International Heart and Vascular Disease Journal. Volume 11, № 37, Marth 2023
ISSN: 2311-1623 (Print)
ISSN: 2311-1631 (OnLine)
http://www.heart-vdj.com

Echocardiographic changes in patients who experienced COVID-19 after 6 and 12 months of hospital discharge

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Abstract

Objective. To determine the dynamics of echocardiographic changes in patients who experienced COVID-19 at 6 and 12 months after hospital discharge.

Materials and methods. The study included 85 patients (40 men and 45 women, mean age 50.1 ± 8.7 years) who received inpatient treatment in 2020–2021 for COVID-19 of moderate (n = 49; 58 %) or severe (n = 36; 42 %) course. All patients underwent: general clinical examination with collection of complaints and medical history, physical examination, standard electrocardiography and transthoracic echocardiography.

Results. The dynamics of echocardiographic parameters in the examined patients was not with clinical manifestations after 6 and 12 months. The important findings during 12-month follow-up were the increased frequency of hydropericardium (relative risk (RR) 3.727 at 95 % confidence interval (CI) 2.058–6.749), types 2 and 3 of right ventricular diastolic dysfunction (RR — 9.5 at 95 % CI — 4.33–20.842), significant increases of maximal and mean aortic valve pressure gradients, and mean mitral valve pressure gradient.

Conclusion. It is reasonable to monitor patients with persisting cardiovascular symptoms to prevent severe and

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long-term complications using transthoracic echocardiography after COVID-19.
Key words: COVID-19, SARS-CoV-2, echocardiography.

Conflict of interest: none declared.

Received: 29.11.2022
Accepted: 27.01.2023

For citation: Kanorsky S.G., Panchenko D.I., Bystrov A.O., Moisova D.L., Gorodin V.N., Ionov A.Yu. Echocardiographic changes in patients who experienced COVID-19 after 6 and 12 months of hospital discharge. International Journal of Heart and Vascular Diseases. 2023. 11(37): 15-20. doi: 10.24412/2311-1623-2023-37-15-20

Introduction

Currently, along with studies regarding the management of patients with acute phase of coronavirus infection (COVID-19), clinicians are paying attention to the investigation of its long-term concequences. This interest is confirmed by the rapid increase in the number of publications on the problem of post-covid syndrome [1]. Russian experts agree with the definition of post-covid syndrome that is given in the guidelines of the United Kingdom National Institute for Health and Care Excellence. It is defined as the signs and symptoms that develop during or after COVID-19 and last for over 12 weeks andcannot be explained by another cause [2]. Between 10 % and 30 % of patients experience long-term symptoms after SARS-CoV-2 infection, some of which may be related to cardiovascular system [3]. Since cardiovascular diseases are the main cause of death after discharge from hospital [4], there is the need to conduct studies to assess the state of the cardiovascular system after COVID-19 infection. It is important that the techniques used in them are not only informative, but are also available in routine clinical practice.

We investigated the clinical status and changes in echocardiography parameters in patients 6 months after moderate and severe COVID-19 [5]. We followed-up the examined patients to determine the dynamics of symptoms and detect echocardiographic changes 6 and 12 months after hospital discharge.

Methods

The research was conducted in the Specialized Clinical.

Infectious Diseases Hospital located in Krasnodar 6 and 12 months after discharge of patients from the hospital. The study enrolled 85 patients (40 men and 45 women; mean age — 50.1 ± 8.7 years) who received inpatient treatment between 2020–2021 for moderate (n = 49; 58 %) or severe (n = 36; 42 %) COVID-19.

We did not include in the study patients younger than 18 years old or older than 60 years old. We also excluded those with a history of cardiovascular and/or other diseases that could significantly affect study results (coronary heart disease, chronic heart failure, heart defects, atrial fibrillation/ atrial flutter, hypertension, chronic kidney disease ⩾ 3a stage, cancer, alcohol abuse and mental disorders).

