

Poteshkina N. G.<sup>1,2</sup>, Krylova N. S.<sup>1,2</sup>, Karasev A. A.<sup>1</sup>, Nikitina T. A.<sup>2</sup>, Beloglazova I. P.<sup>1,2</sup>, Kovalevskaya E. A.<sup>1,2</sup>, Parshin V. V.<sup>2</sup>, Lysenko M. A.<sup>1,2</sup>, Ibragimova A. M.<sup>1</sup>, Smorschok V. N.<sup>2</sup>

<sup>1</sup> Pirogov Russian National Research Medical University, Moscow, Russia

<sup>2</sup> Municipal Clinical Hospital #52, Moscow, Russia

## CONDITION OF THE RIGHT HEART IN PATIENTS WITH COVID-19-ASSOCIATED PNEUMONIA: FOLLOW-UP DURING HOSPITALIZATION

|                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Aim</i>                  | Dynamic assessment of the right heart in patients with COVID-19-associated pneumonia of different severity during regression of the systemic inflammatory response (SIR).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <i>Material and methods</i> | This single-center prospective study included 46 patients with the novel coronavirus infection COVID-19 and viral pneumonia according to chest multispiral computed tomography (CT). Laboratory and echocardiographic examinations of patients were performed.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <i>Results</i>              | Based on the results of evaluation with the Clinical Condition Scale (CCS-COVID), patients were divided into two groups: group A, patients with a score from 6 to 9 and group B, patients with a score from 10 to 14. The study results of both groups were evaluated twice: on day 10±2.5 from the onset of symptoms (groups A10 and B10, respectively) and again on day 17±1.8 (groups A17 and B17, respectively). Patients of group B10 had more pronounced SIR (C-reactive protein, 111.38±52.5 mg/l) and a larger volume of ground-glass opacity (38.3±9.6%). At the first stage, higher values of right ventricular global longitudinal strain (RV GLS) were detected in group B10 compared to group A10 (23.2±4.8% vs. 19.9±3.5%, p=0.048). During the regression of SIR intensity and the positive dynamics of CT, lower values of E/A were observed in group B17 (1.0 [0.98; 1.2]) vs. group A17 (1.4 [1.18; 1.5, p=0.015), and e'/a' in group B17 (0.66 [0.58; 0.85]) vs. 0.95 [0.79; 1.12] in group B17 (p=0.010). E/A and e'/a' ratios were correlated with total lactate dehydrogenase fraction (r= -0.452 and p=0.006; r= -0.334 and p=0.050, respectively). |
| <i>Conclusion</i>           | In patients with severe COVID-19-associated pneumonia during regression of SIR intensity, changes in the parameters that reflected RV diastolic dysfunction were observed.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <i>Keywords</i>             | COVID-19; systemic inflammatory response; echocardiography; right ventricle; diastolic function                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <i>For citations</i>        | Poteshkina N.G., Krylova N.S., Karasev A.A., Nikitina T.A., Beloglazova I.P., Kovalevskaya E.A. et al. Condition of the Right Heart in Patients With COVID-19-Associated Pneumonia: Follow-Up During Hospitalization. <i>Kardiologiia</i> . 2023;63(8):26–32. [Russian: Потешкина Н.Г., Крылова Н.С., Карасев А.А., Никитина Т.А., Белоглазова И.П., Ковалевская Е.А. и др. Состояние правых отделов сердца у пациентов с COVID-19-ассоциированной пневмонией: динамическое наблюдение в течение госпитализации. <i>Кардиология</i> . 2023;63(8):26–32].                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <i>Corresponding author</i> | Karasev A.A. E-mail: akara95_2010@mail.ru                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

### Introduction

Patients with COVID-19 are characterized by cardiovascular system involvement [1]. Cardiac abnormalities were shown by echocardiography in 50% of hospitalized patients [2]. Mild-to-severe right ventricular (RV) dysfunction was the most common pathology in the right heart, and pulmonary hypertension, RV dilation, and D-shaped RV were less common [2]. The group authors described hyperfunction of the right heart in patients with COVID-19-associated pneumonia on day 10±2.5 from the onset of symptoms as a response to increased afterload in severe systemic inflammatory response (SIR) [3]. However, there is no data in the available literature on the state of the right heart in patients with COVID-19-associated pneumonia during regression of SIR severity.

