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ANALYSIS OF CLINICAL AND LABORATORY INDICATORS OF MYOCARDITIS AND MYOPERICARDITIS IN PATIENTS WITH COVID-19.

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Abstract

In December 2019, a new respiratory infection caused by a previously unidentified strain of coronavirus, named SARS-CoV-2, was identified in China. This virus belongs to the Coronaviridae family, Nidovirales, and is characterized by a pleomorphic structure with crown-like spikes on its surface, which is why it was named "coronavirus". The size of the viral particles varies from 80 to 160 nanometers, and the genome length, expressed as positive-sense RNA, ranges from 27 to 32 kilobases. The emergence of SARS-CoV-2 led to a global pandemic, named COVID-19.

Keywords: coronavirus disease 2019, severe acute respiratory syndrome virus, erythrocyte sedimentation rate, C-reactive protein, aspartate aminotransferase.

Relevance of the topic: The spread of the COVID-19 pandemic has led to significant changes in the global healthcare system, exacerbating existing problems and revealing new ones. One of the most dangerous consequences of the infection has been the development of cardiovascular complications such as myocarditis and myopericarditis. This is an important direction for studying the mechanisms of the development of myocarditis and myopericarditis caused by COVID-19. It should be noted that the symptoms characteristic of COVID-19 and its predecessor beta-viruses are similar. These common symptoms include fever, body aches, fatigue, dry cough, shortness of breath, and the presence of bilateral opacities on multispiral computed tomography of the chest. Additionally, chest X-rays obtained after admission showed that some patients had opacities in the upper lung fields, which was associated with progressive dyspnea associated with hypoxemia.

Objective: To determine the clinical and laboratory characteristics of myocarditis and myopericarditis in patients with COVID-19, including biochemical markers and instrumental research data;

Research object: This study included 100 patients with myocarditis and myopericarditis due to COVID-19, as well as 50 patients without cardiac complications, who had COVID-19, as part

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of a prospective observational study conducted at the Samarkand branch of the Republican Specialized Scientific and Practical Medical Center during 2022–2024, a total of 150 patients.

Research object: The results of instrumental examinations to assess clinical parameters, including ECG, EchoCG, as well as peripheral blood samples for general and biochemical analyzes, were analyzed.

Study materials and methods. A comparison of demographic characteristics of patients with myocarditis and myopericarditis caused by COVID-19 is shown in Table 1. According to the results of the study, the age of the participants in the two groups was similar. Thus, the mean age in the main group was 45.8±10.5 years, while in the control group it was 46.2±11.0 years, and there was no statistically significant difference (p=0.78).

Table 1

Comparison of demographic characteristics of patients in study groups

Indicators	Base group n=100	Control group n=50	R-value
Age (years)	45.8±10.5	46.2±11.0	0.78
Males (n, %)	65 (65%)	32 (64%)	0.89
Females (n, %)	35 (35%)	18 (36%)	0.89
Weight (kg)	83.2±15.3	71.5±14.0	0.001
BMI (kg/m²)	28.5±4.2	24.8±3.5	0.001
Smoking (n, %)	40 (40%)	10 (20%)	0.005
Alcohol (n, %)	20 (20%)	8 (16%)	0.56
***Note**: Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of less than 0.05*			

We also found that there were no significant differences between the groups in terms of gender distribution in both groups, and this factor did not affect the results of the study. In particular, the main group consisted of 65 men (65%) and 35 women (35%), while the control group consisted of 32 men (64%) and 18 women (36%), which was not statistically significant (p=0.89). Thus, as a result of the study, we identified significant differences between the main and control groups in terms of indicators such as weight, TVI, and smoking habits. At the same time, no statistically significant differences were identified in terms of age, gender distribution, and alcohol consumption. These data emphasize the need to take demographic characteristics into account when interpreting the results of the study.

Figure 1 shows the distribution of patients in the main group by type of complications associated with COVID-19. According to the results of the study, in the main group, 56 (56%) patients had complications such as myocarditis, 27 (27%) patients had pericarditis, and 17 (17%) patients had both myocarditis and pericarditis. No such complications were observed in the

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control group (0%). Thus, the main group consisted of patients with cardiac complications associated with COVID-19, in particular, myocarditis, pericarditis, and their co-occurrence.

