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CONTENT

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ETHICS IN MEDICINE

What do medical doctors' ethics mean? The answer to this question is not simple, but it is a key point when it comes to doctors' working. Ethical thinking does not raise scientific or technical issues, but raises questions about the doctor's behavior and decision-making, questions about values, rights and responsibilities. Doctors face such issues as often as they face scientific, medical and technical issues.

All ethical issues in medicine are not equally challenging. It is relatively easy for some ethical questions to be answered, mainly because there is a well-developed consensus about action in a particular situation (for example, the doctor should always ask for the patient's consent to be the subject of research)[1]. Contrary to this, on some other issues it is more difficult to give an answer, especially for those where there is no generally accepted rule, or in which all alternative responses show some disadvantage (for example, the limitation of resources that are deficient and have impact on human health)[2].

So, again, we come to the initial question: "What exactly is ethics and how does it help doctors to deal with such questions?" Simply put, The World Medical Association and the Medical Ethics Manual define ethics as a study of morality - careful and systematic thinking and analysis of moral decisions and behavior in the past, the present and the future. On the other hand, morality is a valuable dimension of human behavior and decision-making. The language of morality contains nouns such as rights, responsibilities and virtues and adjectives as good, bad (evil), right, wrong, just and unjust[3]. Accordingly, ethics is above all a matter of knowledge, while morality is a matter of action. Their close connection is reflected in the fact that ethics should provide rational criteria so that people (doctors) can decide and / or behave as they should. Doctoral ethics is a branch of ethics that deals with moral issues in medical practice[1].

Ethics is an integral part of medicine since the time of Hippocrates, 5 centuries BC. He is considered to be the founder of medical ethics. From his studies medicine became percept as a profession, because doctors publicly declare and promise that patients' interests will put first.[4]. In recent years, medical ethics has been influenced by the advancement of human rights. In a pluralistic and multicultural world, a world with many moral traditions, the major international treaties that relate to human rights are the basis for medical ethics that is acceptable everywhere, surpassing both national and cultural borders. Additionally, doctors often deal with medical problems that arise as a consequence of human rights violations, such as forcible migration and torture[2].

In addition, medical ethics is closely related to the law. In most countries there are laws that determine how doctors should deal with ethical issues in health care and research. But often ethics prescribes higher standards of behavior than the law, and sometimes doctors' ethics require that

they do not obey laws that require unethical behavior. Likewise, laws vary greatly from country to country, while ethics applies independently of national borders[3].

The duties and responsibilities of doctors are the core and the essence of medical ethics. However, like all human beings, doctors have rights and responsibilities, and medical ethics would be incomplete if they do not deal with the question of how doctors should treat others, be it patients, society or colleagues. In medical ethics, six values are commonly applied: autonomy, benevolence, fairness, dignity, sincerity and honesty.

Ethical responsibilities of doctors can be classified according to their main beneficiaries: patients, society and colleagues (which also include other health professionals). The need to ensure patient's safety as well as to support a healthy lifestyle of doctors is resolved in some countries by limiting the number of hours and the length of shifts that doctors and trainees can handle.[5]. Although such measures can contribute to the health and well-being of the physician, the primary responsibility of self-care depends on the doctor himself. In addition, to avoid such obvious risks to health as smoking, substance abuse and overtime, physicians need to protect and improve their own health and well-being by determining the factor - stress in their professional and personal lives and by developing and renaming appropriate strategies for dealing with it. When failing, physicians should seek help from colleagues and relevant professionals about personal problems that may have a bad influence on their relationship with patients, society, or colleagues [3].

The future of medical ethics depends, in large part, on the future of medicine. By the end of the 20th century and the beginning of the 21st century, medicine developed at a very fast pace and it is difficult to predict its course. Given the unpredictability inherent in the future, medical ethics should be flexible and subject to change and adjustment. However, its basic principles will remain as they are, in particular the values of compassion, competence and independence, along with the care of basic human rights and the commitment to professionalism.

Finally, the question arises about who decides what is ethical? Individuals disagree about what is right and what is wrong, and even when they agree, they do it for various reasons[2]. In some societies, such disagreement is considered normal and people have great freedom to act as they wish, provided that they do not violate the rights of others. However, in more traditional societies, there is greater consensus, as well as greater social pressure to act in a certain way, more than one else. In such societies, culture and religion often play a dominant role in determining ethical behavior [1].

Over the centuries, the medical profession has developed its own standards of behavior for its members, which are expressed in codes of ethics and appropriate documents for its views. Globally, the World Medical Association has adopted a number of ethical attitudes that determine the behavior required by doctors regardless of where they live and work [3].

This brief overview of medical ethics is just a small indicator and step in diving in medical ethics and some of its central issues. The aim is to point out the need for understanding and

continuing thinking about the ethical dimension of medicine, and in particular how to solve the ethical issues that doctors draw during their own practice.

References:

1. Shah N. Ethical issues in biomedical research and publication. J Conserv Dent. 2011; 14:205–7.
2. Pitak-Arnnop P, Hemprich A, Dhanuthai K, Pausch NC. Principlism: The simplicity of complexity, or the complexity of simplicity? J Plast Reconstr Aesthet Surg. 2011;64:978–9.
3. The World Medical Association. Medical Ethics Manual. 2nd ed. [Last accessed on 2011 Oct 10]. Available from: http://www.wma.net/en/30publications/30ethicsmanual/pdf/ethics_manual_en.pdf
4. Louden I. The Hippocratic oath. BMJ. 1994;309:414.
5. Gillon R. White coat ceremonies for new medical students. J Med Ethics. 2000;26:83–84.

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THE EFFECTS OF HYPERBARIC OXYGENATION THERAPY (HBOT) TO SYMPTOMS' MANIFESTATION AND DEVELOPMENTAL GROWTH IN CHILDREN WITH AUTISTIC SPECTRUM DISORDER (ASD) – A PILOT STUDY

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ABSTRACT:

Autistic spectrum disorders (ASD) are a group of neurodevelopmental disorders characterized by significant impairment of social adaptation and communication, as well as with repetitive and restrictive patterns of behavior. According to the World Health Organization these disorders affect approximately 1 in 160 children worldwide. In the past years hyperbaric oxygen therapy (HBOT) has increased its popularity as a treatment for the ASD. In this study, the therapeutic effect of HBOT was measured in terms of symptoms' manifestation and developmental growth. Parents reported significant improvement in several areas of development and decrease of problem behaviors of their autistic children. No physiological side effects of HBOT were registered during the study.

Key words: Autism spectrum disorders, hyperbaric oxygenation therapy, symptom manifestation, developmental growth.

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Introduction:

Autistic spectrum disorders (ASD) are a group of neurodevelopmental disorders characterized by significant impairments of social adaptation and communication, as well as with repetitive and restrictive patterns of behavior. According to the World Health Organization these disorders affect approximately 1 in 160 children worldwide, whereby boys almost 4 times are more susceptible than girls. Despite the core symptoms of ASD, children often display sensory, motor and cognitive impairments, as well as problem behaviors in terms of aggressive behavior, hyperactivity, disturbed sleep and eating problems. All of these cause significant amount of stress to the child, the families and the people working with him/her. The most of the patients with ASD require some level of assistance throughout their whole life. Nevertheless, progress is being made in both identifying risk factors and targeting specific goals for therapeutic programs, that would enable the patients and their families to better adapt to the requirements of the social environment. Although autism is far from being completely understood, new clinical research has enlightened some aspects of the neurobiological basis of the disorder. Results indicate that ASDs are multisystem disorders, affecting the central nervous system, the immune system and the gastrointestinal tract (Fatemi et al., 2012; Careaga et al., 2010; Kemper, 2010). There are clinically significant results indicating cerebellar dysfunctions (Hardy et al., 2013; Fatemi et al., 2012; Welsh et al. 2005); abnormal activation in parts of the occipital and the temporal lobes – the fusiform gyrus and the superior temporal sulcus (Mundy, 2003); frontal lobe abnormalities (Rizzolatti and Craighero,2004; Oberman et al., 2005), as well as structural abnormalities in the limbic system (Minshew et al., 1997; Williams and Minshew, 2007). The cerebellum is responsible for the coordination of motor acts, for rhythmic stereotypical movements and for the processing of sequential sensory information. The fusiform gyrus and the superior temporal sulcus are parts of the social brain circuits, and the same participate in the processing of facial expressions and biological movements. The limbic system is associated with emotional response and processing of the emotionally relevant information. Many investigations recently are directed towards the role of "mirror neurons" in the organization of social behavior (Rizzolatti and Craighero,2004; Oberman et al., 2005) and their relation to the social impairment symptoms in ASD (Fan et al., 2010). Whereas autism previously was considered a disorder with an extremely poor prognosis with only 50% of individuals developing spoken language, it has now been demonstrated that 75–95% of children who receive early intensive intervention develop useful speech by age 5 (Lovaas, 1987; McGee, Morrier, & Daly, 1999; for a review, see Rogers & Dawson, 2009). In the past years hyperbaric oxygen therapy (HBOT) has increased its popularity as a complementary/alternative treatment for the ASD.

Hyperbaric Oxygen Therapy (HBOT) is commonly used to treat carbon monoxide poisoning, to enhance wound healing and for pressure equalization after diving injuries. Among its attributed properties are also increasing blood flow and oxygen to the brain and decreasing inflammation. Thus it has been proven to be efficient in the disorders of the central nervous system,

including cerebral palsy, dementia, fetal alcohol syndrome and traumatic brain injury (Levy, S. E., Human, S.L., 2008). Given that ASDs are related to functional and structural abnormalities of the central nervous system, it has been hypothesized that HBOT might be beneficial for these patients as well (Rosignol, D. A., Rosignol, L. W., 2006). In addition, HBOT is generally considered safe at oxygen pressures below 3.0 ATA and with treatment durations of less than 120 min. The use of HBOT in children appears to be generally safe, even at pressures of 2.0 ATA for 2 hours per day for up to 40 sessions (Ashamalla et al., 1996). The most common side effect of HBOT is middle ear barotrauma, which occurs in approximately 2% of the patients.

Goals and Objectives of the Study:

This study aims to measure the therapeutic effect of HBOT in terms of symptom manifestation and developmental growth, by applying two standardized parent report forms – before and after treatment.

Method

Participants:

The group consists of 22 children with a diagnosis of Autistic spectrum disorder (including Infantile autism, Asperger's syndrome and Atypical autism) and their parents. Children's age is between 3 and 9 years (Mean age = 6 years). Children are unequally distributed by gender – 3 girls and 19 boys.

Materials and procedure:

The study is conducted at the Military Medical Academy MBAL – Varna in the period 2015-2017. All children had a diagnosis of ASD, established by an outside psychiatrist or a neurologist. Additionally, the children underwent a clinical evaluation by a pediatrician before the beginning of the HBOT protocol. Each child underwent 20 consecutive sessions of hyperbaric oxygenation therapy each with duration of 60 minutes at 1,5 ATA. A multiplace hyperbaric chamber was used, so that each child enters with a parent/ a grandparent and a member of the medical staff if necessary. The sessions were well tolerated by the children.

Prior and after HBOT protocol parents were asked to fill in two forms to measure the behavior outcome of the hyperbaric therapy:

Child Behavior Checklist for Ages 1.5-5 and for Ages 6-18 (Achenbach, 2000), translated and standardized for Bulgaria by Stankova (2007). The Child Behavior Checklists (CBCL) are part of the Achenbach System of Empirically Based Assessment and are traditionally used to measure emotional, behavioral and communicative problems in normative and clinical samples.

Developmental Assessment of Young Children (DAYC), translated and standardized for Bulgaria by Koltcheva (2005). This battery is used for the evaluation of children from birth till 6 years of age in five big development areas – Adaptive Behavior, Speech Development, Cognitive Development, Physical Development and Social-Emotional Development. For each of the areas

the examiner determines a "basis" (a minimum of 3 consecutive skills marked as acquired) and a "rooftop" (more than 2 not acquired skills out of 5 consecutive items).

Results

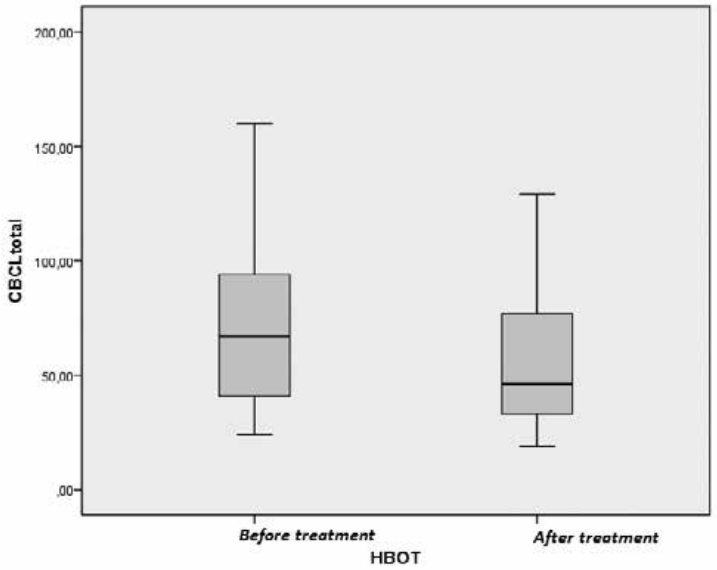
One-sample T test was used to compare CBCL total scores before and after HBOT protocol. We established a significant difference between the scores on the report forms with *t=9,052* (T critical=3.527, df=21, p=0.001),* demonstrating that HBOT is a contributing factor to the reduction of problem behaviors.

Table 1: Descriptive statistics of the Total Score on CBCL before and after the completion of HBOT sessions.

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
CBCLbeforeHBOT	22	72,0000	37,30824	7,95414
CBCLafterHBOT	22	55,0909	30,28737	6,45729

Graph 1: Boxplot of Mean score and Standard deviation on CBCL Total Score.



The items which contributed the most to the reduction of CBCL total score were related to improved eye contact, increased attention span, positive response to social contact, reaction to change, temper tantrums and reduced eating/digestive problems.

The scales of DAYC were administered to all children, so that their developmental delays could be measured. Before the HBOT protocol none of the participants could cover the last age

periods of all scales in DAYC, despite their chronological age. A one-way ANOVA was performed to estimate the effect of HBOT on the development of the children. There was a marked improvement on every scale, although significant results were found only on Adaptive Behavior, Speech and Cognitive Development.

Table 2: Results of one-way ANOVA for the effect of HBOT on the scale results of DAYC. F critical=4.06, df=42.
ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Adaptive Behavior	Between Groups	641,455	1	641,455	4,094*	,049
	Within Groups	6580,182	42	156,671		
	Total	7221,636	43			
Speech Development	Between Groups	1255,114	1	1255,114	9,925*	,003
	Within Groups	5311,318	42	126,460		
	Total	6566,432	43			
Cognitive Development	Between Groups	1375,364	1	1375,364	10,466*	,002
	Within Groups	5519,364	42	131,413		
	Total	6894,727	43			
Physical Development	Between Groups	,000	1	,000	,540	1,000
	Within Groups	2641,545	42	62,894		
	Total	2641,545	43			
Social Emotional Development	Between Groups	105,091	1	105,091	1,668	,204
	Within Groups	2645,909	42	62,998		
	Total	2751,000	43			

Parents reported improved self-help skills, improved receptive speech, acquisition of new words and communicative gestures (pointing), attempts at imitative behavior, improved categorization, improved play in terms of initiation, spontaneity and reciprocity. The results demonstrate that HBOT could be established as an alternative/ complementary therapeutic technique in addition to current behavioral and speech therapy approaches. A restriction of the current study is that only parent report forms were evaluated with no controlling for positive bias. Future research should include multiple respondents report forms and direct evaluation of the enrolled children.