### Objective

Assess the right heart in patients with COVID-19-associated pneumonia of varying severity over time as SIR intensity regression goes on.

### Material and Methods

A single-center prospective study included 46 patients with COVID-19 and positive polymerase chain reaction (PCR+) and viral pneumonia confirmed by chest computed tomography (CCT). Patient ages ranged from 31 to 78 years (mean 55±11 years); 30 (65.2%) patients were male. Respiratory support for patients with acute respiratory failure (ARF) was performed using low-flow oxygen delivery (n=42), mean flow rate of the oxygen mixture was 8.8±1.2 l/min. Inclusion criteria were SARS-CoV-2-positive PCR; viral pneumonia confirmed by CCT.

Exclusion criteria: left ventricular systolic dysfunction shown by echocardiography; severe concomitant pulmonary and cardiovascular pathology: chronic obstructive pulmonary disease, bronchial asthma, cerebrovascular accident with severe neurological deficit, abnormal left ventricular ejection fraction (LVEF), permanent atrial fibrillation, severe renal dysfunction. The NEWS2 and SHOCS-COVID scales were used to assess patients' clinical status [4, 5]. CCT was performed to determine the volume of damaged pulmonary parenchyma using MULTI-VOX software. Hematology and biochemical blood tests were performed to determine the concentrations of troponin I and the N-terminal pro-brain natriuretic peptide (NT-proBNP). Echocardiography was performed using a Siemens SC2000 system with in-depth evaluation of the structural parameters (RV diameter, RV wall thickness), the right atrium (RA), hemodynamic parameters (pulmonary artery systolic pressure (PASP), mean pulmonary artery pressure (mPAP), maximum pressure gradient in the pulmonary artery (PA)), and functional parameters (RV systolic and diastolic function, myocardial performance index (Tei), and RV and RA global longitudinal strain (GLS)).

Patients received combined drug therapy for SARS-CoV-2-associated infection following the temporary guidelines of the Ministry of Health of the Russian Federation, version 9 [6].

The study was conducted following the Good Clinical Practice and the Declaration of Helsinki. The study was approved by the Ethics Committee of the N.I. Pirogov Russian National Research Medical University (Minutes No.203 dated January 21, 2021). All subjects signed the informed consent before being inclusion in the study.

According to the study design, patients were divided into 2 groups based on SHOCS-COVID scores: Group A included 16 patients with moderate COVID-19 (from 6 to 9), Group B comprised 30 patients with severe COVID-19 (from 10 to 14) at the time of inclusion.

Findings of clinical examinations and laboratory tests were evaluated twice in both groups: on Day 10±2.5 from the onset of symptoms (Group A10 (n=15) and Group B10 (n=26)) and re-evaluation on Day 17±1.8 the onset of symptoms when stable normothermia for 48 hours was achieved and levels of acute phase reactants (leukocytes, C-reactive protein (CRP), fibrinogen, ferritin) improved (Group A17 (n=15) and Group B17 (n=26), respectively). Due to worsening course and transfer to the intensive care unit, 1 patient in Group A10 and 4 patients in Group B10 were excluded from the study.

The data obtained were processed using IBM SPSS version 26.0. Normality of the distribution of quantitative indicators was estimated using the Shapiro-Wilk test or the Kolmogorov-Smirnov test. Normally distributed quantitative variables were described using the arithmetic means (M) and the standard deviations (SD), and non-normally distributed quantitative variables were expressed using the medians (Me) and the lower and upper quartiles [Q1; Q3]. The categorical data were expressed by the absolute values and the percentages. The two groups were compared by quantitative variables using the Student's t-test or the Welch's t-test (unequal dispersions), or the Mann-Whitney U-test. Percentages were compared in the analysis of four-fold conjugation tables using the Pearson chi-square test or Fisher's exact test. Pearson's chi-squared test was used to compare percentages in the analysis of multifactor contingency tables. The direction and power of the correlations between the two quantitative variables were evaluated using the Spearman's rank coefficient of correlation and the Pearson correlation coefficient. The differences were statistically significant with p value being less than 0.05.

