https://russjcardiol.elpub.ru
doi:10.15829/1560-4071-2020-3904

ISSN 1560-4071 (print)
ISSN 2618-7620 (online)

COVID-19 infection after recent heart transplantation: a case report

Vechorko V. I.[1,2], Gordeev I. G.[2], Gubareva E. V.[1], Ryndyaeva E. V.[1], Averkov O. V.[1,2]

History of heart transplantation in combination with immunosuppressive therapy and acute viral respiratory infection overlay makes the patient difficult to manage. In case of COVID-19, the setting is complicated by unknown pathogenesis, including its effect on blood, coagulation system, and lung tissue. Current case report discusses the 60-year-old patient with a COVID-19 infection occurred in the immediate postoperative period after heart transplantation.

Key words: SARS-CoV-2, 2019-nCoV, immunosuppression, coronavirus, atypical pneumonia, hypercoagulation, atrial thrombosis, heart failure.

Relationships and Activities: none.

[1]O. M. Filatov City Clinical Hospital № 15, Moscow; [2]Pirogov Russian National Research Medical University, Moscow, Russia.

Vechorko V. I. ORCID: 0000-0003-3568-5065, Gordeev I. G.* ORCID: 0000-0002-3233-4369, Gubareva E. V. ORCID: 0000-0002-0749-7051, Ryndyaeva E. V. ORCID: 0000-0001-8099-4110, Averkov O. V. ORCID: 0000-0002-3010-755X.

*Corresponding author: cardio-15@yandex.ru

Received: 12.05.2020
Revision Received: 14.05.2020
Accepted: 18.05.2020

For citation: Vechorko V. I., Gordeev I. G., Gubareva E. V., Ryndyaeva E. V., Averkov O. V. COVID-19 infection after recent heart transplantation: a case report. *Russian Journal of Cardiology*. 2020;25(5):3904. (In Russ.) doi:10.15829/1560-4071-2020-3904

The pandemic of novel coronavirus infection SARS-CoV-2 (Covid-19) required a review of current standards, including the standards and protocols for the management of various pathologies. Being a viral respiratory infection with an unknown pathogenesis, Covid-19 is especially dangerous for patients with comorbidities and immunodeficiency. Such patients, of course, include people after transplantations. According to study by Pereira, et al. (2020) with a cohort of 90 such patients, sixteen patients died (18% overall, 24% of hospitalized, 52% of ICU). The authors concluded that transplant recipients with COVID-19 appear to have more severe outcomes, although testing limitations likely led to undercounting of mild/asymptomatic cases [1]. Of course, heart recipients are at particular risk [2].

In Russia, according to anti-epidemic measures, the treatment of patients with a suspected or established COVID-19 is carried out in specialized hospitals. O. M. Filatov City Clinical Hospital № 15 in Moscow is a general hospital with a priority area of cardiology, which was completely redesigned to fight infection. We offer a case report of a patient after a recent (less than a month) heart transplantation hospitalized with COVID-19.

Clinical case

A 60-year-old patient was admitted with complaints of fever up to 38,5° C, shortness of breath, weakness, and a tingling under the shoulder blades. He was delivered by the ambulance team from home 4 days after being discharged from another hospital, where he received an orthotopic heart transplantation due to ischemic cardiomyopathy.

These complaints appeared the day after discharge. The patient has a history of myocardial infarction (9 years ago) and hypertension. The epidemiological history was positive: an employee of transplantology center had a positive test for SARS-CoV-2. The patient came to Moscow from another region for surgical intervention.

The patient takes chronic medications: Methylprednisolone 4 mg/day, Tacrolimus 3 mg/day, Mycophenolate mofetil 2 g/day, Trimethoprim/sulfamethoxazole 480 mg/day, Amlodipine 2,5-5 mg/day.

Upon admission to the hospital, the patient had a moderate state and normal consciousness. The body weight was normal. There were a respiratory rate of 22 per minute, spontaneous breathing, SpO_2 of 90%. Blood pressure was 121/80 mm Hg, heart rate — 115 per minute. The heartbeat was regular, without pulse deficit.

According to multi-slice computed tomography (Figure 1), there were bilateral multisegmental areas of ground glass opacity and consolidation, mainly in the subpleural sections (right lung — 15%, left — 10%). The lumen of the trachea, the main and segmental bronchi remained constant.

