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PREFACE

Dear colleges,

This year we are organizing a professional scientific conference "Pulmonary Days Tešanj 2021". This symposium has become traditional and is being held for the tenth time this year. In October last year, a meeting was not organized because of the COVID pandemic. Over the past 20 months, most participants of us have been engaged for the purposes of this pandemic. Since COVID 19 is primarily a respiratory infection, our participation in activities during the pandemic was necessary. We have encountered medical problems and challenges that we have never had before. We have gained many experiences that we did not have before. But we wish that we have gathered scientific interest and a desire to overcome the problems of our everyday medical practice as successfully as possible. Furthermore, we must admit to ourselves, that we did not solve the problem with COVID 19 infection. Recommendations for the treatment of COVID 19 change frequently, sometimes very significantly. That is why we chose COVID 19 infection as the main topic of this year's symposium. The main challenges that remain unsolved are respiratory support and anti-inflammatory treatment of this disease. We hope that the meeting, but also the wider audience, will bring significant benefits. We are certainly looking forward to meeting proven friends again, knowing that we have gathered scientific interest and a desire to overcome the problems of our everyday medical practice.

Prof dr Besim Prnjavorac,
President of organizing committee

POSITRON EMISSION TOMOGRAPHY IN THE MANAGEMENT OF LUNG DISEASES: CURRENT APPLICATIONS AND FUTURE PERSPECTIVES

(Dimitrievska D, Zdraveska M, Todevski D, Tushevaska-Mitkovska M, Chamurovski N, Arbutina S.
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Positron emission tomography (PET) combined with computed tomography (CT) is an established diagnostic modality that has become an essential imaging tool in oncological practice. However, thanks to its noninvasive nature and its capability to provide physiological information, the main applications of this technique have significantly expanded.

In the past 20 years, positron emission tomography (PET), usually with ^{18}F -fluoro-2-deoxy-D-glucose (FDG), has become an important imaging modality in patients with lung cancer. PET is a useful technique to characterize the solitary pulmonary nodule, diagnose primary lung cancer, carry out mediastinal and extrathoracic staging, plan radiotherapy, therapeutic response assessment and detect recurrence. PET may help to determine the ideal site for tissue diagnosis as well as predict prognosis. Combined PET and computed tomography (PET / CT) has the best of both worlds of metabolic and anatomic imaging and may provide optimal disease assessment.

^{18}F -labelled fluorodeoxyglucose (FDG) is the most commonly used radiopharmaceutical for PET scanning and demonstrates metabolic activity in various tissues. Since activated inflammatory cells, like malignant cells, predominantly metabolise glucose as a source of energy and increase expression of glucose transporters when activated, FDG-PET/CT can be successfully used to detect and monitor a variety of lung diseases, such as infections and several inflammatory conditions. The added

value of FDG-PET/CT as a molecular imaging technique relies on its capability to identify disease in very early stages, long before the appearance of structural changes detectable by conventional imaging.

Furthermore, by detecting the active phase of infectious or inflammatory processes, disease progression and treatment efficacy can be monitored.

Key words: positron emission tomography (PET), PET/computed tomography, lung cancer, tumor staging, therapy response, evaluation of inflammatory and infectious lung diseases

DIAGNOSIS AND MANAGEMENT OF COPD IN SERBIA - A GUIDELINES WITH REFERENCE TO ACTUAL COVID-19 SITUATION IN THE REGION

(Ivan Kopitović, Institut of Lung Diseases of Vojvodina)

In Serbia, like in most countries of our ex YU region, the burden of COPD is high and vast majority of the patients are diagnosed at relatively late stages. In our document, we propose an algorithm for treating COPD patients in Serbia based on national experts' opinion, taking into account global recommendations (GOLD) and recent findings from clinical trials that are tailored according to local needs. We identified four major components of COPD treatment based on country specifics: active case finding and early diagnosis in high-risk population, therapeutic algorithm for initiation and escalation of therapy that is simple and easy to use in real-life practice, de-escalation of ICS in low-risk non-exacerbators, and individual choice of inhaler device based on patients' ability and preferences. With this approach we aim to facilitate implementation of the recommendation, initiate the treatment in early stages, improve cost-effectiveness, reduce possible side effects, and ensure efficient treatment. In addition, there would be a small reference to actual COVID-19 situation and their impact to COPD patients.

Keywords: COPD; guidelines; treatment, COVID-19.

DYNAMIC FLOW OF CHANGES IN INTERLEUKIN AND IMMUNOGLOBULIN LEVELS IN COVID-19 INFECTION

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Background: As a newly discovered respiratory infection COVID-19 was presented in most cases as lung interstitial pneumonia. It was considered that around 85 % cases have that clinical manifestation. The other cases were presented as gut infection, generalized myositis, carditis, while other localizations of the disease are fairly rare. It is to be noted that 80 % of PCR positive patients have no symptoms. In pathogenesis of the disease type I of inflammation is predominant in the first phase of the disease. In analysis of pathoanatomy of lungs in severely ill patients alveolar inflammation, exudative form of disease was seen in early phase of the disease. After a few days of clinically manifested disease severe necrosis of alveolar walls was seen. Alveolar spaces in inflamed tissue have poor ventilation. Condensation of alveolar tissue, with no air inside, was seen in many cases.