All patients underwent: general clinical examination with the collection of complaints, medical history, physical examination, standard 12-lead electrocardiography. Additionally we performed a transthoracic echocardiography by standard technique [6] using "Samsung HS70A" ultrasonic device (Malaysia) with 2.0–4.0 MHz sensor in sectoral scanning mode with color Doppler mapping, pulse, continuous wave and tissue Doppler sonography. Visualization of the heart, measuring the sizes of its structures and cavities were performed in the supine and left lateral position in B-mode and M-mode. Local contractile dysfunction of left ventricular myocardium was assessed in 16 segments, and at least 2 segments were considered diagnostically significant.

A chest computed tomography and the measurement of SARS-CoV-2 IgG and IgM titers were performed in each case.

The study was performed in accordance with the standards of Good Clinical Practice and the principles of the Declaration of Helsinki. The local Independent Ethics Committee approved the study protocol. Written informed consent was obtained from all participants before inclusion into the study.

Statistical analysis

We performed the statistical processing of the study results using StatTech v. 2.8.5 (developer — Stattech LLC, Russia). Quantitative indices were assessed for their correspondence to normal distribution using the Kolmogorov-Smirnov criterion. Quantitative indices with normal distribution are described as arithmetic

mean (M) with standard deviations (SD), 95% CI limits. Since data deviated from normal distribution, quantitative data are described as median (Me) with lower and upper quartiles (Q1-Q3). Categorical data are presented as absolute values with percentages. The comparison of two groups quantitative parameters that had a normal distribution was performed using Student's t-test. The Mann-Whitney U-test was used to compare quantitative indicator between two groups that deviated from normal distribution. Qualitative characteristics were compared using the Yates-adjusted x-square test and Fisher's exact test (two-sided). Hypothesis testing for associations between variables was conducted using Pearson correlation coefficient. Statistical significance was set as $p < 0.05$.

Results

All study participants were followed up for 6 and 12 months after the disease. A positive level of SARS-CoV-2 IgM was detected in 47 patients at the 6-month visit and in another 28 patients at the 12-month visit, indicating a recurrent coronavirus infection that did not lead to hospital admission. After the first examination, patients received treatment for chronic heart failure and myocarditis, according to current clinical guidelines.

A general clinical examination of COVID-19 patients revealed the following main signs and symptoms during hospitalization 6 and 12 months after the disease onset (Table 1).

There was a significant regression of a number of clinical manifestations 12 months after the COVID-19 — BP, dyspnea and palpitations rate decreased. Frequency of cardiac arrest, cardialgia, and the lower extremities swelling tended to decrease, but differences in the dynamics did not reach statistical significance.

According to the results of statistical processing none of the presented clinical manifestations correlated with echocardiographic changes in the examined patients.

The main echocardiography data of patients who underwent COVID-19 are presented in Table 2.

The frequency of cardiac complications according to echocardiography in patients who underwent COVID-19 is presented in Table 3.

According to the results, at 12 months after the COVID-19 the relative risk of patients having per-

Table 1. **Number of patients with major clinical signs and symptoms 6 and 12 months after inpatient COVID-19 treatment**

Parameter	During the hospitalization	After 6 months	After 12 months	P2–4	P3–4
Rise of blood pressure > 140/90 mm Hg	68	11	9	0,0001*	0,86
Heart palpitations	64	27	15	0,0007*	0,69
Arrhythmias	21	3	7	0,16	0,47
Chest pain	26	12	5	0,22	0,57
Dyspnea	85	46	21	0,0001*	0,067
Swelling of the lower extremities	46	37	34	0,32	0,95

**Comment. ***$p < 0.05$ using Yates-adjusted x2 test and Fisher's exact test (two-sided).

Table 2. **The results of the echocardiography of the patients after inpatient COVID-19 treatment**

