

COVID-19-induced cardiovascular complexities

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ABSTRACT: This study aimed to investigate the features of the clinical course of COVID-19 in combination with the pathology of the cardiovascular system (CVS). A prospective study was carried out. The main group (n=150) consisted of patients with changes in the cardiovascular system associated with COVID-19, i.e. newly diagnosed CV pathology, and patients with exacerbation of cardiac pathology against the background of COVID-19. The comparison group (n=154) included patients with COVID-19, but without any significant concomitant cardiac pathology. The average age of patients in the main group was 67.7 years (from 47 to 86 years), in the comparison group of 66.1 years (from 48 to 88 years). The study groups were representative and did not differ statistically in the nature of COVID-19 symptoms and the degree of lung involvement. Among the cardiac pathology, progressing or first occurring against the background of infection with COVID-19, in most cases, arterial hypertension of II-III degree (60.0%), coronary heart disease (48.7%), arrhythmias (23.3%) were diagnosed. Echocardiographic abnormalities included right ventricular dysfunction (22.7%), left ventricular contractility disorders (18.7%), with decreased ejection fraction (17.3%), diastolic dysfunction (14.0%), and toxic myocarditis (7.3%). The most significant risk factors were the presence of a burdened medical history (RR=10.39), elevated body mass index over 30 (RR=2.63) and diabetes mellitus (RR=1.55). In patients with COVID-19 in combination with CVS pathology, a relatively high incidence of acute onset (64.0% vs. 44.2%; $p<0.001$), respiratory failure (83.7% vs. 62.0%; $p<0.001$), admission to the intensive care unit (25.3% vs. 11.7%; $p=0.004$), development of acute respiratory distress syndrome (20.0% vs. 9.1%; $p=0.012$), hospital mortality (10.7% vs. 2.7%; $p=0.006$). Cardiac manifestations of COVID-19 included focal or global myocardial inflammation, ventricular dysfunction, heart failure, and arrhythmias. A high frequency of acute onset of the disease, respiratory failure and hospital mortality is determined.

KEYWORDS: COVID-19, SARS-CoV-2, cardiovascular system, clinical course, comparative analysis

INTRODUCTION

According to the World Health Organization, "the prevalence of cardiovascular disease (CVD) has doubled over the past 30 years from 271 million to 523 million cases, and the number of deaths from CVD has reached 18.6 million (17.1-19.7 million)" [1-3].

It is known that "COVID-19 poses a particular danger in terms of decompensation of existing chronic diseases and specific damage to the cardiovascular system (CVS), especially in the case of severe COVID-19 and a high risk of adverse outcomes" [5, 6]. As a rule, the combination of COVID-19 with cardiovascular pathology leads to additional difficulties in diagnosing, choosing management tactics, and treating patients in emergencies [7, 8].

Due to the lack of clinical data on this issue, it is extremely important to address a number of problems that arise in the management of patients with CVD and COVID-19.

The purpose of the study: to study the features of the clinical course of COVID-19 in combination with CVS pathology.

MATERIAL AND METHODS

The study included patients with predominantly initial moderate course of COVID-19. The main group (n=150) consisted of patients with changes in the cardiovascular system associated with COVID-19, i.e. newly diagnosed CVD pathology, and patients with CVD exacerbation due to COVID-19. The comparison group (n=154) included patients with COVID-19, but without any significant concomitant cardiac pathology. The average age of patients in the main group was 67.7 years (from 47 to 86 years), there were 48 men and 102 women. The average age of patients included in the comparison group was 66.1 years (from 48 to 88 years). There were 50 men and 104 women.

By the nature of the symptoms of the disease, the study groups were representative and did not differ statistically in the frequency of occurrence of one or another symptom of COVID-19. Typical manifestations of COVID-19 in patients of the study groups were fever, noted in 86.2% of cases, dry cough (65.4%), fatigue (43.1%), shortness of breath (24.3%), sore throat (15.5%), headache (13.2%), myalgia (13.8%), chills (12.5%), vomiting (7.2%), diarrhea (5.6%), hemoptysis (1.6%) and hyperemia of the conjunctiva (1.6%).

