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RESEARCH ARTICLE

HEART LESIONS IN POST-COVID SYNDROME CLINICAL AND DIAGNOSTIC ASPECTS

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Abstract: Heart lesions in post-covid syndrome occupy one of the key places among the long-term consequences of COVID-19 infection and determine the risk of developing chronic heart failure, arrhythmias and thrombotic complications. The aim of the study was to evaluate the frequency and structure of heart lesions in patients with post-covid syndrome, as well as to characterize the clinical and diagnostic features of cardiac pathology in this group. A study was conducted with the participation of 50 patients aged 22 to 72 years who had suffered from COVID-19 at least 3 months before admission and who complained that they met the criteria for post-covid syndrome. All participants underwent clinical and anamnestic examination, electrocardiography, echocardiography, laboratory examination of the level of highly sensitive troponin and NT-proBNP, and magnetic resonance imaging of the heart was performed when indicated. Signs of heart damage, determined by a combination of clinical, instrumental and laboratory criteria, were detected in 52% of the examined patients. The presence of myocardial damage was associated with a more severe course of the acute phase of COVID-19, a higher prevalence of hypertension and diabetes mellitus, as well as increased concentrations of cardio specific biomarkers. It has been shown that the use of a comprehensive examination algorithm, including echocardiography with assessment of global contractile function and, if necessary, magnetic resonance imaging of the heart, makes it possible to identify both obvious and subclinical forms of cardiac damage in patients with post-covid syndrome.The results obtained emphasize the need for active cardiological monitoring of this category of patients and the development of routing, taking into account the identified nature of heart damage.

Keywords: kidney syndrome, heart lesions, myocarditis, heart failure, arrhythmias, echocardiography, magnetic resonance imaging of the heart, NT-proBNP, troponin, clinical and diagnostic aspects.

INTRODUCTION

The COVID-19 pandemic has demonstrated the significant role of the cardiovascular system both in the acute period of infection and in the stage of long-term consequences. Numerous studies have shown that SARS-CoV-2 is capable of affecting the myocardium and vascular wall, causing myocarditis, acute coronary syndrome, thrombosis and various rhythm disturbances. At the stage of convalescence, some patients form a complex of persistent symptoms, combined by the concept of post-cystic syndrome or post-acute COVID-19 syndrome, in the structure of which a significant share is occupied by cardiac manifestations. Modern reviews indicate that COVID-19 survivors, even with mild course, have an increased risk of developing myocarditis, decreased contractile function of the left ventricle, rhythm disturbances and signs of heart failure, and the duration of such changes can be months or even years after the initial infection [4].

There is no single generally accepted definition of post-covid syndrome yet, but the most commonly used formulation proposed by WHO experts is that post-covid is indicated in the presence of symptoms that appear or persist at least three months after acute COVID-19 infection, lasting at least two months and not explained by an alternative pathology. Typical complaints include shortness of breath, decreased exercise tolerance, palpitations, heart failure, and a feeling of compression or discomfort in the chest. These manifestations are often combined with severe asthenia, cognitive impairment, and symptoms of autonomic dysfunction, which makes it difficult to interpret their association with heart disease and requires careful clinical and diagnostic analysis [1].

According to meta-analyses and large cohort studies, the prevalence of cardiovascular symptoms in the structure of post-covid syndrome reaches 20-30%, and the frequency of objectively confirmed heart damage according to modern imaging methods, including magnetic resonance imaging with contrast, may be even higher due to subclinical forms of myocarditis and diffuse myocardial fibrosis [12]. Of particular importance in this case is the use of echocardiography with strain analysis and MRI of the heart, which allows detecting minimal changes in global longitudinal deformation of the myocardium and foci of edema, which are not manifested by a decrease in ejection fraction and remain inaccessible to traditional diagnostic methods [6].

The mechanisms of cardiac damage in post-covid syndrome are multifactorial and include the consequences of the direct damaging effect of the virus on cardiomyocytes, endothelial dysfunction and micro-thrombosis, persistent low-intensity inflammation, immune-mediated myocarditis and activation of fibrosis. An important role is also played by the initial presence of cardiovascular risk factors and diseases, primarily arterial hypertension, coronary heart disease and diabetes mellitus, which increase the likelihood of the formation of cystic fibrosis and aggravate its course [4].