Conclusions

In the current pilot study, HBOT at pressure of 1.5 atm with up to 100% oxygen was well tolerated by children with ASD. Parents reported significant improvement in several areas of development and decrease of problem behaviors of their autistic children. No physiological side effects were reported. However, since this is a pilot study and the therapeutic effect is only measured through potentially biased parent reports, the efficacy of the therapy for children with ASD cannot be conclusively stated. Further double-blind, controlled trials with direct testing of children need to be performed.

Literature:

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Washington, DC, American Psychiatric Association, 2013
2. Achenbach, T. M., & Rescorla, L. A. (2000) *Manual for the ASEBA Preschool Forms & Profiles*. Burlington, VT: University of Vermont Department of Psychiatry
3. Ashamalla HL, Thom SR, Goldwein JW. Hyperbaric oxygen therapy for the treatment of radiation-induced sequelae in children: the University of Pennsylvania experience. Cancer 1996;77(11):2407–12
4. Hardy, M.W., LaGlasse, A.B. Rhythm, Movement and Autism. Front Integr Neurosci. 2013; 7: 19.
5. Koltcheva, N. *Battery for Developmental Assessment of Young Children. Procedure for validation*. Psychological Studies, 2005
6. Levy SE, Hyman SL, "Complementary and Alternative Medicine Treatments for Children with Autism Spectrum Disorders" Child Adolesc Psychiatr Clin N Am. 2008 Oct; 17(4): 803–ix).
7. Lovaas OI (1987). "Behavioral treatment and normal educational and intellectual functioning in young children with autism". J Consult Clin Psychol. **55** (1): 3–9
8. Mundy P. *The neural basis of social impairments in autism: The role of the dorsal medial-frontal cortex and anterior cingulate system.* Journal of Child Psychology and Psychiatry and Allied Disciplines. 2003;44:793–809
9. Oberman L. M., Hubbard E. M., McCleery J. P., Altschuler E. L., Ramachandran V. S., Pineda J. A. (2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. Cogn. Brain Res. 24, 190–198
10. Rizzolatti G., Craighero L. (2004). The mirror-neuron system. Annu. Rev. Neurosci. 27, 169–192
11. Rogers S.J., Dawson G. *Early Start Denver Model for Young Children with Autism: Promoting Language, Learning and Engagement*. 2009. Guilford Publications Inc. New York
12. Rosignol DA, Rosignol LW. Hyperbaric oxygen therapy may improve symptoms in autistic children. Medical hypotheses (2006) 67, 216-228
13. Stankova M. Clinical and social aspects of the behavior problems in preschool age. 2012. New Bulgarian University, Sofia
14. Welsh JP, Ahn ES, Placantonakis DG. Is autism due to brain desynchronization? Int J Dev Neurosci. 2005;23:253–263
15. World Health Organization: International Classification of Diseases, 10th edition, 2003.

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INTRAVENOUS INDUCTION IN GENERAL ANESTHESIA IS A TRIGER FACTOR FOR S-T SEGMENT VARIATIONS

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ABSTRACT

Background: The most important moment during the induction in general anesthesia is the intubation and the opening of the airway. The manipulation on the larynx during laryngoscopy and airway's manipulations are stressful events producing consecutive changes in hemodynamic. There are several reports indicating that hemodynamic changes during this period may implicate the coronary circulation and may produce variations in the ST-T segment. The aim of this study was to compare, analyze and evaluate the reports of ST changes appearance during intravenous induction to anesthesia in our material and literature.

Method and Material: This academic research has the aim to compare and consult the contemporary literature concerning this problem from MEDLINE, EMBASE and Cochrane Library Databases and Cobiss as well, to the personal data of the authors. The relevant Data, connected to variations in the ST-T segment were selected, analyzed and prepared for discussion.

Results: More than 30 articles and 2 doctoral theses concerning the hemodynamic changes during intravenous induction to anesthesia were consulted. The personal data show that the main changes and ST variations were found at T4 (5 min after the intubation): -0.31±0.4 vs. -0.02±0.3 (p=0.004427). It seems that this is a result of the stress reaction of the body on the laryngoscopy and due to the effects of the released catecholamines.

Conclusion: According to the literature it is obvious that the laryngoscopy and the intubation can provoke hemodynamic instability with appearance of nonspecific variations in the ST-T segment. This is an unwanted event that must be taken into consideration, particularly in the hypertensive patients treated with RAS antagonists, which provokes a remarkable decrease of the BP that is responsible for a coronary vasoconstriction and changes in the size of the ST segment. The main changes in the ST segment are 5 minutes after the intubation.

Key words: intubation, laryngoscopy, vasoconstriction, ECG, ST-T segment.

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Introduction

The induction of anesthesia combined with airway manipulations are stressful events for patients undergoing surgery. The consecutive hemodynamic changes are seen as impaired blood pressure (mostly as hypotension) and tachycardia. The hypertensive disease is followed by structural changes in the cardiovascular system and those patients are very sensitive to the influence of the anesthetics and anesthetic manipulations.

Nowadays, the use of Renin angiotensin system (RAS) antagonists (angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor antagonists), as antihypertensive therapy, is in constant increase. In general, in anesthetic practice, a continuation of the antihypertensive therapy until the morning of surgery is accepted (1,2,3). But, by the evidences it was confirmed that ACE taken on the day of the surgery provoked a hypotension refractory to the therapy with sympathetic-agonists and fluids (4-11). These data indicate that hypertensive patients treated with Renin angiotensin system antagonists (RASa) are more sensitive to anesthesia than the patients treated with beta blockers (1, 12, 13).

Renin angiotensin system is an important system of the body, responsible for the maintenance of blood pressure during the stress. The treatment with RAS antagonists induces a blockade of the RAS that may affect hemodynamic during anesthesia and surgery. It seems that this hemodynamic disturbances compromise the coronary circulation producing variations in the ST-T segment. Trotter and his colleagues in 1992 have investigated the incidence of ST-segment abnormalities during Caesarean section under regional and general anesthesia. They found that significant myocardial ischemia was very infrequent in healthy patients undergoing elective Caesarean section (14).

Recently, the opinions about the use of antagonist of RAS prior to surgery are still controversial. The appearance of changes in ST-T waves as a result of the stress during the induction to anesthesia is an indication of the harmful effect of this procedure (15). In one previous study we hypothesized that non-hypertensive patients were less sensitive to anesthetic stress during the induction to anesthesia and airway's manipulation than hypertensive patients treated with RASa (16).

With the aim to confirm this hypothesis we made an investigation on 60 patients of the non-specific ST variations during the induction to anesthesia in hypertensive patients treated with Renin Angiotensin System Antagonists.

Material and Method

The aim of the study was to compare, analyze and evaluate the effects of airway manipulations to the coronary circulation and the appearance of variations in the ST-T segment.

This academic research was committed at the University Clinic of Anesthesia, Reanimation and Intensive Care at the Medical Faculty at the University "Ss Cyril and Methodius" in Skopje, Republic of Macedonia, during 2015-2017.

The method of this study was to consult and compare the contemporary literature concerning this problem from MEDLINE, EMBASE and Cochrane Library Databases and Cobiss as well, with the personal data of the authors.

The hemodynamic data and the appearance of ST-segment during induction on anesthesia (T0-T5) were analyzed in 60 patients. The data of 30 hypertensive patients chronically treated with RAS antagonists (Group A), were compared to 30 non-hypertensive patients (Group B).

The relevant data, connected to variations in the ST-T segment were selected, analyzed and prepared for discussion.

Results

The results provided from the authors of this research, concerning the blood pressure (BP) and heart rate as mean and SD, in non-hypertensive patients and hypertensive patients (B) chronically treated with RAS antagonists, are presented in the Table 1. There is a significant difference in BP in the preoperative checkup (T 0) in the groups. Despite the antihypertensive treatment, the patients in the hypertensive group have high BP. It was slightly decreased preoperatively (T 1), but a decrease > 20 mm Hg was noted after the induction to anesthesia (T 2). The airways manipulations as stressed procedure did not provoke changes in the study group A and B. There were not noted any remarkable differences in the groups (p=0.3). But in T 4 and T 5, 5 and 10 minutes after the induction, the BP dropped in both groups. The hypotension was developed in the group A (decrease of BP > 30 mmHg). The degree of dropping of BP in the Group A vs. Group B was statistically significantly bigger (p<0.05). There were significant differences in BP between the groups in T0, T1, T2 and T5.

Table 1.
The hemodynamic changes in the groups in different times

	Heart rate/ bpm (M±SD)			Blood Pressure / mmHg (M±SD)		
Time	Group A n=30	Group B n=30	p	Group A n=30	Group B n=30	p
T 0	82.0±17.8	84.8±13.3	0.277190	157.2±18.5	131.0±14.3	0.000001*
T 1	80.9±17.0	82.3±13.2	0.473347	148.3±16.3	127.0±14.3	0.000005*
T 2	79.6±16.5	84.3±14.6	0.193249	129.7±22.3	119.8±14.3	0.014413*
T 3	80.6±16.5	87.2±13.5	0.059429	120.7±27.6	120.0±14.3	0.300712
T 4	80.7±16.3	81.4±13.0	0.706172	103.6±21.9	111.0±14.3	0.344046
T 5	79.1±16.4	80.9±15.1	0.584363	95.0±21.5	108.4±14.3	0.015639*

p <0.05 significant difference;

The variations of the ST-T segments on the ECG monitors of the studied groups are presented in the Table 2.

Table 2.
ST segment variation in the groups

ST / mm	**Study group A**				
time	Valid N	Mean	Minimum	Maximum	Std.Dev.
T 0	30	-0.21	-1.2	0.6	0.475141
T 1	30	-0.223333	-1.2	0.8	0.451575
T 2	30	-0.203333	-1.0	0.9	0.460497
T 3	30	-0.24	-1.2	0.6	0.503505
T 4	30	-0.313333	-1.2	0.	0.478311
T 5	30	-0.246667	-1.4	0.7	0.502911
ST / mm	**Study group B**				
T 0	30	-0.013333	-0.4	0.7	0.278832
T 1	30	0.006667	-0.6	0.8	0.347338
T 2	30	-0.016667	-0.7	0.6	0.331229
T 3	30	-0.003333	-0.7	0.9	0.390829
T 4	30	-0.023333	-0.6	0.8	0.341077
T 5	30	0.003333	-0.6	0.9	0.339861

The average values of the ST segment in the group A (hypertensive patients) were from -0.2 to -0.3 mm, with remarkable differences from the non-hypertensive patients (Group B) where the range was from -0.003 to 0.007 mm.

The ST variations less than 0.2 mm were noted as non-specific variations.

Table 3.
Presentation of the Mann-Whitney U Test of the ST differences in groups

mm	Rank Sum-group A	Rank Sum-group B	U	Z	p-level
T 0	813.5000	1016.500	348.5000	-1.50062	0.133455
T 1	780.0000	1050.000	315.0000	-1.99590	0.045946*
T 2	798.5000	1031.500	333.5000	-1.72239	0.085001
T 3	794.0000	1036.000	329.0000	-1.78892	0.073629
T 4	722.5000	1107.500	257.5000	-2.84600	0.004427*
T 5	760.5000	1069.500	295.5000	-2.28419	0.022361*

P<0.05 significant differences

There is significant difference in the appearance of the ST segment in the study group at T1, T4 and T5.

Table 4.
Analysis of Variance – ANOVA test of the ST segment

Groups	SS effect	df	MS effect	SS error	df	MS error	F	p
Group A	0.238278	5	0.047656	39.93167	174	0.229492	0.207656	0.958932
Group B	0.021111	5	0.004222	20.08800	174	0.115448	0.036572	0.999273

According the ANOVA – test, the differences of the mean values of the ST segments registered in the groups are insignificant, p>0.05 (Table 4).

DISCUSSION

The impact of ST segment monitoring on the patients' outcomes is not known, but this is a useful method for detecting non-specific ST variations or silent ischemia in patients undergoing surgical procedures. In order to obtain accurate data in ST segment, it is important to monitor the assurance of the locations of the electrodes from removal (17 -20). The baseline must be stable and not wandering. There should be little interference from skeletal muscle. The patient must be relaxed and comfortable. There should be a square wave calibration to show that 1 mV is equivalent to 1 cm in height. The identification of the ischemic events is preferably with monitoring of ST segment changes in multiple leads (12 leads), but during the surgery the use of 5 lead monitors is common (21). The appearance of the ST segment at lead II and V of the ECG is with high sensitivity to detect coronary ischemia (22). As significant depression or elevation of ST segment is considered a variation of at least 0-1mV or 1mm. These changes are mostly presented in the coronary attacks or in hypertensive patients with uninspected hypotension or tachycardia (23).

In this study a significant ST depression ($p<0.05$) was found in the group of hypertensive patients treated with RAS antagonist without other characteristic changes, particularly without any clinical and anamnesis signs regarding the presence of an acute coronary attack. With a careful analysis of the degree of ST depression and the character and depth of inversion of the T waves, correlations between these findings with developed hypotension (>30 mmHg) in the Group A were found.

There are several reports about the interaction of hypotension in patients who received angiotensin-converting enzyme inhibitors (ACEIs) before a surgical procedure, suggesting that interactions between ACEIs and anesthesia may be neither beneficial nor predictable (24-28). The answer of such hypotension is hidden in the pharmacology of the antagonist of RAS. The RAS antagonists produce vasodilatation via several mechanisms: a direct sympathetic blockade, increases the half life of the peptides of vasodilatation (bradikinins, prostaglandins), inhibitions of the angiotensin 2 (AT-2), decrease release of aldosteron and ADH with consecutive impairment of the retention of Na ions and water. The vasoconstrictor activity of RAS, via (angiotensin) AT-2 is disabled and the stress-responses of the regional circulation and the control of the endothelial tonus is decreased (29, 30).

The developed hypotension is emphasized by the drugs used in the induction of anesthesia and is refractory to the therapy with sympathetic-agonists. In this study the morning intake of the RASa was avoided (more than 12 hours), but despite of this, a remarkable hypotension was noted. We speculate that the reason for this was the using of RASa; in this study the majority of the patients received ACEI's (26/4).