Methods: We analyzed patients treated in COVID division of Department of Pulmonology in General Hospital Tešanj. Analyses of IL-6 and IgM and IgG were performed. For all patients standardized diagnostic tool were performed, which include blood cells count, SE, biochemical analyzes, blood gases analyses and other according to clinical situation. For all patients chest X-ray was performed and lung CT scan, if needed.

Results: Out of all 970 patients treated in first 15-month period of pandemic, for 220 of them complete IgM and IgG measurement was performed. For 76 patients out of all, analyses of immunoglobulin level

on admission day were completed. Median of IgM level in mild group was 0.18 COI, in moderate group 2.25 COI and in severe group 0.01. Measurement of IgG show the next results: for mild, moderate and sever group – 9.16 COI, 8.195 COI and 1.30 COI respectively. It is to be seen that the severe group has the lowest levels of both, IgG and IgM, but mild group has the highest levels. Difference was seen more in IgM measurements than in IgG. Preliminary results of collected data made by Kruskal-Wallis method showed no normal distribution and the results were analyzed with non parametric Mann – Whitney sum of ranks. The measurement of IL-6 showed great variability even on a daily basis. IL-6 was in substantial correlation with inflammatory parameters, but with no normal distribution parametric statistical analysis was impossible. On daily basis IL-6 increased in some patient from 4.6 pg/ml to 2600 pg/ml in time frame of 12 hours. Moreover, if a great variation of some parameter is present, absolute value of this parameter is not appropriate to be used in decision making. But substantial increase in short time is to be considered as appropriate in decision making process for therapy.

Conclusion: Measurement of IgG and IgM showed the lowest levels in the group with severe clinical picture, and the highest levels in the mild group on the day of admission to the hospital. Lack of well immunological response was seen in the severe group. Measurement of IL-6 showed great variability, on daily basis, but the result of increased level in short time was relevant for decision making of therapy with tociliumab.

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BRONCHOSCOPY IN THE COVID INTENSIVE CARE UNIT

(Doc dr Spasoje Popević, University of Belgrade - Faculty of Medicine
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SARS-CoV-2 infection is spread primarily by respiratory droplets and microdroplets, although aerosol transmission may also occur. Bronchoscopy belongs to the group of procedures that create aerosol (AGP) and must be performed with special care, respecting all protection measures of both medical staff directly involved in performing the intervention, and the space and other patients.

The most common vital indications for bronchoscopy in the intensive care unit are: unexplained worsening of hypoxemia in patients on non-invasive or invasive mechanical ventilation, microbiological sampling (tracheobronchial aspirates or bronchoalveolar lavage) in order to select appropriate antimicrobial therapy, to remove mucus plugs (atelectasis, subatelectasis), in hemoptysis or when bronchoscopically guided intubation is required. The most common bronchoscopy techniques will be presented and their significance for each of these indications will be described.

The lecture will show our experiences in the application of bronchoscopy and interventional pulmonary procedures in COVID intensive care units of the Clinic for Pulmonology UKCS and COVID Hospital "Batajnica", which is the largest institution of its kind in Europe.

Key word: COVID 19, Bronchoscopy, Intensive care unit

COVID 19 and COPD

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Occuring due to sistematic reaseraches of 15 studies (2473 hospitalised patients, among them more than 500 critically ill cases) impact of COPD was analized on outcome of COVID-19 infections.

Risk factors for worse outcome: older age and cardiovascular comorbidities (CVC). COPD occurs mainly in later life and is associated with CVC. COPD is associated with poorer outcomes. Reasons: increased sensibility to viral infections and increased ACE2 expression in COPD. Thrombosis and coagulopathy are common features of severe COVID-19. Pre-existing endothelial dysfunction in COPD predisposes to vascular complications during COVID-19. The relationship between the use of inhaled corticosteroids (ICS) and COVID-19 is still unclear. ICS may reduce the ability of SARS-CoV-2 to reproduce, but it can also minimize important antiviral mechanisms. ICS prevents exacerbations when eosinophils in the blood are high, but increases the risk of pneumonia can be seen, when eosinophils in the blood are low. Thus, the use of ICS in COPD with COVID-19 can be a double-edged sword. Isolation of patients with COPD can lead to: short-term reduction of viral infection but in the long run can cause a decrease in physical activity and quality of life, as well increased symptoms and risk of exacerbations and mortality. Mechanisms that may increase sensitivity to COVID-19 in COPD can increas pulmonary ACE2 receptors expression. Reduced antiviral defense, dysfunction of endothelial cells and increased coagulopathy may wors the clinical course of COVID-19. Effects of ICS and COVID-19 in COPD: ICS prevent exacerbations of eosinophilic COPD; Corticosteroids reduce SARS-CoV-2 replication; ICSs reduce ACE2 expression by reducing type 1 interferon production. ICS

can reduce antiviral defense. What's the influence for clinical outcomes of COVID-19 in patients with COPD? There is no evidence of an increase in frequency COVID-19 in COPD. Patients with COPD have an increased risk of poorer COVID-19 outcome, including mortality.