Parameter	During the hospitalization	After 6 months	After 12 months	P2–4	P3–4
LVPWd, mm	42,8 ± 0,8	44,5 ± 1,2	44,4 ± 1,1	0,19	0,91
LV EF, % (by Simpson)	52,9 ± 2,9	60,9 ± 2,7	59,5 ± 2,2	0,06	0,85
IVSd, mm	13,4 ± 0,4	10,9 ± 0,4	10,9 ± 0,4	0,001*	0,30
LV PW, mm	11,4 ± 0,4	10,6 ± 1,7	11,4 ± 1,5	0,17	0,94
STIS, %	34,1 ± 5,1	49,2 ± 4,1	58,7 ± 6,8	0,013*	0,29
STPW LV, %	27,8 ± 5,1	55,7 ± 6,6	62,7 ± 6,0	0,0001*	0,45
AVOA, mm	18,6 ± 0,4	18,5 ± 0,5	17,4 ± 0,5	0,12	0,15
AV MPG, mm Hg	12,1 ± 0,8	16,8 ± 1,2	20,7 ± 1,3	0,0004*	0,04*
AV APG, mm Hg	3,4 ± 0,3	4,4 ± 0,2	4,8 ± 0,5	0,04*	0,81
LV SVI, ml/m^2	23,2 ± 1,6	24,3 ± 2,0	22,8 ± 1,6	0,73	0,76
LV MMI, g/m^2	106,2 ± 6,7	109,5 ± 8,3	97,6 ± 6,2	0,39	0,31
LA VI, ml/m^2	26,4 ± 1,7	26,9 ± 1,6	24,7 ± 1,4	0,39	0,26
RV SVI, ml/m^2	14,2 ± 0,8	11,1 ± 1,3	12,1 ± 1,4	0,19	0,84
RV WT, mm	4,8 ± 0,2	5,5 ± 0,3	5,0 ± 0,2	0,60	0,16
RV EF, % (by Simpson)	51,6 ± 3,9	51,2 ± 3,2	60,1 ± 3,7	0,17	0,03*
RV FAC, %	42,2 ± 2,0	39,1 ± 3,4	42,7 ± 3,1	0,71	0,41
RAVI, ml/m^2	27,3 ± 1,7	31,9 ± 2,3	29,8 ± 2,0	0,17	0,50
RA ESV, cm^2	12,0 ± 0,7	12,9 ± 1,0	13,1 ± 1,0	0,17	0,57
MV fibrous ring velocity (lateral), cm/s	10,1 ± 0,7	12,2 ± 0,6	11,4 ± 0,5	0,21	0,32
MV APG, mm Hg	1,1 ± 0,1	1,6 ± 0,2	2,0 ± 0,2	0,002*	0,10
MV regurgitation, %	17,1 ± 2,1	13,5 ± 1,6	10,1 ± 1,4	0,009*	0,076
TV fibrous ring velocity (septal), cm/s	11,4 ± 0,6	10,7 ± 0,6	10,0 ± 0,3	0,10	0,44
TV regurgitation, %	14,3 ± 2,5	15,6 ± 1,9	14,0 ± 2,0	0,34	0,52
PA diameter, mm	24,8 ± 0,8	28,5 ± 0,9	27,9 ± 0,7	0,003*	0,53
PA right branch diameter, mm	18,8 ± 0,6	20,3 ± 0,6	19,2 ± 0,5	0,50	0,21
MPGPA, mm Hg	19,8 ± 1,9	23,9 ± 1,7	22,2 ± 1,2	0,09	0,46

Comment. n — number of patients,
*$p < 0.05$ using Kruskal-Wallis test.

doi: 10.24412/2311-1623-2023-37-15-20

Table 3. **Frequency of cardiac complications according to echocardiography in patients who underwent COVID-19**

Parameter	During the hospitalization	After 6 months	After 12 months	P2–4	P3–4
Hypokinesis, n	48	39	31	0,16	0,73
Hydropericardium, n	11	62	41	0,05*	0,63
LVDD types 2–3, n	11	48	9	0,06	0,31
RVDD types 2–3, n	6	68	57	0,0004*	0,25

**Comment. ***p < 0.05 using Yates-adjusted x2 test and Fisher's exact test (two-sided).

sistent hypokinesis was 0,646 (95% CI 0.461–0.905), hydropericardium was 3,727 (95% CI 2.058–6.749), left ventricular type 2–3 diastolic dysfunction — 1.222 (95% CI 0.534–2.798), right ventricular type 2–3 diastolic dysfunction — 9.5 (95% CI 4.33–20.842). Thus, in a year after the COVID-19 the frequency of detection of hydropericardium and diastolic dysfunction of the right ventricle did not decrease, but, on the contrary, increased.

