery in patients with reperfused acute myocardial infarction (AMI) and to find an optimal dose of dobutamine in these patients.
Methods: Consecutive patients with coronary reperfusion after AMI underwent DOB and measurement of DE (Baseline). In DOB segmental systolic wall thickening (SWT) was measured on three short axis slices at rest and during dobutamine at 5, 10 and 20$\mu g*kg^{-1}*min^{-1}$. All slices were divided into 6 equiangular segments and dysfunctional segments were identified by SWT $<$ 50% of normal reference segments. For each segment the extent of DE was measured 10 minutes after 0.1mmol/kg of Gd-DTPA. Segmental SWT was reexamined at rest after a median of 7.4 months (follow-up) and compared to baseline. Thereafter, sensitivity, specificity and accuracy of DOB and DE at optimal cut-off values to predict segmental recovery were calculated.
Results: Fifty patients were evaluated (age 56±12years, 42 males). A total of 248 segments were dysfunctional at baseline with presence of DE in 193 segments. DOB showed best diagnostic performance at $10\mu g*kg^{-1}*min^{-1}$ of dobutamine (Sens.67%, Spec.63%, Acc.66%) and a cut-off value for SWT of 2.0mm. DE showed similar diagnostic performance (Sens.68%, Spec.65%, Acc.67%) at a cut-off value of 45.7%. Combined analysis of DOB10 and DE revealed no improvement of diagnostic performance (Sens.63%, Spec.71%, Acc.66%).

Diagnostic performance of DOB and DE

	AUC	95%CI	Sensitivity	Specificity	Accuracy	Cut-off
DOB 5	0.632	0.56-0.71	63	60	62	1.8
DOB10	0.68	0.61-0.75	67	63	66	2.0
DOB20	0.68	0.61-0.75	67	61	65	2.4
DE	0.73	0.67-0.8	68	65	67	45.7
DOB10+DE			63	71	66	2.0/45.7

AUC: area under the curve, CI: confidence interval. Sensitivity, specificity and accuracy are given in %. Cut-off values are given in mm for DOB5-20 and in % of the segmental area for DE.

Conclusion: Early prediction of segmental myocardial recovery after reperfused AMI is possible with DOB and DE. A dose of dobutamine higher than $10\mu g*kg^{-1}*min^{-1}$ or combined analysis of DOB and DE does not improve diagnostic performance.

P1454 Microvascular obstruction detected by cardiovascular magnetic resonance in stress condition (CMR) in patients with first anterior acute myocardial infarction (AMI)

D. Piotrowska, L. Kownacki, O. Rowinski, M. Golebiowski, G. Opolski, L. Krolicki. *Medical University, of Nuclear Medicine and of Cardiology, Warsaw, Poland*

Background: Despite its prognostic importance, accurate assessment of microvascular reperfusion after pPCI in AMI is difficult.
Purpose: Assessment of impaired microvascular reperfusion after successful pPCI (TIMI3) of infarct related artery with CMR.
Methods and Materials: 44 patients with first anterior AMI who underwent successful pPCI were included into the study. CMR was performed on 1.5 T scanner between 3 and 10 days after pPCI. Myocardial perfusion was assessed at rest and in stress condition during infusion of adenosine (140μg/kg b.w./min.) by first-pass perfusion imaging. Microvascular obstruction ("no-reflow" region) was defined as hypoenhancement seen 1 to 2 minutes after contrast injection on T1 weighted contrast-enhanced images acquired with the use of an inversion-recovery segmented gradient-echo sequence.
Results: Microvascular obstruction was found in 32/44 studied subjects. The mean mass of "no reflow" region was 11,4g (range 0g to 64g) and correlated with infarct size (r=0.713, p=0.0001) and ESV (r=0.457, p=0.002) and reversely with ejection fraction (r= -0,362, p=0,016). The patients with "no-reflow" mass over 5 g (24/44 subject) had significantly lower EF (34% vs 44%, p=0,001), increased EDV (164ml vs 140 ml, p=0,007), ESV (108ml vs 79ml p=0,001), and infarct size (62g vs 37g). Till now 22 patients underwent successfully second CMR scan at 8 months. Infarct size decreased form 65 to 43g in patients with "no-reflow" mass over 5 g at baseline CMR (11 cases) compared to 3 g reduction (from 36g to 33 g) in patient with "no-reflow" mass $<$ 5g.
Conclusion: The prevalence of no-reflow phenomenon revealed on MRI images is frequent in AMI patients early after successful PCI and is associated with severe decreased left ventricle function early after AMI. Infarct size reduction in patients with severe "no-reflow" may be due to wall thinning at follow up.

COMPUTED TOMOGRAPHY

P1455 Feasibility of contrast enhanced computed tomography of the coronary arteries using Dual-source MDCT without heart rate lowering premedication

J. Rixe, A. Rolf, G. Conradi, C.W. Hamm, T. Dill. *Kerckhoff Heart Center, Cardiology Dept., Bad Nauheim, Germany*

Background: Multi-detector computed tomography (MDCT) permits visualization of coronary arteries, but due to a temporal resolution of 165 ms, its utilization has been limited to patients with a heart rate below 60/min. We investigated the feasibility of coronary artery visualization in a large cohort of patients without precedent heart rate control using Dual-source computed tomography (DSCT).
Methods: DSCT (330 ms tube rotation, 83 ms temporal resolution, 64 x 0.6 mm collimation) was performed in 165 unselected patients (mean age 64±11.4 y). For data acquisition, 60 - 80 ml of iodine contrast agent were injected at 5 ml/s, image reconstructions were rendered in 5%- intervals of the RR- cycle with 0.6 mm slice thickness and 0.3 mm increment.
Data sets were evaluated by two expert readers in consensus as to the visibility and evaluability of the coronary arteries as well as to the presence of motion artefacts.
Results: Of 2541 coronary segments included, visualization without artifacts was possible in 2509 cases (98.7%); mean heart rate was 65± 10.5/min.
Only two segments were considered unevaluable because of motion artefacts.
Data reconstruction at 65 or 70% of the RR- cycle provided for best image quality (39 and 51% of all patients). Data sets with best image quality at 65% were gained from patients with a significantly lower heart rate (57.5±4.5/min vs. 65.0±5.7/min, $p < 0.05$) compared with data sets preferably rendered at 70% of the cardiac cycle.
For heart rates $>$ 85/min, a systolic reconstruction at 45% also provided for satisfactory results.
Conclusion: In comparison to earlier MDCT- scanner generations, DSCT provides for non-invasive coronary angiography without motion artefacts at a wide range of heart rates and thus might become, in experienced hands, a valuable tool in first line diagnosis of coronary artery disease.

P1456 Diagnostic accuracy of 64-slice Multi-Slice Computed Tomography coronary angiography to assess in-stent restenosis in 182 patients

J.D. Schuijf[1], F. Cademartiri[2], F. Pugliese[1], J.W. Jukema[2], D. Ardissino[3], P.W. Serruys[2], G.P. Krestin[2], E.E. Van Der Wall[3], P.J. De Feyter[2], J.J. Bax[3]. *[1]Leiden University Medical Center, Cardiology, C5-P, Leiden, Netherlands; [2]Erasmus Medical Center, Radiology and Cardiology, Rotterdam, Netherlands; [3]Azienda Ospedaliero-Universitaria di Parma, Radiology and Cardiology, Parma, Italy*

Purpose: Evaluation of coronary stents still posed considerable problems with 4- and 16-slice Multi-Slice Computed Tomography (MSCT) but may have improved with 64-slice MSCT. However, few data are currently available. The purpose of the present study was to evaluate the diagnostic accuracy of 64-slice multi-slice computed tomography (64-slice MSCT) coronary angiography in the follow-up of patients with previous coronary stent implantation.
Methods: 64-slice MSCT angiography was performed in 182 patients (152 (84%) males, aged 58±11 years) with previous stent (≥2.5mm diameter) implantation (n=192) using either a Sensation 64 (Siemens, Germany) or Aquilion 64 (Toshiba, Japan). At each center, coronary stents were evaluated by two experienced observers and evaluated for the presence of significant (≥50%) in-stent restenosis. Quantitative coronary angiography served as the standard of reference.
Results: A total of 14 (7%) stented segments were excluded because of non-diagnostic image quality. In the interpretable stents, 20 of the 178 (11%) evaluated stents were significantly diseased, of which 19 were correctly detected by 64-slice MSCT. Accordingly, sensitivity, specificity and positive and negative predictive value to identify in-stent restenosis in interpretable stents were 95% (CI: 85% to 100%), 93% (CI: 90% to 97%), 63% (CI: 46% to 81%), and 99% (CI: 98% to 100%), respectively.
Conclusion: In-stent restenosis can be evaluated with 64-slice MSCT with good diagnostic accuracy. In particular a high negative predictive value of 99% was observed, suggesting that 64-slice MSCT may be particularly valuable as a non-invasive method to exclude in-stent restenosis.

P1457 Assessment of significant coronary artery stenoses with computed tomography number of the contrast medium in the reference lumen proximal and distal to the stenotic lesion using multislice CT

H. Kitabata[1], A. Kuroi[1], T. Tanimoto[2], T. Yamano[1], Y. Matsuo[1], S. Takarada[1], T. Kubo[1], T. Imanishi[1], Y. Tomobuchi[1], T. Akasaka[1]. *[1]Wakayama medical university, Cardiovascular medicine, Wakayama, Japan; [2]Wakayama Medical University, Cardiovascular medicine, Wakayama, Japan*

Background: Multislice computed tomography(MSCT) is a recently developed

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

noninvasive imaging modality, which may achieve high level of reliability and accuracy in the visualization of coronary artery. However, false positive rate of the examination is relatively high, mainly due to severe calcifications and residual motion artifacts.
Purpose: We measured CT number of the contrast medium in coronary arteries proximal and distal to the lesions, and evaluated a correlation between the percent change of the CT number ((CT number proximal to a lesion – that distal to the lesion) divided by the CT number proximal to the lesion × 100%) and a degree of stenoses assessed by invasive coronary angiography (CAG).
Methods: We enrolled 42 patients (35male, mean age 67±10 years) who underwent both CAG and MSCT using a scanner with 40 detector rows. We evaluated 100 segments and they were classified as normal (33/100), 50% stenosis (27/100), 75% stenosis (11/100), or 90-99% stenosis (24/100) according to the results of CAG.
Results: The percent change of the CT number were 3.3±3.7% in normal segments, 6.6±8.1% in 50% stenotic lesions, 19.7± 14.2% in 75% stenotic lesions, and 22.2±16.8% in 90-99% stenotic lesions. There was a significant difference between the percent change of the CT number in non-significantly stenotic segments (<50%) and that in significantly stenotic lesions (>75%). Furthermore, there was a significant correlation between the percent change of the CT number by MSCT and the degree of stenoses by CAG(r=0.51).
Conclusions: The measurement of the CT numbers of the contrast medium in the coronary artery lumen proximal and distal to the stenotic lesion by MSCT may provide higher accuracy in the assessment of the degree of the coronary stenosis. This novel method would be useful even if it is difficult to assess the coronary artery lumen directly on MSCT because of severe calcification.

P1458 Anatomically adjusted tube current modulation reduces radiation dose estimates in cardiac 64-slice CT angiography in patients after bypass graft surgery

F. Hermann, E. Hendrich, T. Meyer, M. Hadamitzky, U. Lang, C. Schwarzer, S. Martinoff, J. Hausleiter. *Deutsches Herzzentrum Munich, Radiology Dept., Munich, Germany*

Purpose: Owing to the longer scan range, a substantial radiation burden is associated with computed tomography angiographies (CTA) in patients with aorto-coronary bypass grafts. Recent developments in CT technology have improved the spatial and temporal resolution of 64-slice CTA which is associated with a further increase in radiation dose, if the signal-to-noise ratio shall be kept constant. An anatomically based algorithm ("CareDose") has been developed for dose savings in CT studies. The objective of this prospective investigation was to evaluate the impact of the "CareDose" algorithm on radiation dose and image quality during 64-slice CTA in patients after bypass surgery.
Methods: Radiation dose was estimated for 125 consecutive patients undergoing 64-slice CTA with ECG-dependent dose modulation after surgical coronary revascularization. In the later 80 patients the "CareDose" algorithm was used in addition to ECG-dependent dose modulation.
Results: The overall radiation dose estimate was 14.7±1.9 mSv (0.62±0.09 mSv/cm scan length). In patients without and with "CareDose" the estimated doses were 0.65±0.10 vs. 0.60±0.07 mSv/cm scan length, respectively (p<0.01). This significant 8% reduction in radiation dose was not associated with a reduction in diagnostic image quality as assessed by image noise, signal- and contrast-to-noise ratios as well as qualitative parameters.

Anatomically based dose-saving algorithm

	without CareDose	with CareDose	p-Value
Dosis per cm scan length	0.65±0.10	0.60±0.07	<0.01
Image noise	73.3±17	73.7±20	n.s.
Signal-to-noise ratio	5.3±1.5	5.5±1.7	n.s.
Contrast-to-noise-ratio	3.8±1.2	4.1±1.4	n.s.

Conclusions: Anatomically adjusted tube current modulation allows for a significant reduction of effective radiation dose with maintained diagnostic image quality. This dose saving algorithm is recommended in all patients undergoing 64-slice bypass graft CTA.

P1459 Accurate and noninvasive assessment of aortic valve area and coronary stenoses by 64-row multidetector computed tomography in patients with aortic stenosis

M. Katayama[1], F. Kureha[2], K. Tamita[2], A. Yamamuro[2], T. Tani[2], K. Tanabe[2], Y. Kihara[2]. *[1]Institute of Biomedical Research & Innovation, Cardiology Department, Kobe, Japan; [2]Kobe General Hospital, Cardiology, Kobe, Japan*

Background: Recent advancement of 64-row multidetector computed tomography (64-MDCT) provides noninvasive assessments not only on the coronary artery trees, but also on the left ventricular shape and valvular morphology. Patients with aortic stenosis have a higher prevalence of coronary artery lesions, and clinical evaluation of coronary stenoses is essential to avoid unexpected clinical outcomes, especially in elder patients. The aim of this study was to assess the feasibility to measure aortic valve area (AVA) and coronary artery stenoses simultaneously by using 64-MDCT.
Methods: Twentysix patients (72±10 years old) with aortic stenosis underwent both 64-MDCT and transthorachic echocardiography (TTE). In contrast enhanced 64-MDCT images, AVA was reconstructed at the cross-sectional transverse level at the mid systole of ECG-gating cardiac cicle, and was measured by planimetry. The AVA was compared to that by the continuity equation in TTE. The coronary tree of each patient was evaluated for >75% diameter stenosis by experienced observers and was compared to the invasive angiography.
Results: The values of AVA measured by 64-MDCT were very close to those measured by TTE (0.87±0.36 cm^2 vs 0.74±0.34 cm^2), and the regression analysis showed a significant correlation between 64-MDCT and TTE (R=0.896, p<0.0005). Prevalence of coronary artery disease was 46% (12 of 26 patients). Invasive coronary angiography was followingly underwent in 16 of 26 patients who showed massive calcifications and stenotic lesions in 64-MDCT. The sensitivity of 64-MDCT in detecting significant coronary artery stenosis was 100% and its specificity was 83%. The positive and negative predictive value was 90% and 100%. By 64-MDCT, conventional coronary angiography was eventually avoided in 10 of 26 patients.
Conclusion: Using 64-MDCT, noninvasive and simultaneous assessments of AVA and coronary artery stenoses are reliable. This results suggest that 64-MDCT is a powerful and noninvasive tool for assessing concomitant coronary artery stenoses in patients with aortic stenosis.

P1460 Left atrial and left atrial appendage volumes in various cardiac diseases as determined by multislices computed tomography (MSCT) imaging

L. Christiaens[1], N. Varroud Vial[2], P. Ardilouze[3], B. Lequeux[4], J. Mergy[3], J. Allal[3]. *[1]cardiologie C.H.U. La Miletrie, Dmc Cardiologie, Poitiers Cedex, France; [2]cardiologie CHU La Miletrie, cardiology, Poitiers, France; [3]Radiologie CHU La Miletrie, radiology, Poitiers, France; [4]Cardiologie CHU La Miletrie, cardiology, Poitiers, France*

Purpose: Left atrial (LA) volume is related to cardiovascular morbidity, and is usually measured using trans-thoracic echocardiography. The association of multislice computed tomography (MSCT) imaging, and of the new 3D reconstruction software, allows direct cardiac chamber volume measurement without geometrical assumptions.
Aim of study: Measurement of LA maximal (LA max) and minimal volumes (LA min), and left atrial appendage maximal volume (LAA max,), during the cardiac cycle.
Methods: Measurements were performed using a 64-MSCT scan with contiguous multiphase short-axis images generated from axial MSCT data and semi-automated 3D segmentation technique.
Results: 88 patients, in sinus rhythm, were studied: 62 men, age: 63±13 years, 20 pts ischemic cardiomyopathy (ICM), 20 pts hypertrophic cardiomyopathy (HCM), 20 pts dilated hypokinetic cardiomyopathy (DCM), 20 pts without cardiomyopathy (Normal), 8 with surgical mitral regurgitation (MR). Close correlation was observed between LAmax and LAAmax volumes (r = 0.69, p < 0.0001). Preliminary results of this ongoing study in Table (results).

Results

	LA max	LAA max	LA max/BSA	p	LA min/BSA	Atrial EF
Normal	104±24 ml	8±3 ml	55±9 ml/m^2		31±8 ml/m^2	44±9%
ICM	104±26 ml	8±3 ml	56±13 ml/m^2	ns	34±12 ml/m^2	39±11%
DCM	121±32 ml	11±6 ml	63±15 ml/m^2	ns	42±17 ml/m^2	34±15%
HCM	126±36 ml	10±6 ml	64±19 ml/m^2	0.06	44±17 ml/m^2	32±11%
MR	180±88 ml	14±7 ml	101±48 ml/m^2	0.0002	74±39 ml/m^2	28±14%

BSA: body surface area, p: correlation between indexed LAmax for each group of cardiomyopathy and the "normal" group; atrial EF: ejection fraction of left atrium = (LAmax –LA min)/LA max.

Conclusion: 64 MSCT is a useful tool for the assessment of the left atrial volumes and emptying without geometrical assumptions.

ECHO IN VASCULAR DISEASE

P1461 Abnormal regional myocardial deformation properties and increased aortic stiffness in normotensive patients with aortic coarctation despite successful correction: an ABPM and strain rate study

G. Di Salvo[1], G. Pacileo[2], G. Limongelli[2], S. Gala[2], B. Castaldi[2], M. Verrengia[2], A. Rea[2], P. Caso[2], M.G. Russo[2], R. Calabro'[2]. *[1]Naples, Italy; [2]Second University of Naples, Chair of Cardiology, Naples, Italy*

The long-term follow-up data subsequent to a successful repair of aortic coarctation (AoC) show that life expectancy remains reduced. Previous standard echocardiographic studies demonstrated normal or increased systolic cardiac function in patients after successful repair of AoC. Strain rate (SR) imaging is a new technique able to detect subclinical myocardial abnormalities. We investigated whether young patients late after successful AoC repair, without hypertension, as assessed by 24-ABPM and exercise test, already show abnormal myocardial deformation properties and their relationship with aortic stiffness. We studied 166 subjects: 83 AoC non-hypertensive patients (mean age 12±4 years)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

late after successful repair of AoC; 83 age-sex matched subjects as controls. Peak systolic SR (1/sec) for both regional longitudinal and radial function was assessed. Aortic (AO) stiffness index was calculated from the echocardiographically derived thoracic AO diameters and the measurement of blood pressure obtained by cuff sphygmomanometry.
Results: Left ventricular (LV) ejection fraction was significantly increased in AoC patients, while regional longitudinal SRs were significantly reduced (SR: -1.1±0.9 vs –2±0.5, p<0.0001) in patients. Ao stiffness index was significantly increased in AoC patients (12±9, p<0.0001). At multilinear regression analysis, age at repair (p:0.005; Coeff.: -0.201; SE: 0.027) and aortic stiffness index (p=0.0029; Coeff.: 0.334; SE: 0.423), predicted longitudinal SR.
Conclusions: Despite the presence of a successful repair for AoC, in absence of hypertension, longitudinal deformation properties are significantly impaired. Moreover, the degree of longitudinal SR impairment is correlated with age at repair and aortic stiffness. Early repair can delay the onset of hypertension in postcoarctectomy patients, but cannot change the innate structural and functional abnormalities of the aorta and their deleterious effect on myocardial deformation properties.