Bronchi were not narrowed; the bronchial walls were thickened. Diaphragm, mediastinum, and pleural cavities were without pathological findings. There was a pericardial fluid with a diameter of up to 32 mm. Mediastinal lymph nodes were not enlarged (up to 9 mm). Report: CT pattern of bilateral multisegmental pneumonia, high level of suspicion COVID-19 infection, moderate severity (CT1). Hydropericardium.

According to the first echocardiography (upon admission), the heart chambers had normal sizes and contractility. Left ventricular (LV) walls were thickened. Mild mitral and tricuspid regurgitation. Grade 1 LV diastolic dysfunction. There were large hydropericardium (up to 3,2 cm). Diastolic collapse of the right atrium and right ventricle. Visceral pericardial layer had depositions.

Three days later, a repeated echocardiogram (Table 1) (Samsung Medison HS60-RUS) showed left atrial dilatation. The left ventricle was D-shaped. LV walls were thickened. Grade 1 mitral and tricuspid regurgitation was identified. LV local and global systolic function were not impaired. Pericardium was without findings. In left atrial appendage, a mobile echo-bright formation 27x11 mm in size, probably a thrombus, was visualized. During the week, its size changed to 27x11 mm. It was decided to not use transesophageal echocardiography. The electrocardiogram is shown in Figure 2.

There were following laboratory findings: hemoglobin level of 77 g/l (hypochromic anemia, anisocytosis), which changed to 100 g/l after blood transfusion; absolute ($0,7\times10^9$/L, followed by a decrease to $0,3\times10^9$/L) and relative lymphopenia; an increase in C-reactive protein level to 70 mg/L and a further decrease to 22 mg/L; an increase in D-dimer level to 800 ng/ml; an increase in procalcitonin level to 0,5 ng/ml, followed by a decrease to 0,1 ng/ml.

The initial diagnosis of COVID-19 infection was made according to clinical, investigational, and epidemiological criteria, and was subsequently confirmed by repeated polymerase chain reaction (PCR) with an interval of 2 days.

The treatment was carried out using the following medications: IV azithromycin, IV ampicillin/sulbactam, intranasal interferon-alpha; therapy with tacrolimus, mycophenolate mofetil, methylprednisolone was continued. Anticoagulants were used: initially — enoxaparin (0,4 ml/day); after detecting left atrial appendage thrombus — rivaroxaban (20 mg/day), subsequently switched with warfarin.

Pericardiocentesis was performed — serous-hemorrhagic fluid of 960 ml was evacuated (hemorrhagic effusion with lymphoid reaction, single mesothelial