When distributing patients according to the volume of lung damage, it was noted that up to 25% of lung tissue damage was diagnosed in 20.8% of patients from the comparison group and in 22.7% from the main group; up to 50% - in 68.8% of patients from the comparison group and in 68.0% - from the main group; up to 75% - in 10.4% and in 9.3% - from the main group; cases with more than 75% lung involvement were not observed in both study groups.

The research materials were subjected to statistical processing using the methods of parametric and non-parametric analysis. Accumulation, correction, systematization of initial information and visualization of the obtained results were carried out in Microsoft Office Excel 2016 spreadsheets. Statistical analysis was carried out using the IBM SPSS Statistics V.26 program (developer - IBM Corporation). When comparing mean values in normally distributed sets of quantitative data, Student's t-test was calculated. Differences in indicators were considered statistically significant at a significance level of $p < 0.05$.

Ethical approval

The review board and ethics committee of Center for the Development of Professional Qualifications of Medical Workers approved the study protocol and informed consents were taken from all the participants.

RESULTS AND DISCUSSION

The study of the clinical characteristics of cardiovascular pathology in patients with COVID-19 (main group) made it possible to determine that in most cases they were diagnosed with stage 3 hypertension (AH) (88 or 58.7% of persons), arterial hypertension (AH) II-III degree (90 patients (60.0%)), risk degree 4 was exhibited with a significantly higher frequency 67.3% (101 patients) than risk 3 (32.7%) (49 persons), with an almost equal incidence of coronary heart disease (IHD) 2 and 3 degrees (48.7% or 73 patients) and 48.0% or 72 patients). Moreover, heart failure corresponding to NYHA stage 3 was detected more often 68.0% (102 patients) than NYHA 4 (32.0%) (48 patients).

Pathological conditions with cardiac arrhythmias were detected in 23.3% (35 out of 150) of cases. Among the arrhythmias, the most frequently detected were atrial fibrillation (AF) in 11.3% (17 out of 150; including new-onset AF) (Table 1).

Ventricular extrasystoles (PVC) were diagnosed in 5.3% (8 of 150), AV block in 2.0% (3 of 150) of cases, ventricular tachycardia (VT) was reported as a complication of COVID-19 in 7 (4.7%) of patients of the main group (Table 1).

Echocardiographic anomalies registered in patients of the main group included right ventricular (RV) dysfunction with overload (dilation) (22.7%; 34 of 150), impaired LV wall contractility (18.7%; 28 of 150), LV systolic dysfunction with decreased EF (17.3%; 26 of 150), diastolic dysfunction II (pseudonormal type) or III (restrictive) types (14.0%; 21 of 150), and pericardial effusion (toxic myocarditis) (7.3%; 11 out of 150).

Half of the patients of the main group (49.3%; 74 out of 150) could observe 1 pathological condition on the part of the cardiovascular system, a combination of 2 changes in the part of the cardiovascular system was detected in 32.0% (48 out of 150) of cases, patients with 3 pathologies of the cardiovascular system had 14.0% (21 out of 150), and with 4 CCC pathologies (4.6%; 7 out of 150). Decompensated heart failure was diagnosed in 10.7% (16 out of 150) of cases of COVID-19 associated cardiovascular syndrome.

Acute onset of COVID-19 pneumonia was observed more often in the main group than in the comparison group (64.0% or 96 out of 150) versus 44.2% (68 out of 154), respectively ($2=11.259$; $p<0.001$). The average duration of hospitalization after the onset of the disease in the study groups did not differ statistically ($p=0.537$) and amounted to 6.4 ± 0.8 (from 3 to 11) days in the comparison group, and 5.7 ± 0.7 (from 3 to 11) days in the main group (from 2 to 8) days.

Patients from the main group had a history of various kinds of chronic respiratory pathology more often ($p = 0.042$) than in the comparison group, the incidence of COPD was 16.0% (24 out of 150) and 7.8% (12 out of 154) in the main and comparison group, respectively (Table 3).

Also, other comorbid conditions were more typical for patients of the main group. Thus, chronic cerebrovascular insufficiency was diagnosed in 12.0% (18 out of 150) and 2.6% (4 out of 154) ($p = 0.004$) of cases, chronic kidney disease in 22.7% (34 out of 150) and 9.1% (14 out of 154) cases ($p=0.003$), diabetes mellitus in 18.0% (27 out of 150) and 5.2% (8 out of 154) cases and obesity with a body mass index (BMI) of more 30 was noted in 35.3% (53 out of 150) and 23.4% (36 out of 154) of cases in the main and comparison groups, respectively.