P1462 Coronary ectasia - without concurrent stenosis - associated with impaired perfusion in myocardial contrast echocardiography testing

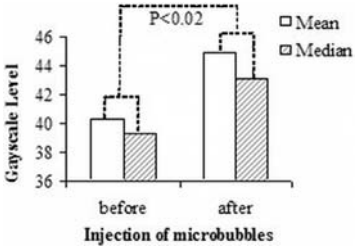
C. Aggeli, G. Giannopoulos, G. Roussakis, E. Christoforatou, G. Marinos, C. Vlachopoulos, A. Androulakis, C. Stefanadis. *1st Cardiology Dept, Hippokration Hospital, University of Athens Medical School, Athens, Greece*

Background and aim: Coronary ectasia has been correlated in the past to decreased coronary blood flow velocity. However, the impact of this condition on myocardial perfusion at rest and during increased workload has not been adequately evaluated. The purpose of the present study was to assess myocardial perfusion in patients with ectatic coronary arteries, using stress-contrast echocardiography.
Methods: Twenty-five subjects (10 females, age 67±7) with ectatic coronary artery segments shown on coronary angiography (CAG) - with ectasia defined as vessel diameter >1.5 times the diameter of adjacent arterial segments - without stenoses >50% and 20 controls with normal coronary arteries (matched for age, sex, presence of diabetes, smoking history and dyslipidemia) were submitted to dobutamine stress echocardiography (four-staged protocol at doses 10-40 μg/kg/min with use of atropine as required to achieve 90% of age-adjusted target heart rate). Concurrent myocardial contrast echocardiography (MCE) study was performed. Sonovue, Bracco contrast agent was used and the studies were performed with a Sonos 5500 (Philips Medical Systems) echocardiography machine. The acquired images were recorded, and reviewed by two experienced readers, who were blinded as to the coronary angiography findings.
Results: Among patients with ectasia, all had normal perfusion studies at rest, while 21 (84%) showed a reversible perfusion defect at peak stress. On the contrary, only 4 (20%) (p<0.01) of the controls showed a reversible perfusion defect on MCE. The location of the perfusion defects in each patient with coronary ectasia were then compared with the distribution of the artery(ies) with the ectatic segment(s). The observed perfusion defect on MCE corresponded to a coronary artery with ectatic segment(s) in 19 out of the 21 patients with coronary ectasia and perfusion defects on MCE, which means that in 19 out of 25 (76%) patients with ectatic coronary artery segments, the myocardial regions supplied by the ectatic vessels showed impaired perfusion at stress, demonstrable by MCE.
Conclusions: Our findings suggest that ectatic coronary arteries commonly cause significant myocardial ischemia on stress, as shown by MCE, in the absence of significant stenoses on CAG. This may be taken into account in the clinical evaluation of these patients and may explain the manifestation of symptoms of ischemia in subjects with non-stenosed, albeit ectatic, coronary arteries.

P1463 Contrast enhanced harmonic imaging for the assessment of carotid plaque neovascularization

T.G. Papaioannou[1], M. Vavuranakis[1], A. Androulakis[2], K. Filis[3], I. Kakadiaris[4], I. Vlasseros[4], G. Lazaros[1], M. Naghavi[5], I. Kallikazaros[5], C. Stefanadis[1]. *[1]1st Dept of Cardiology, Hippokration Hospital, Athens, Greece; [2]State Cardiac Dept, Hippokration Hospital, Athens, Greece; [3]Dept of Surgery, Hippokration Hospital, Athens, Greece; [4]Dept of Computer Science, Univ. of Houston, Houston, United States of America; [5]Association for Eradication of Heart Attack, Houston, United States of America*

Neovascularization and inflammation are thought to be related to atherosclerotic plaque vulnerability. Contrast enhanced ultrasound has been recently used for the quantification of VV density in coronary plaques. Postmortem studies showed that patients with symptomatic carotid atherosclerosis have plaques that are characterized by a dense network of vasa vasorum (VV). Our purpose was to examine whether surface contrast enhanced ultrasound (SCEU) is able to detect features of neovascularization in carotid plaques. Mehtods. Among 20 pts with coronary artery disease screened with Duplex carotid ultrasound, seven patients (mean age 69.3±10.9 years, 6 males) had plaques without superficial luminal calcification, plaque echolucency within the plaque and luminal stenosis <80%. Duplex ultrasound and harmonic imaging were used to image carotid plaques before and after the injection of 2.5cc solution of microbubbles. Image sequences were acquired continuously for 2min and were digitally stored and processed. Images at the same point within the cardiac cycle base on the ECG were extracted for the analysis. Mean and median grayscale level (GL) was calculated for each plaque before and after the injection of microbubbles.
Results: The seven plaques that were studied had an average luminal stenosis was 40±5%. The injection of microbubbles induced a significant increase in both mean GL (from 40.3±20.3 to 44.9±24.5, p=0.018) and median GL (from 39.3±21.9 to 43.0±23.9, p=0.019).



Conclusion: Harmonic imaging revealed that injection of microbubbles induced a significant increase in the echolucency of plaque area possibly indicating the presence and the extent of neovascularization. Further histological studies are needed to verify this hypothesis and validate the proposed technique.

P1464 Evaluation of plaque stabilization with carotid intima-medial elasticity measured by a transcutaneous ultrasonic-based tissue characterization system

T. Yamagishi[1], K. Kato[2], Y. Koiwa[3], K. Omata[4], H. Hasegawa[5], H. Kanai[1]. *[1]Tohoku Kosai Hospital, Department of Internal Medicine, Sendai, Japan; [2]Matsushita Electric Industrial Co., Ltd., Healthcare Business Company, Yokohama, Japan; [3]Graduate School of Medicine, Tohoku Univ., Department of Medical Sciences, Sendai, Japan; [4]Miyagi University of Education, Health Administration Center, Sendai, Japan; [5]Graduate School of Engineering, Tohoku Univ., Department of Electronic Engineering, Sendai, Japan*

Purpose: We attempted to classify carotid plaque tissues in terms of arterial wall elasticity instead of the echogenicity on B-mode scanning, and investigated the effect of statin on plaque stabilization by carotid elasticity distribution in patients with hypercholesterolemia.
Methods: In a total of 220 subjects including healthy volunteers and patients with untreated hypercholesterolemia and carotid plaques, simultaneous measurements of intima-media thickness (IMT) and elastic modulus in the circumferential direction (Eθ) were performed by the new high-resolution Doppler technique, "Phased Tracking Method" (Circulation 2003, 107:3018). Elasticity was estimated at intervals of 80 μm in the depth direction and 400 μm in the axial direction and calculated from the wall strain and the blood pressure and then the distribution of the elasticity was displayed as a 2D cross-sectional color image. The effect of fluvastatin (30 mg/day, n=34) was assessed during 12-month with elasticity distribution and serum markers.
Results: From observation of various tissues, the elasticity library with transcutaneous ultrasound was obtained as follows; lipidcore, 22±15; calcification, 674±384; lipidcore- and calcification-free plaques, 173±69; smooth muscle, 104±32; blood clot, 85±68; fibrosis, 273±173 (Eθ, kPa). The statin reduced LDL-C, hsCRP, IMT and Eθ significantly (p <0.05). Histogram analysis of the data revealed a decrease in areas corresponding to Eθ of 20-200 kPa and an increase in relatively hardened areas of ≥250 kPa for the subgroups showing increased Eθ, which were thought to be a decrease of lipid/smooth muscle-rich tissue and/or an increase of collagen fibers by using the elasticity library.
Conclusions: The present non-invasive echographic carotid arterial elasticity data suggested that this method is useful for classification and evaluation of atherosclerotic plaques that increase with progressing lipid deposition and the measurement data may reflect chronological and histopathological changes.

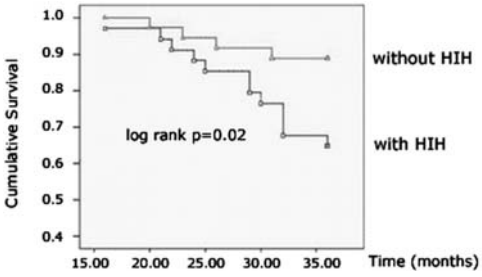
P1465 The effect of hemodialysis induced hypotension on mortality and its relation to aortic elasticity: a three-year outcome analysis

D. Duman, B. Erdogan, B. Karadag, G.M. Sahin, R. Demirtunc. *Istanbul, Turkey*

Background: Hemodialysis induced hypotension (HIH) is one of the most serious complications in renal replacement therapy. The pathogenesis of HIH is multifactorial and may include impaired aortic elastic properties. The present study was undertaken to determine aortic elastic properties in patients undergoing chronic hemodialysis with and without HIH and to asssess the effect of HIH on mortality.
Methods: Aortic elastic properties and left ventricular (LV) functions were evaluated in 70 chronic hemodialysis patients with (n = 34) and without HIH (n = 36). After 36 months follow-up, we evaluated total mortality.
Results: Patients with HIH in comparison to patients without HIH, had lower aortic

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

strain (5.0±3.8% vs. 7.8±3.0%, $p < 0.005$) and distensibility (2.3±1.9 vs. 3.2±1.7 $cm^2/dyn/10^3$, $p < 0.01$). In a logistic regression model, LV systolic dysfunction, coronary artery disease (CAD) and decreased aortic distensibility were found to be the main predictors of HIH. During follow-up, 12 of 34 of patients with HIH died compared with 4 of 36 without HIH (Log rank, P= 0.02) (Figure). However, in a multivariate proportional hazards model after adjustment for age, sex, duration of dialysis, diabetes, CAD, LV systolic dysfunction, serum albumin level and the use of β-blockers and long-acting nitrates, HIH did not increasedthe risk of death.



Kaplan Meier Survival Analysis

Conclusion: These data suggest that HIH is strongly associated with impaired aortic elastic properties. Although survival is significantly shorter in patients with HIH compared to without HIH, there is no independent effect of HIH on mortality.

P1466 Aortic dilatation in obstructive sleep apnea syndrome

C. Meuleman, F. Boccara, E. Di Angelantonio, E. Ederhy, S. Janower, F. Raoux, G. Dufaitre, L. Boyer-Chatenet, B. Fleury, A. Cohen. *hopital saint antoine, cardiology, Paris, France*

Purpose: Obstructive sleep apnea syndrome (OSAS) has been associated with an increased risk of arterial hypertension (AH), coronary artery disease, heart failure and death. Whether OSAS influences aortic root size has not been fully investigated. The aim of our study was to investigate aortic root diameter and aortic stiffness in OSAS.
Methods: Using transthoracic Doppler echocardiography, we evaluated 104 OSAS patients (Pts) (mean age 52.14±8.94 years, 92 men), with no overt cardiovascular disease. The following parameters were off-line measured: aortic diameter at Valsalva sinuses, aortic regurgitation (AR) grade, left ventricular (LV) mass, LV ejection fraction (LVEF, Simpson rule), systolic pulmonary artery pressure (sPAP). Aortic stiffness (carotid-femoral pulse wave velocity (PWV) was measured non-invasively using SphygmoCor technology in 75 pts.
Results: Mean duration of OSAS was 4.57±3 years and 86% of pts had a treatment with continuous positive airway pressure. AH was documented in 38 pts. The mean aortic root diameter was 34.95 mm (26,4-44,6 mm). The main results are presented according to aortic diameter tertiles. Seventeen pts (16.3%) had aortic root diameter > 39 mm.

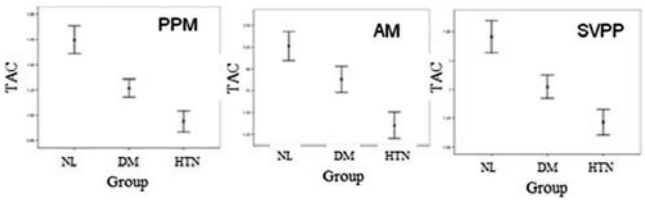
	Group 1 N = 35	Group 2 N = 35	Group 3 N = 34	Pearson correlation
Mean aortic root diameter (mm)	30.5±2.13	35.14±1.06	39.32±1.83	
Mean age (yrs)	50.35±8.97	50.25±8.53	55.93±8.34	0.27 (0.08,0.44)
Men	71%	97%	97%	0.45 (0.28,0.59)
BMI (kg/m^2)	32.39±5.45	32.28±6.66	36.72±30.29	0.05 (-0.15,0.25)
AH (%)	43%	37%	29%	-0.18 (-0.36,0.01)
Apnea-hypopnea index	59.61±40.92	50.73±30.41	54.76±36.18	0.11 (-0.11,0.32)
PWV (m/s)	9.79±2.68	9.52±1.62	9.74±1.86	-0.05 (-0.27,0.18)
LVEF (%)	60.82±3.42	60.14±1.48	60.12±1.82	-0.13 (-0.31,0.07)
sPAP (mmHg)	31.31±5.3	29.96±6.25	29.82±4.29	-0.11 (-0.31,0.11)
AR	5 (14%)	3 (9%)	7 (21%)	0.09 (-0.11,0.27)

On univariate analysis, AH was not a predictor of aortic root dilatation. However, PWV was a significant predictor of aortic root dilatation ($p<0.05$).
Conclusions: These results suggest that aortic root diameter enlargement is associated with OSAS, independently from the presence of AH. This observation could represent a link between the increased prevalence of aortic dissection and OSAS.

P1467 A comparison of methods for assessing total arterial compliance

B. Haluska[1], J. Brown[2], S.G. Carlier[3], T.H. Marwick[2]. *[1]University of Queensland, Department of Medicine, Brisbane, Australia; [2]University of Queensland, Medicine, Brisbane, Australia; [3]Cardiovascular Research Foundation, New York, United States of America*

Background: Reduced total arterial compliance (TAC) is associated with HTN, ischemia and reduced exercise capacity. However the optimal technique of assessing TAC is unclear. We compared three methods of estimating TAC in a large group of patients with and without cardiovascular risk to determine which may be the most robust.
Methods: We studied 320 pts (170 men; age 55±10) with and without cardiovascular risk. TAC was determined by 1) the pulse-pressure method (PPM) based on the two element Windkessel, 2) the area method (AM), which uses an integral variation of the Windkessel, and 3) the stroke volume/pulse pressure method (SVPP) a ratio of stroke volume and PP. Arterial waveforms were obtained using radial applanation tonometry and a transfer function was used to calculate central pressure from radial pressure. Clinical data, risks factors and TAC by all three methods were then compared.
Results: Correlation was good between all methods: PPM/AM .83, PPM/SVPP .94 and AM/SVPP .80 (all p< .0001). TAC by the PPM was 1.24± .50, by the AM 1.84± .89 and by the SVPP 1.44± .53 (all p< .0001). Analysis of the subgroups showed significant differences between the groups for all three methods, and PPM showed the largest group differences with the smallest standard deviations (Figure). The independent correlates of patient group in linear regression models were all the same–age, HTN and TAC (all p< .0001) and the variance and model strength were all similar (F= .74; R2 =.46; p< .0001).



Conclusions: Normal and abnormal values of TAC vary according to method, and should be expressed. Each technique shows good correlation with each other and similar values. The PPM appears to be slightly more robust in determining differences between groups with and without cardiovascular risk.

P1468 Elastic properties of aorta is reduced in patients with slow coronary flow phenomenon

N. Arat, H. Altay, I. Sabah. *Turkiye Yuksek Ihtisas Hospital, Cardiology, Ankara, Turkey*

Background: Increased stiffening and decreased distensibility of the large arteries are associated with the presence of coronary artery disease and has been related to increased cardiovascular mortality in different populations. Aim: Aim of this present study was to investigate the elastic properties of the aortic wall in patients with slow coronary flow phenomenon (SCFP).
Material and method: We studied 20 patients with SCFP (age: 40± 12 years) and 15 normal control subjects by echocardiography. Aortic strain (%), distensibility ($cm^2 \times dyn^{-1} \times 10^{-6}$), and stiffness index were calculated from the echocardiographically derived thoracic Ao diameters (mm/m^2). The measurement of pulse pressure was obtained by cuff sphygmomanometry.
Results: There was no difference in the left ventricular ejection fraction, left ventricular end-diastolic and end-systolic diameters, left atrial diameters, left ventricular mass index between SCFP and control groups. Maximal aortic diastolic diameter was increased in patiens with SCFP compared with control group ($p<0.05$). Ao distensibility and aortic stiffness index were lower and Ao strain was higher in the patiens with SCFP compared with control group ($p<0.05$).

Table 1

	Patients with SCFP	Patient with NCF	p
AoSDI (mm/m^2)	18.8±3.5	18.4±3.3	NS
AoDDI (mm/m^2)	17.2±3.1	16.4±2.9	0.044
Ao strain (%)	11.9±4.7	7.6±2.9	0.035
Ao distensibility	2.5±0.4	5.3±0.7	0.024
Ao stiffness index	3.5±1.2	5.9±2.8	0.034

Comparison of the aortic elastic properties between the patients with slow coronary flow and normal coronary flow. SCFP; slow coronary artery phenomenon, NCF; normal coronary flow, AoSDI; aortic systolic diameter index, AoDDI; aortic diastolic diameter index, NS; non-significant.

Conclusion: Reduced thoracic aortic elastic properties in patients with SCFP, assessed by echocardiography, apart from demonstrating subclinical atherosclerosis may also contribute to the etiopathogenesis of the SCFP necessisating more aggressive primary preventive measure.

P1469 Vascular-coronary coupling: large artery stiffness is a determinant of coronary flow velocity reserve

M. Saito[1], H. Okayama[1], K. Nishimura[1], A. Ogimoto[1], T. Ohtsuka[1], T. Yoshii[2], K. Inoue[2], G. Hiasa[2], T. Sumimoto[2], J. Higaki[1]. *[1]Ehime university graduate school of medicine, Toon, Japan; [2]Kitaishikai hospital, Ozu, Japan*

Backgrounds: Population studies have shown that increased large artery stiffness is an independent predictor of cardiovascular events. In a normal elastic aorta, the pressure wave reflects from the periphery and returns to the heart during diastole. As the aorta stiffens, the velocity of the pressure wave increases, and the reflected pressure wave eventually reaches the heart during systole rather than diastole. Consequently, the diminished elasticity of the stiff aorta, combined

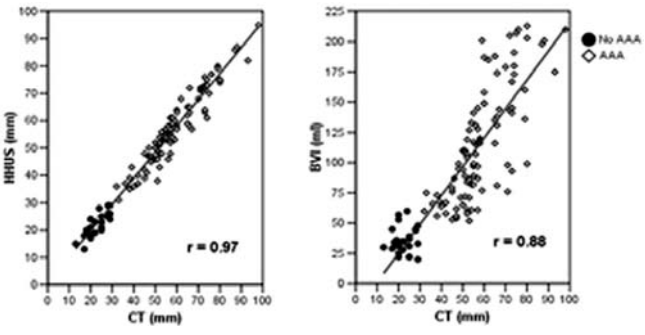
Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

with the absence of diastolic augmentation from the reflected pressure wave, has the potential to reduce coronary perfusion pressure and coronary blood flow. Experimental studies have shown that a stiff aorta is associated with decreased coronary blood flow. However, a link between large artery stiffness and coronary microvascular function in the clinical setting has not been fully demonstrated previously. Thus, the goal of this study was to evaluate the relationship between large artery stiffness and coronary flow velocity reserve (CFVR).
Methods: The study enrolled 102 consecutive subjects (mean age 62 ±10) without coronary and peripheral arterial disease. After 15 min of rest, measurements were obtained of brachial-ankle pulse wave velocity (baPWV), augmentation index (AIx) from a carotid pulse tracing, and transthoracic echocardiographic parameters, including coronary flow velocity in the left anterior descending coronary artery. In addition, coronary flow velocity during hyperemia was measured during an intravenous infusion of adenosine triphosphate (0.14 mg/kg/min). CFVR was defined as the ratio of hyperemic to basal coronary velocity.
Results: Subjects with decreased CFVR (<2.5; n = 40) had significantly higher baPWV (1848±360 cm/sec vs. 1548±333 cm/sec, P<0.0001), greater AIx (25±11% vs. 16±20%, P<0.05) and greater pulse pressure (PP) (64±13 mmHg vs. 54±13 mmHg, P<0.001) than those with normal CFVR (n = 62). Multivariate analysis among age, gender, hemodynamic parameters, metabolic variables, left ventricular mass index, E/A ratio, baPWV and AIx revealed that AIx and PP were independent predictors of CFVR (r = -0.32, P<0.0001 and -0.25, P<0.05, respectively).
Conclusion: Our data suggest that high AIx and PP are linked to a reduction of coronary flow velocity reserve, which may partially explain the higher cardiac event rate in patients with increased large artery stiffness.