It could be taken into consideration also, that during this hypotension the coronary blood supply is impaired, and a misbalance between the myocardial oxygen demand and its utilization is developed (30,31). In this short period of time the myocardium suffers from ischemia which is seen as a down-sloping ST- depression existing in this study from minimum -0.6 to maximum of -1.2 mm (M= 0.3). The size of the ST segment at T0 was evidently different in both groups (-0.21mm$\pm$0.4 vs. -0.01mm$\pm$0.2), but statistically insignificant ($p>0.05$), what was expected considering the diagnoses (hypertensive vs. non-hypertensive). At the time T3 (during the laryngoscopy) there was noted no difference in the size of the ST segment between the study groups ($p=0.07$). The main changes were found at **T4**: -0.31±0.4 vs. -0.02±0.3 ($p=0.004427$*), 5 minutes after the intubation. It seems that this is a result of the stress reaction of the body on the laryngoscopy and due to the effects of the released catecholamine.

Conclusion

The laryngoscopy and the intubation of the hypertensive patients treated with RAS antagonists provoke a remarkable decrease of the BP that is responsible for a coronary vasoconstriction and changes in the size of the ST segment. The main changes in the ST segment are 5 minutes after the intubation. None of the size of the ST abnormality was in the ranges for serious myocardial ischemia. According to the received results of ST segment in this study, we found that they did not match the criteria for ischemia in electrocardiography (less than 1.0 mm at 80 min after J point), and we concluded with the statement that these ST-segment changes are nonspecific abnormalities.

References

1. Fleisher LA, Beckman JA, Brown KA. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary. J Am Coll Cardiol 2007; 50:1707–1732.
2. Smith I, Jackson I. Beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers: should they be stopped or not before ambulatory anaesthesia? Current Opinion in Anesthesiology 2010, 23:687–690.
3. Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg 2001; 92:26–30.
4. Mirenda VJ, Grissom TE. Anesthetic Implication of the renin-angiotensin System and angiotensin – Converting Enzime Inhibitors. Anesth Analg 1991; 72: 667-83.

5. Behnia R, Molteni A, Igic R. Angiotensin-converting enzyme inhibitors: mechanisms of action and implications in anesthesia practice. Curr Pharm Des 2003; 9:763-76.
6. Cittanova ML, Zubicki A, Savu C, et al. The chronic inhibition of angiotensinconverting enzyme impairs postoperative renal function. Anesth Analg 2001; 93:1111-15.
7. Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. Anesthesiology 1994; 81:299 –307.
8. Brabant SM, Bertrand M, Eyraud D, et al. The hemodynamic effects of anesthetic induction in vascular surgical patients chronically treated with angiotensin II receptor antagonists. Anesth Analg 1999; 89:1388-92.
9. Matchar DB, McCrory DC, Orlando LA, et al. Systematic review: comparative effectiveness of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers for treating essential hypertension. Ann Intern Med 2008; 148:16-29.
10. Costa VV,Caldas CA, Nunes NGL, Siebra SP, Saraiva AR. Influence of Angiotensin-onverting Enzyme inhibitors on Hypotension after anesthetic induction. Is the Perioperative discontinuation of this drug Necessary? Revist Bras de Anest 2009; 59:710-32.
11. David LR.et al. Predictors of Hypotension After Induction of General Anesthesia. Anesth Analg 2005; 101: 622–8).
12. Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg 2001; 92:26–30.
13. Kheterpal S, Khodaparast O, Shanks A, et al. Chronic angiotensinconverting enzyme inhibitor or angiotensin receptor blocker therapy combined with diuretic therapy is associated with increased episodes of hypotension in noncardiac surgery. J Cardiothorac Vasc Anesth 2008; 22:180– 186.
14. Trotter T. N., Langton A., Barker P., Rowbotham D. J.; Perioperative continuous monitoring of ST-segment changes in patients undergoing elective Caesarean Section, British Journal of Anaesthesia 1992; 69: 352-355.
15. Righetti A, Crawford MH, O'Rourke R, Hardarson TH, Schelbert H., Daily PO, Deluca M, Ashburn W, ROSS J.; Detection of Perioperative Myocardial Damage after Coronary Artery Bypass Graft Surgery; 1977, Circulation, 55 (1): 173-178.
16. Sholjakova M., Jovanovski Srceva M. Non Specific S-T Segment Variations During Intravenous Induction In Anesthesia In Hypertensive Patients Treated With Renin Angiotensin System Antagonists, J Anesth Crit Care Open Access 2017, 8(1): 00293.
17. Drew BJ, Califf RM, Funk M, et al. AHA Scientific Statement: Practice standards for electrocardiographic monitoring in hospital settings. Circulation. 2004;110:2721-46.
18. Sheppard LP, Channer KS. Acute coronary syndromes, Contin Educ Anaesth Crit Care Pain, 2004; 4 (6): 175-180.
19. Fredberg CK, Zager AE ; "Nonspecific" ST and T-Wave Changes, Circulation, 1961; 23 :655-661 http://circ.ahajournals.org .

20. K. Johnson. AACN, Practice alert; ST segment monitoring, Revised 05/2009:1-4.
21. Jari A. Laukkanen1,2*, Timo H. Ma¨kikallio2,3, Rainer Rauramaa4,5, and Sudhir Kurl1; Asymptomatic ST-segment depression during exercise testing and the risk of sudden cardiac death in middle-aged men: a population-based follow-up study; European Heart Journal 2009; 30, 558–565 doi:10.1093/eurheartj/ehn584.
22. Abdou Elhendy, MD, PHD, Ron T. van Domburg, PHD, Jeroen J. Bax, MD, PHD, Jos R. T. C. Roelandt, MD, PHD, FACC; The Significance of Stress-Induced ST Segment Depression in Patients With Inferior Q Wave Myocardial Infarction JACC 1999, 33, (7), :1909–1915.
23. Coriat P , Richer C , Douraki T , Gomez C , Hendricks K , Giudicelli JF , Viars P : Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. Anesthesiology 1994, 81(2):299-307, (PMID:8053578).
24. Juan Carlos Villalba G. : Electrocardiographic changes in the ST segment during anesthesia: Things to consider, Rev Colomb Anestesiol 2012; 40 (3):175-176 – DOI: 10.1016/j.rcae.2012.06.006.
25. Rodrigez LBH, Batista A. Monteiro F., Duarte JS. ST-segment elevation during general anesthesia for non-cardiac surgery: a case of takotsubo, *Brazilian Journal of Anesthesiology*, *2015; 65 (5) :403-406.*
26. Singh PM, Shah D, Trikha A ; Recurrent intraoperative silent ST depression responding to phenylephrine, J Anaesthesiol Clin Pharmacol. 2012; 28(4): 510–513.
27. Dominiak P. Modulation of sympathetic control by ACE inhibitors. Eur Heart J 1993; 14(Suppl 1):169 –72.
28. Gombar S, Khanna AK, Gombar KK. Perioperative myocardial ischaemia and infarction - a review. Indian J Anaesth [serial online] 2007 [cited 2017 Feb 20]; 51:287. http://www.ijaweb.org/text.asp?2007/51/4/287/61158.
29. Mandim BLS, Achá RES, Fonseca NM, Zumpano F, ; Cardiac arrhythmias and ST changes in the perioperative period of elderly patients submitted to transurethral prostatectomy under spinal anesthesia. Comparative study; Rev. Bras. Anestesiol. 2004; 54(2) :1-11 http://dx.doi.org/10.1590/S0034-70942004000200006.
30. Yang JH, Hahn JY, Bin Song Y, Choi SH , Choi JH , Lee SH , Jeong MH , Choi DJ , Park JS, Park HS , Gwon HC; Angiotensin receptor blocker in patients with ST segment elevation myocardial infarction with preserved left ventricular systolic function: prospective cohort study; BMJ 2014;349:g6650 doi: 10.1136/bmj.g6650 (Published 14 November 2014).
31. Colson P, Ryckwaert F; Coriat P., : Renin Angiotensin System Antagonists and Anesthesia, Anesthesia & Analgesia, 1999, 89:1143–1155 doi: 10.1213/00000539-199911000-00012.
32. Brabant, S., Bertrand, M., Eyraud, D., Darmon, PL., Coriat, P; The Hemodynamic Effects of Anesthetic Induction in Vascular Surgical Patients Chronically Treated with Angiotensin II Receptor Antagonists, Anesthesia & Analgesia, 1999, 89 (6) :1388-1398.

ИНТРАВЕНСКИ ВОВЕД ВО АНЕСТЕЗИЈАТА КАКО ПРЕДИЗВИКУВАЧ НА ВАРИЈАЦИИ ВО S-T СЕГМЕНТОТ

АПСТРАКТ

Вовед и цел: Круцијален момент при интравенскиот вовед во анестезијата е интубацијата и обезбедувањето на слободен дишен пат. Манипулациите при ларингоскопијата и ослободувањето на дишните патишта предизвикуваат промени во хемодинамиката. Постојат повеќе списи кои наведуваат дека хемодинамиските промени во текот на овој период може да ја засегнат коронарната циркулација и да предизвикаат варијации во ST-T сегментот. Целта на оваа студија е да се спореди нашиот материјал со наводите во литературата околу појавата на промени во ST сегментот при интравенска индукција во анестезијата.

Метод и материјал: Оваа проспективна студија ги споредува резултатите на авторите од вклучени 60 болни со податоците од современата литература околу овој проблем. Релевантните податоци, поврзани со варијациите во ST-T сегментот, достапни на MEDLINE, EMBASE, Cochrane Library Databases, како и Cobiss, беа селектирани, анализирани и подготвени за дискусија.

Резултати: Сопствените резултати на авторите покажуваат дека главните промени и ST варијации се случуваат во Т4 (5 минути по интубација): -0.31±0.4 vs. -0.02±0.3 (p=0.004427). Се чини дека тоа се должи на стрес-одговорот на организмот на ларингоскопијата, како и на ефектот на ослободените катехоламини.

Заклучок: Според освртот врз литературата јасно е дека ларингоскопијата и интубацијата може да предизвикаат хемодинамиска нестабилност со појава на неспецифични варијации во ST-T сегментот. Тоа е несакан сучај на кој секогаш треба да се мисли, особено кај хипертензивните пациенти кои се третирани со RAS антагонистите, кои предизвикуваат значаен пад на артериският крвен притисок, кој е пак одговорен за коронарната вазоконстрикција и промените во големината на ST сегментот. Главните промени се случуваат 5 минути по интубацијата.

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PNEUMOTHORAX TREATMENT IN PATIENTS WITH EMPHYSEMATOUS LUNG DISEASE WITH TWO DIFFERENT SURGICAL TECHNIQUES. EVALUATION OF COMPLICATIONS, RISKS AND BENEFITS

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ABSTRACT

Objective: to compare the outcomes of thoracotomy and video-assisted thoracoscopic surgery (VATS) in the treatment of pneumothorax in patients with emphysematous lung disease.

Method and Material: in prospective study we analyzed the level of postoperative complications, duration of drain presence, total drain collection, site infections, length of hospital stay (LOHS) and recurrence of pneumothorax in two groups of patients. Group OT (n=12) included patients undergoing open thoracotomy and group VATS (n=12) underwent VATS for primary pneumothorax treatment.

Results: Demographic data between the groups was homogenous. Duration of drain presence was 4.08 vs. 3.8 days in respect to the groups. Statistically significant large amount of drain collection was found in the OT group (604.1 ml vs. 391 ml). Length of hospital stay was statistically longer in group OT (p=0.02). Two patients had recurrent pneumothorax in VATS group.

Conclusion: According to our study patients, who undergo VATS, postoperatively have lower amount of drain collections, have drain presence for less days, have less days spent in the hospital, but have increased recurrence rate. Even though our study has small number of patients included, it opens a door to larger study to confirm the results.

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Introduction

Spontaneous pneumothorax in patients with emphysematous lung disease or large bullae is a common finding. Even though this is a self limiting benign condition some controversies regarding its treatment (surgical, conservative, different surgical techniques) are still present (1). Authors are mostly confirmative that presence of air leakage (5-7 day) after the drainage is an indication for surgical treatment, but these reports are still not particular which surgical approach is the best treatment option for these patients (2).

On the other hand, surgeons and clinicians debate that open thoracotomy and Video Assisted Thoracoscopic Surgery (VATS) show different results in the treatment of this condition. Many authors advocated that VATS for the treatment of spontaneous pneumothorax as a first line treatment is correlated to lower morbidity and mortality rates. But interestingly most results confirm that the recurrence rates of pneumothorax after VAST are higher and more common (3, 4, 5). Therefore, different thoracic associations still give different guidelines in the usefulness and relevance to the results (2, 6).

In the present study we evaluated and compared the safety and effectiveness of spontaneous pneumothorax treatment in patients undergoing thoracotomy and VATS. We analyzed the level of postoperative complications, air leakage, site infections, length of hospital stay (LOHS) and recurrence rate of pneumothorax in patients undergoing open thoracotomy and VATS.

Material and method

The study was undertaken as a prospective (pilot study) after the Institutional approval at the Clinic for Thoracic Surgery in Skopje, during the period from January 2016 to July 2017.

Inclusion and Exclusion criteria. This study included 24 consecutive patients (aged 18-55, BMI <30 m^2) with emphysematous lung disease who had spontaneous pneumothorax, previously treated with pleural drainage and in whom (per guidelines) [2] air leak persisted- one week after the pleural drainage**.** All patients with secondary pneumothorax due to trauma, underlying malignances, pulmonary diseases (empyema, carcinoids) and all patients with cardiology problems (EF<50% and severe arrithmogenic events) were not included in the study. Patients were divided into two groups according to the surgical technique treatment that was done, (Group OT, patients in whom open thoracotomy was done and Group VATS, patients in whom VATS was done).

Surgical procedure choice. Preoperatively all patients had conventional x-ray and computed tomography (CT scan 2-5 mm intervals) for assessing the underlying disease. Choice of surgical procedure was based on the size, site, degree of the collapsed lung and desmoplastic range evaluation. All patients underwent general anesthesia with double lumen tube. Both techniques were undertaken in lateral decubitus position (contralateral hemitorax –sane side on the surgical table) and after the finishing of either of the procedures 1or 2 chest drains were placed. For the Open thoracotomy technique: via 15-25 cm incision rib spreader was applied on the affected hemitorax. For the VATS technique: The video equipment was positioned on either side of the patient, one utility incision up to 5 cm and two additional ports were applied, without rib spreading. All patients in whom conversion from VATS to conventional thoracotomy was needed were excluded from additional analyses.

Analyzes. In all patients' demographic characteristics: (age, gender, BMI), side of the pneumothorax, number of bullas, comorbidities, laboratory findings and duration of surgery were evaluated. Additionally, in both groups of patients we analyzed the occurrence of postoperative complications: air leak, late recurrence of the pneumothorax (occurrence of pneumothorax on the side of the operation after one-month period, confirmed by x-ray), ICU admission, postoperative bleeding, drain presence (in terms of days), drain collection (for the first 3 days in total volume in terms of ml) and length of hospital stay. Analysis of mean parameters and standard deviation in both groups and between the groups was done with parametrical (paired and unpaired t-test) depending on the distribution.

Results

We analyzed data from 24 patients with emphysematous lung disease who underwent surgical treatment for primary spontaneous pneumothorax. Out of them 12 underwent VATS and (12) underwent open thoracotomy treatment. Demographic and clinical characteristics in patients are given in Table 1.