Despite a significant number of publications on the problem of COVID-19, the issues of clinical and diagnostic characteristics of heart lesions in the structure of the post-covid syndrome remain insufficiently studied. There is insufficient data on the ratio of symptomatic and subclinical forms, on the relationship of the detected changes with the severity of the infection, as well as on the possibilities of routine imaging and laboratory diagnostics in daily practice. This determined the relevance of this study, the purpose of which was to assess the frequency and structure of heart lesions in post-covid syndrome and analyze their clinical and diagnostic aspects in patients who sought specialized help.

METHODOLOGY & MATERIALS

A prospective single-center observational study was conducted on the basis of the cardiology department of a multidisciplinary hospital. The study included 50 consecutive patients aged 22 to 72 years (average age 49.6±12.3 years) who had undergone laboratory-confirmed SARS-CoV-2 infection at least 12 weeks before the start and who complained that they met the criteria for post-covid syndrome. All patients signed informed voluntary consent, the study protocol was approved by the local ethics committee and complies with the provisions of the Helsinki Declaration.

The inclusion criteria were the presence of a history of confirmed PCR or antigen test for SARS-CoV-2, completion of the acute period of the disease at least three months before the examination, as well as the presence of at least one symptom potentially related to the cardiovascular system, including shortness of breath, palpitations, heart failure, decreased exercise tolerance, periodic discomfort or chest pain.

The exclusion criteria were pronounced structural heart diseases known before COVID-19 (dilated or hypertrophic cardiomyopathy, severe acquired and congenital valve defects), severe chronic heart failure of NYHA functional class IIIB–IV, end-stage chronic renal failure, oncological diseases in the active phase, as well as refusal to participate in the study [11].

The examination included a carefully collected medical history with an assessment of the severity of COVID-19 infection, data on the need for hospitalization, oxygen support or mechanical ventilation, as well as information on the presence of cardiovascular risk factors and concomitant pathology, primarily hypertension, type 2 diabetes mellitus, obesity, coronary heart disease, and chronic lung diseases. Physical examination, measurement of blood pressure and heart rate in a sitting position and after a small standard load, assessment of functional status using a six-minute walking test were performed.

The laboratory part of the study included general and biochemical blood analysis, determination of the level of highly sensitive troponin I, N-terminal fragment of brain natriuretic peptide (NT-proBNP), C-reactive protein and, if necessary, D-dimer. 12-lead electrocardiography was performed in all patients. According to the indications, daily Holter ECG monitoring was performed, primarily in people with complaints of heart failure, episodes of tachycardia, fainting or fainting states.

Echocardiography was performed according to a standard protocol on an expert-class ultrasound machine with an assessment of the size of the heart chambers, the left ventricular ejection fraction using the modified Simpson biplane method, diastolic function, and pulmonary artery pressure. In some patients, the global longitudinal strain of the left ventricle was evaluated by speckle-tracking echocardiography. In the presence of clinical and laboratory indications to exclude myocarditis or other structural pathology of the myocardium, patients underwent magnetic resonance imaging of the heart with gadolinium contrast according to a standard protocol using Lake Louise criteria for the diagnosis of myocarditis.

Cardiac damage in the structure of the post-covid syndrome was determined in the presence of at least one of the following signs that were absent before the infection: recurrent systolic dysfunction of the left ventricle with an ejection fraction of less than 50%; signs of myocarditis detected by MRI of the heart (myocardial edema, late contrast of the myocarditis

type); clinically significant rhythm and conduction disturbances requiring drug correction; persistent increase in the level of NT-proBNP or troponin I, excluding alternative causes.

Statistical processing was carried out using standard application software packages. Quantitative indicators were described in the form of an average value and a standard deviation, qualitative indicators were described in the form of an absolute number and a percentage. To compare the two independent groups, the Student's t-test or the nonparametric Mann–Whitney criterion were used, depending on the type of distribution, and the Pearson's $\chi 2$ criterion was used for frequency analysis. The differences at the $p<0.05$ level were considered statistically significant.

RESULTS

The study included 22 men (44%) and 28 women (56%). The average age was 49.6±12.3 years. 20 patients (40%) had a mild acute phase of COVID-19, 18 (36%) had a moderate acute phase, and 12 patients (24%) had a severe course requiring hospitalization and oxygen support. Arterial hypertension was detected in 21 people (42%), type 2 diabetes mellitus in 9 (18%), obesity in 14 (28%), coronary heart disease in 7 (14%).
The generalized clinical characteristics of the examined are presented in Table 1.