P1470 New ultrasound devices for abdominal aortic aneurysm detection - comparison with the computerized tomography

R. Vidakovic[1], O. Schouten[1], H.H.H. Feringa[1], M. Dunkelgrun[1], S.E. Karagiannis[1], S.E. Hoeks[1], E. Merks[1], A.N. Neskovic[2], N. Bom[2], D. Poldermans[2]. *[1]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; [2]Clinical Hospital Center "Zemun", Cardiology, Belgrade, Serbia*

Background: Screening for abdominal aortic aneurysm (AAA) of patients at risk might become more cost-effective if a simple, inexpensive and reliable ultrasound (US) device becomes available. A hand-held US device might be a promising tool.
Aim: To compare the diagnostic potential of a newly developed hand-held 2D duplex US device (HHUS) and hand-held US scanner for the three-dimensional assessment of volumes, based on Bladder Scan technology (BVI), with the computerized tomography (CT) in patients with AAA.
Methods: In total, 120 patients (70±10 years, 101 men) were screened for the presence of AAA (diameter >3cm on CT). All patients underwent first examination by CT, and then by both HHUS and BVI. Using the HHUS the aortic diameter was measured at 4 levels in millimetres. With the volume scan the aortic volume was measured at 6 pre-defined symmetric topographic points around the umbilicus in millilitres. Maximal diameters (CT and HHUS) and volumes (BVI) were used for analyses.
Results: In 96 (80%) patients an AAA was diagnosed by both CT and HHUS, presenting the agreement between the methods of 100%, kappa 1.0. Sensitivity, specificity, positive and negative predictive value of the HHUS in detection of AAA were 100%, respectively. Maximal aortic diameter by CT correlated closely with maximal aortic diameter by HHUS (r=0.97, p<0.0001), as well with the maximal volume by the BVI (r=0.88, p<0.0001). Using cut-off of >50 ml for the presence of AAA by BVI; sensitivity, specificity, positive and negative predictive value of the BVI in detection of AAA were 97%, 100%, 100% and 87%, respectively. The agreement between the two methods was 97%, kappa 0.92.



Conclusion: This study shows that a simple hand-held US devices can effectively identify patients with an AAA as confirmed by a CT.

ECHO IN ARRHYTHMIAS

P1471 Improvement of left ventricular deformation after catheter ablation for isolated paroxysmal atrial fibrillation in patients with normal ejection fraction: a 2-dimensional strain study

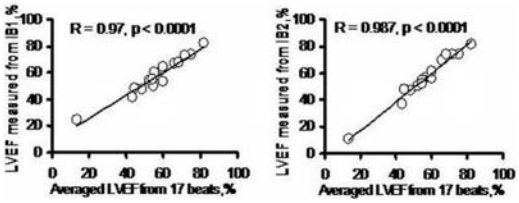
P. Reant, S. Lafitte, P. Jais, F. Sacher, N. Derval, A. Deplagne, M. Hocini, J. Clementy, M. Haissaguerre, R. Roudaut. *CHU de Bordeaux, Universite Bordeaux II, Echocardiography and Cardiology, Bordeaux-Pessac, France*

Background: Paroxysmal isolated atrial fibrillation (AF) is generally associated with normal left ventricular (LV) ejection fraction. Recently, echocardiographs have been implemented by 2-dimensional (2D) strain technique, a new tool based on speckle tracking which allows accurate evaluation of the three components of LV deformation (circumferential, radial and longitudinal strains). Objective: The aim of this prospective study was (1) to evaluate whether 2D strain evaluation could point out alteration of LV deformation in patients with paroxysmal AF and normal ejection fraction in comparison with controls; (2) to evaluate the evolution of the different strain components after AF catheter ablation.
Methods: Patients with isolated paroxysmal AF were investigated with a VIVID7 (General Electric) before ablation, at 1 month (M1) and at 6 months (M6) after catheter ablation.
Results: Twenty five successive patients (mean 58±12 years, 5 women) with isolated paroxysmal AF (mean since 8 years) and 25 controls were investigated. Before ablation, no significant difference was observed in term of LV ejection fraction between the 2 groups (p ns). In patients with paroxysmal AF, global longitudinal strain (GLS) and global circumferential strain (GCS) were significantly reduced compared to controls: GLS was -17.8±2.9% vs -21.4±2% in controls (p<0.001) and GCS was -15.4±4.1% vs -21.1±2.8% in controls (p<0.001). In contrast, no significant difference was observed for the global radial strain (GRS). After ablation, GLS increased from -17.8±2.9% to -19.3±2.3% (M1)(p<0.05), and to -19.3±2%(M6)(p=0.07), and GCS increased from -15.4±4.1% to -15.7±2% (M1)(p ns), and -16.3±1.7% (M6)(p ns). GRS was not significantly modified (from 41.7±17% to 37.1±12.4% (M1)(p ns) and 44.3±14% (M6)(p ns)).
Conclusions: Paroxysmal AF induced subclinical LV dysfunction as demonstrated by the decrease in longitudinal and circumferential strains in patients with normal ejection fraction. In our patients, this LV dysfunction tends to be improved after AF catheter ablation.

P1472 Assessment of ventricular function in atrial fibrillation: single beats with equal preceding and pre-preceding R-R intervals allow accurate estimation of LV systolic and diastolic function

A. Bajpai[1], A. Kiotsekoglou[2], I. Savelieva[1], C. Dougal[1], G.R. Sutherland[1], A.J. Camm[1]. *[1]St George's, University of London, Cardiovascular Sciences, London, United Kingdom; [2]St George's, University of London, Cardiological Sciences, London, United Kingdom*

The irregular rhythm during AF makes it difficult to estimate the LV function. Echo indices are usually averaged over 3-5 cycles which is unreliable. In AF, values need to be averaged over 13-17 cycles in order to obtain <1.5% variability from true values. LV systolic function in AF has positive linear relationship to the ratio of preceding (RR_1) and pre-preceding (RR_2) cycle lengths.
We studied 18 randomly selected patients with AF and measured indices of LV systolic and diastolic function. Each parameter was measured over 17 cardiac cycles & the average value was compared with single values from selected beats (IB) with $RR_1 = RR_2$. Two kinds of IB were identified-those with longest (IB1) and shortest (IB2) equal RR_1 & RR_2 intervals. Systolic parameters included stroke output using aortic VTI, ejection fraction (EF) by Simpson's method and LV longitudinal function using 2D-guided M-Mode. Diastolic indices were transmitral peak E wave velocity & deceleration time (EDT) and pulmonary venous flow velocity and deceleration time.
A strong correlation was noted between all values from IB1 & IB2, and the average value from 17 consecutive cycles (r= 0.95-0.99 for parameters of systolic function; p<0.0001, and 0.83-0.96 for diastolic function; p<0.0001). Mean relative error for EF from index and averaged beats was < 1%, and between <1% - 3% for LV volumes and EDT. Values were not significantly different between IB1 & IB2.



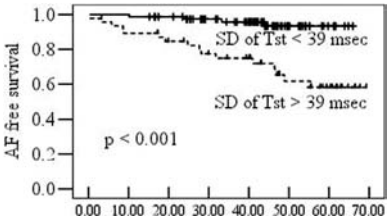
Conclusion: Measurements obtained from single beats with equal preceding and pre-preceding cycle lengths provide accurate assessment of LV systolic and diastolic function in AF and remove the need to average over multiple cardiac cycles.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1473 Left atrial dyssynchrony assessed by tissue Doppler and strain imaging in predicting future development of atrial fibrillation in patients with heart failure

G.Y. Cho, S.H. Kim, M.K. Kim, W.J. Park, S.H. Jo, H.S. Kim, Y.J. Choi, D.J. Oh, C.Y. Rhim. *Hallym University Sacred Heart Hospital, Hallym University, Anyang, Korea, Republic of*

Background: New onset atrial fibrillation (AF) in heart failure (HF) is associated with increased morbidity or mortality. We sought to evaluate whether atrial dyssynchrony can predict new development of AF in HF.
Methods: A total 158 patients (age 63±10, women 34%, mean ejection fraction (EF) = 35±13%) who hospitalized for HF and had no history of AF underwent conventional and tissue Doppler echocardiography. Tissue Doppler imaging was performed using 4 atrial walls (septum, lateral, inferior, and anterior). Atrial dyssynchrony was defined as standard deviation (SD) of time to peak velocity (Ts) or peak strain (Tst) or strain rate (Tsr) of 4 atrial walls during reservoir and booster period.
Results: During the mean follow up of 43±15 months, 21 patients (13.3%) developed new onset AF. The feasibility of SD of Ts, Tst, and Tsr during reservoir period were 96%, 80% and 60% and Ts and Tsr during booster period was 89% and 53%. There was no significant difference in baseline EF, LV volume, and diastolic parameters in patients with or without new onset AF. Univariate predictors of new onset AF were left atrial (LA) dimension and volume, LA fractional shortening (FS), early diastolic tissue velocity of annulus, and atrial dyssynchrony during reservoir period. However, atrial dyssynchrony during booster period was not predictive. By multivariate Cox regression model, atrial dyssynchrony based on strain (p = 0.005) or strain rate (p = 0.026), LA FS (p = 0.039) were independent predictors of new onset AF. The optimal cut off point of SD of Tst was 39 msec with 80% sensitivity and 71% specificity.



Conclusion: Atrial dyssynchrony based on strain during reservoir period can predict future development of new AF in heart failure.

P1474 Left atrial asynchrony before and after electrical cardioversion: mechanical resynchronization and improvement of atrial function after one month of sinus rhytm

E. Rondano, C. Piccinino, G. Sarasso, G. Marti, P. Devecchi, G. Bellomo, P.N. Marino. *Novara, Italy*

Dispersed intraatrial conduction because of atrial fibrillation (AF) is associated with cavity remodelling and loss of its filling and emptying properties. Cardioversion (CV) should remodulate atrial function through recovery of mechanical synchronism. In order to assess if CV of AF to sinus rhythm (SR) is associated with improvement of atrial mechanical synchrony, 54 patients with AF (30 males), mean age 69±8.6 years, with (n=52) or without structural heart disease were studied. Echocardiographic evaluation was performed 1 week before electrical CV in all patients and 1 month later only in those patients (n=26) who reached and maintained stable SR. Atrial volume (indexed to surface area) was calculated from the anterior-posterior diameter (parasternal long axis view) and area (4-chamber view) according to the formula: 4.2*diameter/2*area/2. Two-dimensional strain (speckle tracking technique) was used to estimate the peak and the standard deviation (SD) of the time-to-peak (% of R-R' interval) of the deformation of 6 segments arbitrarily identified along the septum, the roof and the lateral wall of the atrial cavity, as imaged in a 4-chamber view. Brain natriuretic peptide (BNP) was also measured 1 week before in all patients and 1 month after CV, if SR was maintained. There was a significant decrement in atrial volume after SR was restored (from 66.7±19.1 to 56.4±21.0 cm^3/m^2; p=0.004) together with an increase in mean peak strain (from 4.8±2.7 to 7.0±3.6%, p=<0.001). There was no change in time-to-peak of individual strains before and after CV (from 53±13 to 51±12%; p=0.67), but the SD significantly decreased (from 20.4±7.0 to 15.8±7.7%; p=0.05) suggesting improved atrial mechanical synchrony. Also BNP decreased significantly (from 125±108 pg/ml to 76±90 pg/m; p=0.03) and its change corresponded to the reduction in atrial volume (P=0.016). A multiple logistic regression analysis including age, duration of AF, presence or absence of mitral regurgitation, atrial volume, peak strain and SD of time-to-peak strain, identified SD as the only predictor of maintenance of SR post CV (p=0.06). It is concluded that in patients that maintain SR 1 month after CV: 1) left atrial asynchrony is significantly decreased and this improvement favourably modulates atrial strain, volume and dismission of BNP, 2) the extent of atrial asynchrony pre CV can predict maintenance of SR at 1 month.

P1475 Comparison of echocardiographic abnormalities in patients with and without ischaemic cerebral events and the diagnostic utility of echocardiography in this group: a study of 22,473 patients

S. Sulfi[1], D. Balami[1], A. Suliman[1], A. Kapur[2], R.A. Archbold[1], K. Ranjadayalan[2], A.D. Timmis[1]. *[1]Newham University Hospital, Cardiology Dept., London, United Kingdom; [2]London Chest Hospital, London, United Kingdom*

Background: Transthoracic echocardiography (TTE) is commonly performed in patients with ischaemic stroke or transient ischaemic attack (TIA). However, the diagnostic utility of echocardiography in this patient group has not been systematically evaluated.
Methods: Data was collected prospectively into a purpose built database from all patients undergoing echocardiography in a district general hospital from 1997 to 2006. Of 22473 patients aged ≥35 years undergoing TTE, data were available in 22245, of whom 824 (3.7%) were being investigated for ischaemic stroke/TIA. The group had a mean age of 66±14 years (range: 35-103), and 49.9% were male.Multiple structured queries were performed to identify clinical findings considered to have therapeutic implications. The prevalence of these abnormalities were compared between patients with ischaemic stroke/TIA (group 1, n=824) and those without ischaemic events (group 2, n=21,421)
Results: There was no significant difference in the age distribution between the two groups (67±13 vs 66±14)but there were more males in group1 (57.3% vs 49.6%, p<0.0001)
Group 1 had significantly increased prevalence of patent foramen ovale (0.61% vs. 0.15%, p=0.001), intra cardiac thrombus (0.85% vs. 0.36%, p=0.03) and atrial septal aneurysm (1.21% vs. 0.32%, p<0.0001). There were no significant differences in the prevalence of dilated cardiomyopathy (0% vs. 0.17%), mitral stenosis (0.61% vs. 0.51%) or intra cardiac mass (0.24% vs. 0.28%). Most important individual predictors of an ischaemic cerebral event were atrial septal aneurysm [odds ratio (OR): 3.51, 95% confidence Interval (CI):1.75-70.1, p<0.001], Patent foramen ovale (OR:3.44, 95% CI:1.27-9.30, p= 0.02) and intra-cardiac thrombus (OR:2.79, 95% CI:1.27-6.18, p=0.01)
Only 29 patients (3.5%) among those with ischaemic stroke/TIA had a clinically signficant abnormality identfied in the TTE.
Conclusions: 1. The abnormalities of atrial septum are the most potent independent predictors of ischaemic cerebral events. The results of ongoing trials will help determine whether PFO closure protects against these.
2. This review of current clinical practice reveals that the diagnostic yield from transthoracic echocardiography in patients with ischaemic cerebral events is very low. We recommend that TTE should be done more selectively in patients more likely to have a cardiac source of emboli.

P1476 Embolic events and paroxysmal atrial fibrillation. An echocardiographic assessment study

A. Navazio, N. Muia, E. Lo Jacono, M. Azzarone, G. Tortorella, M. Calzolari, O. Gaddi, M. Pantaleoni, L. Brandi, U. Guiducci. *Department of Cardiology, Arcispedale S. Maria Nuova, Reggio Emilia, Italy*

Background: Although it is known that atrial fibrillation (AF) is associated with an increased incidence of stroke, there is only limited evidence regarding the association between paroxysmal AF and embolic events.
Aim: The aim of the current study was to determine echocardiographic indices associated with an increased risk of embolic events in patients with paroxysmal AF.
Methods: Patients with recurrent episodes of paroxysmal AF and without patent foramen ovale, significant atheromatic plaques in the aortic arch, heart failure, valvular disease or on anticoagulation therapy were included in the study. All patients underwent transthoracic and transesophageal echocardiography in less than a month from the last episode of AF and the history of stroke was recorded. The echocardiographic indices studies were: left atrial (LA) size, left atrial appendage (LAA) flow velocities, LAA fraction and the presence of thrombi or spontaneous echocontrast in the left atrium (visually graded, 0-4 +)
Results: 105 patients were included in the study; 27 with a history of stroke (Group A) and 78 without (Group B).The demographic and echocardiographic characteristics of the two groups are shown in the table. Patients with a history of stroke had significantly lower left atrial appendage flow velocities, lower LAA fraction and more commonly present spontaneous echocontrast

	Group A (n=27)	Group B (n=78)	p
Age (years)	65±7	64±8	NS
LA size (mm)	43.5±4	42.3±5	NS
Presence of thrombi	6 (22%)	24 (30%)	NS
LAA fraction (%)	35.8±9.7	45.2±9.2	0.003
LAA filling flow velocity (cm/sec)	44.3±12.4	62.3±14.2	0.001
LAA emptying flow velocity (cm/sec)	37.4±13.2	51.3±16.6	0.003
Spontaneous echocontrast	7 (26%)	31 (39%)	0.055

Conclusions: Patients with recurrent episodes of paroxysmal AF and history of stroke had echocardiographic characteristics consistent with more impaired left atrial function compared to patients with paroxysmal AF but without stroke his-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

tory. These echocardiographic indices may be a useful marker of predicting future embolic events, suggesting the need for anticoagulation

P1477 Changes of left atrial structure and function after catheter ablation and electrical cardioversion for atrial fibrillation

J.I. Choi, S.M. Park, W.J. Oh, M.Y. Park, S.H. Shin, S.J. Hong, H.N. Pak, D.S. Lim, Y.H. Kim, W.J. Shim. *Korea University Anam Hospital, Cardiology, Seoul, Korea, Republic of*

Purpose: The reverse remodeling of left atrial (LA) size and improvement of LA function after cardioversion in atrial fibrillation (AF) are well documented. However, the detailed evaluation of LA structure and function has not been performed according to the different methods of restoring sinus rhythm. The objective of this study was to assess whether the morphological and functional changes of LA after radiofrequency catheter ablation(ABL) differ from those after electrical cardioversion (ECV) in AF.
Methods: The AF patients who had maintained sinus rhythm for 3 months after either ECV (n=30, male:24, 58.6±9.3 years) or ABL (n=33, male:27, 55.9±10.2 years) were studied. Two dimensional and Doppler echocardiography were performed at baseline, 1 week, 1 month, and 3 months. LA dimensions, mitral inflow velocity, and tissue Doppler imaging of mitral annulus were examined.
Results: LA dimensions decreased after procedure with similar trends in both groups ($p<0.05$ for all variables), but were larger in the ECV group than that of the ABL group from baseline to 3-month follow up period. There were no difference in late diastolic velocity of mitral annulus (A') and early transmitral peak velocity (E) between the ABL and ECV groups. But late transmitral peak velocity (A) increased from 1 week to 3 months only in the ECV group (ECV: 42.1±14.4 to 56.7±14.8 cm/s, p=0.000; ABL: 38.7±12.5 to 44.8±16.7 cm/s, p=NS). In sub-group analysis with persistent AF patients with similar LA size (40-49mm anteroposterior diameter; ECV: n=21, ABL: n=8), A and A' significantly increased 1 week to 3 months after restoration of sinus rhythm in both groups but were higher in the ECV group at each follow up point than that of theABL group. In the patients with paroxysmal AF, A and A' significantly decreased after ablation and did not recover to the baseline level at 3 months (A; 56.8±21.5 before ablation, 46.6±13.2 at 1 week, 47.9±18.3 cm/s at 3 months, $p<0.05$: A'; 9.4±2.0, 6.9±1.9, 8.0±1.4 cm/s, $p<0.05$) Conclusion: This study demonstrates that reverse morphological remodeling of the LA occurs in patients undergoing both successful ABL and ECV for AF. But LA function assessed by the A and A' velocity were lower in theABL group than that of the ECV group after procedure. These findings suggested the degree of functional reverse remodeling of LA after restoration of sinus rhythm by ABL was lower than that of ECV. Since the decreased A and A' by ABL did not recover to the baseline levels until 3 months after procedure, meticulous anticoagulation therapy should be considered in these patients.