Key words: COPD, COVID-19, clinical outcome.

COVID-19 AND COAGULOPTAHY

(Jusufović Edin, Medical Faculty Tuzla and Health Center Tuzla, BiH,)

Changes in the coagulation system of COVID-19 patients generally show enhanced coagulation and thrombosis. Complications of severe and critical COVID-19 are acute respiratory distress syndrome, pulmonary embolism (PE), pulmonary thrombosis and hypercoagulable state. COVID-19 inpatients develop DVT in ~60% and PE in >45% cases, even when prophylactic anticoagulation is used. The most often used and useful coagulation test are D-dimer, Fibrinogen, PT (prothrombin time) with aPTT (activated partial thromboplastin time) and platelet count. The most common pattern of coagulopathy observed in patients hospitalized with COVID-19 is characterized by elevations in fibrinogen and D-dimer levels, and mild prolongation of PT/aPTT. Rarely severe COVID-19 infection and multiorgan failure progress to a coagulopathy with disseminated intravascular coagulopathy (DIC), which is reflected by thrombocytopenia, prolongation of the PT/aPTT, elevation of D-dimer, and decreased fibrinogen. The International Society on Thrombosis and Haemostasis has published criteria for DIC, with sensitivity of 91% and a specificity of 97%. Monitoring platelet count, PT±PTT, D-dimer, and fibrinogen are recommended only in hospitalized patients. Worsening of these parameters, indicates progressive severity of COVID-19 when aggressive critical care may be needed. However, an elevated D-dimer should not be used as a sole criterion for hospital admission or mandate imaging for DVT/PE unless other signs or symptoms of DVT are present, which may be suspected if: D-dimer levels change from normal to abnormal, there is a rapid increase in D-dimer on serial monitoring, and/or clinical signs or symptoms occur. Imaging studies to diagnose PE or DVT should be pursued in these

scenarios. Last up-to-date research has given an algorithm for anticoagulation treatment in COVID-19 patients. Thromboprophylaxis in prophylactic dose is recommended for all hospitalized patients (strongly in ICU), as well as in obstetric cases in the absence of bleeding, despite abnormal coagulation. Anticoagulation is generally not used in outpatients, in whom it may be used only in selected individuals, when Rivaroxaban 10 mg daily for 31 to 39 days should be used.

Key words: COVID-19, Coagulopathy.

RADIOLOGICAL MANIFESTATIONS OF COVID-19 PNEUMONIA

(Ruža Stević, Center for Radiology Imaging - Magnetic Resonance
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Radiological methods play an important role in the diagnosis and monitoring of COVID-19 pneumonia. In most health care institutions, first a radiograph of the lung is performed, followed by a computed tomography (CT). The findings on the radiography of the lungs in patients with COVID-19 pneumonia occur after symptoms have already developed, so at the beginning of the disease in most cases the radiography is without pathological changes.

COVID-19 is manifested by a wide range of radiographic findings from discrete ground-glass opacity, reticular changes to extensive consolidations. The most common changes visible on radiography in the early phase of the disease are reticular changes in the first four days, and often, the first radiographic signs can be peripherally localized changes in the appearance of ground-glass. In the advanced stage of the disease bilateral consolidations can be seen. Most often a combination of the previously mentioned changes is present. In about 90% of cases, the changes are bilateral, predominantly peripheral, and more extensive in the lower parts of the lungs. In the most severe cases, the lungs are completely affected by the changes. Unilateral changes do not exclude COVID-19 pneumonia and are most often presented in the form of consolidation or pleural effusion. Pneumothorax and pneumomediastinum may be seen in some patients, especially those on mechanical ventilation. In a small number of cases, the manifestations of COVID-19 pneumonia are atypical and represent a serious differential diagnostic problem. Computed tomography is a more sensitive method for detecting

and displaying the extent of changes in the lungs. Often, in patients with signs of respiratory infection and normal radiography, CT reveals ground glass opacity changes or consolidations. In addition, it is much more precise in monitoring the evolution of changes in the lungs during the disease.

Conclusion: Radiological manifestations of COVID-19 pneumonia are diverse and can be different in the same patient depending on the stage of the disease and the extent of the changes. Therefore, it is necessary to know the clinical facts about the patient in order to draw the correct conclusion based on the radiological findings.

Key words: COVID 19, Chest X ray, CT scan

ANTIINFLAMMATORY STRATEGY IN COVID19

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The worsening of clinical picture in patients with severe form of COVID-19 often occurs rapidly, and such severe form of disease is caused by overreaction of the body's immune system known as "cytokine storm". Cytokine storm is a condition of uncontrolled systemic inflammation caused by an excessive amount of cytokines, and it leads to failure of multiple organs, even death. The concept of cytokine storm was first recognized in acute graft vs. host reaction in the process of transplantation of hematopoietic stem cells, and later was discovered in other diseases (malignancies, rheumatic diseases, sepsis).