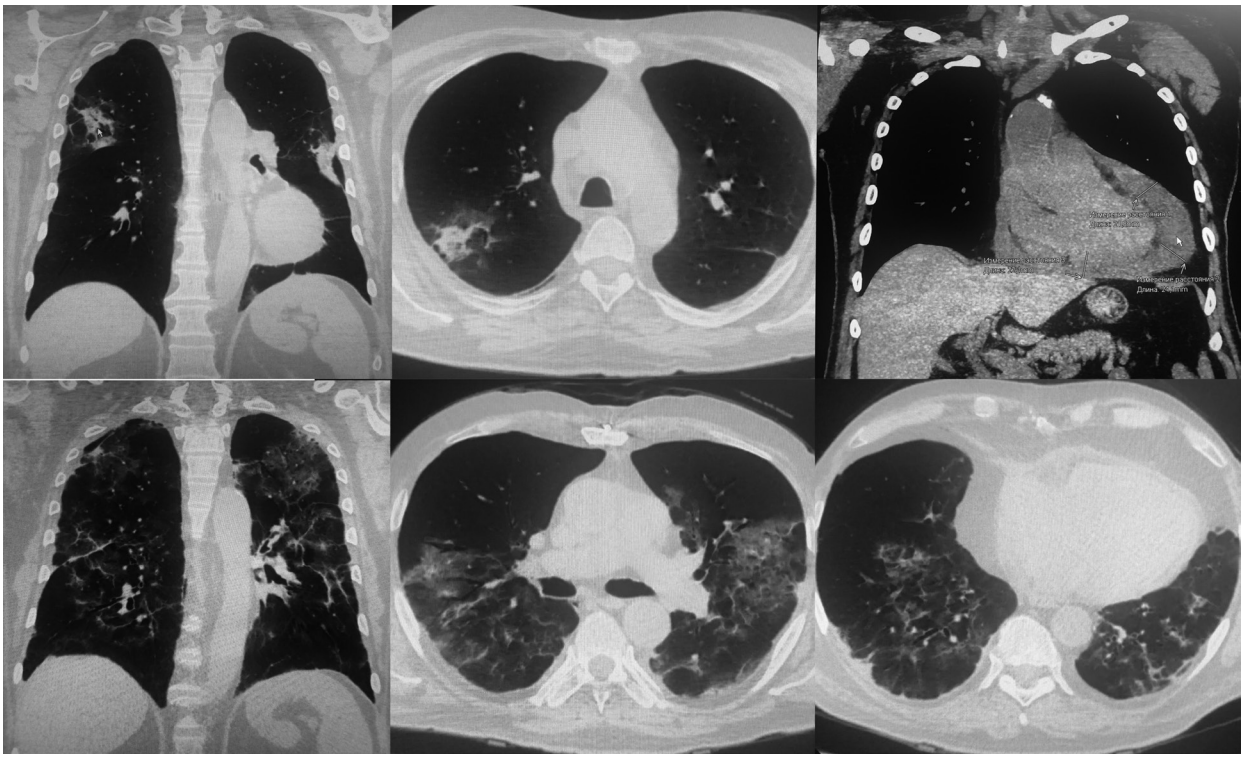

Figure 1. Lung and cardiac computed tomography scan.

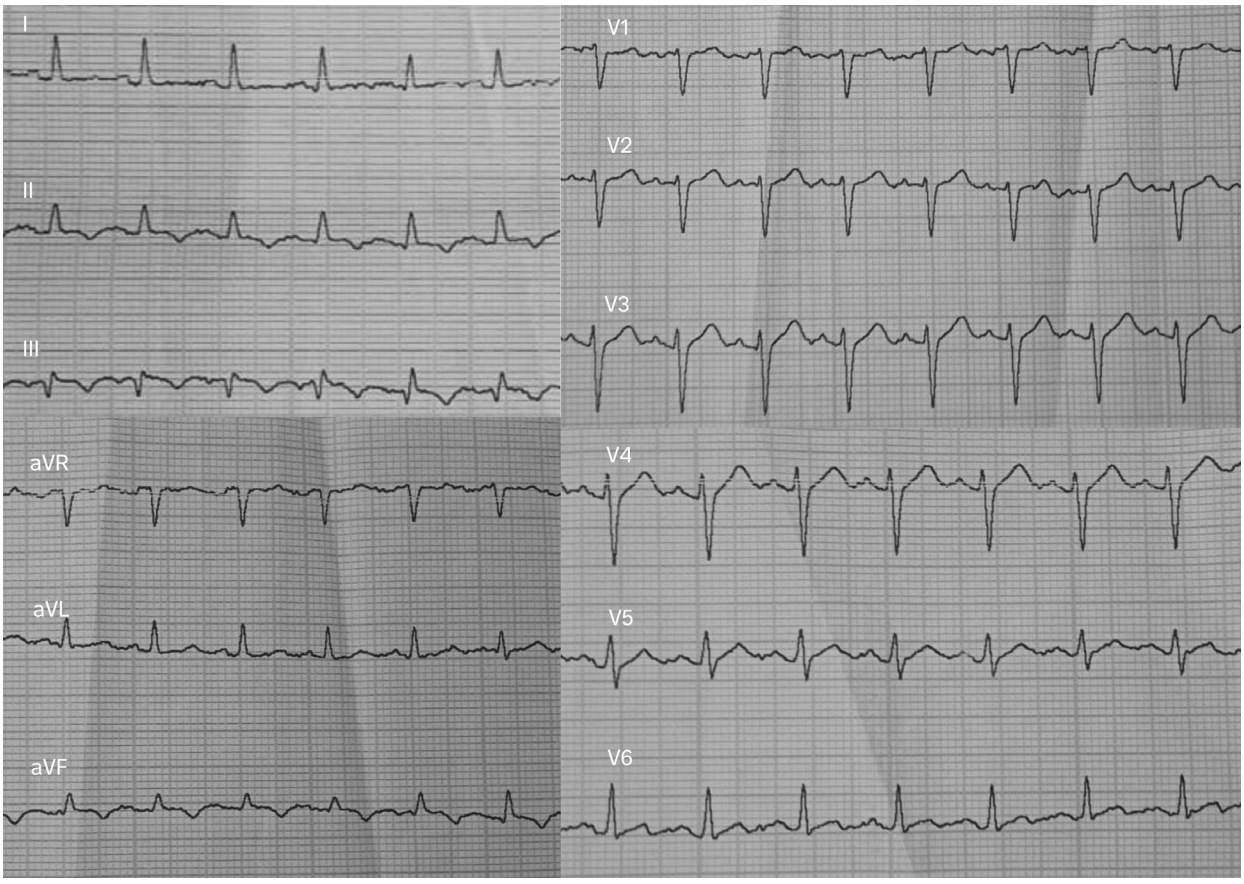

Figure 2. Electrocardiogram.