P1478 Value of routine echocardiography after radiofrequency ablation

B.A. Schaer, A. Maurer, C. Sticherling, P.T. Buser, S. Osswald. *University Hospital, Basel, Switzerland*

Background: Echocardiography after radiofrequency ablation (RFA) is a standard procedure in many centres to rule out pericardial effusion. However, there is only limited data available about the incidence of post-procedure effusion in different forms of tachycardia.
Aim: Evaluation of the usefulness of routine echocardiography (echo) after RFA.
Methods: 364 consecutive pts who underwent RFA were studied. 3 pts who did not have any echo and 37 pts who did not have a postprocedure echo were excluded. In the remaining 324 pts, echos before (n=177) and within 24 hours after RFA (n=324) were analysed regarding pericardial effusion or other procedure-related complications. An effusion was defined as being small, if it was less than 5mm in distension in endsystole.
Results: 40% of patients were female, mean age was 54.5 (±16.6;range 15-89) years. RFA was performed for AV-nodal-reentry-tachycardias (AVNRT) in 131 pts (40%), atrial flutter in 91 pts (28%), AV-reentry-tachycardias (AVRT)/WPW in 45 pts (14%), atrial fibrillation in 22 pts (7%), ventricular tachycardias in 19 pts (6%), and other forms of tachycardia in 17 (5%) No valvular or aortic damage was seen. In 3 pts, a small effusion was present before and after RFA and thus not attributed to the procedure. In 7 pts (2.2%), small post-procedural effusions were observed. Control echos never showed progression and no effusion was considered to be hemodynamically relevant. In 3 pts, no echo was available before RFA, nevertheless the effusion was thought to be due to RFA. Mean age of patients with effusion after RFA was 66 years. Effusion was significantly more often present in 4/22 pts after a-fib ablation (18.2%), than after AVNRT ablation (2 pts; 1.6%) or after AVRT ablation (1 pt; 2.2%), p values < 0.05. Only one of these effusion was suspected based on procedure circumstances, the other six were detected "by chance" and the procedure had been unremarkable.
Conclusion: The occurrence of procedure-related complications other than pericardial effusion is close to zero. The incidence of pericardial effusion is low and, as they were hemodynamically irrelevant, does not justify routine post-procedure echocardiography. However, due to the much more complex procedure in a-fib ablation, routine echocardiography should be performed in this group of patients.

ASSESSING AND TREATING HYPERTENSION

P1479 Adrenergic activation in mild renal failure: regional patterns and relations with metabolic and cardiac abnormalities

G. Seravalle[1], F. Quarti Trevano[2], F. Pieruzzi[2], S. Genovesi[2], A. Stella[2], G. Grassi[2], G. Mancia[2]. *[1]Ospedale St. Luca - Istituto Auxologico Itali, Cardiology Dept, Milan, Italy; [2]S. Gerardo Hpt, Clinica Medica, Monza, Italy*

Objective: Patients with mild renal failure are characterized by a marked increase in muscle sympathetic neural outflow. No data are available on whether this adrenergic activation 1) is generalized to the whole circulation and 2) is related to the metabolic (insulin resistance) and cardiac (left ventricular hypertrophy) abnormalities frequently detected in this condition. Design and Methods. In 16 patients (8 females, 8 males, age 60.4±2.4 yrs, mean ± SEM) with mild renal failure (creatinine clearance ranging from 36 to 66 ml/min), we measured beat-to-beat arterial blood pressure (Finapres), heart rate (EKG, HR) and efferent postganglionic muscle sympathetic nerve traffic (microneurography, MSNA) during a 20 min resting period. Measurements also included 1) glucose and insulin assay (radioenzymatic method) and HOMA index calculation, 2) echocardiographic assessment of left ventricular mass index (LVMI) and 3) microneurographic recording of skin sympathetic nerve traffic (SSNA).
Results: For similar blood pressure values, patients with mild renal failure displayed MSNA values significantly greater than those found in age-matched controls, both when expressed as bursts incidence over time (51.3±2.8 vs 38.4±3.5 bs/min, $p<0.05$) and as bursts incidence corrected for heart rate (70.5±3.2 vs 54.8±5.6 bs/100 hb, $p<0.05$). In contrast, both HR and SSNA values detected in renal failure patients were not significantly greater than those found in healthy controls (HR: 72.2±3.1 vs 70.5±1.4 b/min, p=NS; SSNA: 12.3±1.3 vs 14.4±1.8 bs/min, p=NS). Furthermore, in renal failure patients with (n=6) and without (n=10) insulin resistance (HOMA index: 5.5±1.8 vs 1.4±0.2 a.u., $p<0.05$) MSNA values were superimposable (67.2±3.3 vs 70.5±4.2 bs/100 hb). Similarly, renal failure patients with (n=8) and without (n=8) left ventricular hypertrophy (LVMI: 130.5±5.3 vs 93.1±2.8 g/m^2, $p<0.05$) displayed not significantly different MSNA values (72.1±4.0 vs 73.9±4.1 bs/100 hb).
Conclusions: Thus in mild renal failure sympathetic activation does not appear to be generalized to the whole circulation, the cardiac and the skin district not displaying the adrenergic overdrive seen in the muscle circulation. They also show that, in contrast to what found in other pathologic states, sympathetic activation is not related to insulin resistance or potentiated by left ventricular hypertrophy.

P1480 Nicotine increases chemoreflex sensitivity to hypoxia in non smokers

J.F. Argacha, O. Xhaet, M. Gujic, D. Adamopolos, S. Beloka, C. Dreyfuss, J.P. Degaute, P. Van De Borne. *Erasme, Cardiology, Anderlecht, Belgium*

Background: The carotid body chemoreceptor contributes to cardiovascular regulation and represents the first line of defense against hypoxia. The effects of nicotine on chemoreflex regulation in non-smoking humans are unknown.
Method: We conducted a prospective, randomized, crossover, and placebo controlled study in 20 male non-smokers to test the hypothesis that nicotine increases chemoreflex sensitivity. The effects of two intakes of 2 mg nicotine tabs and placebo on sympathetic nerve activity to muscle circulation (MSNA), minute ventilation (Ve), blood pressure (BP) and heart rate (HR) during normoxia and 5 minutes of moderate isocapnic hypoxia (10%O_2, 90%N_2) were assessed in 10 subjects. Maximal end expiratory apneas were performed at baseline and at the end of the fifth minute of hypoxia. In a second experimental setting, we studied the ventilatory response to a more marked progressive isocapnic hypoxia in 10 other volunteers.
Results: T he second intake of nicotine increased mean BP during normoxia (from 87±2 to 92±3 mmHg $p<0.05$) and moderate hypoxia (from 87±2 to 93±3 mmHg $p<0.01$). Nicotine increased heart rate throughout the study ($p<0.05$). MSNA and Ve were not modified by nicotine during normoxia or moderate hypoxia. However, nicotine increased sympathetic activity markedly when apneas were allowed to continue until O_2 saturation decreased below 85% (511±44% increase in activity after the first intake, and 436±43% increase after the second intake, vs. 387±56% and 338±31 with placebo, respectively, $p<0.05$). Nicotine also increased the ventilatory response when O_2 saturation decreased to less than 85% in the second set of experiments ($p<0.05$).
Conclusion: This is the first study to demonstrate that nicotine increases peripheral chemoreflex sensitivity to large reductions in arterial oxygen content in healthy, male non-smokers.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

P1481 Exercise training restores baroreflex control of sympathetic nerve activity in hypertensive patients

M. Laterza[1], L.D.J. Matos[1], M.J.N. Alves[1], F. Roveda[1], I.C. Trombetta[1], A.M.W. Braga[1], E.M. Krieger[1], C.E. Negrao[2], M.U.B. Rondon[2]. *[1]Heart Institute(Incor), Univ Sao Paulo, Sao Paulo, Brazil; [2]Heart Institute and Sch Phys Ed and Sport,USP, Sao Paulo, Brazil*

Purpose: Previous studies demonstrated that exercise training improved baroreflex control of heart rate in hypertension. However, the effects of exercise training on baroreflex control of sympathetic nerve activity in hypertensive patients are unknown. We hypothesis that: 1) Exercise training would improve baroreflex control of muscle sympathetic nerve activity (MSNA) and heart rate in patients with hypertension; and 2) Exercise training would reduce MSNA and blood pressure in hypertensive patients.
Methods: Twenty never-treated hypertensive patients were randomly divided into two groups: Exercise-trained (n=11, 46±2 years) and untrained (n=9, 42±2 years) patients. An additional age-matched normotensive exercise trained group (n=12, 42±2 years) was also studied. Baroreflex control of MSNA (microneurography) and heart rate (ECG) was assessed by stepwise intravenous infusions of phenylephrine and sodium nitroprusside and analyzed by linear regression. Blood pressure was non-invasively monitored on a beat-to-beat basis. Exercise training consisted of three 60-min exercise sessions/week for four months.
Results: Under baseline conditions (pre intervention), blood pressure and MSNA were similar between hypertensive groups, but significantly increased when compared with the normotensive group. Baroreflex control of MSNA and heart rate was similar between hypertensive groups, but significantly decreased when compared with the normotensive group. In hypertensive patients, exercise training significantly reduced blood pressure ($P<0.01$) and MSNA ($P<0.01$) levels and significantly increased baroreflex control of MSNA and heart rate during increases ($P<0.01$ and $P<0.03$, respectively) and decreases ($P<0.01$ and $P<0.03$, respectively) in blood pressure. The baseline (pre intervention) difference in baroreflex sensitivity between hypertensive patients and normotensive individuals was no longer observed after exercise training. No significant changes were found in untrained hypertensive patients.
Conclusions: Exercise training restores the baroreflex control of MSNA and heart rate in hypertensive patients. In addition, exercise training normalizes MSNA and decreases blood pressure levels in these patients.

P1482 Brain natriuretic peptide and early cardiovascular adaptations in essential hypertension

D. Chatzis, C. Tsioufis, P. Pavlidis, E. Taxiarchou, D. Tsiachris, D. Tousoulis, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: Left ventricular (LV) diastolic dysfunction and aortic stiffening represent markers of adverse cardiovascular prognosis, closely associated in the early stages of essential hypertension (EH). In the present study, we tested the hypothesis whether brain natriuretic peptide (BNP) could be the intermediate link between the abovementioned parameters.
Methods: We studied 254 non-diabetic subjects with newly diagnosed stage I-II EH, without LV hypertrophy, and 62 normotensive controls matched for age, sex and smoking status. All the participants underwent a complete echocardiographic examination, as well as non-invasive measurement of carotid-femoral pulse wave velocity (c-f PWV) and determination of BNP levels. LV diastolic function was estimated by averaging the medial mitral annulus systolic and diastolic velocities (Em_{av}, Am_{av}) obtained in 5 consecutive cardiac cycles.
Results: The two groups did not differ regarding BNP concentrations. Hypertensives exhibited greater Am_{av} values and c-f PWV, as well as significantly lower Em_{av} and Em_{av}/Am_{av} ratio. A univariate analysis showed that BNP was significantly associated with office pulse pressure, LV mass index, Em_{av} and Em_{av}/Am_{av} ratio ($p<0.05$ for all cases). However, multiple regression analyses revealed that the main determinants of Em_{av}/Am_{av} ratio were c-f PWV ($p<0.05$), age and office diastolic BP ($p=0.03$ for both cases), while those of c-f PWV were Em_{av}/Am_{av} ratio, age and office SBP ($p<0.05$ for all cases).
Conclusions: BNP plasma levels are not independently related to indexes of LV diastolic function or large artery stiffness. Our findings weaken the role of BNP as a potent mediator of hypertensive structural and functional cardiovascular adaptations in newly diagnosed essential hypertension.

P1483 The effect of therapeutic reduction of sympathetic hyperactivity on baroreceptor reflex sensitivity in essential hypertension

J. Burns, D.A.S.G. Mary, A.F. Mackintosh, S.G. Ball, J.P. Greenwood. *Leeds Teaching Hospitals NHS Trust, Cardiology, Leeds, United Kingdom*

Purpose: Essential hypertension (EHT) and left ventricular hypertrophy (LVH) have been associated with sympathetic activation and cardiovascular risk, and are accompanied by impairment of baroreceptor reflex sensitivity controlling the heart rate (BRS). We planned to determine whether therapeutic reductions of sympathetic output and left ventricular mass (LVM) influenced the BRS impairment.
Methods: We measured muscle sympathetic nerve activity (MSNA) by peroneal microneurography, LVM by magnetic resonance imaging (MRI) and BRS by the Valsalva manoeuvre in two matched groups of 15 patients with newly diagnosed, untreated EHT and LVH. Equipotent anti-hypertensive regimens were given to the two groups. One group received Valsartan and Moxonidine (V/M), and the other Bendroflumethiazide and Amlodipine (B/A).The V/M and B/A groups were similar at baseline in terms of age (54±3.1 and 50±2.0 years), mean blood pressure (123±3.8 and 124±4.1 mmHg), heart rate (68 ±2.1 and 70±2.7 beats/min), body surface area (1.92±0.04 and 2.04±0.05 m^2), LVM index (LVMI) (85±5.2 and 83±3.5 g/m^2), MSNA (64±2.6 and 61±2.1 bursts/100 cardiac beats) and BRS (3.9±0.64 and 4.7±0.64 ms/mmHg).
Results: There were no significant changes in heart rate and body surface area. During both V/M and B/A therapy mean blood pressure (MBP) significantly (paired t test) decreased ($P<0.0001$) by 19±2.3% and 20±2.8% and LVMI decreased ($P<0.0001$) by 15±1.5% and 11±1.3%. MSNA significant decreased ($P<0.0001$) during V/M therapy by 17±2.9%, but not during B/A therapy. BRS decreased ($P<0.02$) during B/A therapy by -23±8.7% but not during V/M therapy. During V/M therapy there was a greater (unpaired t test) decrease of MSNA ($P<0.0001$) by 17.2±3.4% and LVMI ($P<0.04$) by 3.4±1.9% compared to B/A therapy, but these were not accompanied by significant improvement of BRS by V/M therapy.

	MBP (mmHg)	LVMI (g/m^2)	MSNA (bursts/100 beats)	BRS (ms/mmHg)
V/M Change	-25±3.5	-13±1.6	-11±1.6	0.50±0.93
B/A Change	-27±4.4	-10±1.3	-0.1±1.3	-1.03±0.43
Difference	2.7±5.6	3.0±1.9	10.6±2.1	1.55±1.0

Data expressed as mean ± SEM.

Conclusions: The results show that the therapeutic reduction of LVM and sympathetic activity does not improve the impairment of BRS in EHT, suggesting other mechanisms are responsible for BRS impairment.

P1484 Baroreflex sensitivity is depressed in patients with Sickle Cell Disease (Hb S)

W.A. Martins, H.F. Lopes, C. Mady, G.M. Riccio, E. Arteaga, F.M. Consolim-Colombo. *Sao Paulo, Brazil*

In patients with Sickle Cell Disease (Hb S) cardiovascular autonomic dysfunction has been described. In the present study we analyzed the cardiovascular reflex control of heart rate and baroreflex sensitivity (BRS) in 16 patients with homozygous inheritance of Hb S disease (HbS), in 13 with "sickling" trait (ST), in 13 iron-deficiency anemia (ID) and in 13 health volunteers (NL). The groups were matched by age (from 20 to 30 years), gender and ethnicity, and had a normal cardiac size by thorax Rx; patients with anemia did not present signs and symptoms of heart failure.
Methods: non invasive arterial blood pressure (BP) and heart rate (HR) were continuously recorded with FINAPRESS at rest (5 min) and during different standardized maneuvers: "diving" (20s), tilt table test (5 min), and IV infusion of a bolus of phenyleprine (100 m g) and sodium nitroprusside (50 m g) to calculate BRS (HR/BP index). Changes in HR and BP in response to all procedures were compared in each group and among groups using multiple anova tests.
Results: Hb levels were, respectively for HbS, ST, ID and NL groups: 8,4±2, 14,3±2, 9,3±2 and 13,9±1 g/dl. BP and HR were similar among groups at baseline.

HR and BP alterations in all groups

test/group	Hb S	ST	DI	NL
Delta HR diving (bpm)	6±2*	12±3	6±1*	12±2
Delta HR tilt t. (bpm)	8±1#	20±3	20±2	16±1
BP/HR index nitroprusside	4,5±0,3	4,7±0,4	10,4±0,6	9,7±0,6
BP/HR index phenyleprine	11,3±0,6	13,5±0,8	19,8±1,1	18,8±0,9

*$p<0,05$ Hb S and DI vs ST and NL groups, #$p<0,05$ Hb S vs all other groups, †$p<0,05$ Hb S and ST vs all DI and NL groups.

Conclusion: Our data indicates that young patients with Sickle Cell Disease and "sickling" trait exhibit depressed baroreflex sensitivity. Moreover, a significant a significant alteration in the parassimpathetic control (demonstrated during diving maneuver) are associated with low levels of HB.

P1485 Urinary albumin excretion and cardiac structural adaptations in essential hypertensive subjects: correlations from the Hippokration Hellenic Hypertension (3H) study

K. Dimitriadis, C. Tsioufis, D. Tsiachris, I. Skiadas, E. Taxiarchou, P. Missovoulos, D. Tousoulis, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: Microalbuminuria (MA) is an integrator of subclinical atherosclerotic damage and a potent marker of cardiovascular risk. The aim of the study was to determine the prevalence of MA in a large cohort of hypertensives and to investigate the relationships of urinary albumin excretion, expressed as the albumin to creatinine ratio (ACR), with left ventricular mass and left atrial dimensions.
Methods: A total of 1178 consecutive essential hypertensive subjects [604 men,

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

aged 56 years, office blood pressure (BP)=144/90 mmHg] that were included in the Hippokration Hellenic Hypertension (3H) study, an ongoing greek registry of hypertension-related target organ damage, were considered for analysis. According to ACR values determined as the mean of two non-consecutive morning spot urine, hypertensives were divided into those with MA (ACR=22-300 mg/g in men and ACR=30-300 mg/g in women) and those without MA (ACR<22 mg/g in men and ACR<30 in women). Furthermore, all participants underwent complete echocardiographic examination.

