

Original article

Reprint

Features of echocardiography parameters in acute coronary syndrome in combination with post COVID-19 syndrome

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Abstract:

Objective: to evaluate echocardiographic changes in patients with acute coronary syndrome (ACS) combined with post COVID-19 syndrome (PCS).

Materials and methods. The study included 118 patients (61 men and 57 women) with ACS+PCS. All patients were subjected to the echocardiography (EchoCG) on the first day, in addition to coronary angiography and general clinical examination methods. The comparison group included 121 patients with ACS but without PCS.

Results. In the ACS+PCS group, the following parameters were statistically significantly more frequently recorded than in the ACS group: elevated blood pressure (risk ratio, RR 2.327; 95% confidence interval, CI 1.582–2.699), tachycardia (RR 2.067, 95% CI 1.415–3.730), dyspnea (RR 2.022, 95% CI 1.495–2.736), weakness (RR 4.077, 95% CI 2.946–5.643), and insomnia (RR 1.893, 95% CI 1.519–2.358); $p < 0.001$. According to EchoCG results, in the ACS+PCS group of patients, an increase in the mean pulmonary artery pressure, expansion of its diameter, and mitral valve regurgitation were noted ($p < 0.001$). Of the cardiac complications, the most common were left ventricular apical thrombus (RR 1.785, 95% CI 1.304–2.444), left ventricular aneurysms (RR 1.736, 95% CI 1.234–2.443), along with hypokinesia and akinesia (development of myocardial infarction) (RR 1.673, 95% CI 1.275–2.196; $p < 0.05$).

Conclusion. Patients who experienced ACS in combination with PCS exhibited more pronounced EchoCG changes vs. patients without PCS.

Keywords: acute coronary syndrome, new coronavirus infection (NCI), post COVID-19 period, echocardiographic changes, post COVID-19 syndrome

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Introduction

Cardiovascular diseases (CVD) hold their leading positions in terms of mortality and fatality rates both in the Russian Federation and worldwide [1]. However, the recent pandemic of the new coronavirus infection (NCI) has aggravated the course of CVD [2]. The number of arrhythmia cases (extrasystoles, atrial fibrillation), acute cardiovascular events (heart attacks, strokes), and decompensated heart failure has increased significantly. So did the progression of chronic diseases, along with the number of complaints of chest pain unexplained by any other reasons [3]. The World Health Organization (WHO) has identified post COVID-19 syndrome (PCS) as a separate nosology, according to which it represents signs and symptoms that developed during or after the NCI and continue after 12 weeks, which cannot be explained by any other reason [4]. According to the etiological structure of the fatal outcome after the NCI, cardiovascular catastrophic events predominated [5], such as acute coronary syndrome (ACS), which substantiates the relevance of conducting studies to assess the morphological structure of the heart and its condition both during the acute event and in dynamics. It is extremely important that the

studies are available and easily applicable in routine clinical practice.

Objective – to evaluate EchoCG changes in patients with ACS in combination with PCS.

Materials and methods

We conducted a prospective cohort study. A total of 118 patients were included in the main group (57 women and 61 men). The mean age was 57.5 ± 6.2 years for women and 53.7 ± 8.3 years in men. All patients were transported to the regional vascular center by an ambulance team.

All patients included in our study were diagnosed with ACS in accordance with the clinical guidelines, Acute Coronary Syndrome without ST Elevation of the Electrocardiogram [6] and Acute Coronary Syndrome with ST Elevation of the Electrocardiogram [7], approved by the Scientific and Practical Council of the Russian Federation Ministry of Healthcare.