Although different therapeutic modalities are recommended to alleviate the cytokine storm, up until now no universal and specific recommendations for the treatment of COVID-19 have been issued. In some countries, anti-inflammatory therapy is prescribed regularly, and in some countries it can only be used in clinical trials. Recent published studies have examined cytokine blockade directed at specific cytokines, such as interleukin (IL) -1 and IL-6 or the Janus kinase pathway (JAK) and a potential for effective treatment for COVID-19 was shown. Also, *in vitro* and *in vivo* studies are underway for exploring therapeutic usage of traditional anti-inflammatory medicaments, such as corticosteroids and colchicin. Systemic corticosteroids have been shown to be effective in moderate to severe COVID-19 in patients on oxygen therapy, but the timing of initiation of this therapy and the dose of dexamethasone (or methylprednisolone) have not been determined precisely

IL-6 is a key inflammatory cytokine in Cytokine Releasing Syndrome (CRS). Clinical trials have shown that rapid clinical improvement

and lower mortality rates in patients with severe COVID-19 could be associated with cytokine storm blockade using tocilizumab, a monoclonal antibody that acts as an antagonist of the IL-6 receptor. The panel of authors of the European Respiratory Society and the American Thoracic Society proposes that therapy with this monoclonal antibody be suggested for hospitalized patients with COVID-19 who need oxygen therapy or ventilatory support, but not for patients whose disease does not require oxygen therapy or who have not received corticosteroid therapy.

Given that cytokine storm is caused by different cytokines in different diseases, it is important to keep in mind that treatment must be individual, because the stage at which each cytokine contributes to the development of the disease may vary. Therefore, the combination of antiviral and anti-inflammatory therapy represents a very important segment of the treatment of patients with COVID-19.

Key Word: COVID 19, Inflammation, Cytokine

Reference

1) Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med.* 2020; 8(5):475-81.

2) Behrens EM, Koretzky GA. Review: Cytokine Storm Syndrome: Looking Toward the Precision Medicine Era. *Arthritis Rheumatol.* 2017; 69(6):1135-43.

3) James D. Chalmers, Megan L. Crichton, Pieter C. Goeminne, et al. Management of hospitalised adults with coronavirus disease-19 (COVID-19): A European Respiratory Society living guideline. *European Respiratory Journal* 2021; 57: 2100048; DOI: 10.1183/13993003.00048-2021.

ATYPICAL LUNG CARCINOID

(Case record)

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Carcinoid tumors of bronchopulmonary localization are slow-growing tumors, characterized by a quite good prognosis, even in the presence of regional lymphogenic metastases, opened to adequate surgical treatment. Primary lung carcinoid accounts for about 2% of all primary lung tumors. The tumor is growth out of Kulchitski's neuroendocrine cells, localized in the mucosa of the bronchial tree, on the basis of which we distinguish: typical carcinoid (KCC 1), atypical carcinoid (KSS 2) and small cell carcinoid (KCC 3). Tumors with more expressed cellular atypia, high mitotic activity and foci of necrosis are considered as atypical carcinoid or anaplastic carcinoid. The method of choice in the treatment of carcinoid lung tumors is surgical, based on three main principles: - complete removal of the tumor within healthy tissue, maximum preservation of the non-involved lung parenchyma and ipsilateral lymph node dissection. The authors present a case of atypical carcinoid localized in the left upper bronchus in a 44-year-old man who was inoperable at the time of diagnosis and after oncological treatment (chemo and radiotherapy) a left pulmectomy was successfully performed.

Key words: Atypical carcinoid, Pulmectomy

PNEUMOTHORAX AND PNEUMOMEDIASTINUM IN PATIENT WITH COVID19 INTERSTITIAL PNEUMONA

(Nusret Ramic, Clinical Hospital for Lung Surgery, UKC Tuzla, BiH)

A new disease that causes atypical pneumonia called COVID-19, which started from the Chinese province of Wuhan, quickly turned into a pandemic. Although the diagnostic test of choice is standard lung radiography, it is confirmed that CT is useful in identifying complications associated with this new infection.

Spontaneous pneumomediastinum, pneumothorax, and pleural effusion have recently been marked as unusual complications of severe COVID-19 pneumonia infection. The presumed pathophysiological mechanism is diffuse alveolar injury that leads to alveolar rupture and air leak.

Also, a significant number of patients with COVID-19 pneumonia require tracheal intubation. In the same period, there was an increased incidence of severe forms of pneumomediastinum in intubated patients with COVID-19 pneumonia for which a surgical treatment option was required. The presumed pathophysiological mechanism in these patients is alveolar injury and tracheobronchial tree injury as well as the use of high pressure in ventilation.

In this paper, we will present a series of cases of COVID-19 pneumonia with extra pulmonary and life-threatening complications in patients that are hospitalized in COVID hospital PHI UKC Tuzla and in the Respiratory Center PHI UKC TUZLA and give guidelines for the treatment of these severe complications.