Table 1. *Demographic and clinical characteristics in patients*

	OT n=12	VATS n=12
Age (mean ± sd)	43.1 ±17.4	43.8 ± 12.3
Gender (n/%)		
Male	10/83.3%	7/58.3%
Female	2/16.7%	5/41.7%
Hypertension (n/%)	9/75%	8/66.7%
Diabetes mellitus	1/8.3%	2/16.7%
Smoker	10/83.3%	8/66.7%
Duration of surgery(min)	124.1±66	138.7 ± 32.8
Bullas ligated (mean ± sd)	1.9 + 1.2	1.7+0.6

In both of the groups most patients were male and the demographic data were comparable. Mean age between the both groups was not significantly different (p=0.83). Most of the patients were smokers and hypertension was present in 75% and 66.7% of the patients in respect to the groups. 3 patients in Group OT had other health issues (cerebral tumor extirpated, chollolithiasis and renal stones) while in group VATS, two patients has cerebral vascular insult previously. Left sided pneumothorax was present in 5 patients (41.7%) in group OT while in group VATS in 3 patients (25%). Number of bullas ligated was not significantly different between the groups (p=0.5).

Table 2. *Postoperative complications and length of hospital stay*

	OT N=12	VATS N=12
Drain presence-days (mean ± sd)	4.08 ± 1.2	3.8 ± 1.3
Drain collection-ml (mean ± sd)	604.1± 199	391.6 ± 281 *
Recurrence (n/%)	/	2/16.7%
Site infection (n/%)	1	/
LOHS (mean ± sd)	14.3 ± 3.2	10.2 ± 4.8 *

*Sd=standard deviation; n=number; * p<0.05; LOHS=length of hospital stay*

Chest drain was present postoperatively on average of 4.08 days in group OT and 3.8 days in group VATS. Drain presence (in days) was not statistically significant, but drainage collection (in ml) was statistically higher in group OT. Bleeding (more than 500 ml plain blood in one day) was found in one patient in OT. Length of hospital stay was statistically longer in group OT (p=0.02). Air leakage postoperatively was present in 2 patients in group OT and in one patient in group VATS.

Discussion

Our study confirms that VATS is safe surgery approach for patients with primary spontaneous pneumothorax. The experience of non systematic knowledge so far, confirms that VATS procedure in elderly (>75 years) patients and in children is safe and useful technique without specific affiliation to precise outcome (7, 8).

Sudduth et al. (2017) performed a systematic review and meta analysis in order to define optimal surgical technique for pneumothorax treatment. In their research, 6907 patients' data were analyzed (1988 - 2015) within the PubMed. Results of the study showed that there have not been multicenter researches comparing properties and clinical parameters with risk factors in different population to potentiate open thoracotomy or VATS (9). Thus, we do not have enough knowledge based on diseases or based on performed researches.

Historically, surgical treatment for pneumothorax has been debated for decades. Open thoracotomy is advocated as too aggressive treatment to have major affect on the postoperative mortality and morbidity. Authors like Cattaneo SM. (10) and Kaseda S. (11) confirmed that patients who undergo open thoracotomy for the treatment of pneumothorax and lung carcinoma have higher incidence of pulmonary complications, need aggressive pain treatment and have higher mortality rates. In our study there were no major complications or mortality and the pain management was not evaluated, so these aspects cannot be discussed for now.

On the other side, VATS is not novel approach in the surgery and various publications with different, relatively small samples of patients exist that confirm the advantages of this technique over the others in terms of length of hospital stay and postoperative complications (12,13,4,5).

In the current study we discovered that in patients who underwent VATS, chest drains were removed earlier compared to the patients who underwent OT. Similar to us, these finding were

confirmed in the study of Mouroux J. et al (14) (in sample size of 100 patients) and in the study of Li WW. (15), even though in both studies no statistically significant difference was found.

Differently to our study in the both above citied (14,15) studies time of surgery was found to be significantly shorter during VATS. For our study OT patients' duration of surgery was on average 124 minutes versus 138.7 minutes in VATS group. The differences between the studies' results might be due to the method of time measurement (authors don't give precise method what duration of surgery means) while in our study me measured the time of surgery from the start of anesthesia to extubating). Additionally, in our study the number of bullas ligated in both groups was not statistically different so we cannot exclude this factor as a reason for longer duration. Some authors argue that the routine for VATS has the biggest influence for the duration of the procedure (14).

The matter of drain collection in total depends on the amount of tissue trauma, irrigation, type of the surgery and several other factor (2,6,15). In our study statistically higher amounts in terms of ml (for the first 3 days in total volume) was found in the OT group which might be due to the larger trauma involved.

Literature reviews that air leak as a primary postoperative complication after pneumothorax appears to occur similar following both of techniques. In our study 16.7% of the patients with OT had persistent air leak (longer than 7 days) and 8.3% of the patients in VATS. Similar percentage (<8%) was found in the study of the Joshi V. et al. (3) where 163 patients were evaluated. Air leak after VATS may be due to rapid re-insufflation of the lung that may cause a tear in staple line or grasping of the lung with endoscopic instruments.

Recurrence rate of pneumothorax after conservative management (chest drainage, needle aspiration has been reported to be between 16-52% (5). Differently, these rates are lower after surgery, but literature proves that higher recurrence rates are expected after VATS (2-14 %) compared to (0-7%) in open thoracotomy (16,17,18). For our study this was proved and 16.7% of the patients (2 patients) only in group VATS had late recurrence. Increased recurrence rates in VATS may be due to inadequate exposure of the chest cavity and subsequent incomplete detection and resection of all bullae. Literature debates that surgeon experience and the lack of detailed pleural examination are the two most crucial factors that determinate recurrence (5, 16).

Several studies have found out that after VATS, inflammatory response was lower. This was truth in our study where only one patient in OT group had site infection. Additionally, in the terms of global inflammatory response we cannot discuss due to the fact that in the present study inflammatory response is not evaluated.

Conclusion

According to our pilot study there is no doubt that VATS is here to stay. Patients with emphysematous lung disease are heterogeneous group of patients and their treatment is a real challenge. Even though scientific data of comparing one technique to the other is limited from our study,

we can conclude that in terms of drain collection, drain presence and length of hospital stay VATS performs favorably.

Limitation

Limitation of this study is that it was not randomized double blind study. The recruitment of patients to specific group was based on several factors (the size, site, degree of the collapsed lung and desmoplastic range evaluation). Sample size is small, but however this study raised several questions that need to be answered in larger randomized studies.

References:

1. Light RW. Management of spontaneous pneumothorax. Am Rev Respir Dis 1993; 148: 245–248.
2. MacDuff A, Arnold A, Harvey J. BTS Pleural Disease Guideline Group. Management of spontaneous pneumothorax: British Thoracic Society Pleural Disease Guideline 2010. Thorax 2010; 65(Suppl 2): 18–31.
3. Joshi V., Kirmani B, Zacharias J. Thoracotomy versus VATS: is there an optimal approach for treating pneumothorax? Ann R coll Surg Engl 2013;95:61-4.
4. Naunheim KS, Mack MJ, Hazeerlrigg SR et al .Safety and efficiency of video assisted thoracic surgical techniques for the treatment of spontaneous pneumothorax. J Thoracic Cardiovascular Surg 1995: 109; 1198-203.
5. Fatimi SH, Hanif HM., Azziz S et al. How VATS has changed the management of spontaneous pneumothorax in the 21 st century. J Pak Med Assoc 2012; 62:1041-5.
6. Baumann MH, Strange C, Heffner JE. Management of spontaneous pneumothorax: an American College of Chest Physicians Delphi consensus statement. Chest 2001; 119: 590–602.
7. Yim APC Thoracoscopic surgery in elderly population. Surg endossc 1996;10:880-2.
8. Yim APC, Low JM, Ng SK et al. Video assisted thoracoscopic surgery in pediatric patients. J PediatrChild health 1995;31:192-6.
9. Sudduth CL, Shinnick JK, Geng Z, et al. Optimal surgical technique in spontaneous pneumothorax: a systematic review and meta-analysis. *Journal of surgical research*.2017 ;2010: 32-46.
10. Cattaneo SM.,Park B., Wilton A. Use of Video-Assisted Thoracic Surgery for Lobectomy in the Elderly Results in Fewer Complications Ann of Thorac Surg 2008;85(1):231-6.
11. Kaseda S, Aoki T, Hangai N, et al. Better pulmonary function and prognosis with video-assisted thoracic surgery than with thoracotomy. Ann Thorac Surg. 2000;70(5):1644-6.
12. Qureshi R, Nugent A, Hayat J, et al. Should surgical pleurectomy for spontaneous pneumothorax be always thoracoscopic? Interact Cardiovasc Thorac Surg 2008; 7: 569–572.
13. Nakajima J, Takamoto S, Murakawa T, Outcomes of thoracoscopic management of secondary pneumothorax in patients with COPD and interstitial pulmonary fibrosis. Surg Endosc 2009; 23: 1536–1540.
14. Mouroux J.Elkaim D, Padovani B, et al. Video-assisted thoracoscopic treatment of spontaneous pneumothorax: Technique and results of one hundred cases. J Thorac Cardiovasc Surg 1996;112:385-91.
15. Li WW, lee Rl, lee Tw at al. The impact of thoracic surgical access on early shoulder function: video-assisted thoracic surgery versus post lateral thoracotomy. Eur.J.Cardiothorac Surg 2003;23(3):390-6.
16. Ng CS, Lee Tw, Wan S et al: Video assisted thoracic surgery in the management of spontaneous pneumothorax: the current status. Postgrad Med J. 2006; 82:210-4.
17. Walter DA, Forty J, Morritt GN. video assisted thoracic surgery versus thoracotomy for spontaneous pneumothorax Ann Thorac Surge 1994: 58:372-6.
18. Cole FH, Cole FH jr, Khandekar A et al: video assisted thoracic surgery for spontaneous pneumothorax? Ann Thorac Surg 1995 ;60:931-3.

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APPLYING CVVHDF THERAPY USING AN "OXIRIS FILTER" AFTER CARDIAC SURGERY IN PATIENTS WITH PREOPERATIVE METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) INFECTION

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ABSTRACT

Aim: Methicillin resistant staphylococcus aureus (MRSA) is a hazardous and potentially life threatening *Staphylococcal bacteria*, which is known for its resistance to essentially all beta-lactamic antibiotics. Infections with MRSA can be classified as either hospital acquired or community associated.

The aim of this study was to present the use of oXiris filter in the CVVHDF therapy of hospital MRSA in 72 years old female patient.

Materials and Methods: The ability of oXiris filter is to remove inflammatory mediators via membrane binding. This is enabled by its AN69™ membrane, which has the ability to remove compounds by absorption. Oxiris filter for continuous venovenous hemodiafiltration (CVVHDF) is used for elimination and filtration of large molecules in patients on CVVHDF. This filter can remove different compounds, and the same can also filtrate immune complexes and inflammatory components. The Oxiris filter is suitable in patients with endocarditis, pancreatitis, after transfusion or in septic patients. In addition, high-risk patients are treated with an Oxiris filter, in order to prevent potentially bacterial growth, and reproduction as well as to disable the spreading of the primary infection.

Results: In this clinical case, hospital MRSA found preoperatively in 72 years old patient, was successfully treated with CVVHDF therapy using oXiris membrane.

Conclusion: CVVHDF therapy with oXiris membrane can be suggested as therapeutic option for hospital MRSA infections.

Key words: CVVHDF (Continuous veno-venous hemodiafiltration), MRSA, Oxiris, pneumonia, sepsis.

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Introduction

Infections with MRSA can be classified as either hospital acquired or community associated. Hospital infections with MRSA develop usually in patients with weakened immunity or progressed primary disease, or in patients that have been subjected to long term hospitalization or antibiotic treatment. Community and hospital acquired MRSAs are usually different epidemiologically, phenotypically and genetically. Community acquired MRSA is more virulent, spreads faster, and adapt quicker to the conditions of the host than hospital acquired MRSA.

Methicillin resistant staphylococcus aureus (MRSA) is commonly inhabited on the skin, in the mucous membrane of the nose and in clinically healthy people. It can also be classified as a transient form of bacterial flora of various skin rabbits, carbuncles and furuncles. One in four healthy people have the bacteria in their nose or on their skin without demonstrating any symptoms of an active infection. If the bacteria enters a healthy organism, it can cause an infection that is local and is usually expressed as carbuncles, furuncles and cellulite. On the other hand, serious infections of the heart, lung or bones are observed in immuno-compromised people.

Cardiac surgical patients with extracorporeal circulation have an increased risk of dissemination of the otherwise normal bacterial flora. They also have a change in their immune response and thus have an increased tendency to develop more severe clinical signs and symptoms. Therefore, early recognition of systemic changes, including typical signs and symptoms observed in cardiac surgery patients during the first 48 – 72 hours after surgery, as well as appropriate response with adequate and aggressive therapy is critical. Continuous veno-venous haemodiafiltration (CVVHDF) with an Oxiris filter may be a therapeutic option in these urgent cases.

Newly introduced Prismaflex eXeed system has two different options for managing critically ill patients, such as septic, or patients already in septic shock. SepteX™ and oXiris™ are proprietary disposable sets, used only in conjunction with the Prismaflex system. The base membrane comprising the filter in the oXiris set is AN69™, which is the most widely used Continuous renal replacement therapy (CRRT) membrane with unique property to remove compounds by absorption (membrane binding). The ability of oXiris membrane is to remove inflammatory mediators via this mechanism. Furthermore, due to specific modification of the membrane, one additional set of molecules targeted for absorptive removal is related to endotoxins. These endotoxin fragments act as an inflammatory stimulus in many septic episodes. Finally, due to the increased bleeding risk following CRRT, heparin is immobilized to the blood-contacting surface of the oXiris membrane.

Oxiris filter for continuous venovenous hemodiafiltration (CVVHDF) is used for elimination and filtration of large molecules in patients on CVVHDF. This filter can remove different compounds, and also can filtrate immune complexes and inflammatory components. The Oxiris filter is suitable in patients with endocarditis or if patients are septic. In addition, high-risk patients are treated with an Oxiris filter, in order to potentially prevent bacterial growth and reproduction, as well as to disable the spreading of the primary infection.

The hypothesis of this study was that the CVVHDF therapy with Oxiris filter can be used for treating hospital MRSA infections. Consequently, the aim of this study is to present a clinical case of the use of Oxiris filter during CVVHDF therapy of hospital MRSA detected preoperatively in the intra-nasal membrane of 72 years old patient.

Case Report

A female seventy-two (72) year old patient was admitted for surgical treatment of the mitral and tricuspid valve. Patient's history revealed pneumonia, which had been treated a year before admission. At the moment of hospitalization, patient complained with fatigue and heart palpitations as subjective symptoms.

Preoperatively, comprehensive biochemical analyses, chest x-rays, microbiological analyses and selective coronary angiography of the coronary blood vessels were conducted. However, due to acute hemodynamic instability, the patient was urgently admitted for surgical procedure, without having completed all necessary pre-operative microbiology tests.