Table 1 – Clinical characteristics of the examined patients (n=50)

Indicator	Meaning
Average age, years	49,6±12,3
Men / women, n (%)	22 (44) / 28 (56)
Severity of COVID-19, n (%): mild / moderate / severe	20 (40) / 18 (36) / 12 (24)
Acute phase hospital admission, n (%)	19 (38)
Oxygen support needed, n (%)	14 (28)
Hypertension, n (%)	21 (42)
Type 2 diabetes mellitus, n (%)	9 (18)
Obesity, n (%)	14 (28)
Coronary heart disease, n (%)	7 (14)
The average distance of a six-minute walk, m	425±64

By the time of the examination, the median time from infection to inclusion in the study was 6 months. The main complaints of patients were increased fatigue, decreased exercise tolerance, shortness of breath during habitual activity, palpitations and heart failure, periodic discomfort or chest pain. At the same time, a significant part of the patients noted a combination of several symptoms, which is characteristic of the multisystem nature of the post-covid syndrome.

According to a combination of clinical, instrumental and laboratory criteria, signs of heart damage were detected in 26 patients, which accounted for 52% of the sample. This group included individuals with newly developed systolic or severe diastolic left ventricular dysfunction, documented clinically significant rhythm disturbances, increased levels of cardio-specific biomarkers, and/or signs of myocarditis according to cardiac MRI. The remaining 24 patients had no objective signs of structural or functional myocardial damage, despite the presence of complaints, and were assigned to the group without heart damage.

Among 26 patients with heart damage, 4 had mild COVID-19, 12 had moderate COVID–19, and 10 had severe COVID–19. In the group without heart damage, the indicators were distributed differently: a mild form was noted in 16 people, a moderate form in 6, and a severe form in only 2. Thus, the share of severe COVID-19 in the anamnesis among patients with heart damage was 38.5%, while in the group without heart damage it was 8.3%, which indicates a significant association of the severity of the acute process with the subsequent formation of post-cortical cardiac damage.

According to echocardiography, systolic dysfunction of the left ventricle with an ejection fraction of less than 50% was detected in 10 patients (20% of the total sample, 38.5% of the group with heart damage). 14 people (28% of the total sample) showed signs of diastolic dysfunction, such as relaxation disorders or pseudo-normalization, and in most cases, they were combined with clinical symptoms of shortness of breath and decreased exercise tolerance. In patients without heart damage, the ejection fraction remained within the normal range in the vast majority of cases, and the reported complaints were more often attributed to deconditioning and concomitant pulmonary pathology.

Special attention should be paid to the results of magnetic resonance imaging of the heart performed in 18 patients with suspected myocarditis or with a persistent increase in troponin levels. 7 of them (38.9% of those examined by MRI, 14% of the entire sample) showed signs of active or past myocarditis according to Lake Louise criteria in the form of foci of edema and late subepicardial or medial contrast. These data are consistent with the results of a meta-analysis, which demonstrated that the prevalence of myocarditis in the post-covid period can exceed the acute phase and

reaches about 7.4%, and when using MRI of the heart, the frequency of detection of myocardial damage is significantly higher than when relying only on clinical criteria.

Daily ECG monitoring was performed in 32 patients with complaints of palpitations and interruptions. Clinically significant rhythm and conduction disturbances requiring observation and, in some cases, drug correction were detected in 9 of them (18% of the total sample). The structure of arrhythmias was dominated by paroxysmal atrial fibrillation recorded in 4 patients, supraventricular tachycardia in 3 and frequent polymorphic ventricular extrasystole in 2. Most of these patients also had signs of structural or biochemical damage to the myocardium, which indicates the complex nature of post-cortical cardiac damage.

Laboratory examination showed an increase in the level of highly sensitive troponin I above the upper limit of the reference range in 11 patients (22%) and an increase in the concentration of NT-proBNP in 13 (26%). At the same time, all cases of increased troponin and 12 out of 13 cases of increased NT-proBNP were observed in the group with heart damage. This pattern confirms the diagnostic significance of cardio-specific biomarkers in assessing the effects of COVID-19 on the myocardium and is consistent with research data on persistent myocardial damage in post-covid syndrome.

For a detailed analysis of the clinical and diagnostic features, a comparative characterization of patients with and without signs of heart damage was performed. The main results are presented in table 2.