Table 1. Clinical characteristics of cardiovascular disease in patients with COVID-19

Clinical characteristics	Main group (n=150)	
	n	%
Average systolic arterial blood pressure, mm Hg Art.	134.8±12.6	
Average diastolic arterial blood pressure, mm Hg Art.	85.4±9.2	
Arterial hypertension Stage 1	60	40.0%
Arterial hypertension Stage 2	54	36.0%
Arterial hypertension Stage 3	36	24.0%
NYHA 3	102	68.0%
NYHA 4	48	32.0%
Risk 3	50	33.3%
Risk 4	100	66.7%
Arrhythmias	35	23.3%

Table 2. Comparative characteristics of comorbidities

Comorbidities	Comparison group (n=154)	Main group (n=150)	p
Obesity with a BMI over 30	36 (27.3%)	53 (35.3%)	<0.05
Diabetes	8 (5.2%)	27 (18.0%)	<0.001
Chronic obstructive pulmonary disease	12 (7.8%)	24 (16.0%)	<0.05
Chronic cerebrovascular insufficiency	4 (2.6%)	18 (12.0%)	<0.01
chronic kidney disease	14 (9.1%)	34 (22.7%)	<0.01
Creatinine. $\mu\text{mol/l}$	76.7 ± 1.6 (49–98)	82.4 ± 1.6 (54–102)	<0.01
Glomerular filtration rate. ml/min	94.5 ± 0.6 (85–102)	88.9 ± 1 (71–98)	<0.001
Chronic liver disease	9 (5.8%)	12 (8%)	>0.05
Alanine aminotransferase U/l	28.6 ± 2.6 (17–180)	34.5 ± 5.2 (14–243)	>0.05
Aspartate aminotransferase U/l	31.8 ± 2.4 (20–142)	39.6 ± 3.3 (10–174)	<0.05
Total cases with comorbidities	70 (45.5%)	88 (58.7%)	<0.05

When compared with the comparison group, patients of the main group had higher rates of liver and kidney damage upon admission. Although the results of the analysis of the state of liver function were practically similar in both groups, in patients of the main group, renal failure at admission was significantly higher. This was evidenced by higher creatinine levels ($82.4\pm 1.6 \mu\text{mol/l}$ versus $76.7\pm 1.6 \mu\text{mol/l}$) and lower estimated glomerular filtration rate (GFR) ($88.9\pm 1.0 \text{ ml/l}$) versus $94.5\pm 0.6 \text{ ml/min}$) in the main group than in the comparison group. Next, the relationship between risk factors and CCC lesions in patients with COVID-19 was assessed (Table 3). A statistically significant relationship in the development of heart damage can be traced with a burdened family history of CVD, overweight (BMI > 30) and diabetes mellitus.

Despite the comparability of the initial CT data of the lungs between the study groups, 7 days after hospitalization, a higher incidence of respiratory failure (RF) was determined in the main group. So, in total, 62.0% (93 out of 150) patients were without DN in the main group, and 83.7% (129 out of 154) in the comparison group ($p < 0.001$) (Figure 1).

Table 3. Correlation of risk factors for cardiovascular pathology in patients with COVID-19

	RR (95% CI)	p
Non modified		
Family history of CVD	1.95 (95% CI 1.6-2.4)	<0.001
Modified		
BMI over 30	1.3 (95% CI 1.0-1.7)	<0.05
Smoking	0.80 (95% CI 0.6-1.1)	>0.05
Diabetes	1.7 (95% CI 1.4-2,1)	<0.001