An additional criterion for inclusion in the study was a history of NCI that met the criteria for the diagnosis of PCS specified in the clinical guidelines, Characteristics of the

Clinical Course of Long COVID Infection. Therapeutic and Rehabilitation Procedures [8]. In compliance with the amendments made to the International Classification of Diseases, 10th revision, ACS occurs in people after coronavirus infection with confirmed SARS-CoV-2 infection three months after the onset of COVID-19. In patients included in our study, the diagnosis of previous COVID-19 was established in accordance with the recommended laboratory diagnostic methods specified in the temporary clinical guidelines, Prevention, Diagnosis and Treatment of New Coronavirus Infection (COVID-19), version 18 (October 26, 2023), approved by the Scientific and Practical Council of the of the Russian Federation Ministry of Healthcare [9].

The comparison group included 121 patients (62 men and 59 women) with a diagnosis of ACS but without PCS (there was no indication in the anamnesis of the presence of a diagnosis of NCI confirmed by the polymerase chain reaction method or the detection of immunoglobulins of classes A, M, G to SARS-CoV-2 by the immunochemical method [8]). Both groups were comparable in terms of their gender and age composition.

All patients underwent EchoCG using a General Electric color ultrasound scanner (USA) according to the standard for examining patients with ACS. The study included one- and two-dimensional scanning using pulsed and continuous wave Doppler ultrasonography, as well as color-coded Doppler blood-flow mapping. When analyzing resting EchoCG, we assessed the end-diastolic dimension (EDD) of the left ventricle (LV), which was measured along the long axis at the level of the papillary muscle heads, end-diastolic volume (EDV) of the LV, end-diastolic volume index (EDVI) of the LV, end-systolic dimension (ESD) of the LV, end-systolic volume (ESV) of the LV, and end-systolic volume index (ESVI) of the LV. To calculate the global contractility of the LV and the ejection fraction (EF) of the LV, a quantitative assessment of two-dimensional echocardiograms was used, viz., the biplane method of disk summation (modified Simpson method), taking into account the LV EDV and LV ESV. The mean pulmonary artery pressure (mPAP) was calculated as the ratio of the flow acceleration duration in the right ventricular (RV) outflow tract to the ejection duration.

The study was approved by the Ethics Committee of Novosibirsk State Medical University of the Russian Federation Ministry of Healthcare (Novosibirsk, protocol No. 155 of November 29, 2023) and the Research Topic Committee (protocol No. 1 of October 25, 2023; Current Issues of Prevention, Diagnosis and Treatment of Internal Diseases). Each patient signed informed consent to participate in the study in accordance with the ethical requirements of the WHO.

Statistical analysis was performed using the SPSS 17.0.5 software package. Taking into account their normal distribution, our data are presented as mean values of quantitative parameters (M) and their standard deviations (SD). Comparison of populations by quantitative variables (parametric analysis) was carried out using Student's t-test for unrelated samples. Comparison of groups by categorical variables was performed using Pearson's and Fisher's chi-squared tests. Risk ratio (RR) with 95% confidence interval (CI) was estimated for each variable.

Results

The main group included 118 patients, while the comparison group included 121 patients. The main group patients were diagnosed with ACS. The clinical characteristics of the patients are presented in Table 1. Statistically significant differences were observed for various characteristics: elevated blood pressure (RR 2.327, 95% CI 1.582-2.699; $p < 0.001$), tachycardia (RR 2.067, 95% CI 1.415-3.73; $p < 0.001$), shortness of breath (RR 2.022, 95% CI 1.495-2.736; $p < 0.001$), weakness (RR 4.077, 95% CI 2.946-5.643; $p < 0.001$), and complaints of insomnia (RR 1.893, 95% CI 1.519-2.358; $p < 0.001$). All symptoms listed in Table 1 occurred for the first time after the NCI.

