

## CARDIAC ULTRASOUND ALTERATIONS IN INDIVIDUALS WITH PNEUMONIA RELATED TO COVID-19 INFECTION

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**Abstract:** COVID-19 exhibits a broad spectrum of cardiac effects during its acute phase. Notably, troponin levels are elevated in 8 to 28% of cases, but clear signs of systolic myocardial dysfunction are uncommon. More frequently observed is subclinical myocardial dysfunction, often identified as a reduction in the global longitudinal strain of the left ventricle (LV GLS). During hospitalization, up to 80% of patients demonstrate this change. LV GLS is a significant independent predictor of in-hospital mortality and plays a vital role in risk assessment for follow-up care. This study presents initial findings on the long-term cardiovascular impact of COVID-19 one year post-hospitalization. We previously observed that patients who had COVID-19 pneumonia exhibited a decline in LV GLS and deformation parameters in the apical and some middle segments of the LV myocardium one year after discharge, a negative trend compared to data from three months post-discharge. The study aims to investigate the frequency and clinical relevance of long-term myocardial damage post-COVID-19. To achieve this, we analyzed patient data, categorizing them based on their LV GLS values one year after hospital discharge. This approach helps in understanding the long-term myocardial damage and its clinical implications following COVID-19.

**Key words:** arterial hypertension, inflammation, cytokines.

**Target:** to compare clinical and echocardiographic parameters in patients with proven COVID-19 pneumonia, depending on the magnitude of global LV longitudinal strain (LV GLS) one year after discharge.

**Material and research methods:** The recruitment of patients was carried out from September 2021 to February 2022. All examined gave written informed consent to participate. Inclusion criteria: documented diagnosis of COVID-19-associated pneumonia, willingness of the patient to participate in observation. Exclusion criteria: chronic diseases in the acute stage, a history of oncological diseases lasting less than 5 years, tuberculosis and other diseases accompanied by pneumofibrosis, HIV, hemodynamically significant heart defects, chronic hepatitis. Exclusion criteria: unsatisfactory imaging on echocardiography (EchoCG), dilated, restrictive and hypertrophic cardiomyopathy, pregnancy detected during the observation period, oncological diseases, refusal to participate.

58 patients who had COVID-19 pneumonia were examined after a year  $\pm$  2 weeks. after discharge, the mean age was  $53.0 \pm 16.7$  years (from 18 to 84 years); 56.8% of them are men. The parameters of global and segmental longitudinal myocardial deformity of the left ventricle were studied in all examined patients with optimal visualization quality in echocardiography (EchoCG). Patients were divided into groups depending on the LV GLS value: group 1 - with normal LV GLS ( $< -20\%$ ) - 26 people, group 2 - with depressed LV GLS ( $\geq -20\%$ ) - 32 people. The groups did not differ in age ( $p = 0.145$ ), severity of lung

injury during hospitalization ( $p = 0.691$ ), duration of hospitalization ( $p = 0.626$ ) and frequency of stay in intensive care units (ICU) ( $p = 0.420$ ).

Hospitalization data are obtained from extracts from case histories. The severity of lung injury was assessed in accordance with current recommendations [4], and the maximum volume of lung injury was analyzed. According to CT data, during hospitalization, 16 (27.9%) patients had mild lesions, 20 (34.5%) had moderate lesions, 17 (29.3%) had severe lesions, and 5 (8.6%) - critical. 9 (15.5%) patients underwent treatment in intensive care units (ICU) (Table 1).

**Table 1. Comparison of clinical data of hospitalization in patients with COVID-19-associated pneumonia**

Parameters		Group with normal LV GLS ( $\leq -20\%$ ) n=26	Group with LV GLS disorders ( $\geq -20\%$ ) n=32	<i>p</i>
Duration of hospitalization	days	13.6 $\pm$ 3.7	17.2 $\pm$ 4.3	0.634
Mild pneumonia	n (%)	5 (19.2)	11 (34.4)	0.308
Moderate pneumonia	n (%)	9 (34.6)	11 (34.4)	0.834
Severe	n (%)	8 (30.7)	7 (21.9.3)	0.413
Critical pneumonia	n (%)	8 (30.7)	9 (28.1)	0.873
ICU admission	n (%)	4 (14.7)	5 (15.6)	0.486

A year after discharge, all examined patients underwent CT scan of the lungs, echocardiography using an expert-class ultrasonic diagnostic system Vivid S70. EchoCG data were analyzed on an IntelliSpace Cardiovascular workstation with TomTec software (Philips, USA). The linear dimensions of the cavities and wall thickness of the heart, chamber volumes, and ventricular systolic function were assessed in accordance with the recommendations, taking into account gender differences and indexation to body surface area [5].