Key words: COVID 19, Pneumothorax, Pneumomediastinum

PERICARDIAL EFFUSION IN LONG-COVID SYMPTOMATOLOGY - REASON FOR TREATMENT?

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Aim: To present the therapeutic modality of pericardial effusion in long-COVID symptomatology.

Methods: This was a prospective study and included 146 patients who underwent echocardiographic examination, 30 days after acute phase of COVID-19. Patients who were placed on mechanical ventilation, patients who had pulmonary thromboembolism or acute coronary syndrome during the acute period of the disease, patients who had an ejection fraction of the left ventricle <50%, patients who were diagnosed with pericarditis during acute illness or clinical signs of heart failure (or had elevated N-terminal (NT)-pro hormone BNP (NT-proBNP) value), with verified renal or hepatic dysfunction were excluded from study, including patients with diabetes mellitus type 1, patients with cancer, connective tissue disease, or pregnant women. The existence of cardiovascular risk factors (hypertension, diabetes mellitus type 2, hyperlipidemia), the presence of previous ischemic heart disease, maximum values of D-dimer and CRP (during the first 15 days of the disease) were taken into analysis.

Results: Effusion was verified around the right atrium (RA) in 104 patients (3.85 ± 1.75 mm), in 135 patients next to the free wall of the right ventricle (RV) (5.24 ± 2.29 mm), in front of the apex of the left ventricle (LV) in 27 patients (2.44 ± 0.97 mm), next to the lateral wall of LV in 35 patients (4.43 ± 3.21 mm), behind the posterior wall of LV in 30 patients (2.83 ± 1.62 mm). Of the total number analyzed, 18 patients

were treated with ibuprofen (600 mg, three times daily), while three patients required the use of methylprednisolone (0.5 mg per kg).

Conclusion: The question of the meaning of echocardiographic examination of patients in long-COVID symptomatology is raised, given the low rate of decision on treatment of patients with verified effusion.

Keywords. COVID-19, Heart, Echocardiography.

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STEROID INDUCED HYPERGLYCEMIA IN COVID 19 INFECTIONS

(Albina Sinanovic, MD, General Hospital Tesanj, BiH)

At the end of 2019. year ,in Wuchan (China) was discovered novel coronavirus, named sars-Cov-2, which spread all over the world, causing global pandemic of COVID -19. Sistemic steroids (SS) stands out , among therapeutic treatment for COVID 19 in severe ill patients, reducing mortalities.

The steroid treatment, for severe ill patients in COVID 19 recomended by WHO (World Health organizations), include dexamethason or the other SS drugs in equivalent doses (pronison or hydrocortison).

Despite consequences of SS, clinical improvement of patients in COVID 19, overridden side effects.

Use of SS is associated with numerous adverse effects and SS induced hyperglycemia is among the most important ones.

SS decreases periferal insulin sensitivity, increases hepatic gluconeogenesis, trigger insulin resistance, inhibit pacreatic insulin production and secretion, worsenes glycemc control in patients with previously known diabetes mellitus, and also causes new-onset of hyperglycemia .

Persistent hyperglycemia contributes to severity of COVID 19, prolonged hospital stay (particulary Intensiv care unit stay), impact clinical outcomes, increases mortality and morbidity in COVID 19.

Optimal glycemc control, during COVID 19 treatment, is crucial, so the menagement of steroid induced hyperglycemia is chalenge in daily rutine.

The evidence and consensus for the management of steroid induced hyperglycemia in COVID 19 is lacking.

This review presents currently available and so far published, clinical practice guidelines for the management of SS induced hyperglycemia in COVID 19 infections.

Key words: COVID 19, Hyperglycemia, Sitemic steroids

COVID-19 AND RENAL COMPLICATIONS

(Irejiz Nedžada, General Hospital Tešanj, BiH)

Kidney injury may be a severe complication of acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who infects the host using the angiotensin-converting enzyme 2 (ACE2) as its receptor, which is expressed in several organs including the lungs, heart, kidneys, and intestines. Kidney complications are relatively common, and acute kidney injury (AKI) is a life-threatening complication in patients with COVID-19. Various pathophysiological mechanisms can contribute to AKI include kidney tubular injury (acute tubular necrosis) with septic shock, microinflammation, increased blood clotting, and probable direct infection of the kidney.

The impact of COVID-19 disease affects not only patients with pre-existing kidney disease or kidney transplantation. De novo kidney disease is commonly seen in hospitalized patients with COVID-19, particularly those with severe disease that require intensive care. In such patients, the incidence of AKI is very high and is associated with high mortality. Most patients with COVID-19-related AKI who recover continue to have low kidney function after discharge from the hospital.