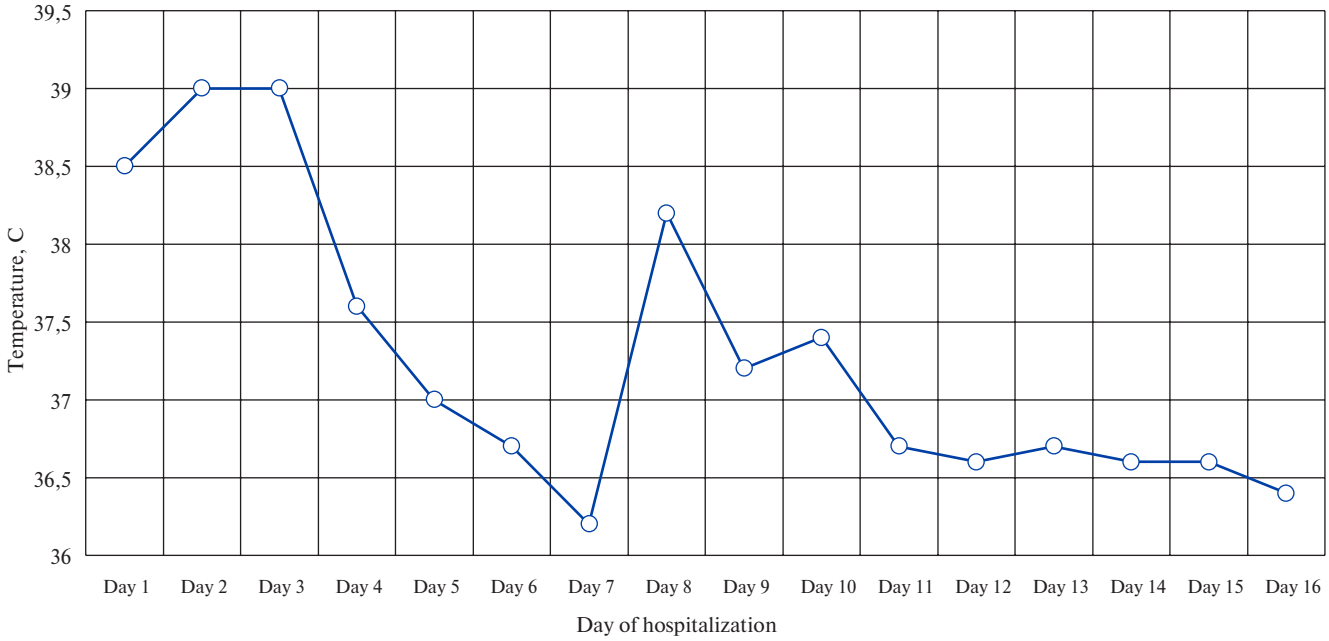

Figure 3. Temperature curve.

Table 1

Echocardiographic data after pericardiocentesis

Parameter	Value	Standard
Aortic annulus, mm	25	до 40
Aortic valve opening, mm	21	15-26
Left atrial size, mm	36x56	30-40
LV EDV, ml	64	67-155
LV ESV, ml	27	22-58
LVEF (Simpson biplane), %	57	52-74
Diastolic thickness of IVS, mm	13	6-11
Diastolic thickness of LVPW, mm	11	6-11
Effective stroke volume, ml	36	-
Right ventricle, ml	27	<33
Right atrial size, mm	28x34	28-40
Pulmonary artery diameter, mm	18	-
Aortic valve: leaflets are not thickened. Vmax — 1,2 m/s, PGr — 6,6 mm Hg. Aortic insufficiency is not detected. Aortic root — 3,7 cm.		
Mitral valve: leaflets are not thickened. Mitral insufficiency — grade 1. Vmax — 0,9 m/s, PGr — 3,9 mm Hg.		
Tricuspid valve: leaflets are not thickened. Tricuspid insufficiency — grade. Vmax — 0,6-0,9 m/s		
Pulmonary valve: insufficiency — grade 1. Vmax 0,9 m/s, PGr 3,3 mm Hg.		
The inferior vena cava is not dilated, collapses with inspiration >50%.		
Abnormally located LV chords. In left atrial appendage, a mobile echo-bright formation 27x11 mm in size, probably a thrombus, is visualized.		