Results: 149 patients (12.6%) had MA and when compared to those without MA (n=1029) were older (58 vs 55 years, $p<0.05$), exhibited higher office systolic BP (149 vs 144 mmHg, p=0.001) and greater prevalence of type 2 diabetes (25 vs 12%, $p<0.0001$) and metabolic syndrome (50 vs 30%, $p<0.0001$). Moreover, microalbuminurics compared to normoalbuminurics had higher left ventricular mass index (LVMI) (108.9 vs 102 g/m^2, p=0.007), relative wall thickness (0.45 vs 0.43, $p<0.0001$), as well as left atrial diameter (3.98 vs 3.88cm, p=0.03) and left atrial volume (47.04 vs 43.23ml, p=0.003), independently of confounders. In the total population, ACR was associated with age (r=0.182, p=0.002), office systolic BP (r=0.109, $p<0.0001$), LVMI (r=0.219, $p<0.0001$), relative wall thickness (r=0.199, p=0.001) and left atrial volume (r=0.168, p=0.035). Regarding, left atrial volume it was related to office systolic BP (r=0.193, p=0.006), LVMI (r=0.352, $p<0.0001$) and relative wall thickness (r=0.166, $p<0.05$). By multiple regression analysis it was revealed that only age and office systolic BP were independent predictors of ACR ($p<0.05$ for both).

Conclusions: Among hypertensives that participated in the 3H study, 12.6% had MA and were characterized by increased left ventricular mass and left atrial dimensions. Moreover, the close association of LVMI and left atrial volume with albuminuria, supports that cardiac adaptations are important in the interpretation of the ACR-related risk.

P1486 Management of elderly patients with hypertension and orthostatic intolerance

G.-A. Dan, A.R. Dan, A. Buzea, C. Mitroi, C. Adam. *Colentina University Hospital, Cardiology, Bucharest, Romania*

Symptomatic orthostatic hypotension (hoT) and syncope are often seen in elderly patients (pts.) with long standing systemic hypertension (HBP). The management of elderly with concomitant HBP and hoT is challenging. The purpose of our opened prospective study was to evaluate 3 randomly assigned antihypertensive regimens in elderly pts. with HBP and associated symptomatic hoT with or without syncope. Between 2003 and 2006 we included 139 treated hypertensive pts. with symptomatic hoT including syncope, mean age 76± 13 yrs, mean systolic blood pressure (SBP): 161±14 mmHg. After a 5-7 days washout period the pts. were randomly assigned to: group A - 47 pts., treated with clonidine, group B - 47 pts., treated with moxonidine, and group C - 45 pts, treated with amlodipine. Medication was uptitrated to the maximal tolerated dose or a low-dose thiazide diuretic was added in order reach the target BP guidelines level. During the follow-up period (FU) of 18±4mo BP measurements were repeatedly performed (supine, orthostatic, and ABPM) and a tilt-test was performed at the beginning and the end of the study. The number of syncopal episodes, the tilt test response and the quality of life (QL) EQ-5D score were monitored.

Results: After the FU period SBP did not significantly differ between the three groups and did not reach the target. QoL score improved significantly in both clonidine and moxonidine groups (p: 0.05 vs. amlodipine, 0.05 vs. basal). The number of syncopal episodes decreased significantly in the clonidine group (p: 0.03 vs. basal), but not in the moxonidine and amlodipine groups. At the end of the FU period the drop in BP during the orthostatic measurement was significantly smaller in clonidine group (28±12 mmHg vs. 38±11 mmHg in moxonidine group and 47±11mmHg in amlodipine group group, p: 0.05). The number of tilt elicited syncopal or symptomatic hoT episodes was also significantly decreased in the clonidine group.

Conclusions: Management of HBP in pts. with orthostatic intolerance remains difficult. The old drug clonidine, by virtue of its peripheral effects, seems to be an efficient and well tolerated treatment in this difficult case.

P1487 PPARa stimulation with clofibrate exerts a blood presure lowering effect through different mechanisms in a time-dependent manner

A. Sanchez-Mendoza[1], M.L. Ibarra-Lara[1], L.G. Cervantes-Perez[1], F. Perez-Severiano[2], J.C. Martinez-Lazcano[2], G. Pastelin-Hernandez[1]. *[1]National Institute of Cardiology, Pharmacology, Mexico, Distrito Federal, Mexico; [2]National Institute of Neurology, Neurochemistry, Mexico, Distrito Federal, Mexico*

Peroxisome proliferator-activated receptors (PPARs) are a family of nuclear receptors that, upon activation with selective ligands, work as transcription factors. Recently, they have been implicated at different levels, in functioning of the cardiovascular system. Our aim was to study if PPAR a -stimulation with clofibrate exerts a lowering effect over blood pressure in rats with hypertension secondary to aortic coarctation and to explore a possible mechanism. Male Wistar rats (250-280g) were randomly distributed into three groups: 1) Sham-operated vehicle-treated; 2) Aortic coarctated vehicle-treated (AoCo-V); and 3) Aortic coarctated clofibrate (100mg/kg)-treated (AoCo-C). The treatment lasted for 1 or 21d starting the day of the surgery. At the end of the treatment, we meassured intracarotid blood pressure and obtained the hipertrophic kidney (HK) to measure, reactive oxygen species (ROS), peroxidated lipids, expression, and activity of superoxide dismutase-1 (SOD-1), catalase, and nitric oxide synthase-3 (NOS-3). PPAR a -stimulation by clofibrate lowered blood pressure at both 1d (111.2±2.3, 156.8±9.4, and 125±4.7 mmHg, for sham, AoCo-V, and AoCo-C, respectively); and 21d-treatment (110.1±6.1, 175±10.1, and 133.8±10.8 mmHg, for sham, AoCo-V, and AoCo-C, respectively). ROS increased after 1d in HK from AoCo-V rats and clofibrate partially prevented this effect (0.77±.2, 2.5±1, and 1.01±0.5 nmoles DFC/mgprot/min, for sham, AoCo-V, and AoCo-Clof, respectively). ROS were not modified after 21d of treatment in either group. The expression of SOD-1 increased significantly upon PPAR a -stimulation after 1d of treatment (3.6-fold) and returned to normal values by day 21 SOD-1 activity increased slightly in response to clofibrate. The activity of catalase increased in HK from AoCo-C at 1d and returned to normal at 21d. NOS-3 expression was not different after 1d treatment but was significantly higher in HK from AoCo-C at day 21. Angiotensin II receptors (AT1 and AT2) were inversely modified at day 21 of treatment in response to clofibrate treatment. AT1 expression decreased compared to AoCo-V, while AT2 increased in HK from AoCo-C compared to AoCo-V. Our results suggest that, in the early development of hypertension secondary to AoCo, the stimulation of PPAR a induces an increase in the antioxidant defences leading to an improvement of the endothelial factors that modulate the blood pressure. While in the subchronic phase, factors such as endothelial NOS and angiotensin II receptors seem to play a major role controlling the blood pressure.

P1488 Comparison of telmisartan with carvedilol in preventing atrial fibrillation recurrence in hypertensive patients: a multicentre study

D. Galzerano[1], S. Caselli[2], R. Breglio[3], G. Conforti[3], G. Saetta[3], B. Tuccillo[3], D. Lama[4], G. Paolisso[3], P. Capogrosso[3]. *[1]Cardiology Division, San Gennaro Hospital, Napoli, Italy; [2]La Sapienza University, Cardiology, Rome, Italy; [3]San Gennaro Hospital, Cardiology, Napoli, Italy; [4]II University, Geriatrics, Napoli, Italy*

Background: In antihypertensive therapy, blood pressure (BP) control and a lower incidence of atrial fibrillation (AF) is a pharmacological goal. The renin–angiotensin–aldosterone system (RAAS) plays an important role as a mediator of atrial remodeling in AF. Aim: To compare the antihypertensive treatments of telmisartan (an angiotensin receptor blocker [ARB]) with carvedilol (a β-blocker) in preventing the recurrence of AF in hypertensive patients with a history of recent atrial fibrillation.

Methods: We studied 144 mild hypertensive outpatients (systolic BP > 130, 80, < 100 mmHg). All patients were in sinus rhythm and had experienced one and four ECG-documented episodes of AF in the previous 6 months. Following a 1-week placebo period, patients were randomized to telmisartan 80 mg daily or carvedilol 25 mg daily and monitored for 1 year. The two groups were comparable regarding left ventricular (LV) mass, LV ejection fraction and left atrial diameter. BP and 24-hour ECG were recorded monthly. Each patient was asked to report any episodes of symptomatic AF and to undergo an ECG as early as possible.

Results: A total of 124 patients completed the study (telmisartan n = 66, carvedilol n = 58). After 12 months, mean BP values were significantly reduced in both groups with no significant difference between the two groups (telmisartan 154/97 to 123/75 mmHg, $p < 0.001$; carvedilol 153/94 to 125/78 mmHg, $p < 0.001$). An AF episode (symptomatic or asymptomatic) was reported in 13.6% of telmisartan patients versus 36.2% carvedilol ($p < 0.007$, $\chi 2$ test). Left atrial diameter, assessed by echocardiography, was lower in the telmisartan group but not significantly different (telmisartan 3.4 ±2.3 cm; carvedilol 3.6±2.4 cm).

Conclusions: Telmisartan appears more effective than carvedilol in preventing new episodes of AF in hypertensive patients with recurrent AF. Our results further suggest that ARBs, which target the RAAS by binding to angiotensin type 1 (AT1) receptors, could favourably affect electrical and structural atrial remodeling in hypertensive patients.

P1489 Candesartan produces great regression in the electrocardiographical left ventricular hypertrophy in patients with metabolic syndrome

A. Calderon, V. Barrios, C. Escobar Cervantes, V. Gonzalez-Pedel, A. Acena, S. Garcia, J. Ortega, R. Fernandez, E. Asin. *Madrid, Spain*

Introduction: The association of metabolic syndrome and left ventricular hypertrophy increases with exponential difference the cardiovascular risk in hypertensive patients. We have analysed the effect of candesartan in the electrocardiogram (ECG) improvement of left ventricular hypertrophy in patients with or without metabolic syndrome in the population of the SARA study.

Methods: The SARA trial is an open, single-arm, prospective study designed to evaluate the efficacy of a 12-month candesartan-based regimen (8mg, 16mg, +add-on therapy) for the ECG-LVH regression in uncontrolled hypertensive patients in daily clinical practice. 202 patients were included, (61.3±18.5 yrs; 56% females) 27.4% of which were diagnosed of metabolic syndrome according to NCEP-ATPIII criteria. At baseline and at study end, ECGs were performed and sent to a core lab to be blindly analyzed by a unique investigator. Cornell (CDP)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

and Sokolow (SDP) voltage duration product, Cornell voltage (CV) and Sokolow voltage (SV) were determined. ECG-LVH criteria were SDP≥2880 mm x ms and CDP≥2440 mm x ms.
Results: The basal prevalence of left ventricular hypertrophy were 26.6% (CDP) and 29.3% (SDP). At the beginning, the patients with metabolic syndrome presented higher systolic blood pressure (164 mmHg vs 160 mmHg, p=0.012), without any differences as to diastolic blood pressure, age, sex and ECG variables. In the patients with metabolic syndrome there was a higher decrease for SDP (-247 vs -27 mm x ms, p=0.045), SV(-1.73 vs -0.53 mm, p=0.045), CV (-1.92 vs -0.51 mm, p=0.036) and CDP(-157 vs -49 mm x ms, p=0.15). When the study was finished there was a left ventricular regression according to CDP and SDP in 25% of the patients with metabolic syndrome and 19% in patients without metabolic syndrome (p=0.065). The predictive factors of left ventricular hypertrophy regression were high diastolic blood pressure (p=0.048) and high values of SDP, SV and CV.
Conclusions: Candesartan produces more decrease of electrocardiographical parameters of left ventricular hypertrophy in patients with metabolic syndrome than in patients without metabolic syndrome. Candesartan produces left ventricular regression in 25% of the patients with metabolic syndrome, considering diastolic blood pressure and left ventricular hypertrophy ECG criteria as the major predicting factors. Candesartan is an efficient therapy in the treatment of hypertensive patients with metabolic syndrome.

P1490 Exaggerated blood pressure variability aggravates hypertensive cardiac remodeling through the angiotensin II-mediated inflammation

N. Takayama, H. Kai, H. Kudo, A. Ikeda, D. Fukui, T. Mori, T. Iaizumi. *Kurme University School of Medicine, Cardiology Department, Kurume, Japan*

Purpose: It has been reported that hypertensive patients with large blood pressure (BP) variability have greater risk of cardiovascular events and exaggerate end-organ damages. However, the pathogenesis is unknown. The aims of this study were to investigate the effects of exaggerated BP variability on hypertensive cardiac remodeling and the underlying mechanism.
Methods: We performed bilateral sino-aortic denervation (SAD) or sham operation in spontaneous hypertensive rats (SHRs). Seven weeks after the operation, 24-hour BP was monitored telemetrically in SAD+SHRs and sham+SHRs.
Results: SAD+SHRs showed greater BP variability parameters, such as standard deviation and covariance of mean BP, compared with sham+SHRs. At Week 7, both groups showed concentric LV hypertrophy, and SAD enhanced LV hypertrophy. SAD+SHRs enhanced myocardial fibrosis by 4.7-fold, relative to sham+SHRs. Perivascular macrophage infiltration was evident in SAD+SHRs, but not in sham+SHRs. SAD remarkably upregulated expressions of myocardial angiotensinogen and monocyte chemoattractant protein-1 (MCP-1). To determine the role of angiotensin II in the BP variability-induced cardiac remodeling, nondepressor dose of angiotensin II receptor blocker, candesartan, was orally given to SHRs after SAD operation (SAD+Cand+SHRs). The small dose of candesartan significantly reduced the SAD-enhanced LV hypertrophy and myocardial fibrosis without any effects on BP variability. Moreover, in SAD+Cand+SHRs, the SAD-induced MCP-1 upregulation and macrophage accumulation were almost reversed to the levels of sham+SHRs.
Conclusion: Exaggerated BP variability aggravates hypertensive cardiac hypertrophy and fibrosis through chronic activation of inflammatory process. And, angiotensin II would play a key role in the activation of the inflammatory process, independently of the presser effect.

P1491 Tissue Doppler assesment of left atrial appendage function by transesophageal echocardiography in systemic hypertensive patients in sinus rhytm and its relation with NT-proBNP levels

E. Tenekecioglu[1], T. Peker[2], M. Yilmaz[1]. *[1]Siirt State Hospital, Cardiology, Siirt, Turkey; [2]Bursa Postgraduate Education Hospital, Cardiology-2, Bursa, Turkey*

The aim of this study is to assess LAA function as indicated by LAA blood flow velocities by pulsed wave(PW) flow by TEE and wall contraction velocities by TDI and its relation with NT-proBNP in hypertensives.
Methods: TEE was performed in 48 hypertensive in sinus rhythm, aged 40 to 55 with normal systolic function and in 20 control subjects without cardiovascular disease, aged 43 to 54.PW sample was obtained at proximal third of appendage with the optimum parallel Doppler alignment to LAA blood flow.In the same view TDI pulsed sample was placed at proximal third of medial (TDI-M) and lateral (TDI-L) free wall of LAA.A triphasic flow pattern of D1 (early diastolic outflow) before P-wave, followed by biphasic waves of D2(emptying velocity) and D3(filling velocity) were identified by both methods.NT-proBNP levels were measured by Roche Elecsys test.
Results: A triphasic PW flow and TDI pattern was recorded in all of 68 (%100) patients from TDI-L and TDI-M walls. In hypertensive group PW late emptying and filling velocities($p<0.05$) and TDI velocities of both medial and lateral walls($p<0,05$) were significantly reduced compared with control group.The LAA emptying velocities and TDI D2 velocities of both medial and lateral walls in hypertensives had a significant negative correlation with diastolic blood pressure,systolic blood pressure, left atrial diameter and NT-proBNP levels.With TEE, LA SEC was present in 10(%22) of 48 hypertensive patients.No thrombus was detected in hypertensive group.In hypertensive group NT-proBNP values were significantly higher compared to control group($p<0.01$).
Conclusion: In patients with hypertension, marked elevation of afterload imposed on left atrium involve both left atrium and LAA, resulting in impairment of LAA function assessed by PW and TDI analysis of LAA. The findings suggest that measurement of LA appendage blood flow velocities and TDI can be used to predict contractile function by TEE,elevated left ventricular filling pressure was correlated with elevated NT-proBNP levels in patients with hypertensive patients.

P1492 The association between viscosity and cardiovascular risk may reflect the central systolic stress response to light activity: an exercise hemodynamic study

J. Sharman[1], D. Holland[2], K. Kostner[1], H. Fairweather[1], G. Macdonald[1], T.H. Marwick[1]. *[1]University of Queensland, Department of Medicine, Brisbane, Australia; [2]University of Queensland, Medicine, Brisbane, Australia*

Purpose: Increased blood viscosity is associated with early atherogenesis and increased cardiovascular (CV) risk. While the mechanism of these associations is unclear, it may be related to increased arterial wave reflection during activities of daily living. This study aimed to test this hypothesis.
Methods: Twenty pts (14 males; aged 61±12y) with polycythemia rubra vera (n=16) or hemachromatosis (n=4) were studied at rest and during cycle exercise at 50% of maximal heart rate, before and after venesection (500ml, volume replaced with saline) to elicit an acute decrease in plasma viscosity at stable blood pressure (BP). Radial tonometry was used to derive central BP and augmentation index (AIx) as a marker of arterial wave reflection. Healthy controls (n=20) underwent the same protocol without venesection.
Results: Venesection caused a significant decrease in plasma viscosity (1.46±0.10 to 1.41±0.11; $p<0.05$), protein and hemoglobin ($p<0.05$ for all) in the pt group, but these parameters did not significantly change in the controls ($p>0.50$ for all). Exercise AIx was significantly reduced in response to venesection, despite lack of significant change in mean arterial pressure, central or peripheral BP. Resting and exercise hemodynamics were not significantly changed in controls (Table). In patients, exercise AIx was significantly related to plasma viscosity ($r=0.35$; $p<0.01$).

Hemodynamics of patients and controls

		Controls (n=20)		Patients (n=20)	
		Pre Rx	Post Rx	Pre Rx	Post Rx
AIx (%)	Rest	11±14	9±13	27±11	25±11
	Exercise	4±12	2±12	31±11	25±10*
MAP (mmHg)	Rest	84±10	82±8	100±8	100±8
	Exercise	88±12	90±8	111±12	108±10
Heart rate (bpm)	Rest	59±10	58±10	72±12	66±10*
	Exercise	93±13	96±8	92±12	95±15
Central SBP (mmHg)	Rest	101±12	98±10	124±10	125±11
	Exercise	106±15	107±11	138±16	134±14

Rx=treatment; *$p<0.001$ compared to pre Rx.

Conclusions: Acute reduction in plasma viscosity lowers the magnitude of arterial wave reflection during light activity. Our findings imply that the increased CV risk associated with viscosity may be related to central hypertension during activities of daily living.