IMPACT OF DIABETES MELLITUS ON PULMONARY HYPERTENSION – OPTIMIZATION OF TREATMENT

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Introduction. Diabetes mellitus (DM) is the most common comorbidity of patients with cardiovascular disease, and its treatment is based primarily on the use of biguanides (metformin), then sulfonylureas and meglitinides, thiazolidinediones (pioglitazone), dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon like peptid -1 (GLP-1) receptor agonists, sodium glucose co-transporter 2 (SGLT-2) inhibitors and insulin (linspro, glulisine, aspart, short and intermediate acting, glargine, glargine u-300, detemir, degludec). Proper selection of therapy according to the specific effects of a particular drug group is imposed as imperative in the treatment of both cardiovascular patients and cardiovascular patients with pulmonary hypertension. Pulmonary hypertension (PH) is an increase in blood pressure at the level of the pulmonary vasculature, or an increase in resistance of blood flow through the pulmonary vessels (arteries or veins). It can be arterial (PAH; increase in mean pulmonary arterial pressure at rest above 25 mmHg, or during loading above 30 mmHg measured by catheterization of the right heart), venous, due to left heart disease, hypoxic, thromboembolic and caused by diseases that

directly affect the pulmonary blood vessels, as well as PH with unclear and / or caused by multifactorial mechanisms.

Aim. To present specificity of particular DM treatment modality, and demonstration of necessity of use of certain substance as supportive therapy in the treatment of pulmonary hypertension.

Methods. Article has a descriptive character and present narrative review of the literature that cover the topic of the article.

Review. DM further complicates the clinical picture in patients with PH. DM affects the progression of endothelial dysfunction, increases pulmonary vascular resistance, leading to right ventricular afterload and right ventricular dysfunction. It also affects left ventricular dysfunction and systemic vascular remodeling and is associated with increased left ventricular hypertrophy and systemic vascular resistance. Endothelial dysfunction leads to unopposed vasoconstriction and increased arterial tone. It has also been found to be associated with the worsening prognosis of patients with PAH. DM has also been linked to thicker epithelial and capillary basal laminas of the alveoli, which further impairs perfusion in the pulmonary system. All of the above makes it imperative to optimize therapeutic modality in DM patients for the purpose of better regulation of DM, which will also benefit PH therapy itself.

There are no large-scale randomized cardiovascular (CV) outcome trials for the use of metformin, as a representative of biguanide, for the onset of cardiovascular events. There is no evidence of benefit in patients with heart failure, although experimental evidence has been found on mice in improving diastolic function. There is also experimental evidence of benefit of metformin in models with pulmonary hypertension. Metformin can stimulate cardiac glucose uptake and combination therapy with bosentan and metformin in pulmonary arterial hypertension patients provides improvements in important outcomes such as exercise capacity and pulmonary haemodynamics, compared with bosentan alone. There is also experimental evidence that metformin can reverse

pulmonary hypertension through inhibition of aromatase and estrogen synthesis in a manner likely to be mediated by AMP-activated protein kinase. Through the ACE trial (Effects of Acarbose on Cardiovascular and Diabetes Outcomes in Patients with Coronary Heart Disease and Impaired Glucose Tolerance) acarbose as a representative of a sulfonurea derivative showed no benefit in preventing a cardiovascular incident, nor did nateglinide in NAVIGATOR trial (Nateglinide And Valsartan in Impaired Glucose Tolerance Outcomes Research). CAROLINA (CARDiovascular Outcome Study of LINAgliptin Versus Glimepiride in Type 2 Diabetes) study confirmed the safety of glimepiride in reducing cardiovascular risk, but is believed to increase cardiovascular risk in patients with DM and to increase mortality in cardiovascular patients with DM, especially in patients with heart failure (HF) and DM, and no vasodilatory effect has been demonstrated that would benefit patients with pulmonary hypertension. Use of pioglitazone is interesting because of its effect on fatty acid oxidation, and indications have been given that pioglitazone could reverse pulmonary hypertension and prevent right heart failure. Experimentally, DPP-4 was expressed in epithelial cells, endothelial cells, smooth muscle cells, and inflammatory cells in the lung, and it seems that sitagliptin attenuated right ventricular systolic pressure (RVSP), right ventricle remodeling, pulmonary arterial medial layer hypertrophy, inflammatory cell infiltration, and endothelial-mesenchymal transition (EndMT) and monocrotaline (MCT) - induced PH rats. GLP-1 causes coronary microvascular dilation and increased flow but does not affect peripheral tone. GLP-1R immunohistochemistry suggests that GLP-1 coronary vasodilation is indirectly mediated by ventricular coronary cross talk. Liraglutide may have both preventative and therapeutic effects on pulmonary vascular remodeling. There is also evidence that GLP-1 mediates the protective effects of DPP-4 on pulmonary vascular and RV remodeling in experimental PH, which may be attributed to the inhibitory effect on EndMT. The effect of liraglutide is reflected in the increase in myocardial glucose uptake, in