Intra operatively the patient was stable and no complications were encountered. A reconstruction of the mitral and tricuspid valves with annuloplasty as well as right atrial resection with atrioplasty was performed.

Postoperatively, the patient was timely extubated and haemodynamically stable with decent blood gas analysis (PaO2 45Hg Pa CO2 95 mmHg), good diuresis (2150 ml per 24 hours) and sufficient peripheral oxygen saturation (SpO2 98%) (Table 1). Postoperatively, during the next 12 hours, the patient destabilized with a decrease in peripheral oxygen saturation, deterioration of blood gas analysis and disruption of hemodynamic parameters. Clinically, dyspnea and tachypnea were evident. Blood counts and biochemical tests were performed along with an X-ray. All parameters suggested a potentially respiratory system infection. Moreover, microbiological analyzes of preoperatively taken samples demonstrated the presence of intra-nasal MRSA.

Due to the urgency of the case, CVVHDF with Oxiris filter was indicated.

During the following hours, however, respiratory failure deepened requiring intubation and mechanical ventilation. In addition, the patient was placed on dialysis for 48 hours.

Clinical condition improved significantly after the first 12 hours. Both, biochemical parameters (Table 2) and X-ray finding (Table 3) improved. Subsequently, the patient was taken off of dialysis and was extubated. As soon as the condition improved the patient was transferred to the general ward. Finally, the patient was discharged from the hospital in stable condition on the 12th post-operative day.

Conclusion

Haemofiltration, especially ultrahemofiltration with a large reverse fluid volume, has evolved remarkably from an "experiment" to a standard and highly efficient life-saving procedure used for the prevention and treatment of various infective conditions including, but not limited to sepsis and septic shock.

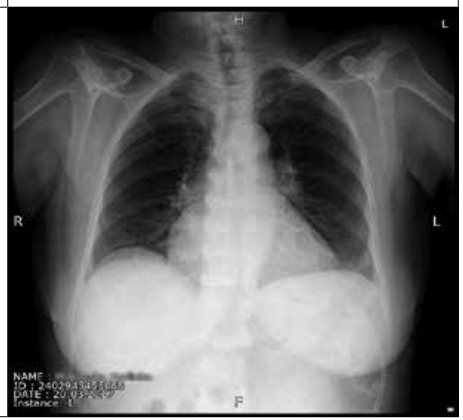
Table 1. *Blood gas analysis*

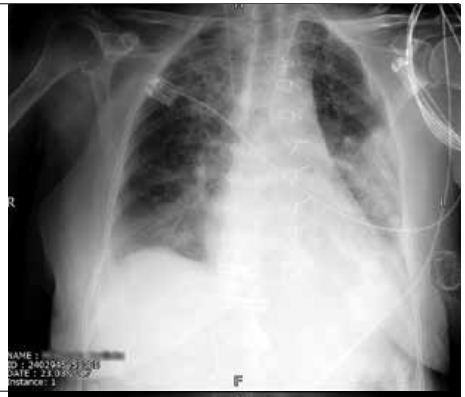
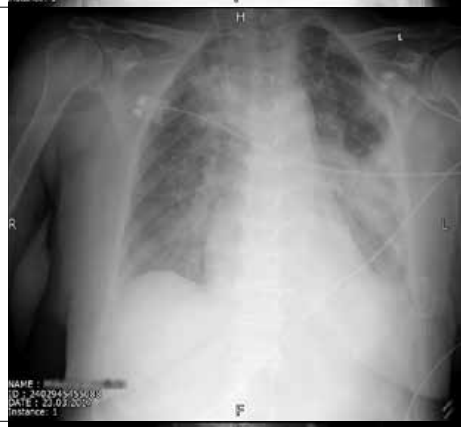
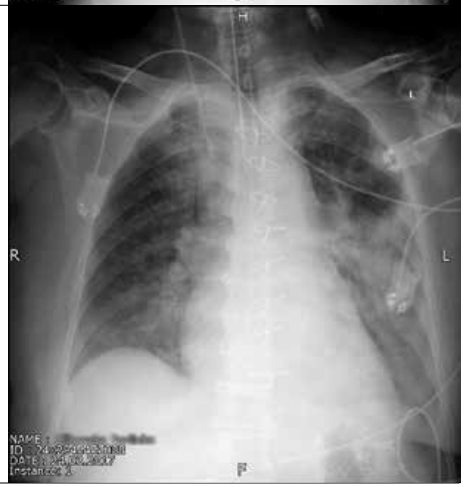
	pH	PO_2	PCO_2	HCO_3	SpO_2	Na	K	Glycaemia	Lactate	BE	M.V.
Before operation	7,4	43	88	26	94	142	3,8	5,2	1,03	1,6	No
Intra operation	7,49	30	199	22	98	136	3,21	4,5	0,8	-0,1	Yes
Day of operation	7,2	36	150	17,4	97	143	3,8	12,7	2,93	-8,4	No
First day	7,32	44	95	22	96	148	4.0	11.4	4.8	-3.4	No
Second day	**7,49**	**31**	**52**	**23**	**88**	**143**	**4,2**	**11,2**	**6.3**	**0**	**No**
Third day	7,39	32	161	19	98	139	4,2	9,1	1,5	-4,7	Yes
Fifth day	7,43	37	82	24	94	137	3,86	6	0,4	0,8	No

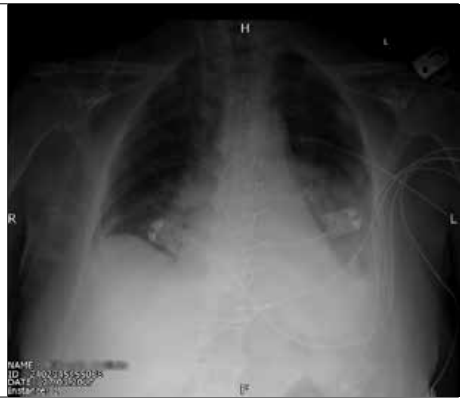
Table 2. *Laboratory analyses*

Date	17.03.2017	22.03.2017	23.03.2017	24.03.2017	26.03.2017	31.03.2017
White blood cells	4,99	16,9	17,33	17,65	8,18	9,74
CRP – C reactive protein			183		72	35
Procalcitonin			1,46		0,23	
Creatinin	62	62	61		37,9	57
Urea	5	4,2	6,7		3,3	4,2

Table 3. *X-ray of lungs*

Date	X – ray finding	X – ray picture
20.03.2017	The lungs are without X-ray signs of pathological parenchymal consolidation. Costo-phrenic sinuses are free of fluid.	

23.03.2017 morning	Pulmonary edema bilaterally in the lung parenchyma. Left in the lower lobe is a reduced lung transparency with suspicion of inflammatory infiltration. Pleural effusions are seen bilaterally in the costophrenic sinuses.	
23.03.2017 afternoon	Condition after sternotomy median, with visible 8 intact wires. Constant lung changes, with pathological parenchymal consolidation right in the upper and lower lungs and left in the middle and basal lung parts, with shaded two CF sinuses, and there is no exclusion of a small pleural effusion in the same.	
24.03.2017	Constant lung changes, with pathological parenchymal consolidation to the right in the upper and lower lungs, left in the middle and basal lung parts most suited for inflammation A small pleural effusion left.	

27.03.2017	Condition after sternotomy, with visible 8 intact wires. The lungs are with steady changes in the middle and basal sides bilaterally, with pathological parenchymal consolidation left basally, as well as shaded CF sinus on the same side of the present pleural effusion. The right CF sinus is free.	

References

1. *Antimicrobial resistance: the example of Staphylococcus aureus*. J Clin Invest 2003; 111(9): 1265−73.
2. *Definition of MRSA*, Centers for Disease Control and Prevention, USA, 12. 4. 2013.
3. Centers for Disease Control and Prevention. Methicillin-resistant Staphylococcus aureus (MRSA) infections. Accessed April 17, 2011.
4. Stein B, Pfenninger E, Grunert A, et al.: Influence of continuous haemofiltration on haemodynamics and central blood volume in experimental endotoxic shock. Intens Care Med 1990, 16: 494-499.View Article.
5. Grootendorst AF, van Bommel EF, van der Hoven B, et al.: High volume hemofiltration improves right ventrictular function in endotoxin-induced shock in the pig. Intens Care Med 1992, 18: 235-240.View Article.
6. Bellomo R, Tipping P, Boyce N: Continuous veno-venous hemofiltration with dialysis removes cytokines from the circulation of septic patients. Crit Care Med 1993, 21: 522-526. View ArticlePubMed.
7. Fisher CJ Jr, Agosti JM, Opal SM, et al.: Treatment of septic shock with the tumor necrosis factor receptor: Fc fusion protein. N Engl J Med 1996, 334: 1697-1702. 10.1056/NEJM199606273342603View ArticlePubMed.
8. van Hamersvelt HW, Eggenhuizen E, Hejinis G, et al.: Convective and diffusive clearance of large molecules during continuous veno-venous hemodiafiltration [abstract]. J Am Soc Nephrol 1999, 10: 198A.

9. Kellum JA, Johnson JP, Kramer D, et al.: Diffusive versus convective therapy: effects on mediators of inflammation in patients with severe systemic inflammatory response syndrome. Crit Care Med 1998, 26: 1995-2000. 10.1097/00003246-199812000-00027View ArticlePubMed.
10. Lonneman G, Koch KM, Shaldon S, Dinarello CA: Studies on the ability of hemodialysis membranes to induce, bind and clear human interleukin-1. L Lab Clin Med 1988, 112: 76-86.
11. Bellomo R, Bladwin I, Cole L, Ronco C: Preliminary experience with high volume hemofiltration in human septic shock. Kidney Int 1998, 53 (suppl 66): S182-S185.
12. Reeves J, Butt WW, Shann F, et al.: Continuous plasmafiltration in sepsis syndrome. Crit Care Med 1999, 27: 2096-2104. 10.1097/00003246-199910000-00003View ArticlePubMed.
13. Tetta C, Bellomo R, Brendolan A, et al.: Use of adsorptive mechanisms in continuous renal replacement therapies in the critically ill. Kidney Int 1999, 56 (suppl 72): S15-S19.View Article.
14. Kellum JA: Immunomodulation in sepsis the role of hemofiltration. Minerva Anesthesiol 1999, 65: 410-418.
15. Bellomo R: Continuous hemofiltration as blood purification in sepsis. New Horizons 1995, 3: 732-737.PubMed.
16. Bellomo R, Kellum JA, Gandhi C, et al.: The effect of intensive plasma water exchange by hemofiltration on hemodynamics and soluble mediates in canine endotoxemia. Am J Respir Crit Care Med 2000, in press.
17. Toft P, Kehler D, Brandslund I, et al.: The immunological effects of continued veno-venous haemodiafiltration in critically ill patients. Crit Care 1999, 3: 159-165. 10.1186/cc370PubMed CentralView ArticlePubMed.
18. Alkhunaizi AM, Schrier RW: Management of acute renal failure: new prospectives. Am J Kidney Dis 1996, 28: 315-328.View ArticlePubMed.
19. Braun N: Expression of adhesion molecules and activation markers on lymphocytes and monocytes during hemofiltration. Blood Purif 1997, 15: 61-76.View ArticlePubMed.

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ORO-MAXILOFACIAL METASTASES- REAR PRESENTATION OF THYROID FOLLICULAR CARCINOMA

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Abstract

All clinicians must be aware that malignant tumors in the oro-facial region may be the first evidence of the dissemination of an unknown tumor from different primary site. Thyroid malignancy are reported to represent only 2% of facial sceleton metastases and 4.2-6.1 % of all jaw metastases, therefore metastases in the oro-facial region may be indications of thyroid cancer in the background [1,2]. We present a rare, but educational case in revealing, evaluation and treatment of follicular thyroid carcinoma presented with orofacial metastases. As to our knowledge this is the first reported case from Macedonia.

Key words: oro-facial metastases, Follicular, Thyroid, Carcinoma

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Introduction

All clinicians must be aware that malignant tumors in the oro-facial region may be the first evidence of the dissemination of an unknown tumor from different primary site. Oro-maxilofacial malignancies present 1% of the whole metastatic sites of different malignacies and the mostly common involve metastases orginating from breast and lung carcinoma [1].

On the other hand, thyroid malignancy are reported to represents only 2% of facial sceleton metastases and 4.2-6.1 % of all jaw metastases, therefore metastases in the oro-facial region may be indications of thyroid cancer in the background[2,3].

Overall in Macedonia, incidence of thyroid carcinoma according to the European Cancer Observatory ECO report is 44 cases per 100000 population [4]. No further data is presented of which type of thyroid carcinoma is the most frequent in Macedonia, but global observatories refer that the follicular thyroid carcinoma is the second most frequent type worldwide (15-20%), right after the papillary carcinoma (60%) [4].

Primary presentation of follicular thyroid carcinoma with metastases in the oro-facial region is extremely rare. Varadarajan et al. has done a systematic review of 41 oro-facial metastatic case reports and his data confirmed that follicular thyroid carcinoma was found to be present in 21 cases [5]. We present a challenging diagnostic case of oro-maxillo-facial malignancy due to follicular thyroid carcinoma. To our knowledge this is the first case reported from Macedonia.

Case Report

In December 2016, a 67 aged patient was addmitted to the University Clinic for Maxillo-facial Surgery due to severe pain in the lower jaw area (potentiated with mouth opening and swallowing), a visible swelling of the face, retro-auricular tumor mass (palpably not painful) and severe swelling behind the right molar. Anamnestically, patient had reduced appetite for several months, had difficulty in swallowing, was a smoker, had regulated hypertension and regulated diabetes type I.

Computed tomography (CT) of the head showed destructive lesion of the mandibula and sweling of the right parotid gland, after what fine needle aspiration and incisional biopsy was done. Obtained biopsy results pointed to malignant tumor in the right parotide gland and at the ramus of the mandibula and total extirpation of the right parotid gland and partial mandibular resection at the level of the ramus was done**.** The dissected material patho-histological analyses (malignant epithelial neoplasm with predominantly follicular reorganized architectural arrangement with vascular invasion) and immunohistochemically differentiation [thyroid transcription factor 1(TTF1) (+), thyroglobulin (+), chromogranin (weak positivity), cytokeratin19 (CK19) (focal positivity)] pointed to assumption that metastatic follicular carcinoma of the thyroid gland was the diagnosis.

Subsequently, after several weeks patient was addmited to the Clinic for Thoracic Surgery for further treatment. At admission, based on the CT scan of the neck and chest (Images 1, 2, 3) indication for total thyroidectomy was established (due to suspection and working diagnoses for thyroid carcinoma).