P1493 Impaired vasodilator capacity in normotensive offspring of hypertensive parents

N. Taha, M. Abdel-Kader, E.S. Mohammad, H.M. Ali. *Al-Minia University, Cardiology, Minia, Egypt, Egypt*

Background: Blood pressure (Bp) levels appear to have strong familial tendencies. An estimated 30-60% of the variation of the BP between individuals, after adjustment of age and sex, is attributed to gene factors. Recent reports suggest occurrence of endothelial dysfunction in development of essential hypertension. The defective nitric oxide production results in reduced vasodilator capacity of the blood vessels, with consequent increase in the peripheral resistance and Bp.
Aim of work: is to address the genetic familial factor in hypertension through

Abstract P1491 – Table 1

	PW-D1 (cm/s)	PW-D2 (cm/s)	PW-D3 (cm/s)	TDI-M D1 (cm/s)	TDI-M D2 (cm/s)	TDI-M D3 (cm/s)	TDI-L D1 (cm/s)	TDI-L D2 (cm/s)	TDI-L D3 (cm/s)	NT-proBNP (pg/ml)
HTN	13±7	32±5	26±23	4.08±1.6	9.52±2.1	6.89±3.7	5.3±1.9	12±3.4	7.99±2.7	414.2±231.0
Control	18±4	55±21	51±27	7.12±3	13.87±4	10.43±5	6.9±2	15.6±5.1	14±5.3	35.6±16.4
p	<0.05	<0.001	<0.001	<0.05	<0.05	<0.05	=0.06	<0.05	<0.01	<0.01

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

the evaluation of vasodilator capacity in normotensive offsprings of hypertensive parents.
Patients and methods: 80 Subjects (15 to 35 years old) were classified according to ambulatory Bp monitoring (ABPM) into: Group 1: 40 subjects with normal Bp but one or both of their parents is hypertensive; 24 subjects had only one hypertensive parent (Group 1A), while 16 subjects had both parents hypertensive (Group 1B). Group 2: 40 subjects with normal Bp and normotensive parents served as controls. Both groups were subjected to: History taking, Clinical Examination, FBS and PPBS, lipogram, ANPM, Colored Duplex Ultrasound to test the vasodilator capacity before and after reactive hyperaemia and Glceryl trinitrate (GTN)-mediated dilatation.
Results: Flow mediated dilatation (FMD) was lower in group 1 than in group 2 (5.71±3.63 vrs 13.99±5.95, $p<0.001$). Meanwhile, GTN mediated dilatation was not different (16.55±6.63 vrs 13.99±5.45, p=0.408) thus rendering the dilatation ratio significant (0.36±0.23 vrs 0.94±0.08, $p<0.001$). Furthermore, the same pattern was also observed comparing Group 1A with group 1B (8.1±1.86 vrs 2.11±2.39, $p<0.001$ for FMD; 18.8±7.11 vrs 14.11±5.35 p=0.187 for GTN and 0.49±0.13 vrs 0.17±0.20 $p<0.001$ for the dilatation ratio) Conclusion: Offspring of hypertensive parents have obvious endothelial dysfunction preceding their development of hypertension. This trait is inherited to them from their hypertensive parents, and is more evident if was inherited from both parents. This may be due to a genetic defect in nitric oxide (NO) synthesis pathway either in production of NO synthase enzyme (NOS) isoforms, co-factors for NOS induction and inhibition and/or L-arginine which is the. NO substrate or its analogues.

P1494 N-terminal pro-brain natriuretic peptide and pulse pressure in patients with essential hypertension

E. Rosello-Lleti[1], M. Rivera Otero[1], A. Salvador[1], L. Grigorian[2], J.R. Calabuig[2], L. Mainar[2], V. Mora[2], V. Bertomeu[3]. *[1]Valencia, Spain; [2]Santiago, Spain; [3]Alicante, Spain*

Purpose: N-terminal pro-brain natriuretic peptide (NT-proBNP) is a useful biomarker in heart failure. We assessed the hypothesis that NT-proBNP maybe useful in the characterization of patients diagnosed with essential hypertension (HT). The purpose of this study was to compare NT-proBNP with systolic (SBP), diastolic (DBP), pulse pressure (PP) and with left ventricular mass index (LVMI) in asymptomatic patients with HT without dilated, ischemic or valvular cardiomyopathy or permanent arrythmia.
Methods: We have studied 260 patients, age 60±13, which had been diagnosed of HT and 40 age-matched controls. A HT questionnaire and echo-Doppler study were performed on these patients. All plasma samples were centrally analysed and NT-proBNP (pg/ml) was determined. We also measured SBP, DBP, PP (mm Hg) and LVMI (g/m^2).
Results: For the whole population NT-proBNP levels were 147±266, SBP 148±20, DBP 87±11, PP 62±18 and LVMI 126±29. In the control group we found 41±23. In the HT non-hypertrophic group we found 41±35 and in the hypertrophic patients NT-proBNP was 274±13, $p<0.0001$. When we divided NT-proBNP in quartiles and we compared with SBP values (144±18, 146±17, 148±22, 159±23), we found $p<0.0001$. When we divided NT-proBNP in quartiles and we compared with PP (56±13, 58±14, 61±19, 72±20), we found $p<0.0001$. When we correlated NT-proBNP with SBP and PP we found r=0.3, $p<0.0001$ and r=0.4, $p<0.0001$. The ROC curve of NT-proBNP for detection of hypertrophy yielded an AUC of 0.89±0.2, $p<0.0001$. From the ROC for NT-proBNP, the optimal cut-off value (199 pg/ml) had a specificity and sensitivity of 100% and 39% for detection of hypertrophy. Furthermore, to investigate wether NT-proBNP levels are independent predictors of hypertrophy a logistic regression was performed. When the multivariate model was applied, NT-proBNP was a strong predictor of hypertrophy ($p<0.0001$).
Conclusions: In this study we found that SBP and PP are related with NT-proBNP levels in a group of asymptomatic patients with HT. NT-proBNP was a strong predictor of hypertrophy. These results agree with the utility of NT-proBNP in the characterization of HT patients and the importance of controlling SBP in patients diagnosed with HT.

P1495 Association of serum testosterone and arterial compliance in essential hypertension

X. Li[1], X.Q. Xu[2], T.M. Tong[1], L.X.Z. Lu[1], Z.H.F. Zhang[1], Z.Y.L. Zhou[1], C.K.J. Cao[1], H.J. Huang[1]. *[1]First Affiliated Hospital of Nanjing Medical, Cardiology Department, Nanjing, China, People's Republic of; [2]First Affiliated Hospital of Nanjing Medical, Department of Cardiology, Nanjing, China, People's Republic of*

Purpose: High androgen levels are presumed by many to explain the higher incidence of cardiovascular disease in men than in women. Large (C1) and small (C2) arterial compliance is considered as sensitive markers for cardiovascular disease. Therefore, whether testosterone is associated with arterial compliance need to be investigated.
Methods: According to the definition of hypertension of systolic blood pressure(SBP) and/or diastolic blood pressure (DBP) ≥140/90mmHg, 356 subjects were divided into four groups; (i) a male control group (MCG), (ii) a male hypertensive group (MHG), (iii) a female control group (FCG), and, (iv) a female hypertension group (FHG). Arterial compliance indexes were measured with the CVProfilor DO-2020 CardioVascular Profiling System. Serum testosterone (T) was measured using enzyme chemiluminescenceand method. Insulin was measured using a radioimmunity kit. Insulin was measured using a radioimmunity kit.
Results: (1) The levels of C1 and C2 in both hypertension groups were lower than those in the control groups. T in MEH was lower than in MNC, but there was no difference in T between FNC and FEH. (2) T was significantly positively correlated with C1 and C2, negatively correlated with blood pressure, triglyceride, fasting blood glucose, body mass index and insulin resistance index in males. T was negatively correlated with body mass index in females. (3) Multivariate regression analysis showed that age, C1, C2 and T were risk factors of SBP in males, while age, C1, C2 and heart rate were risk factors of SBP in females.
Conclusions: Arterial compliance was decreased in hypertension. The reduced serum testosterone might contribute to hypertension and the decreased arterial compliance in middle-aged males.

P1496 Hypertension, multiple cardiovascular risk factors and mortality: The Singapore Cardiovascular Cohort Study

J. Lee[1], S. Ma[2], D. Heng[1], S.K. Chew[1], K. Hughes[3], E.S. Tai[4]. *[1]National University of Singapore, Comm, Occup & Fam Med, Singapore, Singapore; [2]Ministry of Health, Singapore, Singapore; [3]National University of Singapore, Comm, Occup & Fam Med, Singapore, Singapore; [4]Singapore General Hospital, Endocrinology, Singapore, Singapore*

Purpose: Limited information is available from prospective population based cohorts in Asia with regards to the effect of hypertension, either alone or in combination with other CVD risk factors. The aim of this study was to examine these effects in Chinese, Malays and Asian Indians living in Singapore.
Methods: A prospective study, the Singapore Cardiovascular Cohort Study (SCCS) has been conducted using 3 previously conducted cross-sectional studies including: Thyroid Heart Study (1982-1984), the National Health Survey (1992) and the National University of Singapore Heart Study (1993-1995). Prospective follow-up was done by using the unique identity number to link baseline data with the Singapore National Registry of Deaths to obtain mortality data up to 31st December 2004. Hypertensive (HTN) individuals were defined as having SBP ≥140mmHg and/or DBP≥90mmHg and/or currently being treated for hypertension. HTN individuals were further grouped according to the presence of other CVD risk factors as defined by the recommendations of the JNC-7. Outcomes included all-cause and CVD (ICD-9 410-410, 430-438) mortality. Cox proportional hazards regression will be used to obtain adjusted hazard ratios (HR) and 95% confidence intervals (95%CI) for mortality.
Results: The study included 5830 individuals (81757py, mean follow-up time 14yrs). HTN individuals with ≥2 CVD risk factors had the highest risk of all-cause (adjusted HR 2.3;95%CI 1.9-3.0) and CVD (adjusted HR 4.2; 95%CI 2.8-6.2) mortality compared to non-hypertensive individuals. An increasing risk of mortality was found for increasing number of CVD risk factors in HTN participants. Of these risk factors, the presence of diabetes mellitus and smoking significantly contributed to all-cause mortality whilst elevated total-C/HDL-C ratio, diabetes and smoking significantly contributed to CVD mortality in HTN participants.
Conclusions: An increased risk of mortality was found for HTN individuals with concurrent CVD risk factors. This suggests that, in Asia as with other populations, the identification and treatment of concomitant co-morbidities is an important part of the management of the hypertensive individuals.

P1497 The value of ambulatory arterial stiffness index (AASI) in patients with metabolic syndrome

I. Pop, C. Matei, M. Rugina, C. Ginghina, E. Apetrei. *Institute of Cardiovascular Diseases, Cardiology, Bucharest, Romania*

Aims: The purpose of this study was the evaluation of the ambulatory arterial stiffness index (AASI) in hypertensive patients (pts.) with or without metabolic syndrome (MetSyn).
Methods: One hundred ninety-five hypertensive patients (47% male, age >21years, medium age 57.9 years) underwent a 24-hour ambulatory blood pressure monitoring (ABPM) in our Cardiology Department were evaluated regarding medical history, renal function and presence of metabolic syndrome (International Diabetes Foundation criteria). The device used for ABPM was BR-102 (Schiller AG, Switzerland) and AASI was calculated for each patient as 1–regression slope of plotted diastolic against systolic blood pressure values. Statistical analysis was done with EpiInfo 2000 statistical software package, version 3.3.2.
Results: In our study group there was no difference in the mean AASI value between men and women, stratified by age. The patients were divided in two groups according to absence (group A, 131 pts.) or presence (group B, 64 pts.) of MetSyn. There were no statistically significant differences between this groups regarding age, sex, history of important cardiovascular diseases. The mean AASI was found statistically different between groups A and B only for men between age 51-60 (0.46 vs. 0.64, $p<0.05$), and 71-80 (0.57 vs. 0.35, $p<0.05$). We observed increasing of AASI with age (0.36 for age 21-30 compared to 0.67 for age 71-80, $p< 0.05$), but younger male patients in group B had lower AASI compared to corresponding patients in group A (0.36 vs. 0.44, p= ns). Mean AASI increases with age in people with the same BMI category, less evident for obese patients (BMI over 30) - see figure 1. Also, there is no statistically significant difference

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

between mean AASI in normal compared to overweight or obese patients over 41years-old (0.54 vs.0.48 vs. 0.48).
Conclusions: AASI increase statistically significant with age and there is no difference in mean values of AASI between male and female, adjusted by age. Presence of metabolic syndrome or obesity in hypertensive patients does not influence the AASI value in the same age category.

P1498 Blood pressure control rate by ambulatory blood pressure monitoring in hypertensive patients with coronary heart disease

J. Segura[1], M. Gorostidi[2], J. Sobrino[3], A. De La Sierra[2], J.L. Llisterri[4], J. Alonso[5], J.R. Banegas[6], L.M. Ruilope[3] on behalf of the Spanish Society of Hypertension ABPM Registry. *[1]Hospital 12 De Octubre, Hypertension Unit. Nephrology Department, Madrid, Spain; [2]Aviles, Spain; [3]Barcelona, Spain; [4]Valencia, Spain; [5]Toledo, Spain; [6]Madrid, Spain*

We studied the effectiveness of blood pressure (BP) control outside the clinic by using ambulatory BP monitoring (ABPM) among a large number of hypertensive subjects treated in primary care centers across Spain (N=34563). This study is included in a project comprising a nation-wide network in which more than 900 primary-care physicians send ABPM registries together with clinical records to a central database via internet since June 2004.
This analysis focused on patients presenting coronary heart disease (CHD), according the information provided by their primary care. Office-based BP was calculated as the average of 2 readings. Twenty-four-hour ABPM was performed using a SpaceLabs 90207 monitor under standardized conditions.
We identified 2188 patients with CHD. A total of 632 patients (28.9%) had their office BP controlled, 1187 (54.3%) were controlled according to daytime ABPM ($p<0.001$), and 790 (36.1%) were controlled when 24-h ABPM was considered ($p<0.001$). The proportion of office resistance or underestimation of patients' BP control by physicians in the office (office BP $\geq$140/90 mm Hg and average daytime ambulatory BP $<$135/85 mm Hg) was 43.6%, and the proportion of isolated office control or overestimation of control (office BP $<$140/90 mm Hg and average daytime ambulatory BP $\geq$135/85 mm Hg) was 19.5%.
In hypertensive patients presenting CHD, ambulatory-based hypertension control was better than office-based hypertension control. Daytime ABPM revealed that true BP control is near twice higher than office BP control. However, the burden of underestimation and overestimation of BP control at the office is highly remarkable. Physicians should be aware that the likelihood of misestimating BP control is higher in these subjects.

P1499 Ambulatory blood pressure pattern in patients with congestive heart failure

R. Hermida[1], J.R. Gonzalez-Juanatey[2], D.E. Ayala[3], C. Calvo[1]. *[1]University of Vigo, Bioengineering & Chronobiology Labs., Vigo, Spain; [2]Hospital Clinico Universitario, Cardiology and Coronary Unit, Santiago, Spain; [3]University of Vigo, Bioengineering & Chronobiology Labs., Vigo, Spain*

Purpose: A recent trial demonstrated that a non-dipping blood pressure (BP) pattern and increased nighttime diastolic BP were predictors of congestive heart failure (CHF) in elderly men [JAMA. 2006;295:2859-2866]. Several small studies, based on low-reproducible 24h ambulatory BP monitoring (ABPM), have also suggested that patients with CHF are commonly characterized by a prevalent non-dipping BP pattern. Accordingly, we have investigated the circadian BP pattern in patients with CHF who were evaluated by 48h ABPM.
Methods: We studied 106 patients with CHF (67 men and 39 women), 66.5$\pm$12.9 years of age. BP was measured at 20-min intervals from 07:00 to 23:00h and at 30-min intervals at night for 48h. Blood samples and 24h urine collection were obtained the same day before starting ABPM. Physical activity was simultaneously monitored every minute by wrist actigraphy to accurately calculate the diurnal and nocturnal BP means for each patient.
Results: The prevalence of non-dipping among patients with CHF was 73.6%. Most important, 30.2% of the patients presented a high-risk riser pattern (nighttime BP above daytime mean). Daytime and 24h means of systolic BP were comparable between dippers and non-dippers ($P>0.169$). For diastolic BP, there was no difference between groups in nighttime mean, while daytime and 24h means were significantly lower in non-dippers. Accordingly, ambulatory pulse pressure (PP) was larger in non-dippers for the entire 24h ($P<0.001$). Despite the limited sample size, non-dippers, compared to dippers, presented a tendency for lower HDL-cholesterol and glomerular filtration rate, and higher levels of glucose, serum creatinine, fibrinogen and 24h urinary albumin excretion.
Conclusions: Patients with CHF have a large prevalence of blunted nighttime decline in BP. One-third of the patients in this study presented a riser pattern, associated to a very high cardiovascular risk. In CHF, non-dipping is also associated to alterations in relevant markers of cardiovascular risk, and increased prevalence of microalbuminuria and chronic kidney disease. Patients with CHF should be evaluated by ABPM in order to establish a proper time-specified therapeutic regimen that could reduce the prevalent high-risk non-dipper pattern.

P1500 Pulse pressure predicts myocardial silent ischaemia in asymptomatic type 2 diabetics

M. Gomez[1], D. Sanmiguel Cervera[1], J.L. Diez Gil[1], K. Garcia Malpartida[1], I. Roldan Torres[1], M.T. Tuzon Segarra[1], P. Aguar Carrascosa[1], A. Salvador Sanz[2], A. Hernandez Mijares[1], A. Rincon De Arellano Castellvi[1]. *[1]Hospital Dr. Peset, Valencia, Spain; [2]Hospital La Fe, Cardiology, Valencia, Spain*

Pulse pressure (PP) denote arterial stiffness and is a better predictor of coronary disease than systolic or diastolic blood pressure in older adults. Whether this is also true in asymptomatic type 2 diabetics is less known.
Purpose: To examine the relationship between PP and the presence of silent myocardial ischemia (SMI) in type 2 diabetics (DM2).
Methods: we performed a cross-sectional study recruiting DM2 men without any known cardiovascular, medullar or pelvic disease. PP was calculated as the difference between the averaged systolic blood pressure (SBP) and diastolic blood pressure (DBP) readings measured with non-invasive 24-h ambulatory blood pressure monitoring (ABPM). SMI detection followed a predetermined protocol including 24h ECG ambulatory monitoring and an exercise test. A myocardial perfusion imaging test was performed if necessary.
Results: eighty-one asymptomatic DM2 men were included. Eleven patients (13.6%) had SMI. Patients with SMI were older (average 60.8 y. vs 54.8 y.) with a trend towards longer DM2 (median 12 y. vs 5 y.). Clinical and analytical parameters were similar between groups with and without SMI. Patients with SMI had a greater PP (62.0 mmHg vs 49.97 mmHg; $p < 0{,}001$). PP showed a good discrimination power to differentiate between the presence or absence of SMI (area under the ROC curve: 0.80; 95% CI 0.68-0.92; p=0.001). For a PP value of 51 mmHg a 91% sensitivity and 58% specificity was obtained. After adjusting for possible confounders, the odds ratio of PP to predict SMI was 3.13 (95% CI 1.13-8.67) for every 10 mmHg in PP increase.
Conclusions: Increased levels of pulse pressure are associated with SMI in asymptomatic DM2 men. To determinate PP with ABPM seems to be useful in the selection of DM2 patients with higher risk of coronary artery disease.