Table 2 – Comparative characteristics of patients with and without heart disease

Indicator	Heart damage (n=26)	Without heart damage (n=24)	p
Average age, years	52,1±11,4	46,7±12,8	<0,05
Men, n (%)	13 (50,0)	9 (37,5)	>0,05
History of severe COVID-19, n (%)	10 (38,5)	2 (8,3)	<0,05
Hypertension, n (%)	15 (57,7)	6 (25,0)	<0,05
Type 2 diabetes mellitus, n (%)	7 (26,9)	2 (8,3)	<0,05
Left ventricular failure, %	49,2±6,1	58,3±4,7	<0,001
Diastolic dysfunction, n (%)	13 (50,0)	1 (4,2)	<0,001
Increased troponin I, n (%)	11 (42,3)	0 (0)	<0,001
Increase in NT-proBNP, n (%)	12 (46,2)	1 (4,2)	<0,001
Distance of a six-minute walk, m	398±62	452±58	<0,05

As can be seen from the presented data, patients with heart damage were on average older, more likely to have a history of severe COVID-19 requiring hospitalization, as well as a higher prevalence of hypertension and diabetes compared with people without objective signs of cardiac damage. Patients with heart damage have worse indicators of contractile and diastolic function of the left ventricle, higher levels of cardio specific biomarkers and lower exercise tolerance according to the six-minute walking test.

The results obtained confirm that post-ductile heart disease is multifactorial in nature and forms at the junction of the initial cardiovascular vulnerability and the severity of the infection. It is noteworthy that even among patients with a relatively mild or moderate course of the acute phase of COVID-19, cases of structural myocardial damage and clinically significant arrhythmias have been identified, which underscores the need for careful cardiological monitoring of all patients with post-covid syndrome, and not just those who have suffered a severe course of the disease [10]. These observations are consistent with data from international studies demonstrating an increased risk of cardiovascular events and chronic cardiac complications in patients who have had COVID-19, regardless of the initial severity of the disease [7].

From the point of view of clinical and diagnostic aspects, the consistent application of a multi-stage examination algorithm is of particular importance. At the first stage, thorough medical history collection, assessment of complaints, objective examination and registration of a standard ECG are key. Already at this level, it is possible to identify some of the rhythm disturbances and indirect signs of myocarditis [3]. However, for a full assessment of the structural and functional state of the myocardium, echocardiography is required, which makes it possible to diagnose both severe systolic dysfunction and more subtle changes in diastolic function. The addition of echocardiography with global longitudinal strain analysis increases the sensitivity of detecting subclinical myocardial damage, especially in patients with preserved ejection fraction [5].

The use of cardio specific biomarkers, primarily highly sensitive troponin I and NT-proBNP, complements instrumental methods, allowing the detection of persistent myocardial damage and latent myocardial dysfunction. In our study, increased levels of troponin and NT-proBNP were almost always combined with echocardiographic or MRI signs of heart damage, which confirms their diagnostic value [2].

Magnetic resonance imaging of the heart occupies a special place in the diagnosis of post-cystic myocarditis and allows not only to visualize focal or diffuse edema of the myocardium, but also to assess the presence of fibrosis, as well as to differentiate inflammatory changes from ischemic damage. The signs of myocarditis identified in some of our patients confirm that in a subgroup of patients, post-covid syndrome is associated with a long-lasting inflammatory process in the myocardium, which is consistent with international data regarding chronic active myocarditis as one of the severe forms of COVID [8].

The results of the study confirm the need for targeted cardiological monitoring of patients with post-cystic syndrome, especially in the presence of risk factors and signs of myocardial damage. At the initial treatment of a patient after a COVID-19 infection, a general practitioner or a general practitioner should organize an in-depth assessment of the cardiovascular system, taking into account the severity of the disease, age and concomitant pathology. It is advisable to form high-risk groups that include people over the age of 50, patients with hypertension, type 2 diabetes, obesity, as well as patients who have suffered moderate to severe COVID-19 with the need for hospitalization and oxygen support.

At the outpatient stage, it is recommended that an ECG and standard transthoracic echocardiography be performed in all patients with post-covid syndrome with cardiac complaints, followed by dynamic monitoring at least once every 6-12 months. If a decrease in the left ventricular ejection fraction, diastolic dysfunction, significant rhythm disturbances, or increased levels of troponin I and NT-proBNP are detected, the patient should be referred to a cardiologist to resolve the issue of additional imaging, including MRI of the heart with contrast. In practice, it is recommended to take into account that the absence of gross violations according to standard echocardiography does not exclude subclinical myocardial damage, therefore, if complaints and elevated biomarkers persist, a more in-depth examination is justified.

