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ABSTRACT

Purpose of the study: Retrospective assessment of the peculiarities of changes in the clinical and laboratory parameters of patients with COVID-19 and concomitant cardiovascular pathology. **Materials and methods.** A retrospective analysis of medical records of 92 patients was. All patients with COVID-19 underwent routine blood tests, including a complete blood count, coagulation profile, lipid spectrum and liver and kidney function, inflammatory biomarkers. **Results.** According to the results of the study, in the included 92 patients with COVID-19, CVD was found in 32 patients (35.7%). When studying the medical records of patients of the first group with COVID-19 without cardiovascular pathology, the following data of clinical and laboratory parameters were obtained: in the study of a detailed biochemical blood test, an excess of the reference (10-120 μg / l) values of ferritin (192.4 μg / l, p <0.05), C-reactive protein (18.19 mg / l versus the reference 0-5 mg / l, p <0.05), hemostasiogram values: increased fibrinogen (7.25 g / l versus 2.76-4.71 g / l, p <0 , 05), D-dimers (437.8 ng / ml versus 0-255 ng / ml, p <0.05). In the second group COVID-19 with cardiovascular pathology (n = 30), the following data of clinical and laboratory parameters were obtained: when studying a detailed biochemical analysis, an excess of ferritin content was revealed (518.36 μg / l versus 192.4 μg / l, the difference is 169.42%, p < 0.05), C-reactive protein (38.67 mg / L versus 18.19 mg / L, the difference is 112.6%, p <0.05), glucose concentration (7.67 mmol / L versus 4.9 -5.1 mmol / L, p <0.05). **Conclusions.** Thus, it is advisable to involve survivors after COVID-19 in medical rehabilitation programs for faster and better recovery of the functions of various systems (primarily respiratory and cardiovascular), improving the quality of life and reducing the risk of disability.

Key words: COVID-19, cardiovascular disease, inflammatory biomarkers

INTRODUCTION

The pandemic of the novel coronavirus infection (COVID-19), spread by the SARSCoV-2 virus, is a challenge to health systems around the world. The most common manifestation of COVID-19 is the respiratory system. However, this disease is characterized by high activity of inflammation and thrombotic complications, leading to multiple organ lesions. The management of a patient with COVID-19 implies not only the treatment of pneumonia and respiratory failure, but also the timely recognition and treatment of damage to other target organs. According to the results of various studies, hypertension is detected in 15–40% of patients with COVID-19 [6,5]. Currently, we can talk about the prevalence of hypertension in patients with severe forms of COVID-19. So, in the study *Guan et al.* this figure was 23.7%*vs*13.4% - in patients with a relatively mild course of the disease. It is reported that patients with hypertension are 2.6 times more likely to die with COVID-19. The probable mechanisms of the relationship between hypertension and the worst outcome in COVID-19 are correlated with the role of type II angiotensin-converting enzyme (ACE2) [9]. ACE2 is an important link in the renin-angiotensin-aldosterone system (RAAS), which is involved in the pathogenesis of hypertension and other CVDs. The SARS-CoV-2 virus binds to ACE2 receptors on the surface of target cells through a glycoprotein (peplomer) known as the spike S-protein (*spike protein*). The S-protein of the corona of the SARS-CoV-2 virus mimics ACE2 in structure. Further, the virus and the transmembrane domain of ACE2 penetrate into the cell by endocytosis. The SARS-CoV-2 virus causes an imbalance in the ACE2 system, accompanied by a decrease in the level of AT1-7 against the background of an increase in the amount of ATII and activation of the ACE-ATII-AT1-receptor pathway. As a result, acute damage to the lungs, myocardium, blood vessels and other organs, originally caused by the SARS-CoV-2 coronavirus, can worsen. It can be assumed that RAAS inhibitors, providing better control of blood pressure, will partially help to restrain the imbalance of the immune system in hypertension [5]. In patients with hypertension during the period of viral infection, it is necessary to control blood pressure levels and monitor cardiovascular risk.

PURPOSE OF THE STUDY. Of this study was a retrospective assessment features of changes in clinical and laboratory parameters of patients with COVID-19 and concomitant cardiovascular pathology.

MATERIAL AND METHODS. A retrospective analysis of medical records of 92 patients. In all patients, the diagnosis of COVID-19 was confirmed by polymerase chain reaction for the SARS-CoV-2 virus, material obtained using a swab from the nasopharynx and oropharynx. The diagnosis of viral interstitial

pneumonia was revealed in 76 (82.6% of patients) by computed tomography of the lungs, in 16 (12.4%) patients - by standard radiography of the lungs). All patients were divided into 2 groups: the first group - patients with COVID-19 without comorbidity, the second group - patients with coronavirus infection and concomitant ischemic heart disease.