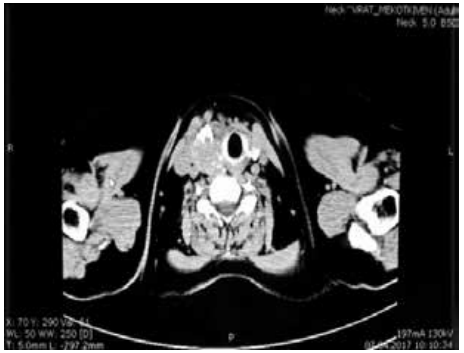
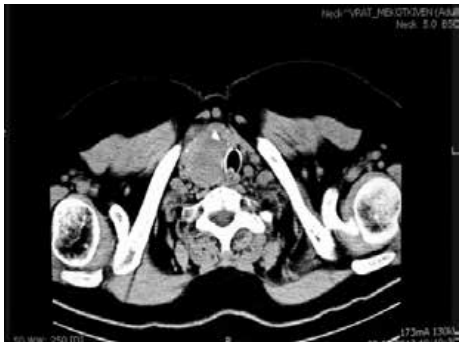
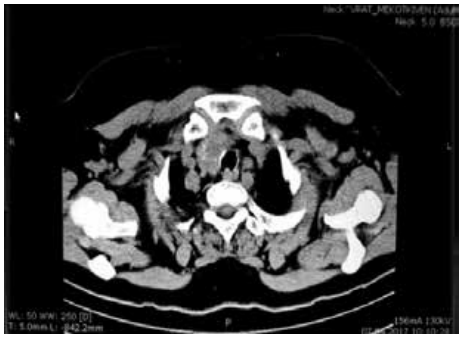


Image 1*: Shows no significant deviation of the thyroid gland and isthmus. The right lobe of the thyroid gland. The chest CT without deviations.*





Images 2 and 3: *show increased right lobe of the thyroid gland, with peripheral calcifications, a non-homogeneous, hypodense zone is detected (relatively demarcated from the environment) and more pronounced hypodense zones are seen in the surrounding parties.*

The patient underwent total thyroidectomy in general endotracheal anesthesia. Standardized thyroidectomy procedure through 5 cm incision in the lower neck was done and two drains were

placed. Surgical material (right lobe, left lobe and isthmus) were sent for patohisthological analyzes. No perioperative and postoperative complications occurred and the patient was discharged on the seventh postoperative day.

Postoperative pathohistological results identified enlarged right lobe (5x3x3) and homogenous left lobe, macroscopically. On the other hand, microscopically the samples from the left lobe were identified as normal thyroid tissue with coloid folicular cells, while as the samples of the right lobe were identified well-differentiated follicular type of thyroid carcinoma with malignant cells present (encapsulated and invades of the capsule with blood vessels). Immunohistochemical, malignant cells for Cytokeratin19 and Calcitonin were negative (-). According to the histopathological findings in the right lobe of the thyroid gland, a III stage (pT3;pN0;pMx:G1) folicular type of thyroid carcinoma was confirmed, which additionally confirmed our clinical and working diagnose.

Postoperatively in addition to the surgery, the patient was sent to the Institute of Pathophysiology, in order to decide on further treatment with radioactive iodine.

Discussion

Cytological recognition of thyroid gland metastases at various places in the body can be a diagnostically and clinical problem. Metastases originating from thyroid carcinoma in the oro-facial region, in the world literature is reported in only 41 case reports. Out of this 41 case reports in half of them (21 cases), follicular thyroid carcinoma was confirmed to be the underlying type for orofacial malignancy [5].

We presented a case of follicular thyroid carcinoma with primary diagnosed dysphagia, face swelling, molar swelling and invasion of mandibular and parotid gland. Literature reports that 41 % of the facial skeleton metastasis in thyroid cancer occur in mandibula and majority of this tumors are presented with swelling and osteolytic lesion as it was the case in our patient [2,3]. Kanchan P. At al. compared the incidence of mandibula versus maxila invasion and confirmed that the mandible is more commonly affected than maxilla with premolar or molar swelling present.

Even tough, follicular carcinoma is unifocal, rarely displays lymphogenic metastases and is slowest growth type (in terms of malignancies in humans), Antunes AA et al [7]. and Lavanya C et al [8]. are discussing that metastatic lesions in these patients are followed by rapid intraoral and extra oral swelling associated with pain granulation like tumors, fractures and disturbed mastication and swallowing. According to these authors, our patient had the typical symptoms that are similar to their case reports. As addition, our patient had firstly diagnosed invasion and destruction of ramus mandible which might be talking of more progressiveness and invasion at this particular patient. This is completely opposite to the literature facts that are displaying a higher propensity for metastases in the mandible's body compared to ramus. [6]

Rarity of our case was also presented in the parotid gland involvement which is exception and only described in one more case report from England. [9]

The complexity of our case interferes with the treatment option. In particular, in our case, our patient was subjected to surgery, where total thyroidectomy was made after previous total parotidectomy and partial resection of the mandibla. In addition to the surgery, post-operatively the patient was sent to the Institute of Pathophysiology for possible radiotherapy with radioactive iodine (I-131) and is set to standard postoperative monitoring.

Literature is deciseve that all sceleton and orofacial metastases should be treated by surgical resection (as in our case), but the finding and resolving of the primary carcinoma is essential [2,3,4]. Faster evaluation and faster approach to optimal therapy for differentiated follicular thyroid carcinoma (total thyroidectomy and radiotherapy) or as some suggested both of them in combination with chemotherapy, have better outcome in these patients. However as in our case, the treatment plan should be formulated with a multidisciplinary team that included surgery, radiology, oncology, pathophysiology.

Conclusion

Follicular thyroid carcinoma is a well-differentiated tumor that originates from hormone-producing follicular cells. Metastases from follicular thyroid carcinoma can be present for years without giving specific clinical symptoms and signs. Every clinitian must reconsider that oro-facial region metastases may be indication of thyroid cancer in the background.

Literature:

1. Friedrich RE, Abadi M. Distant metastases and malignant cellular neoplasms encountered in the oral and maxillofacial region: analysis of 92 patients treated at a single institution. Anticancer Res. 2010; 30:1843–8.
2. Hirshberg A, Shnaiderman-Shapiro A, Kaplan I, Berger R. Metastatic tumors to the oral cavity – pathogenesis and analysis of 673 cases. Oral Oncol. 2008; 44:743–52.
3. Batsakis J. Tumors of the head and neck: clinical and pathological considerations. 2nd ed. Baltimore: Williams & Wilkins; 1979.
4. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer. 2013 Apr;49(6):1374-403.
5. Varadarajan et al. Follicular thyroid carcinoma metastasis to the facial skeleton: a systematic review. BMC Cancer (2017) 17:225.
6. Kanchan P., Gurkaran PS, Sandeep V. et al. Mandibular metastasis revealed papillary thyroid carcinoma: Rare case. Int J Surg Case Rep. 2017; 37: 130–133.
7. Antunes AA, Antunes AP. Gnathic bone metastasis: a retrospective study of 10 cases. Braz J Otorhinolaryngol. 2008; 74:561–5.
8. Lavanya C, Ranganathan K, Veerabahu M. Mandibular metastasis of thyroid carcinoma: a case report. J Clin Diagn Res. 2014; 8:ZD15–6.
9. 9. Whitaker B, Robinson K, Hewan-Lowe K, Budnick S. Thyroid metastasis to the oral soft tissues: case report of a diagnostic dilemma. J Oral Maxillofac Surg. 1993;51:588–593.

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GUIDELINES AND RECOMMENDATIONS OF CARDIOVASCULAR THERAPY FOR PATIENTS WHO UNDERGO NON CARDIAC SURGERY

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ABSTRACT

Most of the patients scheduled for non-cardiac surgery have one or more comorbidities which are treated with certain medical therapy. It is not always clear whether to continue, stop or change this therapy during the perioperative period.

2014 European Society of Cardiology (ESC) and the European Society of Anesthesiology (ESA) guidelines on cardiovascular assessment and management in noncardiac surgery came to the scene. In the same year, 2014 American College of Cardiology (ACC) and American Heart Association (AHA) Guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery were issued, and they also represent the official position of these societies.

The aim of this article is to compare and find the similarities and the differences between the two guidelines concerning perioperative medical therapy.

Key words: anesthesia, guidelines, non cardiac surgery, perioperative medical therapy

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Introduction

Guidelines summarize and evaluate all available evidence, at the time of the writing process, on a particular issue in order to assist health professionals in selecting the best management for each patient, taking into account the impact on the outcome, as well as the risk benefit ratio of the particular diagnostic or therapeutic means.

2014 European Society of Cardiology (ESC) and the European Society of Anesthesiology (ESA) guidelines on cardiovascular assessment and management in non-cardiac surgery, represents the official position of these two societies on the given topic.(1) In the same year, 2014, American College of Cardiology (ACC) and American Heart Association (AHA) issued their Guidelines on perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery and they also represent the official position of these societies.(2)

The major goal of these Guidelines is to provide a step-by-step guidance for clinicians managing cardiac patients undergoing noncardiac surgery. So, these two guidelines focus on the cardiovascular management of patients in whom heart disease is a potential source of complications during non-cardiac surgery.

Part of the guidelines is the perioperative medical therapy incorporated in the risk reduction strategies - pharmacological (ESC&ESA) or recommendations for perioperative therapy (ACC & AHA). In 2016 two editorials were issued on comparison of these guidelines, but perioperative therapy was not analyzed. (3, 4)

Hereby, the two guidelines are presented and the comparison for each group of drugs is given.

Beta-Blocker therapy

Table 1. *Recommendations for beta blocker therapy of ESC&ESA*

Recommendations	Class of recommendation	Level of evidence
Peri-operative continuation of beta blockers is recommended in patients currently receiving this medication	I	B
Pre-operative initiation of beta blockers may be considered in patients scheduled for high-risk surgery and who have 2 clinical risk factors from the RCRI or ASA status 3.	IIb	B
Pre-operative initiation of beta blockers may be considered in patients who have known IHD or myocardial ischaemia.[a]	IIb	B
When oral beta-blockade is initiated in patients who undergo non-cardiac surgery, the use of atenolol or bisoprolol as the first choice may be considered.	IIb	B
Initiation of peri-operative highdose beta-blockers without titration is not recommended.	III	B
Pre-operative initiation of beta blockers is not recommended in patients scheduled for low-risk surgery	III	B

RCRI - revised cardiac risk index; ASA- American Society of Anesthesiologists; IHD - ischemic heart disease.[a] Treatment should ideally be initiated between 30 days and (at least) 2 days before surgery, starting at a low dose, and should be continued post-operatively. The target is a resting heart rate 60–70 bpm and systolic blood pressure>100 mm Hg.

Table 2. *Recommendations for beta blocker therapy of ACC&AHA*

Recommendations	Class of recommendation	Level of evidence
Continue beta blockers in patients who are on beta blockers chronically	I	B
Guide management of beta blockers after surgery by clinical circumstances	IIa	B
In patients with intermediate- or high-risk myocardial ischemia noted in preoperative tests, it may be reasonable to begin beta blockers	IIb	B
In patients with ≥ 3 RCRI factors, it may be reasonable to begin beta blockers before surgery	IIb	B
Initiating beta blockers in the perioperative setting as an approach to reduce perioperative risk is of uncertain benefit in those with a long-term indication, but no other RCRI risk factors	IIb	B
It may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably >1 d before surgery	IIb	B
Beta-blocker therapy should not be started on the day of surgery	III: harm	B

RCRI, Revised Cardiac Risk Index;

Table 3. *Lee's Revised Cardiac Risk Index (RCRI) (5)*

• History of ischemic heart disease
• History of congestive heart failure
• History of cerebrovascular disease (stroke or TIA)
• Chronic kidney disease (creatinine > 170 mmol/L)
• Diabetes mellitus requiring insulin

When the comparison and combination of the two guidelines is made, the results will be following:

1. The two guidelines agree that perioperative continuation of beta blockers is recommended in patients currently receiving this medication.
2. Preoperative initiation of beta blockers
   ESC/ESA guidelines recommend starting a preoperative beta blocker therapy in:
   - Combination of high risk surgery and ≥ 2 RCRI factors or ASA III
   - Known IHD or myocardial ischemia.

   ACC/AHA guidelines recommend starting a preoperative beta blocker therapy in:
   - Intermediate or high risk myocardial ischemia noted in preoperative tests
   - In patients with ≥ 3 RCRI factors.
3. When not to initiate:
   - Low risk surgery (ESC/ESA)
   - Patients without RCRI risk factors (ACC/AHA).
4. Timing of initiation and choice of drugs:
   - Not on day of surgery (ACC/AHA)
   - 2-7 days ideally (ACC/AHA)
   - Not high dose without titration, till heart rate of 60-70 bpm with systolic blood pressure >100mmHg (ESC/ESA)
   - Atenolol or bisoprolol (ESC/ESA)
   - Guide beta blockers according to circumstances after surgery (hypovolemia, pain, blood loss, infection) ACC/AHA

Table 4. *Surgical risk estimation according to the type of surgery or intervention*

Low risk: <1%	Intermediate risk: 1-5%	High risk: >5%
Superficial surgery	Carotid endarterectomy	Emergency major surgery
Endoscopic procedures	Head and neck surgery	Aortic or other major vascular surgery
Eye surgery	Intraabdominal surgery	Pulmonary or liver transplant
Breast surgery	Orthopedic surgery	Duodeno-pancreatic surgery
Gynecology minor	Prostate surgery	Total cystectomy
Orthopedic minor (meniscectomy)	Thoracic surgery	Pneumonectomy
Urology (transurethral operations)	Renal transplant	Operation with large fluid shifts or blood loss

Adapted from Glance et al[6]

Statin therapy

3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) are widely prescribed in patients with or at risk of IHD. Patients with non-coronary atherosclerosis (carotid, peripheral, aortic, renal) should receive statin therapy for secondary prevention, irrespective of non-cardiac surgery. Statins also induce coronary plaque stabilization through pleiotropic effects, which may prevent plaque rupture and subsequent myocardial infarction in the perioperative period.

Table 5. *Recommendations for statins therapy of ESC&ESA*

Recommendations	Class of recommendation	Level of evidence
Peri-operative continuation of statins is recommended, favoring statins with a long half-life or extended-release formulation	I	C
Pre-operative initiation of statin therapy should be considered in patients undergoing vascular surgery, ideally at least 2 weeks before surgery	IIa	B

Table 6. *Recommendations for statins therapy of ACC&AHA*

Recommendations	Class of recommendation	Level of evidence
Statins should be continued in patients currently taking statins and scheduled for noncardiac surgery	I	B
Perioperative initiation of statins use is reasonable in patients undergoing vascular surgery	IIa	B
Perioperative initiation of statins may be considered in patients with clinical indications according to GDMT who are undergoing elevated-risk procedures	IIb	C

GDMT- guide directed medical therapy

According to current guidelines, most patients with peripheral artery disease (PAD) should receive statins. If they have to undergo open vascular surgery or endovascular intervention, statins should be continued afterwards. In patients not previously treated, statins should ideally be initiated at least 2 weeks before intervention for maximal plaque-stabilizing effects and continued for at least 1 month after surgery. According to ESC/ESA guidelines in patients undergoing

non-vascular surgery, there is no evidence to support pre-operative statin treatment if there is no other indication. The recommendations of ACC&AHA include other elevated procedures in the guidelines of perioperative initiation of statin therapy.

