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The Relationship between the Degree of Lung Damage and Indicators of the Hemostasis System in Patients with Cardiovascular Diseases against the Background of COVID-19

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Abstract: In a specialized hospital for the treatment of 63 patients with coronavirus disease, moderate and severe COVID-19 were monitored. These patients were diagnosed with coronary heart disease or arterial hypertension prior to COVID-19. According to computed tomography data, it was found that adherence to hypercoagulation and the severity of the clinical course of coronavirus disease in this category of patients does not depend on the proportion of lung tissue damage. Senile age and an increase in body mass index> 30 kg / m2 were found to be significant factors aggravating the processes of hypercoagulation.

Key words: hemostasis, COVID-19, cardiovascular disease, pneumonia.

Introduction

The problem of cardiac comorbidity in COVID-19 has several aspects: the relationship of concomitant cardiovascular diseases (CVD) with a new viral infection, the severity of its course and the risk of mortality [1].

Infection with SARS-CoV-2 in most patients is mild with flu-like symptoms. At the same time, in many elderly people, especially if they have serious comorbidities, COVID-19 proceeds with severe pneumonia, which can then be complicated by acute respiratory distress syndrome and lead to death [2].

The high activity of plasmin, which is observed in diabetes mellitus, arterial hypertension (AH), coronary heart disease (IHD) and some other cardiovascular diseases, increases the virulence and contagiousness of the SARS-CoV-2 virus through the cleavage of its spike proteins [3]. In

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addition, with COVID-19, changes in hemostasis promote hyperactivation of the sympathetic nervous system, a "vicious circle" is created, and both processes aggravate each other. As a result, the thrombotic process increases and the risk of cardiovascular complications (CVC) increases [4].

Damage to the cardiovascular system is common in COVID-19 [5-7] and its damage is largely determined by the amount of viral inoculum, the size of the immune response, and the presence of concomitant diseases. Myocardial injury occurs in about a quarter of hospitalized patients and is associated with a greater need for mechanical ventilation and higher hospital mortality [8]. However, in the majority of patients with COVID-19, myocardial damage is asymptomatic and cardiovascular diseases are not always diagnosed in a timely manner [9].

Undoubtedly, the severity of the course of coronavirus infection depends on the degree of damage to the lung tissue, at which inhibition of fibrinolysis processes occurs. In addition, with concomitant CVD, such as arterial hypertension (AH), a significant part of the complications is thrombogenic conditions caused by dysregulation of the hemostatic system and endothelial dysfunction [9,10,11]. It is this biological multicomponent system, including the interaction of the vascular wall with blood cells, coagulation and fibrinolytic systems, as well as, in many cases, with insulin resistance, which is responsible for the occurrence of vascular catastrophes [12, 13].

Materials and methods

A prospective study was carried out, which included 63 patients with coronavirus infection aged 49–75 years. Before hospitalization, all patients were registered on an outpatient basis with a diagnosis of coronary artery disease (ESC, 2013) and / or hypertension (ESC, 2018).

The criteria for inclusion in the study were: 1) the presence of stable angina and / or hypertension; 2) COVID-19 associated pneumonia proven by computed tomography (CT); 3) a positive test for COVID-19 based on the polymerase chain reaction (PCR) method in the prehospital stage. Written informed consent was obtained from all participants prior to enrollment. Exclusion criteria: 1) symptomatic (secondary) hypertension; 2) diabetes mellitus; 3) oncological diseases.

The patients underwent clinical examination in a specialized hospital for the treatment of patients with coronavirus infection. In addition to assessing complaints and anamnestic data and

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objective examination, all patients were examined in accordance with the diagnostic capabilities in a pandemic and mass admission: 3-fold daily blood pressure measurement, assessment of blood oxygen saturation (SpO2), calculation of body mass index. In addition to conventional laboratory diagnostic methods on the day of hospitalization, the following hemostasis indicators were studied: PTI (prothrombin index), APTT (activated partial thromboplastin time), international normalized ratio (INR), fibrinogen (FG), prothrombin time (PTT), platelet count (PLT). Depending on the percentage of lung tissue damage, CT data were assessed as:

- CT-1 - less than 25% of the lung volume is affected;
- CT-2 - 25-50% of the lung volume is affected;
- CT-3 —50–75% of the lung volume;
- CT-4 - more than 75% of the lung volume is affected.

Based on CT data, the patients were divided into 3 groups: group 1 - patients with CT-1 and CT-2; group 2 - patients with CT-3 and group 3 - patients with CT-4.

The analysis of the duration of stay of patients in a hospital was carried out. The indications for discharge from the hospital were (within the last three days):

-satisfactory condition of the patient, temperature without antipyretics $<37^0$ C;

- no signs of respiratory failure (shortness of breath, cyanosis, etc.);

-SpO2> 94% (spontaneous breathing).