All patients with COVID-19 underwent routine blood tests, including a complete blood count, coagulation profile, lipid spectrum and liver and kidney function, inflammatory biomarkers. To assess the statistical significance of the differences, the chi-square test, Fisher's exact test, and Mann-Whitney test were used; the limit of significance was considered the probability of error less than 5% ($p < 0.05$).

RESULTS. According to the results of the study, in the included 92 patients with COVID-19, CVD was found in 32 patients (35.7%). The identified 32 patients with cardiovascular diseases suffered from arterial hypertension - 19 patients, coronary artery disease - 9 patients, rhythm disturbances - 1 patient and cerebrovascular diseases - 3 patients (table 1).

Table 1.

Clinical characteristics of patients

Characteristic	Total (n = 92)	Without cardiovascular disease (n = 60)	With cardiovascular disease (n = 32)	P
Men (%)	54 (58.6)	44 (53.3)	22 (68.7)	0.04
Age (years), average	49.1 + 6.92	46.7 ± 7.0	56 + 7.3	<0.001
Temperature (° C) avg.	36.7 + 1.8	37+ 0.9	37.4 + 2.3	0.510
SBP, average	130 + 8.6	126 + 4.9	158+ 6.5	<0.001
DBP, mean	80+ 9.1	78 + 9.1	96.1 + 4.9	<0.001
Heart rate, average	88 + 7.1	87 + 6.4	97 + 3.8	0.021
Concomitant diseases, number (%)				
Diabetes	7 (7.6)	1 (1.6)	6 (18.7)	<0.001
COPD	5 (5.4)	1 (1.3)	4 (12.5)	0.622
Hepatic dysfunction	9 (9.7)	4 (6.6)	5 (15.6)	0.678
Renal dysfunction	9 (9.7)	2 (3.3)	7 (21.8)	0.064

CVD patients had higher mean systolic blood pressure 158.2 ± 6.5, diastolic blood pressure 96.1 ± 4.9, and heart rate 97 + 3.8 ($p < 0.05$). In patients with COVID-19 with CVD, the incidence of diabetes mellitus was 18.7%, which was higher than in patients without CVD. The main clinical manifestations of COVID-19 in the studied patients were: fever in 61 (81.3%) patients, cough in 62 (82.6%) patients, shortness of breath in 42 (56%) patients, muscle pain in 8 (10.6%) patients. %) of patients), rhinorrhea in 3 (4%) patients, diarrhea in 3 (2%) patients) and nausea with vomiting in one patient.

When studying the medical records of patients of the first group with COVID-19 without cardiovascular pathology (n = 60), the following data of clinical and laboratory parameters were obtained: in the study of a detailed biochemical blood test, an excess of the reference (10-120 μg / L) values of ferritin (192.4 μg / L, p <0.05), C-reactive protein (18.19 mg / l versus the reference 0-5 mg / l, p <0.05), hemostasiogram values: increased fibrinogen (7.25 g / l versus 2.76-4.71 g / L, p <0.05), D-dimers (437.8 ng / ml versus 0-255 ng / ml, p <0.05). In the second group of patients, patientsCOVID-19with cardiovascular pathology (n = 32), the following data of clinical laboratory parameters were obtained: when studying a detailed biochemical blood test, an excess of ferritin content was revealed (518.36 μg / l versus 192.4 μg / l, the difference is 169.42%, p < 0.05), C-reactive protein (38.67 mg / L versus 18.19 mg / L, the difference is 112.6%, p <0.05), glucose concentration (7.67 mmol / L versus 4.9 -5.1 mmol / L, p <0.05). The indicators were compared in relation to the first group of patients. According to the results of the hemostasiogram, in comparison with the first group, it was revealed: an increase in the content of fibrinogen (7.91 g / l versus 7.25 g / l, the difference is 9.1%, p <0.05), D-dimers (540.28 ng / ml vs. 437.8 ng / ml, difference 23.408%, p <0.05), international normalized ratio (INR) (1.53 INR (international normalized ratio) vs. 1.34 INR, difference 14.2%, p < 0.05), thromboplastin time (APTT) (17.6 s versus 19.1 s, the difference is 7.85%, p <0.05).