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs)

Table 7. *Recommendations for ACEIs and ARBs of ESC&ESA*

Recommendations	Class of recommendation	Level of evidence
Continuation of ACEIs or ARBs, under close monitoring, should be considered during non-cardiac surgery in stable patients with heart failure and LV systolic dysfunction.	IIa	C
Initiation of ACEIs or ARBs should be considered at least 1 week before surgery in cardiac-stable patients with heart failure and LV systolic dysfunction.	IIa	C
Transient discontinuation of ACEIs or ARBs before non-cardiac surgery in hypertensive patients should be considered.	IIa	C

*ACEIs - angiotensin converting enzyme inhibitors; ARBs - angiotensin receptor blockers; LV - left ventricular. *

Table 8. *Recommendations for ACEIs and ARBs of ACC/AHA*

Recommendations	Class of recommendation	Level of evidence
Continuation of ACEIs or ARBs, perioperatively is reasonable.	IIa	B
If ACEIs or ARBs are held before surgery, it is reasonable to restart as soon as clinically feasible postoperatively	IIa	C

ACEIs - angiotensin converting enzyme inhibitors; ARBs - angiotensin receptor blockers.

There is a difference between the two guidelines concerning the use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs).

The recommendations of ESC&ESA make a distinction between the use of ACEIs or ARBs in LV dysfunction where these drugs should be continued and the use of ACEIs and ARB for treatment of hypertension, where they should be held before surgery. Perioperative use of ACEIs or ARBs carries a risk of severe hypotension under anesthesia, in particular following induction and concomitant beta blocker use. Hypotension is less frequent when ACEIs are discontinued the day before surgery. Although this remains debatable, ACEIs withdrawal should be considered 24 hours before surgery when they are prescribed for hypertension. They should be resumed after surgery as soon as blood volume and pressure are stable. The risk of hypotension is at least as high with ARBs as with ACEIs, and the response to vasopressors may be impaired. In patients with LV systolic dysfunction, who are in stable clinical condition, it seems reasonable to continue treatment with ACEIs under close monitoring during the perioperative period. When LV dysfunction is discovered during pre-operative evaluation in untreated patients in a stable condition, surgery should be postponed if possible, in order to allow for diagnosis of the underlying cause and the introduction of ACEIs and beta-blockers.

The recommendations of ACC/AHA do not include withholding ACEIs or ARBs in certain circumstances, because the studies they analyzed showed a greater deal of hypotension in patients using these medicines perioperativly, but they say that this did not make a difference in 30 day mortality. They find a greater danger if the ACEIs or ARBs are stopped before surgery and they are not continued afterwards.

Calcium Channel Blockers

Both guidelines analyzed the same 11 randomized trials with 1007 patients. The relevance of the randomized trials assessing the perioperative effect of calcium channel blockers is limited by their small size, lack of risk stratification, and the absence of systematic reporting of cardiac death and myocardial infarction. That is why official recommendations were not made. But the analyzed studies showed the following:

- In all patients who underwent non-cardiac surgery under calcium channel blocker treatment, there was a significant reduction in the number of episodes of myocardial ischemia and supraventricular tachycardia,
- Subgroup analyses favored diltiazem.
- Dihydropyridine (nifedipine) use was independently associated to increased incidence of perioperative mortality,
- Heart rate-reducing calcium channel blockers are not indicated in patients with heart failure and systolic dysfunction, because of their substantial negative inotropic effects which may precipitate or worsen heart failure in patients with depressed ejection fraction and clinical heart failure,
- Calcium channel blockers should be continued during non-cardiac surgery in patients with vasospastic angina.

Alpha-2 Agonists

Alpha 2 receptor agonists reduce post-ganglionic noradrenaline output and therefore reduce the catecholamine during surgery. But, the international, large multicenter, blinded POISE-2 study showed that clonidine did not reduce the rate of death or nonfatal MI. Clonidine did increase the rate of nonfatal cardiac arrests and clinically important hypotension. ESC&ESA did not make an official recommendation, but ACC/AHA did.

Table 9. *Recommendations of ACC/AHA*

Recommendations	Class of recommendation	Level of evidence
Alpha-2 agonists for prevention of cardiac events are not recommended in patients who are undergoing noncardiac surgery	III no benefit	B

Diuretics

Diuretics are addressed only in the ESC&ESA Guidelines, but official recommendations are not made. Diuretics are frequently used in patients with hypertension or heart failure. In general, diuretics for hypertension should be continued to the day of surgery and resumed orally when possible. If blood pressure reduction is required before oral therapy can be continued, other antihypertensive agents may be considered. In heart failure, dosage increase should be considered if symptoms or signs of fluid retention are present. Dosage reduction should be considered in patients with hypovolemia, hypotension, or electrolyte disturbances. In general, diuretic treatment, if necessary to control heart failure, should be continued to the day of surgery and resumed orally when possible. In the perioperative period, volume status in patients with heart failure should be monitored carefully and optimized by loop diuretics or fluids. The possibility of electrolyte disturbance should be considered in any patient receiving diuretics.

Antiplatelet Agents

There are two dilemmas concerning dual antiplatelet therapy (DAPT) and surgery. The first question is whether to proceed with the operation or wait until the full course of DAPT is finished. And the second question comes up if we decide to proceed with the operation. The question is whether to stop DAPT or continue perioperativly.

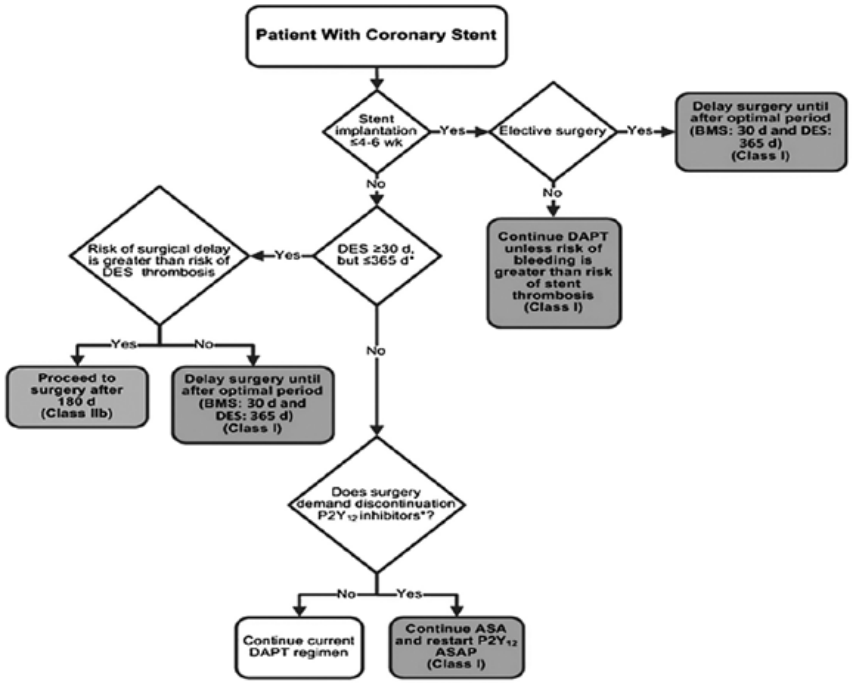
The answer to the first question is the recommendations on the timing of noncardiac surgery in cardiac stable/asymptomatic patients with previous revascularization.

Table 10. *Recommendations of ESC&ESA*

Recommendations	Class of recommendation	Level of evidence
It is recommended that, except for high-risk patients, asymptomatic patients who have undergone CABG in the past 6 years to be sent for non-urgent, non-cardiac surgery without angiographic evaluation.[a]	I	B
Consideration should be given to performing non-urgent, non-cardiac surgery in patients with recent BMS implantation after a minimum of 4 weeks and ideally 3 months following the intervention.[a]	IIa	B
Consideration should be given to performing non-urgent, non-cardiac surgery in patients who have recent DES implantation no sooner than 12 months following the intervention. This delay may be reduced to 6 months for the new generation DES.[a]	IIa	B
In patients who have had recent balloon angioplasty, surgeons should consider postponing non-cardiac surgery until at least 2 weeks after the intervention.	IIa	B

BMS - bare-metal stent; CABG - coronary artery bypass graft surgery; DES - drug-eluting stent.[a] Aspirin to be continued throughout perioperative period.

Figure 1. *Algorithm for Antiplatelet management in patients with PCI and noncardiac surgery in ACC/AHA Guidelines*



The second recommendations are intended to answer the second question: What to do with the DAPT if we decide to proceed with the operation?

Table 11. *Recommendations of ESC&ESA*

Recommendations	Class of recommendation	Level of evidence
It is recommended that Aspirin to be continued for 4 weeks after BMS implantation and for 3–12 months after DES implantation, unless the risk of life-threatening surgical bleeding on Aspirin is unacceptably high.	I	C
Continuation of Aspirin, in patients previously thus treated, may be considered in the perioperative period, and should be based on an individual decision that depends on the perioperative bleeding risk, weighed against the risk of thrombotic complications.	IIa	B
Discontinuation of Aspirin therapy, in patients previously treated with it, should be considered in those in whom hemostasis is anticipated to be difficult to control during surgery. **B**	IIa	B
Continuation of P2Y12 inhibitor treatment should be considered for 4 weeks after BMS implantation and for 3–12 months after DES implantation, unless the risk of life-threatening surgical bleeding on this agent is unacceptably high.	IIa	C
In patients treated with P2Y12 inhibitors, who need to undergo surgery, postponing surgery for at least 5 days after cessation of ticagrelor and clopidogreland for 7 days in the case of prasugrel if clinically feasible, should be considered unless the patient is at high risk of an ischemic event.	IIa	C

Table 12/ *Recommendations of ACC&AHA*

Recommendations	Class of recommendation	Level of evidence
In patients undergoing urgent noncardiac surgery during the first 4 to 6 weeks after BMS or DES implantation, DAPT should be continued unless the relative risk of bleeding outweighs the benefit of the prevention of stent thrombosis.	I	C
In patients who have received coronary stents and must undergo surgical procedures that mandate the discontinuation of P2Y12 platelet receptor–inhibitor therapy, it is recommended that Aspirin to be continued if possible and the P2Y12 platelet receptor–inhibitor to be restarted as soon as possible after surgery.	I	C
Management of the perioperative antiplatelet therapy should be determined by a consensus of the surgeon, anesthesiologist, cardiologist, and patient, who should weigh the relative risk of bleeding with that of stent thrombosis.	I	C
In patients undergoing nonemergency/nonurgent noncardiac surgery who have not had previous coronary stenting, it may be reasonable to continue Aspirin when the risk of potential increased cardiac events outweighs the risk of increased bleeding.	IIb	B
Initiation or continuation of Aspirin is not beneficial in patients undergoing elective noncardiac noncarotid surgery who have not had previous coronary stenting.	III no benefit	C

The summary of the two guidelines is that they both promote the same recommendations:

1. For the patients with a coronary stent, the dual antiplatelet therapy should be continued for 4 weeks for bare metal stents (BMS) and 3-12 months for drug eluting stents (DES) and 1 year for a patients after acute coronary syndrome, irrespective of revascularization strategy, unless the risk of life-threatening surgical bleeding on these agents is unacceptably high. If we discontinue P2Y12 platelet receptor–inhibitor therapy, it is recommended that Aspirin to be continued unless the risk of life-threatening surgical bleeding on this agent is unacceptably high. The P2Y12 platelet receptor - inhibitor should be restarted as soon as possible after surgery, possibly in the first 48 hours.
2. For the patients that take Aspirin, but do not have a stent, should continue Aspirin when the risk of potential increased cardiac events outweighs the risk of increased bleeding. Do not initiate or continue Aspirin if hemostasis is difficult to control. For patients undergoing spinal surgery or certain neurosurgical or ophthalmological operations, it is recommended that Aspirin to be discontinued for at least seven days.

Vitamin K Antagonists

Both guidelines did not make official recommendations concerning vitamin K antagonists, but they both agree that the benefit of anticoagulants must be weighed with the risk of bleeding on a case by case basis. Patients treated with oral anticoagulant therapy using vitamin K antagonists (VKAs) are subject to increased risk of peri- and post-procedural bleeding. If the international normalized ratio (INR) is ≤1.5, surgery can be performed safely; however, in anticoagulated patients with a high risk of thrombo-embolism,for example, patients with:

- AF with a [Cardiac failure, Hypertension, Age ≥75, Diabetes, Stroke – Vascular disease,
- Age 65–74 and Sex category (Female) score of ≥4] or
- mechanical prosthetic heart valves, newly inserted biological prosthetic heart valves, or
- mitral valvular repair (within the past 3 months) or
- recent venous thrombo-embolism (within 3 months) or
- thrombophilia,

discontinuation of VKAs is hazardous and these patients will need bridging therapy with unfractionated heparin (UFH) or therapeutic-dose LMWH. In general, there is better evidence for the efficacy and safety of LMWH, in comparison to UFH, in bridging to surgery. LMWH is usually administered subcutaneously and weight-adjusted for once- or twice-daily administration without laboratory monitoring. In patients with a high thrombo-embolic risk, therapeutic doses of LMWH twice daily are recommended, and prophylactic once-daily doses in low-risk patients. The last dose of LMWH should be administered no later than 12 hours before the procedure. Further adjustment of dose is necessary in patients with moderate-to-high kidney function impairment. It is recommended VKA treatment to be stopped 3 - 5 days before surgery (depending on the type of VKA), with daily INR measurements, until ≤1.5 is reached, and LMWH or UFH therapy to be started one day after discontinuation of VKA or later, as soon as the INR is ,2.0.

In patients with mechanical prosthetic heart valves, the evidence in favor of intravenous UFH is more solid; thus in some centers these patients are hospitalized and treated with UFH until four hours before surgery, and treatment with UFH is resumed after surgery until the INR is within the therapeutic range. On the day of the procedure, the INR should be checked. Consideration should be given to postponing the procedure, if the INR is 1.5. LMWH or UFH is resumed at the pre-procedural dose 1–2 days after surgery, depending on the patient's hemostatic status, but at least 12 hours after the procedure. VKAs should be resumed on day 1 or 2 after surgery, depending on adequate hemostasis with the pre-operative maintenance dose plus a boosting dose of 50% for two consecutive days; the maintenance dose should be administrated thereafter.

Non-Vitamin K Antagonist Oral Anticoagulants

ESC/ESA guidelines elaborate more about non-VKA direct oral anticoagulants (NOACs) than ACC&AHA guidelines do. In patients treated with the NOACs- dabigatran (a direct thrombin inhibitor), rivaroxaban, apixaban, or edoxaban (all direct factor Xa inhibitors), all of which have a well-defined 'on' and 'off' action, 'bridging' to surgery is in the most cases unnecessary, due to their short biological half-lives. An exception to this rule is the patient with high thrombo-embolic risk, whose surgical intervention is delayed for several days. The overall recommendation is to stop NOACs for 2–3 times their respective biological half-lives prior to surgery in surgical interventions with 'normal' bleeding risk, and 4–5 times the biological half-lives before surgery in surgical interventions with high bleeding risk. New tests for better quantification of activity levels of the various NOACs are under development. In general, reduced kidney function or moderate-to-high increased bleeding risk should lead to earlier cessation of NOACs. If patients are pre-treated with dabigatran, which has about an 80% renal excretion rate, the individual

glomerular filtration rate determines the time of its cessation prior to surgery. Kidney function is thus essential for tailoring dabigatran therapy, and earlier cessation is recommended for all NOACs if the bleeding risk is increased.