To calculate the peak systolic pressure in the pulmonary artery (pSPPA), the peak pressure gradient of tricuspid regurgitation and the pressure in the right atrium, estimated by the method of C. Otto et al. [6, 7]. The parameters of global and segmental longitudinal myocardial deformity of the left ventricle were studied in all examined patients with optimal visualization quality. Indicators of LV longitudinal strain were assessed in AFI (Automatic Functional Imaging) mode [5, 8]. The value of the global longitudinal strain (LV GLS) of more than  $-20\%$  was considered to be the lower limit of normal [5]. Group 1 with normal LV GLS ( $< -20\%$ ) included 35 people, group 2 with impaired LV GLS ( $\geq -20\%$ ) - 45 people. The results of the examination were entered into the electronic database. The groups did not differ in age, severity of lung damage during hospitalization,

Statistical analysis was performed using the SPSS 21 software package (SPSS Inc., Chicago, IL, USA) and STATISTICA 12.0. The normality of the distribution of quantitative indicators was checked by the Kolmogorov-Smirnov criterion. Normally distributed quantitative indicators were represented by the mean and standard deviation ( $M \pm SD$ ), in the case of a non-normal distribution, by the median (Me) and the interquartile range [Q1–Q3]. Dichotomous categorical indicators were described by absolute (n) and relative (in %) frequencies of occurrence. Identification of statistically significant intergroup differences in indicators was carried out for normally distributed quantitative indicators using Student's t-test for independent groups, in the absence of normality - using the Mann-Whitney test. Pearson's  $\chi^2$  test was used to identify statistically significant differences between categorical indicators. The critical level of significance was  $p = 0.05$ .

**Results:** in contrast to group 1, the majority of patients in group 2 were represented by men, the body surface area (BSA) in this group was larger (Table 2).

**Table 2. Comparison of clinical characteristics of patients with COVID-19-associated pneumonia**

Parameters		Group with normal LV GLS ( $\leq -20\%$ ) n=26	Group with LV GLS disorders ( $\geq -20\%$ ) n=32	<i>p</i>
Age	years	50.9 $\pm$ 12.9	46.1 $\pm$ 15.9	0.148
Male	n(%)	10 (28.6)	32 (71.1)	<0.001
Height	cm	166.3 $\pm$ 7.8	171.3 $\pm$ 17.7	0.003
Weight	kg	75.8 $\pm$ 13.1	87.8 $\pm$ 18.6	0.002
BMI	kg/m <sup>2</sup>	27.42 $\pm$ 4.65	28.79 $\pm$ 5.03	0.873
body surface area	m <sup>2</sup>	1.8 $\pm$ 0.2	2.0 $\pm$ 0.2	0.486

The groups did not differ in age, body mass index, incidence of obesity and cardiovascular disease. There were also no significant differences in the frequency, structure and duration of arterial hypertension (AH), chronic heart failure (CHF), frequency of heart rhythm disturbances and glycemic profile. In group 2, coronary heart disease (CHD) was diagnosed more often, including in combination with AH. The resolution of symptoms of pneumonia, according to CT data, was observed in most patients of both groups, the statistical significance of the differences in this sign of the group was not shown.

In group 2, there was a tendency towards a smaller thickness of the posterior wall of the left ventricle. After indexing to BSA, this trend increased, and the end-diastolic size, length and stroke volume of the LV in group 2 were lower, as was the cardiac index. There were no significant intergroup differences in LV myocardial mass, type of geometry, and LV ejection fraction (EF). Among the patients of this stage of the study, there were no persons with a decrease in LV EF, as well as with mitral regurgitation of the 2nd degree and above. Group 2 was characterized by a smaller volume of LA emptying, a lower rate of FC MK e', and a smaller integral of the linear flow velocity in the LV outflow tract.

When evaluating the right heart (Table 4), significant intergroup differences in the structural and functional parameters of the right ventricle (RV) were revealed: in group 2, its area, transverse dimensions and sphericity indices were larger, and the fraction of changes in the area of the RV and the speed S' of the tricuspid ring - below The frequency of reduction of global longitudinal deformation of the left ventricle in the long term after the disease was 57.5%. Mean LV GLS in group 2 was significantly worse than in group 1 ( $-17.6 \pm 1.9$  vs.  $-21.8 \pm 1.2\%$ ;  $p < 0.001$ ).