DISCUSSION. The study described the characteristics of patients with COVID-19 with and without cardiovascular disease, and identified risk factors associated with severe disease. In our study, patients with CVD accounted for 35.7%, and hypertension accounted for the largest proportion, which is consistent with the studies [8,14]. CVD was the most common comorbidity in patients with coronavirus and was an independent risk factor for death and other adverse outcomes in patients with SARS [3,1]. About 50% of patients with MRS coronavirus suffered from hypertension and diabetes mellitus [2,7]. A marked increase in coagulation profiles such as D-dimer and PTV was observed in patients with cardiovascular disease. The early stage of CVD was usually accompanied by vascular endothelial dysfunction and organic lesions, whereas oxidative stress and blood pressure can damage the vascular endothelium. Their vicious circle aggravates vascular endothelial damage, and endothelial damage can cause hypercoagulability [11]. SARS-CoV-2 infection can cause direct primary myocardial injury or exacerbate the original myocardial injury. SARS-CoV has been shown to directly affect the heart. Pathological data from patients with COVID-19 showed degeneration and necrosis of cardiomyocytes, so the same

mechanism cannot be ruled out for SARS-CoV-2. Inflammatory biomarkers were significantly increased in CVD patients, indicating that inflammatory cell necrosis promoted the inflammatory response and resulted in myocardial damage by cytokine storms [13]. Their vicious circle aggravates vascular endothelial damage, and endothelial damage can cause hypercoagulability [13]. SARS-CoV-2 infection can cause direct primary myocardial injury or exacerbate the original myocardial injury. SARS-CoV has been shown to directly affect the heart. Pathological data from patients with COVID-19 showed degeneration and necrosis of cardiomyocytes, so the same mechanism cannot be ruled out for SARS-CoV-2. Inflammatory biomarkers were significantly increased in CVD patients, indicating that inflammatory cell necrosis promoted the inflammatory response and resulted in myocardial damage by cytokine storms [13]. Their vicious circle aggravates vascular endothelial damage, and endothelial damage can cause hypercoagulability [11]. SARS-CoV-2 infection can cause direct primary myocardial injury or exacerbate the original myocardial injury. SARS-CoV has been shown to directly affect the heart. Pathological data from patients with COVID-19 showed degeneration and necrosis of cardiomyocytes, so the same mechanism cannot be ruled out for SARS-CoV-2. Inflammatory biomarkers were significantly increased in CVD patients, indicating that inflammatory cell necrosis promoted the inflammatory response and resulted in myocardial damage by cytokine storms [13]. SARS-CoV-2 infection can cause direct primary myocardial injury or exacerbate the original myocardial injury. SARS-CoV has been shown to directly affect the heart. Pathological data from patients with COVID-19 showed degeneration and necrosis of cardiomyocytes, so the same mechanism cannot be ruled out for SARS-CoV-2. Inflammatory biomarkers were significantly increased in CVD patients, indicating that inflammatory cell necrosis promoted the inflammatory response and resulted in myocardial damage by cytokine storms [13]. SARS-CoV-2 infection can cause direct primary myocardial injury or exacerbate the original myocardial injury. SARS-CoV has been shown to directly affect the heart. Pathological data from patients with COVID-19 showed degeneration and necrosis of cardiomyocytes, so the same mechanism cannot be ruled out for SARS-CoV-2. Inflammatory biomarkers were significantly increased in CVD patients, indicating that inflammatory cell necrosis promoted the inflammatory response and resulted in myocardial damage by cytokine storms [15]. Comparing the literature and our results, we have identified many shortcomings in the management and diagnosis of patients with COVID-19. This was due to limited medical resources and time for diagnosis during the outbreak. Finally, the lack of endpoints and proper patient study results, as well as data on

dynamic observation of disease progression, influenced the incidence of complications during the period of mass hospitalization of patients with COVID-19.

CONCLUSIONS. When comparing the values of biochemical blood test parameters in patients with coronavirus infection complicated by cardiovascular pathology with those in patients with coronavirus infection without concomitant pathology, it was revealed: an increase in blood ferritin content by 2.69 times ($p < 0.05$), C- reactive protein 2.13 times ($p < 0.05$), D-dimers - 1.23 times ($p < 0.05$), INR - 1.14 times ($p < 0.05$) and decrease in APTT in 1.09 times ($p < 0.05$). Thus, the discovered comorbid conditions and the position on the diagnosis and management of patients with covid infection should force us to develop step-by-step methods of managing patients both during the period of covid infection against the background of CVD and to trace the postcoid period. It turned out, that older age (≥65 years) and CVD are in our study the leading independent risk factors for patients with COVID-19 and had more severe consequences and worse outcome in the patients we studied. It is advisable to involve survivors after COVID-19 in medical rehabilitation programs for faster and better recovery of the functions of various systems (primarily respiratory and cardiovascular), improving the quality of life and reducing the risk of disability.

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