the repair of left-ventricular disordered function, cardioprotection during ischemia, flow-mediated vasodilation, nitroglycerin mediated dilation, and reduced intima-media thickness. Phlorizin (a nonspecific SGLT inhibitor) and canagliflozin (a SGLT2-specific inhibitor) relaxed pulmonary arteries in a dose-dependent manner. Pretreatment with phlorizin or canagliflozin significantly inhibited sodium nitroprusside (SNP; a nitric oxide donor) - induced vascular relaxation in pulmonary arteries but not in coronary arteries. Through EMPA-REG OUTCOME (EMPAgliflozin cardiovascular outcome event trial in type 2 diabetes mellitus patients - Removing Excess Glucose), the CANVAS (CANagliflozin cardioVascular Assessment Study), and DECLARE-TIMI 58 (Dapagliflozin Effect on CardiovascuLAR Events - Thrombolysis in Myocardial Infarction 58) trial the use of SGLT-2 has its advantages in the treatment of HF, and in line with the above risks through the studies mentioned, could represent the drug of choice in this patient population. Polytherapy is most common in everyday clinical practice, and the combination of metformin and GLP-1 is increasingly tested in ex vivo experiments, to confirm whether metformin can be a GLP-1 stimulator, which could probably also be a turn in the treatment of DM in patients with PAH, given the benefits shown by both drug groups.

Conclusion. In patients with PAH and DM, it is necessary to optimize therapeutic treatment, and GLP-1 agonists should be the first-choice treatment. The addition of metformin to bosentan therapy appears to have an effect on reducing the symptoms of patients with PAH.

Keywords: Pulmonary hypertension, Diabetes mellitus, Treatment.

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MCCONNELL'S SIGN IN CRITICALLY ILL COVID-19 PATIENTS (Poster presentation)

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Aim: To point out the importance of McConnell's sign (severe hypokinesis of the right ventricular free wall with apical sparring), as a predictor in the diagnosis of pulmonary embolism in patients with Coronavirus disease 2019 (COVID-19), which was confirmed with computed tomography (CT) pulmonary angiography.

Methods: This research included 19 patients who had verified McConnell's sign on echocardiographic examination and were diagnosed with COVID-19. All patients were on noninvasive or invasive mechanical ventilation. Signs that indicate pulmonary embolism were examined (McConnell's sign and D-shaped left ventricle; the 60/60 sign did not come into consideration due to difficult views in the same patients, especially the parasternal short-axis (PSAX) view).

Results: The mean age of the patients was 65.17 ± 4.52 years, and from the total number of patients 15 of them were male (78.9%). McConnell's sign was observed in all patients and in 6 patients pulmonary embolism was confirmed. (31%; 4 patients were on non-invasive mechanical ventilation, and 2 on invasive mechanical ventilation). From 6 patients with confirmed pulmonary embolism, 4 had a verified D-shaped left ventricle.

Conclusion: McConnell's sign in critically ill COVID-19 patients does not appear to be a predictive sign of pulmonary embolism. However, verifying the same, along with the D-shaped left ventricle sign, for-

ces us to consider the diagnosis of pulmonary thromboembolism, and is indication for CT pulmonary angiography. Occurrence of McConnell's sign and D-shaped left ventricle should be viewed in correlation with the pharmacological modality of patients, especially with the use of corticosteroids.

Keywords. Pulmonary Embolism, COVID-19, Right Ventricle

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THROMBOPROPHYLAXIS OF PATIENTS AFTER CORONAVIRUS DISEASE 2019 (COVID-19) (Poster presentation)

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Following Coronavirus disease 2019 (COVID-19) routine thromboprophylaxis has not been established. The incidence of venous thromboembolism (VTE) in patients who did not use thromboprophylaxis after COVID-19 was 4.8 patients per 1000, which is similar to earlier data in the posthospital period in patients who were not diagnosed with COVID-19, but were hospitalized. Symptomatic VTE occurs in 0-0.6% of patients 30-42 days after discharge due to COVID-19. Continuation of thromboprophylaxis is recommended if the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE-VTE) score ≥ 4 (Table 1). If the D-dimer values are twice as high as normal with an IMPROVE-VTE score ≥ 2 , that is also an indication for thromboprophylaxis, or if the patient is older than 75 years, and has D-dimer values twice as high as normal. Previous VTE or oncological process in anamnestic data is indication for thromboprophylaxis. The assessment of thromboprophylaxis must be in accordance with the clinical picture of the patient, the findings of computed tomography of the thorax, or the verification of possible VTE. In the case of verified VTE therapeutic regimen is indicated (Table 2).

Key words: Pulmonary embolism, COVID-19, Treatment.