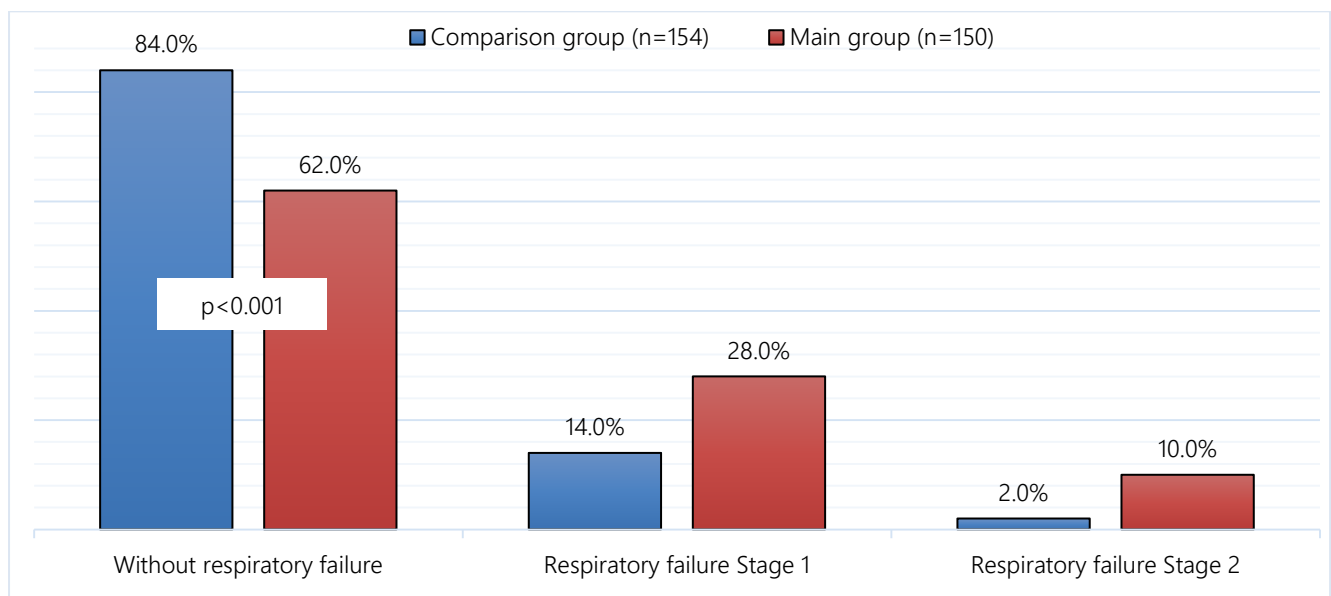


Figure 1. The severity of respiratory failure in the study groups (in %)

Table 4. Complications in study groups

Characteristics	Comparison group (n=154)	Main group (n=150)	p
Transferred to ICU	18 (11.7%)	38 (25.3%)	<0.01
ARDS	14 (9.1%)	30 (20%)	<0.01
Mortality	4 (2.7%)	16 (10.7%)	<0.01

ARDS: Acute respiratory distress syndrome

38 (25.3%) patients in the main group and 18 (11.7%) in the comparison group ($p = 0.004$) needed to continue treatment in the ICU, and the development of an extreme degree of respiratory failure - acute respiratory distress syndrome (ARDS) could be observed with a frequency of 20.0% (30 out of 150) in the main group and 9.1% (14 out of 154) in the comparison group ($p = 0.012$) (Table 4).

The hospital mortality rate was 10.7% (16 out of 150) in the main group and 2.7% (4 out of 154) in the comparison group ($p=0.006$). A number of foreign researchers have made a significant contribution to the study of the problem of the course of COVID-19 in patients with CVD, the results of which are expected to contribute to setting priorities in healthcare resources. So, according to Roth et al. [9] "Population-level studies of changes in CVD mortality provide the broadest view of the overall impact of COVID-19 on CVD. These analyze show a variety of results: from a decrease to a significant increase in CVD mortality during a pandemic" [9].

According to Vasudeva et al. [10], "Among CVDs registered in deaths associated with COVID-19 in all age groups, hypertension (AH) is the most common (19.6%), followed by diabetes mellitus (DM) (15.9%), coronary heart disease (CHD) (10.9%), heart failure (HF) (7.7%), cardiac arrhythmias (7.5%) and cerebrovascular diseases (5%)" [10].