Table 3 – Main directions of management of patients with post-covid syndrome and heart disease

Direction	Specific content of recommendations	Target group of patients	Expected clinical effect
Initial identification of risk factors	Collecting a detailed history of COVID-19, assessing severity, recording data on hospitalization and oxygen support, detecting hypertension, diabetes, and obesity	All patients with post covid syndrome	Determination of the risk group for post-cortical heart disease
Basic cardiological examination	ECG recording, transthoracic echocardiography with assessment of systolic and diastolic functions of the left ventricle, if necessary, a six-minute walking test	Patients with complaints of shortness of breath, palpitations, chest pain, decreased exercise tolerance	Early diagnosis of structural and functional disorders of the myocardium
Laboratory assessment of myocardial injury	Determination of levels of highly sensitive troponin I, NT-proBNP, with indications of C-reactive protein and D-dimer	Patients with suspected myocarditis, heart failure, or persistent myocardial damage	Confirmation or exclusion of myocardial injury, clarification of the degree of risk
Advanced visualization	Appointment of an MRI of the heart with contrast for elevated biomarkers, reduced ejection fraction, persistent arrhythmias or suspected myocarditis	Patients with signs of heart damage according to the initial examination	Verification of myocarditis, assessment of the prevalence of fibrosis, clarification of the prognosis
Drug therapy	Administration and titration of doses of ACE/ARB inhibitors, beta-blockers, mineralocorticoid receptor antagonists, antiarrhythmic drugs and anticoagulants, if indicated	Patients with identified systolic dysfunction, heart failure, arrhythmias, and thrombotic complications	Hemodynamic stabilization, reduction of risk of decompensation and recurrent cardiovascular events
Rehabilitation and supervision	Individually dosed physical activity, blood pressure and heart rate monitoring, scheduled visits to a cardiologist at least once every 6-12 months, correction of therapy based on the results of observation	Patients with post-covid heart disease and people from high-risk groups	Improvement of functional status, increased exercise tolerance, reduction of symptoms of post-covid syndrome
Educational events	Explaining to the patient the nature of kidney-shaped heart disease, the need for long-term follow-up, adherence to the regimen and taking medications, quitting smoking and excessive alcohol consumption	All patients with post-covid syndrome, especially those with confirmed cardiac pathology	Increased adherence to treatment, reducing the likelihood of premature discontinuation of therapy and worsening prognosis

Individuals with confirmed post-covid heart disease are shown to adjust drug therapy in accordance with current recommendations for the treatment of chronic heart failure, hypertension, and rhythm disorders, with an emphasis on early administration of ACE inhibitors or ARBs, beta-blockers, and, if necessary, mineralocorticoid receptor antagonists. Gradual, individually dosed physical rehabilitation under the control of exercise tolerance and cardiac symptoms becomes an important component of management. Patients need to be clarified about the possible association of persistent symptoms with post-ductile cardiac lesion, and the formation of a commitment to long-term follow-up and therapy. At the level of a medical organization, it is recommended to introduce a standard algorithm for the examination and routing of patients with post-covid syndrome, including mandatory assessment of the cardiovascular system.

From a practical point of view, the results of the study indicate the need to include a basic cardiological examination in all outpatient follow-up programs for patients with cystic syndrome, especially in risk groups, which include the elderly, patients with hypertension, diabetes mellitus and severe course of infection. The detection of even subclinical myocardial damage makes it possible to timely adjust drug therapy, optimize lifestyle, determine the frequency of dynamic follow-up and, if necessary, send the patient to a specialized cardiology center on time.

CONCLUSION

The study showed that heart lesions in patients with post-covid syndrome occur in more than half of the examined patients and are represented by both obvious forms of systolic dysfunction and clinically significant arrhythmias, as well as subclinical variants of myocarditis and diastolic dysfunction, detectable only using modern imaging methods and laboratory diagnostics. The presence of heart damage is closely associated with a more severe course of the acute phase of COVID-19, a higher age of patients and the presence of cardiovascular risk factors, primarily hypertension and diabetes mellitus.

A comprehensive clinical and diagnostic approach, including a thorough analysis of medical history and complaints, electrocardiography, echocardiography with assessment of contractile and diastolic functions, the study of cardio specific biomarkers and, if indicated, magnetic resonance imaging of the heart, allows to identify a wide range of post-ductile myocardial lesions and determine further patient management tactics.

The data obtained emphasize the need for active cardiological monitoring of patients with cystic fibrosis and the development of routing, taking into account the nature and severity of the detected heart damage, which is important for preventing the progression of heart failure and reducing long-term cardiovascular risk in this category of patients.
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