Abbreviations: EDV — end-diastolic volume, ESV — end-systolic volume, LV — left ventricle, EF — ejection fraction, IVS — interventricular septum, LVPW — left ventricular posterior wall, Vmax — maximum flow rate, PGr — pressure gradient.

cells). The drainage was removed, further accumulation of fluid according to echocardiography was not found.

During treatment, the state of the patient was stable, the fever decreased with an episode of febrile temperature return (Figure 3). There was no shortness of breath; SpO_2 — 95% (oxygen insufflation of 6 l/min). Hemodynamics was stable.

To continue treatment, the patient was transferred to a specialized institution dealing with patients after

heart transplantation. At discharge, there was an improvement in the form of body temperature normalization, a decrease in C-reactive protein and procalcitonin levels. Anticoagulant therapy with warfarin was administered under the control of INR.

Diagnosis upon transferring:

Primary diagnosis: I25.5 Ischemic cardiomyopathy. Postinfarction cardiosclerosis. Implantation of IABP. Removal of IABP. Orthotopic heart transplantation. Stage 2A heart failure (Strazhesko-Vasilenko Classification), NYHA class II.

Competing diagnosis: U07.1 COVID-19 infection (identified virus). SARS-CoV-2 smears are twice positive.

Comorbidities: I11.9 Stage 3 hypertension, very high risk.

Complications of the primary disease: J12.8 Community-acquired bilateral multisegmental viral pneumonia. Grade II respiratory failure. I31.3 Exudative pericarditis. Pericardiocentesis, pericardial drainage. Drainage removal. I51.3 Left atrial appendage thrombus.

Discussion

This patient had a combination of several pathological processes: immunosuppression, infection against its background, early period after recent major surgical intervention, cardiac disease. An additional complicating factor was the development of left atrial thrombosis, which increase the risk of embolism. Actually, the association of the infectious inflammatory process with the increase in blood coagulation has long been known. However, unknown mechanisms of COVID-19 infection and recent heart transplant heart makes the management of this patient unusual.

In a study by Li F, et al. (2020), there was a first experience of managing such patients in January-February 2020. The first case, a 51-year-old man with a history of heart transplantation in 2003, initially SpO_2 of 99%, without shortness of breath, body temperature of 38,5° C, with characteristic CT changes — ground glass opacity. Then COVID-19 infection was confirmed by PCR test. Apparently healthy patient was discharged after 1-month hospitalization, but with persistent residual changes in lung CT scan. The second patient, a 43-year-old man, was quarantined due to the 2019-nCoV positive test. Then he was hospitalized, but was discharged 2 weeks later due to the double negative PCR test. These authors indicate that the development of the disease and the clinical characteristics of heart recipients differ little from the common ones [3].

Holzhauser L, et al. reported the experience of managing two COVID-19 patients with a transplanted heart (2020). First case is a 59-year-old African-American woman who underwent heart transplantation in 2012 due to non-ischemic cardiomyopathy, also suffering from diabetes, hypertension and chronic kidney disease. The clinical state was severe, with an arterial pH of 7,3, pCO_2 of 32 mm Hg, pO_2 of 64 mm Hg with FiO_2 of 0,8. The condition remained serious. On the seventh day of hospitalization, it was decided to not use extracorporeal membrane oxygenation due to comorbidity profile, age, unfavorable prognosis. On the tenth day, the family was informed of the futility of further treatment and it was discontinued. The second case is a 75-year-old man who underwent heart transplantation in 2000 due to ischemic cardiomyopathy. He admitted in a moderate severity condition. Within 4 days before hospitalization there was a cough, fever up to 38,6° C, diarrhea, weakness and loss of appetite. Upon admission, SpO_2 was 99%. The clinical course worsened on the fifth day: there was a need for oxygen insufflation, single administration of tocilizumab, methylprednisolone. His condition improved and on the eighth day he was discharged. The authors noted that in heart recipients, the immune response to viruses and the transplant-vs-host interaction, against which the infection develops, should be divided. This requires more careful management in order to overcome the response to the virus and avoid cytokine release syndrome [4].