Statistical analysis. Data calculations were carried out using the IBM SPSS Statistics v. 22 (IBM, USA). The results were considered significant at $p < 0.05$. Normally distributed data are presented as $M \pm \sigma$, where M is the arithmetic mean and σ is the root-mean-square (standard) deviation. The degree of correlation of the parameters was determined using the Pearson correlation coefficient (r) in the case of a normal distribution.

Results

The clinical characteristics of the examined patients are presented in Table 1. The groups of patients differed in the percentage of lung tissue damage. The average age of patients in all three groups was> 55 years. The groups of patients did not differ in age, although there was a tendency towards its higher average level in the group of patients with more pronounced damage to the lung tissue (CT-4). Group 1 was dominated by male patients, in the other two groups - female. Most patients suffered from coronary artery disease, exertional angina pectoris II and III

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FC, and the proportion of patients suffering from angina pectoris increased with an increase in the severity of lung damage from 55.1% in group 1 to 68.7% in group 3. In the group of patients with CT-4, there were 100% of hypertensive patients. Anti-ischemic (antianginal) and antihypertensive drug therapy, which was carried out to patients during their hospitalization: 82.4% of patients took acetylsalicylic acid, 18.1% clopidogrel. Angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists were prescribed in 64.7% of patients. B-blockers (82.4%) played a significant role in therapy.

Table 1

Comparative characteristics of groups of patients with different degrees of lung damage according to CT data

Criteria	Group 1 (CT 1-2) N=29	Group 2 (CT-3) N = 18	Group 3 (CT-4) N = 16
Age	59±5,3	57±9,5	64±7,2
Male, n (%)	19 (65,5%)	6 (33,4%)	7 (33,8%)
Female, n (%)	10 (35,5%)	12 (66,6%)	9 (56,2%)
Coronary heart disease, exertional angina, n (%)	16 (55,1%)	10 (55,5%)	11 (68,7%)
AG, n (%)	23 (79,3%)	14 (77,7%)	16 (100%)

Comparison of groups of patients with different degrees of lung tissue damage (Table 2) showed that the amount of PLT significantly differed only in groups 1 and 3 ($p < 0.01$), although this indicator in all groups was within the reference interval. Fibrinogen levels in all groups were increased and significantly differed in patients from groups 1 and 3 ($p < 0.05$).

Table 2

Comparative characteristics of hemostasis indicators in groups of patients with different degrees of lung damage according to CT data

Indicators	Group 1 (CT 1-2) N = 29	Group 2 (CT-3) N = 18	Group 3 (CT-4) N = 16
PLT, x10^9 kl/l	259,17±51,38	236,41±67,52	176,24±41,38*
Fibrinogen, mg/dl	302, 33±85,91	323,76±65,73	325,42±73,14*

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APTT, sec	20,7±4,1	21,7±2,2	19,3±5,6
PTV, sec	17,7±6,1	18,2±10,4	15,4±7,5
PTI,%	84,5±25,1	81,9±35,8	94,3±21,1

Note: * $p < 0.05$, differences between groups 1 and 3

Correlation analysis revealed the following patterns. Correlated with the severity of lung damage: the level of fibrinogen ($r = 0.234$; $p < 0.05$), PLT ($r = -0.171$; $p < 0.05$) and the age of patients ($r = 0.246$; $p < 0.05$). The fibrinogen level and age of the patients had a weak straight line, PLT - a weak negative relationship. Despite the fact that the PLT indicator was weakly associated with the degree of lung damage and a low level of reliability, this parameter correlated more strongly with the BMI level ($\rho = -0.346$; $p < 0.05$).

A shortened APTT is generally considered a sign of hypercoagulability. In 85% of patients, a shortening of this indicator was noted, within 17-20 s, with a norm of 21-35 s. But there was no significant correlation between the volume of lung injury and the shortening of APTT. A more detailed analysis revealed a shortening of APTT in all patients with a BMI> 30 kg / m2, regardless of the extent of lung tissue damage. The increase in PTI and the shortening of PTT, which was observed in 94% of patients, were probably associated with hyperfibrinemia. The volume of lung damage correlated weakly with an increase in PTI in patients of group 3 (CT-4), a large positive relationship was observed in patients over 65 years of age.

It should be noted a longer improvement in the clinical course of the disease, including subjective and objective assessment of the state (NPV, heart rate, SpO2, blood pressure, etc.), in patients of group 2 with adherence to hypercoagulation.

Conclusion

Patients with cardiovascular diseases with COVID-19 are adherent to hypercoagulability regardless of the extent of lung tissue damage. One should not be guided only by the CT picture of lung damage to assess the outcome of the disease in this category of patients. An additional risk factor for blood clots in COVID-19 is the age of the patients and the BMI. In elderly people and with a BMI> 30 kg / m2, hypercoagulation is noted, which may be the cause of frequent cardiovascular accidents in this particular category of people, regardless of the volume of lung tissue damage.

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