Table 1. IMPROVE-VTE score

Data	Score
Previous venous thromboembolism	3
Thrombophilia	2
Paralysis of the lower extremities during hospitalization	2
Active oncological process	2
Immobilization longer than seven days	1
Intensive Care Unit treatment	1
>60 years	1
D-dimer $\geq 2x$ of the reference value	2
Score > 4 - thromboprophylaxis is recommended after hospitalization for up to 42 (45) days	

Table 2. Thromboprophylaxis after COVID-19

Risk	Thromboprophylaxis
Low risk (D-dimer normal, or less than 2x than reference values, without other risk factors)	Neither antiplatelet nor anticoagulant therapy is indicated
Moderate risk (D-dimer greater than 2x than reference values, without other risk factors)	Use of acetylsalicylic acid in prophylactic dose
High risk (D-dimer greater than 2x than reference values and one of the risk factors: immobilization, previous venous thromboembolism, hormonal therapy, body weight > 120 kg or body mass index (BMI) > 35 kg / m ²), oncological process (take into account the risk of bleeding)	Up to 42 days (maximum 45 days) - enoxaparin 40 mg daily, apixaban 2x2.5 mg daily, rivaroxaban 10 mg daily - control by a competent doctor after the mentioned period; "Off-label" use of this therapy in accordance with clinical experience

REVIEW OF THE PATHOLOGY OF THE COVID 19 INFECTION AT COVID DEPARTMENT OF THE GENERAL HOSPITAL TEŠANJ IN 2020

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Introduction: SARS CoV2 (Severe acute respiratory syndrome coronavirus 2) virus causes respiratory tract infections with a diverse clinical picture. The clinical picture can vary from asymptomatic, through general infectious syndrome, pneumonia to ARDS (acute respiratory distress syndrome), including manifestations by other organ systems.

Aim: To analyze the severity of the clinical picture in patients with Covid 19 who were hospitalized at the Covid Department of the General Hospital Tešanj during 2020.

Methods: We analyzed the severity of the clinical picture in patients positive for SARS-CoV-2 who were hospitalized at the Covid Department of the General Hospital Tešanj in the period from 15.03.2020. to 31.12.2020. The severity of the clinical picture is divided into three levels according to radiological findings and oxygen saturation values: mild stage (patients who did not have radiological signs of inflammation or the changes were scarce, with satisfactory saturation (> 92%), without the need for additional oxygentherapy), moderate stage (patients had moderate radiological changes, with satisfactory saturation with oxygen support 5-10 L / min), severe stage (patients with abundant radiological changes, respiratory insufficiency with the need for oxygen support over 10L/min). Data were statistically processed.

Results: Out of the total of 411 patients, 164 (39.90%) were female and 247 (60.10%) male. The total number of patients with mild clinical picture is 119 (28.95%), of which 51 (42,86%) were female and 68

(57,14%) male. Moderate clinical picture was present in 183 (44.53%) patients, of which 80 (43.72%) were female, and 103 (56.28%) male. Number of patients with severe clinical picture was 109 (26.52%), of which 33 (30.28%) were female and 76 (69.72%) male. Among the patients with severe clinical picture there were 37 fatal outcomes and 3 in patients with moderate clinical picture.

Conclusion: Most of the hospitalized patients were male. Most hospitalized patients had moderate clinical picture, possibly because patients with a milder clinical picture were often treated at the primary health care. From the above data, it can be seen that the number of male patients with severe clinical picture is significantly higher than the number of female patients.

Keywords: Clinical presentation, COVID19, Pneumonia

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DIAGNOSIS OF NEW CASES OF DIABETES MELLITUS AND GLUCOSE INTOLERANCE AMONG COVID19 PATIENTS

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Background: COVID19 mostly described as respiratory infection has influence in metabolic stages and function of the whole body. It is known that around 50% of COVID19 positive patients are without any symptoms and signs. Among those with symptoms, the most cases have interstitial pneumonia, while other show malfunction in other organs systems. Coronavirus is vasculotropic and in most cases some impairment of oxygen supply in the tissue can be seen. In some cases we registered glucose intolerance and impaired fasting glucose levels.

Methods: We analyzed patients during a two-month period, we treated 82 patients in COVID division of Pulmonology department of General Hospital Tešanj. Among them, 7 of new Diabetes cases registered before the introduction of steroid therapy. For all patients we performed standard laboratory tools including blood gas analyze, blood cell count, fasting glucose, creatinin, urea, minerals, deep-dimer, transaminase, C-reactive protein and some other laboratory tests if appropriate. For all patients chest X-ray or CT scan was performed, as well as ECG.

Results: During the timeframe of two months we treated 82 patients in COVID division of Pulmonology department of General Hospital Tešanj. Out of all there were 43 male (53.75 %) and 39 female (47.56 %) patients. Among them, we had 7 of new Diabetes cases or glucose intolerance or patients with impaired fasting glucose all registered before the introduction of steroid therapy. Patients were followed-up with average duration of 14 days during hospitalisation. Among new diabetics, maximal glycemia was 28 mmol/L. We introduce insulin in therapy for

5 patients. After the discharge we followed up the patients during 3 months. Among them 5 patients had normal glucose level (fasting glucose or postprandial glycaemia). Among them 2 of patients had Diabetes or glucose intolerance after more than 3 months. Patients treated with high dose of steroids had higher level of glycaemia in new diabetics and in diabetics who were diagnosed before COVID19.

Conclusion: In COVID19 infection, new diabetics or patients with glucose intolerance were registered, but most of them had normal fasting and postprandial glycaemia three months after discharge, even if they were treated with insulin.

Key Words: Diabetes, COVID 19, Glucose intolerance

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