Ren ZL, et al. (2020) summarizes data on heart recipients in context of COVID-19 pandemic. The study included 87 patients, of which 57 had an unfavorable epidemiological history. All preventive and quarantine measures were performed. Four patients had signs of acute respiratory infection, of which 3 had negative PCR test (4^{th} — unknown). According to retrospective assessment of clinical and laboratory data, 21% of patients had lymphopenia. Five patients had an episode of hepatic failure, 6 — renal failure. The authors concluded that in context of COVID-19 pandemic, patients with a transplanted heart, being at high risk, take adequate precautions and do not characterized by an increased danger [5].

In our example, the patient had an increased risk of thrombosis and embolism. For the pathogenesis of SARS-CoV-2 infection, blood coagulation characteristics have been shown [6], but they have yet to be studied. According to study by Panigada M, et al. (2020), a severe inflammatory response triggers changes in blood coagulation, which can be explained by disseminated intravascular coagulation syndrome. However, the authors did not show an increase in the number of platelets. There was an increase in levels of fibrinogen, D-dimer, factors VIII and von Willebrand, which does not characteristic of it, but can partially explain the risk of thromboembolism [7].

The coagulation system is influenced by other regulatory systems, including the sympathetic nervous system, and in case of cardiac disease and heart failure, this effect is enhanced [8]. It should be noted that patients after transplantation of organs, in particular, the heart, have features of the immune system and the related mechanisms of inflammation, and, accordingly, hemostasis. The possible direct effect of SARS-CoV-2 on the coagulation system is not excluded. The widespread use of anticoagulants is effective in patients hospitalized with COVID-19 infection. However, It should be taken into account that only vitamin K antagonists are non-selective anticoagulants that can affect many components of hemostasis. They require control of dose and drug interactions [9, 10]. The risk of thrombotic events is by no means the only one in patients with transplanted organ and COVID-19, but one of the most important.

Conclusion

The spread of a novel infection requires a review of all current recommendations. Perhaps a new situation will entail a revision of the risk factor model and biosocial relationships of the disease development [11]. With the accumulation of data on COVID-19 pathogenesis, the features of managing patients with a different underlying disease will become clear. It is important to remember that humanity is not safe from new pandemics. In parallel with the study of a novel COVID-19 infection as such, it is necessary to develop ideas about working in suspense.

Relationships and Activities: none.

References

1. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in Solid Organ Transplant Recipients: Initial Report from the US Epicenter. Am J Transplant. 2020. doi:10.1111/ajt.15941.
2. DeFilippis EM, Farr MA, Givertz MM. Challenges in Heart Transplantation in the Era of COVID-19. Circulation. 2020. doi:10.1161/circulationaha.120.047096.
3. Li F, Cai J, Dong N. First cases of COVID-19 in heart transplantation from China. J Heart Lung Transplant. 2020;39(5):496-7. doi:10.1016/j.healun.2020.03.006.
4. Holzhauser L, Lourenco L, Sarswat N, et al. Early Experience of COVID-19 in Two Heart Transplant Recipients: Case Reports and Review of Treatment Options. Am J Transplant. 2020. doi:10.1111/ajt.15982.
5. Ren ZL, Hu R, Wang ZW, et al. Epidemiologic and clinical characteristics of heart transplant recipients during the 2019 coronavirus outbreak in Wuhan, China: A descriptive survey report. J Heart Lung Transplant. 2020;39(5):412-7. doi:10.1016/j.healun.2020.03.008.
6. Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past. J Clin Virol. 2020;127:104362. doi:10.1016/j.jcv.2020.104362.
7. Panigada M, Bottino N, Tagliabue P, et al. Hypercoagulability of COVID-19 patients in Intensive Care Unit. A Report of Thromboelastography Findings and other Parameters of Hemostasis. J Thromb Haemost. 2020. doi:10.1111/jth.14850.
8. Buy MZ, Lebedeva AY, Gordeev IG, et al. Heart rate variability and hemostatic parameters in patients with coronary heart disease and chronic heart failure. Russ J Cardiol. 2013;(5):6-11. (In Russ.) doi:10.15829/1560-4071-2013-5-6-11.
9. Canonico ME, Siciliano R, Scudiero F, et al. The tug-of-war between coagulopathy and anticoagulant agents in patients with COVID-19. Eur Heart J Cardiovasc Pharmacother. 2020. doi:10.1093/ehjcvp/pvaa048.
10. Bokarev I, Lusov V, Kirienko A, et al. Venous Thrombosis and Pulmonary Thromboembolism. Russ J Cardiol. 2011;(4):5-12. (In Russ.)
11. Taratukhin EO. Risk factros hierarchy. Russ J Cardiol. 2017;22(9):28-33. (In Russ.) doi:10.15829/1560-4071-2017-9-28-33.