P1501 Relationship between heart rate and microalbuminuria in patients at high-risk for cardiovascular disease: results from the i-SEARCH study

J.-C. Reil[1], N. Danchin[2], M. Thoenes[3], P. Bramlage[4], M. Volpe[5], M. Boehm[6]. *[1]Universitaetsklinikum des Saarlandes, Klinik fuer Innere Medizin III/Kardiologie, Homburg/Saar, Germany; [2]Hospital Europeen Georges Pompidou, Department of Cardiology, Paris, France; [3]Sanofi-Aventis, Paris, France; [4]Technical University of Dresden, Institute of Clinical Pharmacology, Dresden, Germany; [5]University of Roma "La Sapienza", Andreas Hospital, Roma, Italy; [6]Universitaetsklinikum des Saarlandes, Klinik fuer Innere Medizin III/Kardiologie, Homburg/Saar, Germany*

Background: Microalbuminuria (MAU) is an indicator of impaired renal function and a relevant risk predictor for cardiovascular events. An increased heart rate is closely correlated with increased cardiovascular mortality. The International Survey Evaluating Microalbuminuria Routinely by Cardiologists in Patients with Hypertension (i-SEARCH) investigated 21,050 patients with hypertension and risk factors for cardiovascular disease to analyse the relationship between increased heart rate and the prevalence of MAU.
Methods and results: The study was performed worldwide in 26 countries from September 2005 to March 2006. Heart rate, blood pressure, urine albumin and serum creatinine were measured as key parameters. With increasing heart rate ($>$80 bpm to $<$120 bpm) the proportion of patients with MAU increased from 63% to 69%. The odds ratio for MAU increased with increasing heart rate (heart rate 80-100 bpm compared with 60 bpm, OR, 1.47 [95% CI, 1.29-1.68, $p<0.0001$], and heart rate100-120 bpm compared with 60 bpm, OR, 1.56 [95% CI, 1.22-1.99, p=0.0004]). The prevalence of MAU was similar whether patients were receiving beta-blockers or not. On the contrary, the occurrence of MAU was significantly reduced in physically active patients compared with sedentary patients (OR, 0.78; 95% CI, 0.73-0.84, $p<0.0001$).
Summary: These results show, that heart rate is an independent predictor for the prevalence of MAU in hypertensive patients with cardiovascular risk factors. In contrast to beta-blocker therapy, physical activity markedly decreased the occurrence of MAU with increasing heart rates. Further controlled and prospective studies are needed to prove that lowered heart rates in combination with MAU can significantly reduce kidney damage, as well as cardiovascular events.

P1502 Prevalence and correlates of microalbuminuria in essential hypertensive subjects: insights from the Hippokration Hellenic Hypertension (3H) study

C. Tsioufis, K. Dimitriadis, E. Taxiarchou, D. Chatzis, E. Vezali, A. Kakkavas, C. Mihas, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: Microalbuminuria (MA) is a marker of subclinical atherosclerosis progression and it is related to unfavorable outcome. In this study we sought to determine the prevalence of MA in a large cohort of hypertensives and to investigate

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

the relations of the albumin to creatinine ratio (ACR), with diverse clinical and biochemical cardiovascular risk factors.
Methods: A total of 1178 consecutive essential hypertensive subjects [604 men, aged 56 years, office blood pressure (BP)=144/90 mmHg] that were included in the Hippokration Hellenic Hypertension (3H) study, an ongoing registry of hypertension-related target organ damage, were considered for analysis. According to ACR values determined as the mean of two non-consecutive morning spot urine samples, patients were divided into those with MA (ACR=22-300 mg/g in men and ACR=30-300 mg/g in women) and those without MA (ACR<22 mg/g in men and ACR<30 in women). All participants underwent venous blood sampling for estimation of metabolic profile.
Results: 149 patients (12.6%) had MA and when compared to those without MA (n=1029) exhibited higher office systolic BP (149 vs 144 mmHg, p=0.001), left ventricular mass index (108.9 vs 102 g/m^2, p=0.007) and greater prevalence of type 2 diabetes (25 vs 12%, p<0.0001) and metabolic syndrome (50 vs 30%, p<0.0001). Moreover, microalbuminurics compared to normoalbuminurics had lower high-density lipoprotein (49.9 vs 53.5 g/dl, p<0.05), heightened triglycerides (149 vs 122 mg/dl, p<0.0001), fibrinogen (339 vs 321 mg/dl, p=0.04) and homocysteine levels (14.1 vs 12.5 μmol/l, p=0.01). In the total population, ACR was associated with age (r=0.18, p=0.02), office systolic BP (r=0.109, p<0.0001), and triglycerides (r=0.122, p<0.05), while exhibited no relation to fibrinogen and homocysteine (p=NS). Multiple regression analysis revealed that office systolic BP and triglycerides were independent predictors of ACR (p<0.05).
Conclusions: Among hypertensives that participated in the 3H study, 12.6% had MA and were characterized by adverse clinical and biochemical phenotype. These findings suggest that ACR determination is a useful tool to improve cardiovascular risk stratification in this setting.

P1503 The predictive value of relative changes of central blood pressure is independent of age. Results from the Aortic Blood Pressure and Survival (ABPS) Study

P. Jankowski, K. Kawecka-Jaszcz, D. Czarnecka, K. Styczkiewicz, M. Brzozowska-Kiszka, M. Loster, B. Kiec-Wilk, M. Kloch, L. Bryniarski, D. Dudek. *Jagiellonian University Medical College, I Dept of Cardiology and Hypertension, Cracow, Poland*

Background: It is believed that pulsatile component of blood pressure (BP) is not related to cardiovascular events in younger population. However, most published so far studies dealt mainly with brachial BP. We have hypothesized that the predictive value of relative changes of central BP is independent of age.
Methods: The study group consisted of 1109 patients (824 men and 289 women; mean age: 57.5±10.1 years; mean EF: 56.4±12.4%) undergoing coronary angiography. Invasive ascending aortic BP during catheterization was taken at baseline. Pulsatility and pulsatility index were used as measures of the relative BP changes. We defined pulsatility as the ratio of pulse pressure to mean BP and pulsatility index as the ratio of pulse pressure to diastolic BP. The duration of follow-up was 55.0±17.2 months. The primary end point was defined as: cardiovascular death, myocardial infarction, stroke, cardiac arrest or myocardial revascularization. The Cox proportional hazard regression analysis was used to assess the relation between BP-derived indices and long-term event-free survival.
Results: Six hundred and seventeen (56%) patients were below 60 years of age whereas 492 (44%) had ≥ 60 years. The primary end point occurred in 133 (21.6%) younger and 113 (23.0%) older patients. The multivariate hazard ratios of the end point according to age are given in the table. Both measures of the relative BP changes were independent predictors of the event-free survival in the younger and older groups. Moreover, the predictive value of central pulse pressure (a measure of absolute BP changes) in younger patients was not worse compared to older ones.

The results of multivariate analysis

BP-related variables	Age < 60 years	Age ≥ 60 years
Systolic blood pressure per 10 mmHg	1.10 (0.91-1.33)	1.11 (0.91-1.34)
Diastolic blood pressure per 10 mmHg	0.92 (0.77-1.10)	0.92 (0.86-1.27)
Mean blood pressure per 10 mmHg	1.01 (0.84-1.20)	1.02 (0.85-1.21)
Pulse pressure per 10 mmHg	1.15 (1.03-1.29)	1.11 (0.99-1.24)
Pulsatility per 0.1	1.19 (1.06-1.36)	1.18 (1.03-1.35)
Pulsatility index per 0.1	1.11 (1.03-1.19)	1.09 (1.02-1.17)

Adjustments were made for age, gender, ejection fraction, extent of coronary atherosclerosis, NYHA class, heart rate, risk factors and treatment.

Conclusion: Age does not influence the predictive value of central pulsatility and pulsatility index.

P1504 Tissue Doppler versus conventional echocardiography in the evaluation of left ventricular systolic function: a population study

T. Kuznetsova, Y. Jin, L. Thijs, T. Richart, J. D'hooge, P. Claus, L. Herbots, R. Fagard, J.A. Staessen. *University of Leuven, Department of Cardiovascular Diseases, Leuven, Belgium*

Conventional echocardiography enables the assessment of global left ventricular (LV) systolic function (fractional shortening [FS] and ejection fraction [EF]), whereas tissue Doppler ultrasonographic imaging (TDI) makes it possible to specifically evaluate the longitudinal and radial components of regional LV systolic function.
Objective: To compare TDI with conventional echocardiography in the assessment of LV function in a general population.
Methods: We recorded conventional echocardiographic images. Using TDI, we also acquired: (1) natural longitudinal strain (S) and strain rate (SR) from the basal portion of the LV inferior and infero-lateral free walls; (2) and radial deformation of the LV infero-lateral wall. Using stepwise multiple regression, we assessed the independent correlations of the echocardiographic indexes with sex, age, height, weight, body-mass index (BMI), heart rate (HR), systolic and diastolic blood pressures (BP), relative wall thickness (RWT), and end diastolic diameter.
Results: Our study population consisted of 195 normotensive and 137 hypertensive (treated 74) subjects without cardiac diseases (49.7% women, age mean/range 51.5/15-89 years). Mean values ± SD were 23.5±3.8% and 1.36±0.25s-1 for longitudinal S and SR; 58.2±13% and 3.41±0.9s-1 for radial S and SR; 69.2±7.2% for EF, and 39.4±7.2% for FS. Longitudinal S independently decreased with RWT (partial correlation coefficient [r^2]=0.09; P<0.0001) and systolic BP (r^2=0.02; P=0.017). Radial S decreased with BMI (r^2=0.05, P=0.0007). While adjusting for HR, longitudinal SR decreased with RWT (r^2=0.04, P=0.0003) and radial SR decreased with age (r^2=0.03, P=0.005). In contrast, EF and FS increased with age (r^2=0.14; P<0.0001) and RWT (r^2=0.02; P=0.01). Subjects with LV concentric remodeling (RWT>0.43, n=68) had lower S and SR compared to subjects with normal cardiac morphology (24 vs 22% and 1.38 vs 1.30 s-1; P=0.0008 and P=0.03, respectively). Excluding treated hypertensive patients did not alter our findings.
Conclusions: In this first study in a random population sample of echocardiographic TDI, we demonstrated that TDI, in comparison with conventional echocardiography, is a sensitive method for the detection of LV systolic dysfunction, particularly in subjects with LV remodelling and normal EF.

P1505 The prevalence of masked hypertension among healthy offspring of hypertensive patients

T. Makris, M. Daskalaki, O. Papazachou, D. Papadopoulos, E. Sanidas, E. Gialafos, A. Hatzizacharias, V. Votteas. *Laiko General Hospital of Athens, Hypertension Clinic - Cardiology Department, Athens, Greece*

Purpose: Although masked hypertension (MH) is a predictor of cardiovascular disease, its prevalence is still unknown. Aim of our study was to examine the prevalence of MH among healthy offspring of hypertensives (HOH) and to compare the findings to those of healthy offspring of normotensives (HON), matched for age, sex, body mass index and the rest of risk factors.
Methods: One hundred and twenty (50M, 70F) HOH mean age 30±8yrs (group A) and 100 (40M, 60F), HON mean age 29±9yrs (group B) who had clinic blood pressure <140/90 mmHg were studied. The whole study population underwent 24 hour ambulatory blood pressure monitoring (ABPM).
Results: According to ABPM recordings, masked hypertension (daytime systolic blood pressure≥135 mmHg or daytime diastolic blood pressure≥85 mmHg) was determined in 15/120 (9M, 6F) of group A (12.5%) vs 7/100 (5M, 2F) of group B (7%), p< 0.01. Eleven out of 15 of group A (73.4%) with MH had positive family history of hypertension from both parents.
Conclusions: Our findings suggest that the prevalence of masked hypertension is significantly higher in HOH compared to HON. It seems also that the positive family history of hypertension from both parents, is a significant predictor for future development of masked hypertension. To confirm these finings further investigation is needed.

P1506 The detrimental effect of sleep apnea syndrome on target organ damage in a hypertensive population: preliminary data from the Hippokratio Hellenic Hypertension Study (3H Study)

C. Thomopoulos, C. Tsioufis, K. Dimitriadis, D. Tsiachris, E. Vezali, P. Toutouzas, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: Sleep apnea syndrome (SAS) presents with high prevalence among hypertensives, and constitutes an independent risk factor for adverse cardiovascular outcome. We evaluated the effects of SAS on target organ damage (TOD) in an essential hypertensive population.
Methods: A total of 1764 essential hypertensives (51% men, aged 56±13 years) that were included in the Hippokratio Hellenic Hypertension Study (3H Study) (an ongoing registry of hypertension – related target organ damage) were considered for analysis. Left ventricle mass index (LVMI) and relative wall thickness (RWT) were evaluated by echocardiography, while carotid – femoral pulse wave velocity (PWV) was assessed by an automatic device (Complior SP). Renal function was assessed by creatinine levels in a blood sample, while in 24h-urine sample albumin and albumin/creatinine ratio levels were also estimated (the latter was repeated in a further morning urine sample, according to established methods). An Epworth Sleepiness Scale Questionnaire (ESSQ) was used to uncover clinical evidence of SAS after being tested for reliability, and validity in a pilot sub-study.
Results: Among the total population of hypertensives, 212 subjects (12% - 8.5% men) had SAS. Hypertensives with SAS compared to those without SAS demon-

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

strated higher levels of smoking, waist/hip ratio, body mass index (44% vs. 31%, 0.94±0.09 vs. 0.90±0.08 and 31±5 vs. 28.7 ±5 kg/m^2, p<0.05 in all cases) and office diastolic blood pressure (BP) (91±12 vs. 89±12 mmHg, p<0.05), while office systolic BP was similar (145±19 vs. 143±18 mmHg p=NS). LVMI, RWT and PWV were higher in the SAS group (112±32 vs. 104±28 gr/m^2, 0.45±0.09 vs. 0.43±0.08, and 8.24±1.7 vs. 7.87±1.4 m/sec, p<0.05 in all cases). Albeit creatinine levels were similar between the two groups (1±0.2 vs. 0.9±0.2 mg/dl, p=NS), 24h-albumin and albumin/creatinine ratio levels were increased in OSAS hypertensives (23 ±12 vs. 18±11 mg/24h, and 17±8 vs. 11±7 mg/g, p<0.05 for both cases).
Conclusions: Hypertensive subjects with SAS compared to hypertensives without SAS demonstrated significantly higher sub-clinical markers of TOD, a finding suggesting an adverse prognosis in the arm of SAS hypertensives.

P1507 Erectile dysfunction and microalbuminuria in essential hypertension: evidence for two interrelated pathologies of the vasculature

A. Kakkavas, C. Tsioufis, D. Tsiachris, K. Dimitriadis, C. Thomopoulos, D. Tousoulis, C. Stefanadis, I. Kallikazaros.
Department of Cardiology, Hippokration, Athens, Greece

Purpose: Erectile dysfunction (ED) is considered an early sign of sub-clinical atherosclerosis, while microalbuminuria is an established cardiovascular risk factor in essential hypertension. In the present study, we examined the association of ED with urinary albumin excretion, expressed as albumin to creatinine ratio (ACR), in hypertensive males.
Methods: We studied 142 consecutive, newly diagnosed and untreated, male subjects with uncomplicated stage I-II hypertension [mean age=50.6 years, office blood pressure=151/98mmHg]. All subjects were non-diabetics and without clinical atherosclerotic disease. By means of a validated questionnaire, the International Index of Erectile Function score (IIEF-score) was assessed and subjects were divided into those with ED (IIEF-score<26, n=43, 30.3%) and those without ED (IIEF-score> or = 26, n=99). The study protocol included 24-h ambulatory blood pressure monitoring, complete echocardiographic study, routine biochemical tests and ACR determination as the mean of two non-consecutive morning spot urine samples.
Results: Patients with ED compared to those without were older (55±9 vs. 48±7 years, p<0.05), whereas there was no difference regarding smoking status, body mass index, waist to hip ratio, metabolic profile as well as left ventricular mass and geometry (p=NS for all). According to ambulatory blood pressure monitoring measurements, men with ED compared to those without had greater values of 24-h pulse-pressure (50.7±9 mmHg vs. 47.5±7 mmHg, p<0.05) and exhibited higher prevalence of non dipping status (72.5% vs. 47.2%). Regarding urine albumin excretion, a trend towards increased albuminuria values, was observed in hypertensives with ED compared to those without ED (log ACR 1±0.46 vs. 0.95±0.36 mg/gr, p=NS). Multiple logistic regression analysis revealed that, apart from age, the only independent predictors of ED were logACR (Wald=4.5, p<0.05) and non-dipping status (Wald=7.0, p<0.05).
Conclusions: In hypertensives middle-aged maled without clinically atherosclerotic disease ACR in an independent predictor of ED. These findings further support the hypothesis that abnormalities in albumin excretion and erectile function participate in the integrative pathology of diffuse atherosclerosis.

P1508 Integrative approach to unmask sub-clinical target organ damage in hypertensives with obstructive sleep apnea: upper airway and kidneys mirror heart and vessels

C. Thomopoulos, C. Tsioufis, K. Dimitriadis, A. Amfilochiou, D. Tousoulis, P. Toutouzas, C. Stefanadis, I. Kallikazaros. *Department of Cardiology, Hippokration, Athens, Greece*

Purpose: We investigated whether established renal function parameters correlate with sleep parameters and cardiovascular adaptations in hypertensives with obstructive sleep apnea syndrome (OSAS).
Methods: 62 consecutive subjects (49 men, aged 48±7 years, 31 smokers) with stage I-II untreated hypertension and OSAS diagnosed by polysomnography (PSG) [apnea/hypopnea index (AHI)>5], and a control group of 70 untreated hypertensives with negative PSG matched for age, sex, body mass index and smoking status were studied. All subjects underwent aortic stiffness evaluation by carotid – femoral pulse wave velocity (c-f PWV) using a (Complior SP) while serum creatinine levels (SCR), glomerular filtration rate (GFR), and albumin/creatinine excretion ratio (ACR) from a morning urine sample were also determined.
Results: Hypertensives with OSAS compared to hypertensives without OSAS demonstrated similar levels of waist to hip ratio (0.92 vs. 0.92, p=NS), office systolic blood pressure (BP), and pulse pressure (150.7±8.6 vs. 148±14, and 51.7±10 vs. 52.2±12mmHg, p=NS for both cases), while diastolic BP was higher (99±9 vs. 95±8, p=0.03). Left ventricle mass index and relative wall thickness were similar (100± 23 vs. 97±22 g/m^2 and 0.452 vs. 0.455, p=NS for both cases) while c-f PWV was increased in the OSAS group (8.2±1 vs. 7.2±0.9 m/sec, p=0.0001). Metabolic profile was similar in the two groups (p=NS). Albeit SCR and GFR did not differ between the two groups (0.96±0.18 vs. 0.94 ±0.18mg/dl and 114±30 vs. 116±27 ml/min., respectively p=NS for both cases), logACR was significantly higher in OSAS subjects (1.07± 0.31 vs. 0.66±0.38 mg/g, p<0.0001). In different covariance analysis models (ANCOVA), the difference in c-f PWV, and logACR remained significant even after adjustment for confounders(p<0.05 for both cases). In the entire study population c-f PWV was correlated with the presence of OSAS (r=0.40, p<0.001), systolic BP (r=0.25, p=0.01), logAHI (r=0.35, p<0.001), minimum oxygen saturation (min$SatO_2$) (r=0.40, p<0.0001), while logACR was correlated with presence of OSAS (r=0.491, p<0.0001), logAHI (r=0.34, p<0.0001), min$SatO_2$ (r=-0.48, p<0.0001).
Conclusions: The presence of OSAS predicts increased levels of ACR and aortic stiffening in the setting of hypertension, a finding suggesting enhanced subclinical target organ damage. Upper airway impairment in OSAS hypertensive subjects as expressed by AHI and min$SatO_2$ is proportionally correlated with ACR but not with c-f PWV.