Table 1. Clinical characteristics of patients in two groups with acute coronary syndrome

Parameter	Group				<i>p</i>	RR, 95% CI
	Main: ACS and PCS, <i>n</i> =118		Comparison: ACS without PCS, <i>n</i> =121			
	Value/c ount	%	Value/c ount	%		
Mean age, years (M± SD)	55.6±7.5	–	56.5±7.2	–	–	–
Elevated BP>140/90 mmHg	104	88.1	78	64.5	<0.001	RR 2.327, 95% CI 1.582– 2.699
Tachycardia	72	61.0	31	25.6	<0.001	RR 2.067, 95% CI 1.415– 3.730
Cardialgia	27	22.9	15	12.3	0.034	RR 1.392, 95% CI 1.061– 1.825
Shortness of breath	83	70.3	46	38.0	<0.001	RR 2.022, 95% CI 1.495– 2.736
Decompensa ted heart failure	29	24.6	23	19.0	0.297	RR 1.172, 95% CI 0.881– 1.558
Weakness (asthenic syndrome)	88	74.6	12	9.9	<0.001	RR 4.077, 95% CI 2.946– 5.643
Insomnia	36	30.5	9	7.4	<0.001	RR 1.893, 95% CI 1.519– 2.358

ACS, acute coronary syndrome; PCS, post COVID-19 syndrome; RR, risk ratio; CI, confidence interval; BP, blood pressure.

A comparative assessment of the frequency of concomitant CVD was performed between patients of the main group and the comparison group (Table 2). According to our data, hypertension (RR 2.327, 95% CI 1.415-3.730; $p < 0.001$) and life-threatening arrhythmias (RR 1.365, 95% CI 1.035-1.799; $p = 0.049$) were statistically significantly more common in the ACS+PCS group. It should be noted that additional comparison of the main group patients with and without hypertension yielded no statistically significant differences for the same parameters.

The transformation of diagnoses in the ACS+PCS group vs. the comparison group is shown in Figure. According to our results, the ratio of ACS patients with ST elevation of the electrocardiogram and without it in the study groups was similar.

The main EchoCG data in patients with ACS and PCS, as well as in the comparison group, are shown in Table 3.

According to our findings, when comparing EchoCG parameters in the group of patients with ACS and PCS, we observed a statistically significant increase in the mPAP, expansion of the pulmonary artery (PA) diameter, and mitral valve (MV) regurgitation ($p < 0.001$). The Teichholz ejection fraction, biplane method ejection fraction, LV myocardial mass index (LVMI), aortic valve (AV) leaflet opening amplitude, and tricuspid valve (TV) regurgitation were lower in the ACS+PCS group. The values of the interventricular septum (IVS) thickness and RV size were larger in the ACS+PCS group as well. However, the differences in these parameters were not statistically significant.

The incidence of EchoCG cardiac complications in patients with ACS in combination with PCS vs. the comparison group patients is presented in Table 4. Our findings suggest that LV apical thrombus (RR 1.785, 95% CI 1.304-2.444; $p = 0.020$), development of LV aneurysms (RR 1.736, 95% CI 1.234-2.443; $p = 0.036$), and reduced myocardial contractility in the form of hypokinesia and akinesia (RR 1.673, 95% CI 1.275-2.196; $p < 0.001$) were statistically significantly more frequently observed in the ACS+PCS group of patients.

Discussion

Most patients in our main group with PCS complained of elevated blood pressure, tachycardia, cardialgia, shortness of breath, weakness, and insomnia. These findings are similar to the results of studies from other countries. E.g., in the study by A.V. Ballering et al., patients with PCS more often complained of weakness, chest pain, and difficulty breathing/shortness of breath; furthermore, their complaints persisted for up to two years [10]. American scientists examined over 3,000 people with PCS. Their results showed that the most characteristic PCS-related complaints were insomnia and weakness, and they were recorded for a full year after the disease [11]. Of particular interest is the 2021 meta-analysis by Martimbianco et al., which included data on 5,440 patients from 25 observational studies [12]. According to the presented results, the incidence of PCS ranged 4.7–80%. The most common symptoms recorded during the period of 3–24 weeks after the NCI were cardialgia (89%), weakness (65%), shortness of breath (61%), and cough with sputum (59%).