Because of the fast 'on'-effect of NOACs (in comparison with VKAs), resumption of the treatment after surgery should be delayed for 1–2 (in some cases 3–5) days, until post-surgical bleeding tendency is diminished.

Conclusion

Guidelines and recommendations should help health professionals to make decisions in their daily practice. There are some differences between the two guidelines concerning perioperative therapy, but the most of the recommendations are made towards the same purpose. However, the final decisions concerning an individual patient must be made by the responsible health professionals, in consultation with the patient and caregiver as appropriate.

References

1. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014; 130:2215–45.
2. Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J. 2014; 35:2383–431.
3. Kristensen SD. 2014 ESC/ESA Guidelines on Non-cardiac surgery: Cardiovascular Assessment and Management. Are the differences clinically relevant? The European Perspective. J Nucl Cardiol 2016; In press.
4. Port S. 2014 ESC/ESA Guidelines on Non-cardiac surgery: Cardiovascular Assessment and Management. Are the differences clinically relevant? The American Perspective. J Nucl Cardiol; In Press.
5. Lee TH, Marcantonio ER, Mangione CM,et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999; 100:1043–1049.
6. Glance LG, Lustik SJ, Hannan EL, et al. The Surgical Mortality Probability Model: derivation and validation of a simple risk prediction rule for noncardiac surgery. Ann Surg 2012; 255:696–702.

ВОДИЧИ И ПРЕПОРАКИ ЗА КАРДИОВАСКУЛАРНА ТЕРАПИЈА НА ПАЦИЕНТИ ЗА НЕКАРДИЈАЛНА ХИРУРГИЈА

Апстракт

Повеќето од пациентите имаат еден или повеќе коморбидитети кои се третирани со одредена медицинска терапија. Не е секогаш јасно дали за време на периоперативниот период оваа терапија треба да се продолжи, прекине или промени.

Во 2014 година Европското здружение за кардиологија и Европското здружение за анестезија издадоа препораки за кардиоваскуларна процена и постапување за некардијална хирургија. Истовремено во 2014 година и Американскиот колеџ за кардиологија и Американското здружение за срце издадоа препораки за кардиоваскуларна евалуација и справување со пациенти за некардијална хирургија.

Целта на овој труд е да се споредат и да се најдат сличностите и разликите меѓу двата водичи за периоперативната медицинска терапија.

Клучни зборови: периоперативна медицинска терапија, препораки

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EUROANAESTHESIA 2017: "RESIDENTS' TRAINING AND EDUCATION QUALITY IN THE HIHGLIGHT"

The congress of Anaesthesiologists "Euroanaesthesia 2017" was held from 3 June to 5 June in Geneva, Switzerland, and was attended by more than 6,000 delegates, including a large number of trainees in Anaesthesiology. Having in mind the developing countries and the funds needed for a young trainee doctor to participate at the congress, ESA has come up with the subvention of 20 grants worth up to 600 euros in order to enable trainees to become part of Euroanaesthesia 2017. Macedonia is also among the winners of ESA Travel Grant 2017.

The excellent cooperation with the NASC President, as well as the activities of the NASC president (National Anaesthesiologists Societies Committee), has contributed for our country to receive even three ESA Travel Grants and for the first time to take an active part in the activities of the European Association of trainees in anaesthesiology named ESATN (European Society of Anaesthesiology, Trainee Network). ESATN is an association of young doctors, trainees in Anaesthesiology, within ESA with members from all European countries. The beginnings of ESATN as an active participant in Euroanaesthesia, as well as in the Council of ESA, were seen for the first time at Euroanaesthesia 2015. From 2015 to 2017 there was a rapid increase in the number of ESATN members. The ESATN coordinative body also takes an active role as an ESA Council member where elected trainee representatives advocate for the rights, the place, the role and responsibilities of the resident in Anesthesiology as well as the opportunities for higher quality education. In fact, ESATN members who are also active ESA Council members represent the trainees' voice in the name of improving the education, residents' position as well as the place of the trainee in everyday practice.

This year's Euroanaesthesia 2017 has offered a rich program with a huge number of lectures and workshops in the field of Anaesthesiology held by eminent lecturers. Among other things, there were lectures and workshops organized by ESATN, which were intended for the residents in Anaesthesiology as a contribution to better education and exchange of experiences. Lectures and workshops were in the area of regional anaesthesia, obstetric anaesthesia, thoraco-vascular anaesthesia, and management of massive intraoperative haemorrhage. There were meetings and lectures organized by the older trainees who have been sharing their personal experiences and benefits from participating in the trainees exchange program sponsored by ESA. The role and participation of the trainee in the scientific research work, the challenges and opportunities for early profiling of the young trainee in a certain subspecialty, as well as the possibility for academic progress, were also discussed.

Particular emphasis was put on the sharing and exchange of an experience gained from the Trainee exchange program by residents who were last year's three-month grants recipients. They were staying in one of the 36 eminent educational centres across Europe. ESATN supports and encourages the participation of the young trainees in the Trainee Exchange Program as a form of exchange and acquisition of new experiences, as well as the opportunity for better education of the trainee.

Meanwhile, there was also hosted an official meeting of ESATN representatives from all European countries, where our country has participated for the first time. I was certified as a Trainee Representative from the Republic of Macedonia and I've presented the current trends, challenges and problems that every young Macedonian trainee has been facing.

At the meeting were discussed several topics, among which the greatest attention was given to the possibilities for improving the conditions and providing better education for the trainees. The ESATN Coordinative Body members were presented, as well as ESATN's on-going activities for the past year. The position, role and place of the trainee in everyday practice were discussed, as well as the possibilities for improving residents' education. Special attention has been paid to the working conditions, financial benefits and obligatory employment contracts with the hospitals and the young residents in the Southeast Europe Countries. At the meeting were promoted Associations of the trainees of anaesthesia from different countries across Europe, their tasks, duties as well as the way of their functioning and hierarchy. Motivational messages were sent by ESATN's coordinating body and assistance was offered to all countries that have not yet established an association of trainees in Anaesthesiology due to its formation in the future. Discussion about the format of the specialty training programme and the manner of conducting examination due to specialist certification was held in order to obtain a general picture of the similarities and differences that exist in different countries. Also, as a separate topic of interest was the EDAIC test and its importance and meaning in the European Union countries. D-r. Ida Temenugova is the first and so far the only one anaesthesiologist who has passed the EDAIC back in 2014.

The objectives and tasks of ESATN, as well as of the trainee representative of each country, are specifically identified by undertaking activities to improve the education opportunities of the trainees, providing conditions for higher quality education, access to information for congresses, seminars and CME events. In order to establish a network of all trainees across Europe there was created the ESA Trainee Network group on the social networks such as Facebook, Twitter and LinkedIn. The goal of the groups is achieving easier and greater connectivity among the trainees from different countries, facilitating exchange of experiences and knowledge, presenting and solving certain problems that residents are facing, as well as providing access to information for continuous medical education. In fact, the task of the trainee representative of each country consists of continuously providing information for continuous medical education and encouraging further training of trainees from their own country, informing the trainees for all ESA newsletters and all opportunities for sharing experiences , knowledge and skills. During the year there are a

few active meetings with the other trainee representatives from other countries where discussion of current problems, finding and proposing possible solutions for them are done.

I consider that the presence of our country on Euroanaesthesia 2017, as well as the fact that we've become an active member of ESATN for the first time, is of crucial importance for the young trainees in Anaesthesiology due to the fact that this way we are step closer to the latest events in the field of education in Europe and other countries. Indeed, obtaining an ESA Travel Grants as a form of support to the developing countries was a key moment for Macedonia to be equal as other countries and to take an active part in creating proposals and decisions to improve our future and possibilities as anaesthesiologists.

Dr. Filip Naumovski
Resident in Anaesthesiology
and intensive Care Medicine
ESATN National Trainee Representative

Guidelines for Authors

Macedonian Journal of Anaesthesia (MJA) is a scientific journal of the Macedonian Society of Anaesthesia (MSA) and Macedonian Society of Critical Care Medicine (MSCCM). The aim of this specialized medical journal is to speed and promote scientific achievements, novelties', clinical experience's, reviews, controversial topics in anesthesia, reanimation and intensive care.

The Journal is published twice a year (April and November), but additional supplements might be published when needed. MJA publishes original (professional and scientific) articles, review articles, case reports, therapeutic and technological innovation, discussions, critics, impressions from meetings, information for international conferences and reviews of new books or variate.

Manuscripts that are published should have not been published previously. Manuscripts that have been previously published only in form of abstracts are eligible for publishing in the journal but should be followed by additional letter send to the Editor, where the abstract details are noted (abstract number, which book of proceeding or doi, date and place).

The authors are responsible for respecting the ethical guidelines for medical researches, as well as for all that is explained, attitudes, analyses and shown results.

The redaction sends the manuscripts to anonymous reviewing process from international or domestic reviewers and the Editors determine the definitive categorization of the manuscript. Once reviewed manuscript together with the reviewers' remarks is send back to the corresponding author, after what the author is omitted to deliver the final form of the manuscript to the Editorial board within one week.

Editorial board has the right to publish the manuscripts according to the reviewer's priority. The order in which the manuscripts are published does not reflect the scientific value of the article. The Editorial board keeps the rights to make changes to the manuscript to fulfil the criteria.

MANUSCRIPT PREPARATION

Manuscript should be sent together with the accompanying letter from the corresponding authors where declaration that the text has not been published previously is signed. Additional conflict of interests and confirmation by all the authors should be declared in this letter (example: Annex no.1).

The guidelines for authors adhere to the uniform Requirements for Manuscripts submitted to Biomedical Journals:www.nlm.nih.gov.

Language and style of the manuscripts should be clear, simple to according the language, anesthesiological and medical taxonomy.

The manuscript has to be written in **English**, followed by an abstract in Macedonia (after the references section).

Manuscripts should be written in **Microsoft Word** (*.doc format) with **Times New Roman** font and **size 12**. Margins on left, up and bottom should be 3cm and right margin should be 2,5cm.

the inline space should be 2. Do not use Bold or Italic letters for the whole text (only for parts that have to be emphasized). Manuscript should not exceed 10 pages (without the references).

Abbreviations and correct medical terms should be used according to the International Committee of Editors of Medical Journals (http://www.icmje.org). Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

MANUSCRIPT SECTIONS

- Manuscript should be organized in:
- Title page
- Text organized in IMRaD
- Acknowledgments
- Authors Contribution
- References
- Abstract in Macedonian only (For Macedonian Natives)

Review articles, case reports, therapeutic and technological innovation, discussions, critics, impressions from meetings, information for international conferences and reviews of new books or variate may be written in different sequences and manners.

TITLE PAGE

The title of the manuscript written in CAPITAL LETTERS.

Authors Surname and Name initial (Jovanov.J), without academic or other titles.

Name and address of the institution where the authors come from whit the subscribed digits

Abstract in English. Abstract should include up to 250 words and should contain goals of the paper, important elements from the methodology, concisely displayed results and conclusion. Each abstract at the end must have **Key words**: in alphabetical order.

TEXT

- Introduction,
- Matherial and Method,
- Results
- Discussion
- Conclusion

Review articles, case reports, therapeutic and technological innovation, discussions, critics, impressions from meetings, information for international conferences and reviews of new books or variate may be written in different sequences and manners.

Introduction section should include a literature overview in relevance to the elaborated problem. In this sections 3-5 key references are citied and this section should not be longer than 2 pages.

Material and method sections includes detailed description of the performances in the research as well as the statistical analyses used. This section should include: time during what the research was conducted, type of the study, place of where the research was undertaken, randomization or stratification used (clear description of the examined groups), exclusion and inclusion criteria, method, analysis types, apparatus and instruments used and referent values of the examined features (in SI-International System units).

Results are displayed in simple manner with text, images, tables and charts that are submitted in the text where author wants to stand, titled and numbered appropriately. Additionally, on separate document all carts images and tables are send together with the manuscript.

Title and the number of the charts and tables are placed above them while the explanations, abbreviations and comments are placed below. Images title and number is placed below and the image should include proper explanation.

Discussion section emphasize the key finding of the actual research and compares these result to other relevant literature data.

Conclusion section should not include more than 150 words and shoul be drown from the relevant elaborated results.

Acknowledgment and Author contributions sections are displayed after the conclusion and before the reference section.

REFFERENCES

This sections include only the citied references. **The references** are listed in order of appearance in the paper and the citation is standard numbers enclosed in small brackets in the same line with the text ( ).

For each reference if more than three authors appear provide the names of the first three authors and followed by **et a**l.

Examples:

Journal references:

Nirmala BC, Kumari G. Foot drop after spinal anaesthesia: a rare complication. Indian J Anaesth. 2011; 55: 78–79.

Lynch EP, Lazor MA, Gellius JE, et al. The Impact of Posoperative Pain on the Development of Postoperative Delirium. Anesth Analg 1998; 86:781-785.

2. Journal supplements:

AzmanJ, Frkovic V, Bilic L, et al. Korelacija I regresija. Acta Med Croat 2006;60 (suppl I):81-89.

3. Books

Brown, D.L. Spinal, epidural, and caudal anesthesia. In R.D. Miller Miller's Anesthesia, 6th edition. Philadelphia: Elsevier Churchill Livingstone; 2005.p 98-198

4. Doctoral or master thesis

Jelisavac Cosic S.Urokinazni I tkivni aktivator plazminogena i njihov inhibitor u raku dojke (Master thesis).Zagreb: Farmaceutsko-biohemijski fakultet 2004, p.50

5. Electronic reference

Dag Stat. Mackinnon A. Available from :http//www.mhri.cdu.au/biostats.Accessed May 5th 2006.

Webster NR. The anaesthetist as peri-operative physician.Anaesthesia. http://dx.doi.org/10.1046/j.1365- 2044.2000.01722.x

References used from abstracts are marked as **(abstr).,** and from letters with (**letter**)

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Macedonian abstract should include title (in capital letters) and all the needed features as the English abstract only written in Macedonian with Times New Roman, font size 12 with Macedonian support in Microsoft Word.

Prepared manuscript should be submitted electronically to **macedonianesthesiology@gmail.com.**

All manuscripts that don't fulfil the above criteria will not be accepted for reviewing

Accompany letter
ANNEX no.1

I _____. Here by declare that the article _____ (NAME OF THE ARTICLE) has not been previously published (fully or partialy) previously.

We autors_____

_____(FULL NAME AND SURNAMES OF THE AUTORS AND SIGNATURES) are responsible for the etic, profesional and scientific content of the study.

I _____(THE FIRST AUTHOR FULL NAME) declare Conflict of interest or declare non Conflict of interest.

_____(FIRST AND SURNAME OF THE CORESPONDING AUTHOR, …….. (ADRESS), ……,….. (TELEPHONE NUMBER) ……., E-MAIL