**Discussion:** When evaluating the right heart in group 2, structural differences in the pancreas were revealed: the area, transverse dimensions and sphericity indices of the pancreas were greater than in group 1. At the same time, the indicators of systolic function of the pancreas in group 2 were worse, which was expressed in a lower fraction of change area of the pancreas and lower speed S' tricuspid ring. Indicators of LV diastolic function in group 2 were also worse, as evidenced by a smaller volume of emptying of the left ventricle and a lower speed of the fibrous ring of the mitral valve e'. The integral of the linear flow rate in the LVOT, which reflects its pumping function, was also lower in group 2 compared to group 1. Despite the fact that in this group the indices of end-diastolic size (EDS) and LV length were lower, significant differences in EF We didn't receive the LJ.

According to magnetic resonance imaging (MRI), the frequency of a decrease in the index of total longitudinal deformity in convalescents after COVID-19 increases from 2% before 3 months. from the end of the disease to 30% in the period from 3 to 6 months. [9]. Similar figures were obtained by S. Mahajan et al. with transthoracic echocardiography after 1–1.5 months. after discharge: a decrease in LV GLS was observed in 29.9% with a mean value of  $19.7 \pm 4.6\%$  [10]. The frequency of LV GLS decreases in the

long-term period after the disease that we obtained was 57.5%, which significantly exceeds the data of S. Mahajan et al., as well as the frequency of deterioration of LV GLS during MRI [9]. However, it should be noted that such a comparison is rather rough - and due to the low comparability of the clinical characteristics of patients (not all observed by S. Mahajan et al. had a symptomatic course of COVID-19,

The mean value of LV GLS in our patients (total group before separation) after 3 months. after discharge was  $-20.3 \pm 2.2\%$  and in dynamics in a year it worsened significantly in comparison with the survey data after 3 months. after discharge ( $-20.3 \pm 2.2$  vs.  $-19.4 \pm 2.7\%$ ;  $p = 0.001$ ) [3]. In the observation of Chinese colleagues of 46 patients who underwent COVID-19, the value of LV GLS after 3 months after discharge was  $-26.6 \pm 4.4\%$  [11], which is better than that obtained by us, despite the older age of Chinese patients ( $59 \pm 13$  years) and their more frequent stay in the ICU (18.9%). A contribution to the differences in the results of our studies could be made by the difference in vendors [12] - colleagues used the Philips Medical Systems, Andover, MA, USA system.

COVID-19 cohort prospective follow-up of 58 patients MCH Lassen et al. after 2 months after hospitalization, compared with hospital data, did not reveal a significant improvement in LV GLS ( $-17.4 \pm 2.9$  vs  $-17.6 \pm 3.3\%$ ;  $p = 0.6$ ) [13]. This is worse than the values obtained by us, which may be due to the fact that the Danish patients were significantly older -  $62.5 \pm 12.1$  years.

Single center follow-up of 40 patients in the Netherlands FMA van den Heuvel et al. within 4 months. after discharge from the hospital compared with hospitalization data showed a trend towards an increase in LV GLS ( $-18.5$  vs  $-19.1\%$ ;  $p = 0.07$ ). The positive dynamics may be explained by the fact that the studied cohort was older than our patients, but with less comorbidity [14]. However, the values obtained by colleagues also do not reach normal values.

In general, when analyzing literature data on the issue of myocardial deformation in the recovery period after COVID-19, attention is drawn to the lack of a unified approach to the formation of study design, which naturally leads to heterogeneity of the examined contingent and difficulties in comparing the results of various studies. However, it is obvious that patients who, even a year after pneumonia, have a decrease in LV GLS with preserved LV EF, require careful monitoring to prevent the development or timely detection in the future of such conditions as heart failure, LV dysfunction, or arrhythmia.

The data obtained indicate the need for further study of the cardiovascular status of those who have recovered from COVID-19 pneumonia with an increase in the number of observations, a subgroup analysis to identify predictors of violations of the deformation properties of the myocardium, taking into account the treatment carried out in the acute period of the disease, the impact of concomitant cardiovascular diseases, etc.

**Conclusions.** One year after experiencing COVID-19 pneumonia, 58.6% of patients, who initially had normal left ventricular ejection fraction (LV EF), showed reduced global longitudinal strain of the left ventricle (LV GLS). In the group with impaired LV GLS, there was a higher prevalence of men. Additionally, these patients more frequently presented with ischemic heart disease (IHD) alongside hypertension. Furthermore, indicators of left ventricular diastolic function were notably poorer in this group compared to those with normal LV GLS.

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