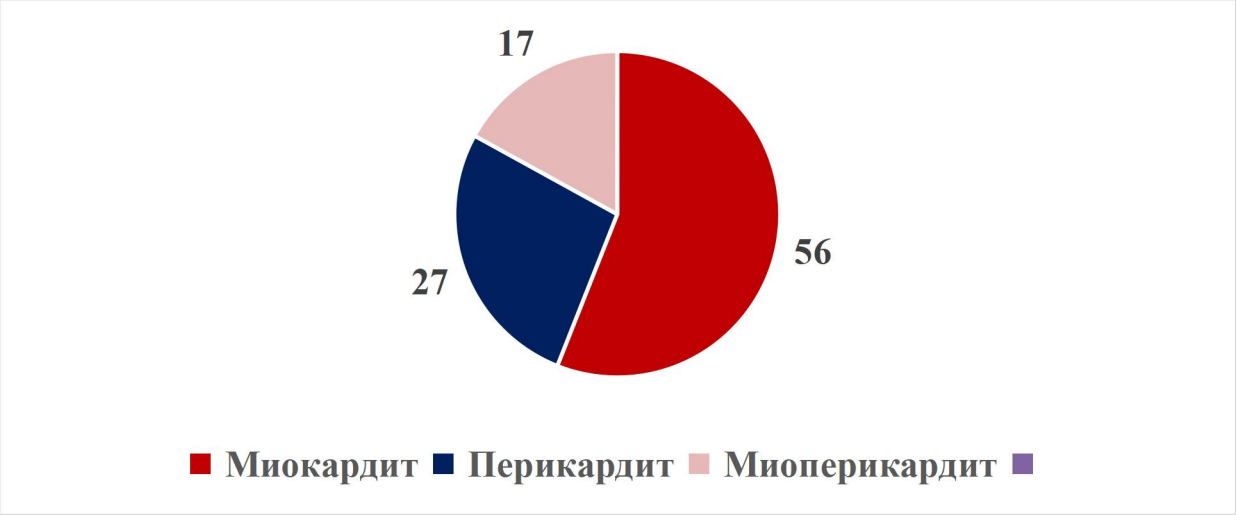

Figure 1. Distribution of patients by frequency of COVID-19 complications

Table 2

Comparative analysis of laboratory indicators of patients in research groups

Indicators	Base group n=100	Control group n=50	R-value
Leukocyte (×10^9/l)	9.7±2.5	6.1±1.5	<0.001
Erythrocyte (×10^12/l)	4.6±0.4	4.8±0.4	0.01
Hemoglobin (g/l)	115.7±12.1	131.2±11.4	<0.001
Platelet (×10^9/l)	202.5±64.9	254.2±51.5	<0.001
Lymphocyte (×10^9/l)	1.2±0.7	2.4±0.4	<0.001
ESR (mm/h)	37.2±12.7	11.4±5.4	<0.001
Note: *Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of p<0.05.*			

The level of lymphocytes was also confirmed to be 1.2±0.7 ×10⁹/l in the main group, which was significantly lower than 2.4±0.4 ×10⁹/l in the control group (p<0.001). In addition, the erythrocyte sedimentation rate (ESR) in the main group was 37.2±12.7 mm/h, which was significantly higher than 11.4±5.4 mm/h in the control group (p<0.001). In conclusion, the results of the study revealed significant differences in laboratory parameters between the main

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and control groups, which once again confirms the importance of these parameters in the diagnosis and monitoring of COVID-19.

The results of the comparison of laboratory parameters between the study groups are presented in Table 3. According to the results, the glucose level in the main group was 6.2±1.2 mmol/l, which was significantly higher than the 4.9±0.8 mmol/l in the control group ($p<0.001$). It was also found that the total protein level in the main group was 68.4±4.1 g/l, which was significantly lower than the 75.8±3.8 g/l in the control group ($p<0.001$). In addition, the results of the study showed that the albumin level in the main group was 34.5±3.7 g/l, which was significantly lower than the 42.1±2.9 g/l in the control group ($p<0.001$). It was also found that the total bilirubin level in the main group was 14.8±5.7 µmol/l, which was significantly higher than the control group's 11.6±3.1 µmol/l ($p<0.001$). The direct bilirubin level was also higher in the main group, which was 5.3±2.1 µmol/l, compared to 3.2±1.2 µmol/l in the control group ($p<0.001$).

Table 3

Comparative examination of laboratory personnel of patients in the study groups

Indicators	Base group n=100	Control group n=50	R-value
Glucose (mmol/l)	6.2±1.2	4.9±0.8	<0.001
Total protein (g/l)	68.4±4.1	75.8±3.8	<0.001
Albumin (g/l)	34.5±3.7	42.1±2.9	<0.001
Total bilirubin (µmol/l)	14.8±5.7	11.6±3.1	<0.001
Bilirubin (µmol/L)	5.3±2.1	3.2±1.2	<0.001
ALT (Ed/L)	45.8±15.2	27.7±8.9	<0.001
AST (Ed/l)	42.3±12.7	24.9±7.4	<0.001
Urea (mmol/l)	6.8±1.6	4.8±1.2	<0.001
Creatinine (µmol/L)	96.2±18.4	78.3±12.4	<0.001
Ferritin (ng/ml)	483.6±152.7	102.8±31.6	<0.001
SRO (mg/l)	22.4±11.3	4.7±1.8	<0.001

Note: *Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of $p<0.05$.*

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Thus, the results of the study revealed significant differences in laboratory parameters between the main and control groups, which is of great importance in the diagnosis and monitoring of COVID-19.