Table 2. Concomitant cardiovascular diseases in patients of two groups

Parameter	Group				<i>p</i>	RR, 95% CI
	Main: ACS and PCS, <i>n</i> =118		Comparison: ACS without PCS, <i>n</i> =121			
	Count	%	Count	%		
Previous functional class II or III angina	27	22.8	21	17.3	0.287	RR 1.181, 95% CI 0.883–1.579
History of acute MI	10	8.47	14	11.6	0.426	RR 0.829, 95% CI 0.507–1.356
History of percutaneous coronary intervention	13	11.0	10	8.3	0.471	RR 1.163, 95% CI 0.792–1.707
History of coronary artery bypass grafting	3	2.5	5	4.1	0.495	RR 0.753, 95% CI 0.305–1.860
Single-vessel coronary artery disease according to coronary angiography	72	61.0	68	56.2	0.450	RR 1.107, 95% CI 0.849–1.444
Multi-vessel coronary artery disease according to coronary angiography	46	39.0	53	43.0	0.531	RR 0.919, 95% CI 0.705–1.199
Hypertension	104	88.1	78	64.5	<0.001	RR 2.327, 95% CI 1.415–3.730
Death of relatives from CVD	27	22.9	24	19.8	0.566	RR 1.094, 95% CI 0.812–1.473
Life-threatening arrhythmias	26	22.0	15	12.4	0.049	RR 1.365, 95% CI 1.035–1.799
Killip>II	22	18.6	24	19.8	0.816	RR 0.962, 95% CI 0.689–1.342

ACS, acute coronary syndrome; PCS, post COVID-19 syndrome; RR, risk ratio; CI, confidence interval; MI, myocardial infarction; CVD, cardiovascular diseases.

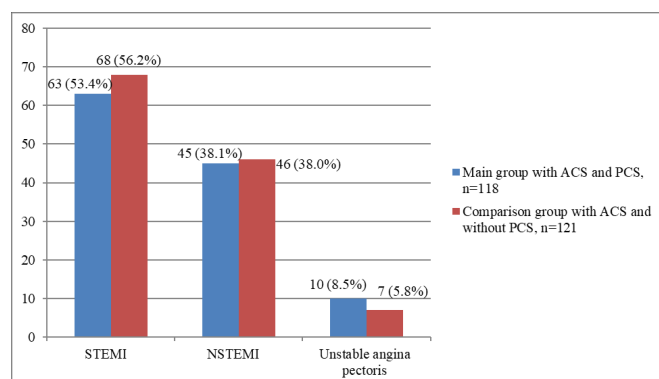


Figure. The structure of acute coronary syndrome in patients of the main group and comparison group.

NSTEMI - myocardial infarction without ST elevation of the electrocardiogram; STEMI - myocardial infarction with ST elevation of the electrocardiogram; ACS, acute coronary syndrome; PCS, post COVID-19 syndrome

Table 3. Echocardiography results in patients of two groups with acute coronary syndrome

Parameter	Group		p
	Main: ACS and PCS, n=118	Comparison: ACS without PCS, n=121	
LVEDD, cm	5.2±0.8	5.9±1.1	0.607
LVEF (according to Teichholz), %	69.5±2.8	71.2±2.7	0.662
LVMI, g/m ²	88±6.7	97±8.2	0.396
IVS, cm	1.1±0.3	0.9±0.4	0.689
LVEDV, mL	74±11.4	81±10.2	0.647
LVEF (based on the biplane method), %	31.2±3.4	32±3.9	0.877
RV size, cm	2.66±0.88	2.44±1.2	0.882
AV leaflet opening amplitude, cm	1.7±0.2	1.9±0.3	0.579
MV regurgitation, %	18.1±2.2	11.5±1.7	0.018
TV regurgitation, %	14.1±2.6	15.7±1.9	0.619
PA diameter, mm	27.5±0.9	23.9±0.8	0.003
mPAP, mmHg	31.8±1.8	23.4±1.7	0.001

ACS, acute coronary syndrome; PCS, post COVID-19 syndrome; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVMI, left ventricular myocardial mass index; IVS, interventricular septum; LVEDV, left ventricular end-diastolic volume; RV, right ventricle; AV, aortic valve; MV, mitral valve; TV, tricuspid valve; PA, pulmonary artery; mPAP, mean pulmonary artery pressure.