P1509 Kidney function and target-organ damage in arterial hypertension

G. Vyssoulis[1], G. Bakris[1], E. Karpanou[2], K. Keramida[2], S.-M. Kyvelou[1], T. Gialernios[1], P. Tapinis[1], D. Cokkinos[2], C. Stefanadis[1]. *[1]Hippokration Hospital, 1st Department of cardiology, Athens, Greece; [2]Onassis Cardiosurgical Center, 1, Athens, Greece*

Purpose: Impaired kidney function has been proposed as an independent cardiovascular risk factor (RF), while arterial hypertension is an established RF and diabetes mellitus is considered as equivalent of coronary heart disease. The aim of this study was to investigate the relationship of kidney function to target-organ damage (TOD) in hypertensives, according to glucose metabolism disorders (GMD).
Methods: The study comprised 9300 consecutive patients with uncomplicated essential hypertension without coronary heart disease, 4959 men and 4341 women, 55.2 years old. Normal sugar metabolism had 6539 patients, impaired glucose tolerance (IGT) had 1562, and type 2 diabetes mellitus (DM) had 1199 patients. All underwent full clinical and laboratory evaluation, after an at least fortnight wash-out period (48%). Serum creatinine (SCr) was measured and glomerular filtration rate (GFR) was calculated. From the ultrasound examination, left ventricular mass index (LVMI) was calculated, while from 24h urine collection α_1 microglobulin (α_1 mgl) and microalbumin were measured and the urinary albumin to creatinine ratio (ACR) was calculated, as was creatinine clearance (CrCl).
Results: In ascending GFR quartiles corrected for GMD, LVMI values increased (129 to 131 to 134 to 139 g/m^2, F=117 p<0.0001), as did LV hypertrophy incidence (32.4 to 36.3 to 44.5 to 53.2% p<0.0001). LVMI corrected for age and GMD, was best related to SCr (r=0.239 p<0.0001) and CrCl (r=-0.183 p<0.0001). These relations were better in DM (r=0.248 & -0.206, p<0.0001) and best in IGT patients (r=0.260 & -0.246, p<0.0001). In ascending corrected GFR quartiles, albuninuria progressively increased (32.5 to 33.7 to 40.8 to 48% p<0.0001), as did α_1 mgl values (6.4 to 6.5 to 7.1 to 7.8 mg/Lt, F=66 p<0.0001), while corrected α_1 mgl was best related to SCr (r=0.240 p<0.0001). Again, in ascending corrected GFR quartiles, ACR increased (32 to 34 to 41 to 48 mg/Lt, F=54 p<0.0001), and corrected ACR was related to SCr (r=0.182 p<0.001), better in patients with IGT (r=0.236 p<0.001).
Conclusions: In patients with arterial hypertension, impaired kidney function is associated with TOD, for every level of GMD. The calculations of GFR or CrCl do not seem superior to the simple SCr measurement.

P1510 Microalbuminuria is very common in patients with hypertension and coronary artery disease: results from the i-SEARCH global survey

N. Danchin[1], M. Volpe[2], M. Thoenes[3], M. Bohm[4]. *[1]Hopital European Georges Pompidou, Cardiology, Paris, France; [2]University of Roma, Rome, Italy; [3]Sanofi-Aventis, Global Medical Affairs, Paris, France; [4]University of Saarland, Cardiology, Angiology and Intensive Medicine, Saar, Germany*

Purpose: Microalbuminuria (MAU) is a predictor of endothelial dysfunction which is believed to be an early step in the atherosclerotic process leading to coronary artery disease (CAD). The International Survey, i-SEARCH, was designed to evaluate the prevalence of MAU in the hypertensive population. The objectives of this analysis were to assess the correlation between MAU and CAD in patients with hypertension, and to increase physician awareness of the importance of MAU screening to identify patients at risk.
Methods: Hypertensive outpatients (seSBP/DBP ≥140/90 mmHg) visiting 1750 study centres in 26 countries worldwide were screened for MAU (albumin excretion rate 30-300 mg/24 h) using reagent strips which detected urinary albumin excretion (UAE) of 10, 30, 80 or 150mg/L. Documented CAD was recorded in the patient population.
Results: Of the 21,050 patients screened, 23% (95% CI, 22-24%) had documented CAD. Of these, 64% had MAU compared with 57% of patients with no CAD. Multivariate analysis showed that patients with CAD were more likely to have MAU than those with no documented CAD, odds ratio (OR), 1.13 (95% CI, 1.04-1.23, p<0.006). There was a shift towards higher UAE in patients with CAD and MAU, compared with patients with no CAD and MAU: 36% (95% CI, 35-38%)

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

of patients with CAD had UAE of 10 mg/L compared with 43% (95% CI, 43-44%) of patients with no CAD, whereas 13% (95% CI, 12-14%) of patients with CAD had the higher UAE of 150 mg/L compared with only 8% (95% CI, 8-9%) of patients with no CAD.
Conclusion: MAU is extremely common in hypertensive patients, especially if they have concomitant CAD. These findings support routine screening for MAU in patients with hypertension to identify patients at cardiovascular risk, and indicates that even stronger efforts should be made to limit endothelial dysfunction by controlling blood pressure.

P1511 E-Tracking (eT) as a new tool in the evaluation of early functional changes in hypertensives without structural remodeling of carotid arteries

J.J. Jaroch[1], K. Loboz-Grudzien[2], A.K. Kowalska[1], Z.B. Bociaga[1], E.K. Kruszynska[1], A.W. Wojszwillo[1], M.W. Woda[1]. *[1]T.Marciniak Hospital, Department of Cardiology, Wroclaw, Poland; [2]Wroclaw University of Medicine, Public Health Department, Wroclaw, Poland*

Background: Little is known about ventriculo-arterial link and relationship between left ventricular (LV) diastolic function and structural remodeling of carotid arteries (c.a.).We aimed to test the hypothesis if e-Tracking (eT) indices of arterial stiffness (a.s.) are an early marker of functional abnormalities and if early functional arterial remodeling precedes LV diastolic dysfunction (d.d).
Material and methods: The study group consisted of 101 subjects, mean age 46,2 years, 36 M and 65 F,43 normotensive (N) and 58 hypertensives (H). eT of c.a. (a new built-in echo walltracking ALOKA system), IMT assessment and echocardiography were performed in each patient.From eT the following a.s. parameters (with blood pressure values introduced into formulas during examination) were calculated:Beta index (beta), Epsilon index (pressure-strain elasticity modulus, Ep), arterial compliance (AC), one-point pulse wave velocity (PWVβ), augmentation index (AI).From echocardiography LVMI, EF, and diastolic function indices (IVRT), early and atrial filling mitral wave (E,A), E/A,E – wave deceleration time (DTE); from TDI: E', A', E'/A', DTE' were evaluated. D.d. was noted in 36 H.
Results: All pts had normal IMT values and preserved LV systolic function.Mean values of eT indices differed significantly depending on pts age and sex.In H mean values of beta (10,7$\pm$3,1) were significantly higher ($p<0,05$) than in N (9,18$\pm$2,85). 73% of H had higher than normal values of beta (established as 8,5 using ROC curve procedure in our normal population) while all of them had normal IMT value.Mean values of Ep and PWV were also significantly higher in H (148,3$\pm$50,6; 7,11$\pm$1,16 respectively) than in N(122,3$\pm$44,9; p=0,01; 6,5$\pm$1,15; $p<0,05$ respectively). Significant correlations between beta and age (r=0,42) and IMT(r=0,36) were noted. In pts with d.d. not only mean values of beta index were significantly higher than in pts without d.d.(10,5 vs 8,87, $p<0,01$), but also 44% pts without d.d. had beta value exceeding normal range in our population. Significant correlations between beta index and IVRT (r=0,22, $p<0,05$), E' (r=-0,29; $p<0,01$), DTE' (r=-0,32; $p<0,05$).
Conclusions: Among e-Tracking carotid artery stiffness indices beta index as well as epsilon index and one point pulse wave velocity can be useful in detection of early functional changes that precede arterial structural remodeling in patients with hypertension which may avoid patients being mistakenly classified as at low risk.Increase of Beta index may precede relaxation abnormalities.

P1512 Predisposition of PPAR-gamma2, ACE, beta1-adrenergic receptors, endothelial NO synthase and AGTR1 genes mutation to caspase levels in hypertensive patients

L. Sydorchuk[1], V. Pishak[1], I. Sydorchuk[2], E. Amosova[3], R. Sydorchuk[1]. *[1]Bukovinian State Medical University, Family Medicine Department, Chernivtsi, Ukraine; [2]Chernivtsi, Ukraine; [3]Kyiv, Ukraine*

Background/Objective: Nitric oxide (NO) is the most important vasorelaxant counteracting to the vasoconstrictive and vasoproliferative hormones of the endothelin and RAAS family such as angiotensin-converting enzyme (ACE) and angiotensin II (AGT). Stimulation of beta1-adrenergic receptors and prolypherative peroxisome activator receptors gamma 2 (PPAR-gamma 2) play a fundamental role in the development of cardiovascular diseases, strokes and insulin resistance appearance. But production of RAAS messengers and receptors activities depends from according genes polymorphism. The aim of study was to investigate the dependence of insertion/deletion (I/D) polymorphism of angiotensin-converting enzyme (ACE) gene, A1166C polymorphism of angiotensin II type 1 receptor (AGTR1) gene, T894G polymorphism of endothelial NO synthase gene (eNOS), Pro12Ala polymorphism of PPAR-gamma2 receptors and beta1-adrenergic receptors (ADRB1) genes on apoptosis intensivness in hypertensive patients.
Design and methods: Study included 268 hypertensive patients (male 127, female 141, mean age 49.06$\pm$8.34) with grade 1-3 AH (15, 130 and 123 patients, respectively). 115 hypertensive 3rd grade patients were complicated with chronic heart failure (CHF). Duration of hypertension was from 5 to 15 years. Target organs injury was evaluated by means of Echo-CG, Reoencephalography, Ultrasonography, ophthalmoscopy, BP Holter-monitoring, ECG Holter-monitoring, clinically laboratory analysis and physical examination. Apoptosis was defined with 1-, 3- and 8-caspase levels by IEA. Genes' polymorphism of ADRB1 (Arg389Gly), PPAR-gamma2 (Pro12Ala), ACE (I/D), eNOS (T894G) and AGTR1 (A1166C) alone or in combination was assessed with PCR based method.
Results: Distribution of polymorphic A1166C AGTR1 genotypes was following: AA genotype was revealed in 66.79% patients, AC genotype – in 27.98%, CC genotype – in 5.23% (p55 years (r=+0.37), in ADRB1 Arg389Arg genotype (r=+0.40) and in ACE DD genotype in 3rd grade hypertensive patients (r=+0.41). In those subjects was revealed the highest levels of caspase': 8-caspase from 1.410$\pm$0.027 EU/ml to 1.830$\pm$0.040 EU/ml ($p<0.000$), 3-caspase from 1.380$\pm$0.043 EU/ml to 1.729$\pm$0.039 EU/ml ($p<0.000$), 1-caspase from 1.229$\pm$0.027 EU/ml to 1.527$\pm$0.038 EU/ml ($p<0.001$). PPAR-gamma2 Ala12Pro, ENOS T894G genes polymorphism were not related to caspase' level.
Conclusion: Arg389 allele of beta-1-adrenergic receptor gene, C allele of angiotensin II type 1 receptor and DD genotype of angiotensin-converting enzyme gene has possible direct association with caspase level in hypertensive patients.

P1513 Progression from hypertension to heart failure

G. Tocci, S. Sciarretta, M. Volpe. *University "La Sapienza", S. Andrea Hospital, Rome, Italy*

Background: During the last two decades, clinical trials on hypertension have consistently demonstrated that lowering blood pressure is effective in terms of reducing risk of major cardiovascular events, including heart failure (HF). Scientific societies and mostly physicians, however, tend to give higher priority to preventing other cardiovascular major endpoints, i.e. myocardial infarction (MI) and stroke, rather than HF.
Aim: In the present study, we specifically analysed incidence per year of new onset HF as compared to other major cardiovascular events, including MI and stroke, in clinical studies on hypertension, up to December 2006.
Methods: For this purpose, we identified international, randomized, controlled clinical studies, performed on hypertension or in patients defined at high cardiovascular risk with a predominant presence of hypertensive patients.
Results: A total of 161.891 hypertensive patients (mean age 65.4 $\pm$7.0 years) were included in the analysis. The incidence per year of HF was quite comparable to that of stroke, accounting for 28% and 30% among total cardiovascular events, respectively. In the same studies MI represented the most frequent event per year, accounting for the 42% of the total events.
New onset of HF was more frequent in old versus young hypertensive patients [RR 2.48, 95% CI (2.13-2.91); $P<0.0001$], as well as in black versus non-black hypertensives [RR 1.98, 95% CI (1.68-2.33); $P<0.0001$]. Moreover HF was the more incident major cardiovascular event in hypertensives affected by diabetes mellitus [RR 3.66, 95% CI (3.19-4.20); $P<0.0001$], as compared to MI and stroke. Finally, according to the level of total cardiovascular risk profile, incidence of HF showed a step-wise increase from low-risk to high-risk hypertensive patients [RR 3.42, 95% CI (3.04-4.01); $P<0.0001$].
Conclusion: Although HF is less considered as major cardiovascular event as copmpared to MI and stroke, its incidence is considerable as well as the incidence of stroke. Moreover in some classes of hypertensives HF represents the most prevalent cardiovasculr event.

P1514 SAH gene variants are associated with obesity-related hypertension in caucasians -the PEGASE study-

C. Hagedorn[1], R. Telgmann[1], E. Brand[2], V. Nicaud[3], J. Schoenfelder[4], S. Hasenkamp[3], F. Cambien[4], M. Paul[1], L. Tiret[4], S.M. Brand-Herrmann[2]. *[1]Leibniz-Institute For Arteriosclerosis Resear, Molecular Genetics of Cardiovascular Disease, Muenster, Germany; [2]University Clinic of Muenster, Internal Medicine.Nephrology and Hypertension, Muenster, Germany; [3]Universtite Pierre and Marie Curie, INSERM UMRS 525, Paris, France; [4]Charite, University Medicine Berlin, Clinical Pharmacology and Toxicology, Berlin, Germany*

Objective: The SAH gene locus has recently been proposed to be involved in obesity-related hypertension in Japanese.
Methods: To independently replicate initial findings in another ethnic group, we scanned the entire SAH gene in 190 Caucasian chromosomes. Six-hundred and fifty-one patients with essential hypertension and 776 controls (PEGASE Study) were genotyped for all identified variants using allele-specific oligonucleotides and single nucleotide polymorphism as well as haplotype analyses were carried out. We additionally performed transient transfection experiments, Northern and Western blots, immunoprecipitation, and acyl-CoA synthetase activity assays.
Results: We identified five polymorphisms in the promoter region (C-1808T, G-1606A, -962ins/del, G-451A, T-67C), two in introns 5 and 7 (T+9/In5C, A+20/In7T), and one missense variant (K359N). Carriage of the -1606A allele was significantly associated with hypertension (odds ratio: 1.28, P=0.049) as was 359N (odds ratio: 1.35, P=0.048) compared to non-carriers. Conversely, for -962del, the odds ratio for hypertension was 0.80 (P=0.042). SAH alleles -1606A and 359N, but not -962ins/del, displayed a raising effect on BMI (P=0.004 and P=0.030, respectively) in hypertensives as well as in controls, after adjustment for BMI in hypertensives, only the odds ratio associated with -962ins/del remained significant (odds ratio: 0.77, P=0.028). Functional analyses in BHK did not reveal differences for SAH 359N- or 359K-containing constructs, formally excluding K359N as the functional variant.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020

Conclusion: We confirm recent evidence that the SAH locus is associated with obesity-related hypertension; in which pathophysiological context SAH variants affect blood pressure remains, however, to be shown.

P1515 Neutrophil elastase gene variation and coronary heart disease

C. Doerdelmann[1], R. Telgmann[1], E. Brand[2], V. Nicaud[3], J. Schoenfelder[4], C. Ruessmann[3], A. Evans[5], F. Cambien[5], M. Paul[1], S.-M. Brand-Herrmann[3]. *[1]Leibniz-Institute for Arteriosclerosis Resear, Department of Molecular Genetics of Cardiovas, Muenster, Germany; [2]Internal Medicine D, Nephrology and Hypertension, Muenster, Germany; [3]Universite Pierre et Marie Curie, INSERM, Paris, France; [4]Charite, Institute of Clinical Pharmacology and Toxico, Berlin, Germany; [5]MONICA Projects, Belfast, United Kingdom*

Neutrophil Elastase (ELA2) has been involved in the complex pathophysiology of cardiovascular disease.
Methods: 2082 chromosomes from participants of the ECTIM Study were scanned for genetic variants and for the common polymorphisms G-761A and S173S (C4890A), 990 patients with MI and 904 controls (Belfast, Glasgow, Strasbourg) were genotyped. For further functional analysis of the polymorphism and a 53bp deletion we designed two expression vectors and two reporter gene vectors. Transient transfection was performed in HEK293T and undifferentiated THP-1.
Results: We identified 11 genetic variants, 2 in the 5'-flanking (G-761A, -852/del53bp), 6 in exonic (R49H, N81N, G93V, S173S, D222Y, P228L) and 3 in intronic gene regions (C+29/in3T, C+149/in3T, C+137/in4T). In Belfast only, 4890A allele carriers had a risk for MI with an odds ratio (OR) of 1.44 (95% CI 1.12-1.86; P=0.005), the OR for MI associated with the -761G/-4890A haplotype with reference to -761G/-4890C amounting to 2.38 (95% CI 1.23-4.57; P=0.01). However, with respect to functional analyses, transcript or protein expression of both allelic constructs (4890A and 4890C), as assessed by kinetic northern and western blot analyses, respectively, did not differ.
Conversely, transient transfection analyses in THP-1 cells demonstrated a significantly higher transcriptional activity (>35%) of the 53bp deletion compared to the non-deleted promoter (P=0.001); the -852/53bp deletion was observed in one patient with premature MI at the age of 28 years whose mother had one at the age of 48 years.
Conclusion: The fact that C4890A was associated with MI in Belfast only, together with the presumed lack of the polymorphisms' functionality, provides little support for a substantial implication of common ELA2 gene variants in overall MI risk. Whether -852/53del play a role in cardiovascular pathophysiology should be evaluated further.

P1516 Antiendothelial cell antibody levels in patients with masked hypertension

T. Makris, O. Papazachou, D. Papadopoulos, E. Sanidas, M. Daskalaki, S. Vichos, A. Hatzizacharias, V. Votteas. *Laiko General Hospital of Athens, Hypertension Clinic - Cardiology Department, Athens, Greece*

Purpose: Recent evidence demonstrate that masked hypertension (MH) is a significant predictor of cardiovascular disease, while, elevated levels of circulating antibodies against endothelial cell surface antigens (antiendothelial cell antibodies – AECA) seem to play an important role at the early stages of atherosclerosis process and of borderline hypertension as well.
Aim of this study was to investigate the presence of AECA in patients (pts) with MH and to compare the AECA title among pts with MH and healthy normotensives (HN), matched for age, sex and body mass index.
Methods: One hundred-thirty (60 M, 70 F) healthy subjects mean age 45±12 yrs who had clinic blood pressure <140/90 mmHg were studied. The whole study population underwent 24 hour ambulatory blood pressure monitoring (ABPM). According to the ABPM recordings, 24 individuals (8M, 16 F) had MH (daytime systolic blood pressure ≥ 135 mmHg or daytime diastolic blood pressure ≥ 85 mmHg - group A) and the remainder 106 subjects (52 M, 54 F) had normal ABPM recordings, group B. IgG and IgM AECA levels were determined by ELISA method. AECA levels were expressed as mean value ± SD. None of the study population had a history of connective tissue disease or any metabolic disorder.
Results: Significantly increased titles of AECA class IgG were found in 8/24 pts of group A (30%) vs 5/106 (4.6%) of group B (p<0,001). Significantly increased titles of AECA class IgM were also found in 6/24 pts of group A (25%) vs.3/80 (3.8%) of group B (p<0,001).
Mean values of both IgG and IgM AECA plasma levels in each group are shown in the table.

	Group A (n=24)	Group B (n=106)	p
IgGAECA (ng/ml)	0.088±0.04	0.052±0.03	<0.001
IgM AECA (ng/ml)	0.096±0.06	0.076±0.02	<0.01

Conclusions: Our results suggest that patients with masked hypertension have significantly higher AECA levels of both classes (IgG, IgM) compared to healthy normotensives. These findings may indicate a possible explanation of the increased cardiovascular risk in MH. The possibility that high AECA levels may be a driving mechanism for the development of MH needs further investigation.

Downloaded from https://academic.oup.com/eurheartj/article/28/suppl_1/1/722750 by guest on 25 September 2020