Table 4 presents a comparative analysis of the levels of cardiac biomarkers between the study groups. According to the results, the level of troponin in the main group was 35.6±8.3 ng/l, which was significantly higher compared to 5.8±1.8 ng/l in the control group ($p<0.001$). Also, the level of D-dimer in the main group was 895.9±378.2 ng/ml, which was also significantly higher compared to 285.4±68.5 ng/ml in the control group ($p<0.001$). In addition, the level of creatine kinase-MB (CK-MB) in the main group was 108.2±33.7 U/L, which was significantly higher than 22.4±8.8 U/L in the control group ($p<0.001$). The level of myoglobin in the main group was 72.6±21.0 ng/mL, while in the control group this indicator was 28.2±8.4 ng/mL, which was significantly higher ($p<0.001$).

4- table

Comparative analysis of laboratory indicators of patients in research groups

Indicators	Base group n=100	Control group n=50	R-value
Troponin (ng/L)	35.6±8.3	5.8±1.8	<0.001
D-dimer (ng/ml)	895.9±378.2	285.4±68.5	<0.001
Creatine kinase-MB (Ed/l)	108.2±33.7	22.4±8.8	<0.001
Myoglobin (ng/ml)	72.6±21.0	28.2±8.4	<0.001
Note: *Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of $p<0.05$.*			

D-dimer levels were significantly higher in the main group, indicating activation of the coagulation cascade and the presence of thrombotic complications in patients with COVID-19. The electrocardiographic parameters of patients in the study groups are compared in Table 5.

Table 5

Electrocardiographic examination of patients in the study groups

Indicators	Base group n=100	Control group n=50	R-value
ChSS (speed/min)	87.2±15.8	72.1±10.3	<0.001
PR-interval (ms)	180±19.3	158.3±15.7	<0.001
QRS (ms)	103.0±12.7	97.2±11.2	0.02

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QTc interval (ms)	454.7±28.6	407.3±19.4	<0.001
ST elevation (mm)	2.5±1.0	0.5±0.2	<0.001
ST depression (mm)	1.5±0.5	0.2±0.1	<0.001
T wave amplitude (mV)	0.3±0.1	0.5±0.1	<0.001
Pathological Q teeth (n, %)	27 (27%)	3 (6%)	<0.001
GTChOB (n, %)	12 (12%)	1 (2%)	0.04
GTO'OB (n, %)	8 (8%)	1 (2%)	0.10
QRS voltage (mV)	1.0±0.3	1.2±0.4	0.03
Ventricular extrasystoles (n, %)	20 (20%)	3 (6%)	0.02
Extrasystoles of compartments (n, %)	15 (15%)	2 (4%)	0.03
Arrhythmias	25 (25%)	4 (8%)	0.01
Note: *Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of p<0.05.*			

According to the results, the heart rate (HR) in the main group was 87.2±15.8 beats/min, which was significantly higher than 72.1±10.3 beats/min in the control group (p<0.001). Also, the PR interval in the main group was 180±19.3 ms, which was significantly longer than 158.3±15.7 ms in the control group (p<0.001). In addition, the QRS complex duration was 103.0±12.7 ms in the main group, and 97.2±11.2 ms in the control group, which was also significantly higher (p=0.02). The QTc interval in the main group was 454.7±28.6 ms, which was significantly longer than the 407.3±19.4 ms in the control group (p<0.001). The ST segment elevation in the main group was 2.5±1.0 mm, while in the control group this indicator was 0.5±0.2 mm, which was significantly higher (p<0.001). At the same time, the ST segment depression was 1.5±0.5 mm in the main group, while in the control group it was 0.2±0.1 mm, and this difference was also statistically significant (p<0.001). The T wave amplitude was 0.3±0.1 mV in the main group, while in the control group it was 0.5±0.1 mV, and it was significantly lower in the main group (p<0.001). In the main group, the presence of pathological Q waves was noted in 27% of patients, while in the control group this figure was 6% and was significantly higher (p<0.001).

In the next phase of our study, echocardiographic parameters of the heart were analyzed in patients who developed myopericarditis or myocarditis as a result of COVID-19. Left ventricular ejection fraction (LVEF) was significantly reduced in patients with myocarditis after COVID-19, averaging 54.3±6.1% compared to 68.1±8.7% in the control group (p < 0.001). In addition, 31% of patients had LVEF <50%, indicating moderate to severe systolic dysfunction; this was observed in only 2% of the control group (p < 0.001). These results indicate that persistent myocardial inflammation and fibrosis processes after COVID-19 infection may lead to a decrease in cardiac contractile function (Table 3.8).