Table 4. Echocardiographic cardiac complications in patients of two groups with acute coronary syndrome

Parameter	Group, count (%)		p	RR, 95% CI
	Main: ACS and PCS, n=118	Comparison: ACS without PCS, n=121		
Hypokinesia and akinesia (development of MI)	59 (54.6)	36 (30.2)	<0.001	RR 1.673, 95% CI 1.275–2.196
Free-flowing pericardial fluid	16 (14.8)	23 (19.3)	0.255	RR 0.369, 95% CI 0.560–1.255
Aneurysm of the LV	8 (7.4)	2 (1.7)	0.036	RR 1.736, 95% CI 1.234–2.443
Apical thrombus of the LV	9 (8.3)	2 (1.7)	0.02	RR 1.785, 95% CI 1.304–2.444

ACS, acute coronary syndrome; PCS, post COVID-19 syndrome; RR, risk ratio; CI, confidence interval; MI, myocardial infarction; LV, left ventricle.

Evaluation of EchoCG changes in patients with ACS in the post COVID-19 period is a relevant direction in cardiology. However, such studies are currently not presented among available publications.

Many published sources examine EchoCG changes in the heart of patients with acute course of NCI. For instance, in the 2020 publication by Y. Li et al., RV longitudinal strain and tricuspid annular plane systolic excursion (TAPSE) are known as predictors of a higher probability of death for the patient [13]. According to the results of another study, e EchoCG was employed to identify dysfunction of both the LV and RV in patients with myocardial lesion against the background of an acute course of NCI. However, these changes partially resolved after two months of observation [14].

In our study, a number of statistically significant EchoCG changes were observed in patients with ACS and PCS, such as an increase in the mPAP and the PA diameter, as well as MV regurgitation. Our findings are partially consistent with other Russian studies, which confirmed an increase in the incidence of CVD (mainly due to the development of hypertension and chronic heart failure) and a tendency to elevated systolic blood pressure in the PA after NCI [15]. At the same time, the authors explain the changes in the right chambers of the heart (including an increase in the mPAP and the PA diameter) by the restructuring of hemodynamics in the remote post COVID-19 period [15].

J. Marazzato et al. (2021) observed changes in systolic blood pressure in the PA in 55% of the studied patients with PCS [16], while 44% of these patients had no previous history of CVD. In addition, 7% of patients had signs of LV and RV dysfunction.

A large meta-analysis that included 52,609 patients from 35 studies confirmed the high risk of developing heart failure,

arrhythmias, and myocardial infarction (MI) in patients who experienced NCI [17].

In our study, we observed EchoCG cardiac complications more often in the group with ACS combined with PCS: hypokinesia and akinesia zones (signs of developed MI), LV aneurysm, and LV apical thrombus were detected. This may be due to vascular endothelial dysfunction, impaired elastic properties of cardiomyocytes, and their damage [18]. Alfaro et al. presented evidence suggesting a sustained increase in the biomarkers of endothelial dysfunction developing against the background of post COVID-19 gas exchange disorders [18]. It is now confirmed that the onset of the CVD development is the manifestation of two leading pathogenic mechanisms: direct viral cytotoxicity and indirect immune hypersensitivity reactions of the body in response to NCI.

Conclusion

Patients who experienced ACS combined with PCS exhibit more severe EchoCG changes vs. patients with ACS alone, which is confirmed by the development of cardiac complications (LV aneurysm, LV apical thrombus, myocardial infarction) and increase in the mPAP, PA diameter, and MV regurgitation. Examining the effect of NCI in patients with ACS is crucial for understanding the pathogenesis of this condition and early diagnosis of severe ACS. The latter can improve the quality of medical care for such patients and reduce the severity of the ACS consequences against the background of NCI.

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