According to the results of our study, it was determined that among cardiac pathology that progresses or first occurs against the background of infection with COVID-19, in most cases AH of II-III degree was diagnosed (60.0%), risk level 4 was set with a significantly higher frequency (67.3%) than the risk of 3 (32.7%), with almost equal incidence of coronary artery disease of the 2nd and 3rd degree (48.7% and 48.0%). Moreover, heart failure corresponding to NYHA stage 3 was detected more often (68.0%) than NYHA 4 (32.0%). Pathological conditions with cardiac arrhythmias were detected in 23.3% of cases. Echocardiographic abnormalities included RV dysfunction with overload (22.7%), LV wall contractility disorders (18.7%), LV systolic dysfunction with decreased ejection fraction (17.3%), diastolic dysfunction (14.0%), and pericardial effusion (toxic myocarditis) (7.3%).

The authors are developing various diagnostic methods, schemes for the treatment and prevention of cardiovascular complications, among which, an important aspect is to establish the significance of genetic polymorphisms for predicting the combined course of COVID-19 with CVD [11, 12]. Direct myocardial injury due to viral damage to cardiomyocytes and the effect of systemic inflammation appear to be the most common mechanisms responsible for heart injury [13].

So, Farshidfar et al. [14] report fulminant myocarditis against the background of COVID-19, which develops as a result of a hyperinflammatory state, cytokine storm, and direct infection of cardiomyocytes.

In studies by Han et al. [15] on the analysis of the main laboratory indicators of heart damage in patients with COVID-19, and their correlation with heart damage and disease severity, it was noted that "a higher concentration in venous blood of specific enzymes of myocardial damage was associated with the severity and lethality of COVID-19". Also, more frequent quantitative hematological abnormalities were previously reported in patients with severe COVID-19, detected by a general blood test (anemia, neutrophilia, neutrophilic shift to the left and lymphopenia) [16]. Various authors noted that the main reasons for poor results are various factors for the occurrence of complications of COVID-19 [6, 10, 14].

According to our data, the most significant risk factors for the development and progression of cardiovascular disease in COVID-19 are the presence of a burdened history of CVD (RR=10.39), elevated BMI over 30 (RR=2.63) and DM (RR=1, 55). At the same time, in half (49.3%) of cases, 1 pathological condition from the side of the cardiovascular system is noted, a combination of 2 changes was detected in 32.0% of cases, patients with 3 pathologies of the cardiovascular system were 14.0%, with 4 pathologies of the cardiovascular system - 4.6 %, and HF decompensation was diagnosed in 10.7% of cases of COVID-19 associated with cardiovascular syndrome.

When comparing the clinical characteristics in patients with COVID-19 in combination with CV pathology, in contrast to the isolated course of COVID-19, a comparatively high incidence of acute onset (64.0% vs. 44.2%; $p < 0.001$), respiratory failure (83.7% vs. 62.0%; $p < 0.001$), hospitalizations in the ICU (25.3% vs. 11.7%; $p = 0.004$), development of ARDS (20.0% vs. 9.1%; $p = 0.012$), hospital mortality (10.7% vs. 2.7%; $p = 0.006$).

The continuing incidence of coronavirus infection, the emergence of new strains and their rapidly changing variations, as well as the lack of knowledge of changes in homeostasis and the characteristics of the course of COVID-19 in situations combined with CV pathology require further study of COVID-19 and the formation of a comprehensive approach to the treatment and prevention of complications in patients with CVD.

CONCLUSION

Against the background of COVID-19, cardiac disorders (progressive or first-time) are manifested by grade II-III hypertension, coronary artery disease, heart failure, various cardiac arrhythmias, and pericardial effusion, which aggravate the course of the underlying disease and its outcome. The most significant risk factors for the development and progression of cardiovascular pathology in COVID-19 are the presence of a burdened history of CVD, elevated BMI over 30, and DM. At the same time, in half of the cases of COVID-19 associated with cardiovascular syndrome, there are two or more pathological conditions from the cardiovascular system. Also, it was found that in patients with COVID-19 in combination with CV pathology, in contrast to the isolated course of COVID-19, a high incidence of acute onset of the disease, respiratory failure, hospitalization in the ICU, development of ARDS and hospital mortality is determined.

DECLARATIONS

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Authors' contribution

All authors contributed equally to this work.

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Competing interests

The authors declare that they have no competing interests.

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