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Table 6

Comparative analysis of echocardiography results in study groups

Indicators	Base group n=100	Control group n=50	R-value
LVEF (%)	54.3±6.1	68.1±8.7	p<0.001
LVEF <50%, n (%)	31 (31.0%)	1(2.0%)	p<0.001
LVEDV, мл	134.3 ±31.6	119.8±34.5	p<0.001
LVESV, мл	56.2±12.3	44.1±12.2	p<0.001
LAVI, мл/м2	41.4±6.8	32.1±5.3	p<0.001
LAVI >34 мл/м2, n (%)	28(28.0%)	3(6.0%)	p<0.001
Left ventricular hypertrophy, n (%)	78(78.0%)	5(10.0%)	p<0.001

Note: *Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of p<0.05.*

Echocardiographic analyses also revealed significant changes in the structure of the left ventricle. In patients with myocarditis due to COVID-19, the left ventricular end-diastolic volume (LVEDV) was 134.3±31.6 ml, compared to 119.8±34.5 ml in the control group (p<0.001). The left ventricular end-systolic volume (LVESV) also increased significantly, reaching 56.2±12.3 ml, compared to 44.1±12.2 ml in the control group (p<0.001). Increased left ventricular end-systolic and end-diastolic volumes indicate that patients have heart failure with left ventricular dilatation and reduced left ventricular ejection fraction. In addition, echocardiographic analyses showed that left ventricular hypertrophy (LVH) was highly prevalent in patients with myopericarditis due to COVID-19. LVH was detected in 78% of patients, compared with only 10% in the control group (p<0.001). LVH may be the result of adaptive remodeling in response to prolonged cardiac workload, increased myocardial pressure, and COVID-19-associated inflammation and fibrosis. The high incidence of hypertrophy indicates a long-term negative impact on the cardiovascular system in patients. Echocardiographic analyses showed significant changes in the structure and function of the right ventricle (Table 3.7). Right ventricular dysfunction was detected in 29% of patients with myopericarditis as a result of COVID-19, compared to only 4% in the control group (p<0.001). Right ventricular dilatation was also observed in 45.1% of patients (p < 0.001). The high incidence of RV dysfunction and dilatation is associated with increased afterload on the right side of the heart and the development of inflammatory processes associated with COVID-19.

Table 7

Comparative analysis of echocardiography results in study groups

Indicators	Base group n=100	Control group	R-value

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		n=50	
Axis dysfunction, n (%)	29(29.0%)	2(4.0%)	p<0.001
Arrow dilatation, n (%)	46(45.1%)	5(10.0%)	p<0.001
Otnoshenie E/A	0.7±0.41	0.9±0.36	p<0.001
Septal e', cm/s	6.1±1.8	7.2±1.6	p<0.001
Lateral e', cm/s	8.2±1.6	9.8±1.4	p<0.001
TAPSE, mm	18.3 ±2.6	22.1±2.1	p<0.001
Septal-lateral otnoshenie E/e	9.3±4.7	8.6±4.3	p<0.001
Note: *Fisher and Mann-Whitney-Wilcoxon tests were used to compare groups with a significance level of p<0.05.*			

In addition, echocardiographic analyses showed that diastolic dysfunction and increased cardiac pressure were significantly more pronounced in patients with myopericarditis as a result of COVID-19. In particular, the E/A ratio was observed to decrease to 0.7 ± 0.41 in the myopericarditis group ($p<0.001$). In addition, the septal e' (6.6 ± 1.8 cm/s) and lateral e' (9.4 ± 3.6 cm/s) indicators were significantly reduced compared to the control group ($p < 0.001$). The septal-lateral E/e' ratio was 9.3 ± 4.7 in the myopericarditis group, indicating increased left atrial pressure. In addition, echocardiographic analyses also showed a decrease in right ventricular systolic function. TAPSE in the main group was 18.3 ± 2.6 mm and was significantly lower than that observed in the control group (22.1 ± 2.1 mm) ($p < 0.001$). The decrease in TAPSE indicates right ventricular systolic dysfunction and decreased blood flow.

CONCLUSION. Thus, according to the results of the study, myocarditis and myopericarditis associated with COVID-19 in the main and control groups were characterized by different clinical manifestations, including tachycardia, shortness of breath and chest pain, as well as elevated biochemical markers of inflammation and myocardial damage (e.g., troponin, C-reactive protein, creatine kinase). Instrumental studies such as ECG and echocardiography can detect changes characteristic of these conditions. This indicates the importance of these parameters in the diagnosis and monitoring of COVID-19.

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