Comparison of echocardiographic parameters in dynamics showed statistically significant increase of maximal and mean pressure gradients on aortic valve from its level during hospitalization to 6 month and further — to 12 month after discharge. Simultaneously, there was a tendency to an increase in the mean pressure gradient on the aortic valve, which reached statistical significance when comparing the index after 12 months with the initial one. There was a tendency to decrease in the amplitude of aortic valve opening.

There was a significant increase in mean pressure gradient in the mitral valve 12 months after discharge.

By the 12 months after hospital discharge there was a significant decrease in interventricular septal thickness with an increase in the percentage of its systolic thickening, a decrease in regurgitation of the mitral valve, as well as decrease in the number of those examined with left ventricular wall hypokinesis. This could indirectly indicate the incidence of myocarditis as COVID-19 complication.

During the observation period the right ventricular ejection fraction and pulmonary artery diameter increased statistically significantly in the examined patients.

Discussion

Only about ¼ of patients who were hospitalized for COVID-19 felt completely cured one year after the SARS-CoV-2 infection [7]. A large study, accounting the presence of symptoms even before COVID-19 developed, showed that the frequency of post-covid syndrome symptoms decreased over time, but persisted in about 1 in 8 of the patients even 2 years after the infection [8].

In our study, patients 12 months after COVID-19 had improved office BP, and the complaints regarding dyspnea and heart palpitations were reported significantly less frequently. Echocardiography parameters changed differently in dynamics. The increased frequency of hydropericardium, diastolic dysfunction of the right ventricle, significant increase of maximal and mean pressure gradients on aortic valve, as well as mean pressure gradient on mitral valve have raised our concerns.

COVID-19 survivors have increased risk of cardiovascular diseases. During the following year, it is several times higher in hospitalized patients, especially in ICU, but complications can occur more frequently even in people who seemed to have fully recovered from a mild infection [9, 10]. Among COVID-19 survivors, within 4 months after infection, the risk of congestive heart failure was about 2.5 times higher compared with those who were not infected [11].

There are still few articles in the current literature presenting echocardiography findings over time in patients who underwent COVID-19 a year ago, and they are not always consistent with each other. According to Ovrebotten T. et al. (2022) dyspnea, fatigue, dizziness and tachycardia in long-term COVID-19 survivors cannot be conclusively confirmed by progressive changes in heart structure and function [12]. One year later, in COVID-19 patients with pneumonia, Yaroslavskaya E.I. et al. (2022) noted increasing changes in ventricular geometry accompanied by worsening of diastolic and systolic left ventricular function, which these authors associated mainly with the development of arterial hypertension and chronic heart failure [13].

In our study, echocardiographic changes were observed in people with no previous significant cardiovascular diseases, which may be associated with decreased elastic properties of the aorta, major arteries, and myocardial damage. These assumptions are consistent with the current understanding of the

mechanisms of cardiovascular lesions in SARS-CoV-2 infection. Possible mechanisms of long-term cardiovascular complications of COVID-19 are believed to include direct and indirect cellular damage mediated by the virus, procoagulant state, immunological response affecting structural integrity of myocardium, pericardium and conduction system, suppression of angiotensin converting enzyme 2 [14]. According to most experts, initially the virus penetrates endothelial cells, causing their inflammation, dysfunction and accelerated apoptosis with the development of thrombosis and rapid progression of atherosclerosis. Further, autoantibodies and immune cells damage many organs, including the heart. Vaccination reduces but does not eliminate the risk of delayed cardiovascular complications [15]. In addition, the researchers cannot exclude the potential risk of antibody-dependent enhancement induced by SARS-CoV-2 in humans.

Conclusions

Given that many millions and presumably even billions of people have been infected with SARS-CoV-2, clinicians are wondering whether the infectious pandemic will be followed by a wave of cardiovascular pathology. Researchers are trying to establish the profiles of people at most risk for cardiovascular disease and complications after COVID-19, the duration of the period of increased risk, and the pathogenesis of the observed pathological changes. Despite the insufficient study of the cardiovascular consequences of SARS-CoV-2 infection, a dynamic follow-up of patients with persisting cardiovascular symptoms and signs to prevent severe and long-term complications, including the use of widely available transthoracic echocardiography, might be beneficial.

Conflict of interest. None declared.

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