## Results

The analysis of clinical and demographic data found that there were more male patients in Group A10 (86.6%) than in Group B10 (57.7%; p=0.030). Patients in Group B10 were older with a mean age of 58±11 years versus 48±10 years in Group A10 (p=0.004).

In Group B10, patients had more severe clinical status as shown by the severity scores – there were significant differences in the NEWS scores (3 [3; 3] in Group A10 and – 4 [3; 5] in Group B10; p=0.002) and the SHOCS-COVID scores (7 [7; 8] in Group A10 and 12 [11; 13] in Group B10; p<0.001). Group B10 patients had a significantly higher body temperature during the study, 37.9±0.7 °C versus 37.2±0.5 °C in Group A10 (p<0.001); lower arterial oxygen saturation (SaO<sub>2</sub>), 90±3% versus 94±2% in Group A10 (p<0.001).

In Group B10, versus Group A10, significantly higher levels of the main SIR marker CRP (111.38±52.5 mg/l versus 63.85±47.5 mg/l; p=0.006) and lactate dehydrogenase (LDH) (355.8 [318; 396.6] U/l versus 278.0 [239.1; 334.6] U/l (p=0.008), respectively), were observed.

The levels of troponin I were normal in both groups. NT-proBNP exceeded the reference values in Group B10 (155 [82; 415] ng/l) and was 115 [56; 189] ng/l in Group A10, but there were no significant differences between the groups (p=0.166).

The volume of damaged pulmonary parenchyma in Group B10 was greater than in Group A10: ground

glass opacity –  $38.3 \pm 9.6\%$  Group B10 and  $15.6 \pm 10.1\%$  in Group A10 ( $p < 0.001$ ). The volume of pulmonary parenchyma consolidations was also greater in Group B10 ( $0.7 [0.2; 2.6] \%$ ) than in Group A10 ( $0.2 [0.2; 0.6] \%$ ;  $p = 0.043$ ) (Table 1).

There were no significant differences between the groups in the echocardiographic structural and hemodynamic parameters (Table 2). As for the RV functional parameters, higher RV GLS values were observed in Group B10 ( $23.2 \pm 4.8\%$ ) compared to Group A10 ( $19.9 \pm 3.5\%$ ;  $p = 0.048$ ).

On Day  $10 \pm 2.5$  of the disease during high-intensity SIR, patients of Group B10 with severe COVID-19 associated pneumonia (SHOCS-COVID score 10–14) had a greater volume of damaged pulmonary parenchyma and, thus, more severe ARF compared to patients of Group A10 with a moderate course of the disease. Patients of Group B10 had higher RV GLS indicative of RV hyperfunction.

The next stage of our work was a comparative analysis of the parameters in Group A17 ( $n = 15$ ) and Group B17 ( $n = 26$ ) during the regression of SIR intensity. Significant differences were found in the SHOCS-COVID scores: 1 [1; 2] in Group A17 versus 2 [2; 5] in Group B17 ( $p = 0.002$ ). On Day  $17 \pm 1.8$ ,  $\text{SaO}_2$  differed in patients: 95 [95; 96] % in Group A17 and 94 [93; 95] % in Group B17 ( $p < 0.001$ ). There were no significant differences between groups in the NEWS2 scores ( $p = 0.210$ ).

In Group A17 and Group B17, SIR indicators improved. NT-proBNP levels differed significantly between the groups: it was significantly higher in Group B17 compared to Group A17, 147 [92; 271] ng/l versus 84 [30; 107] ng/l respectively ( $p = 0.024$ ). Troponin I remained within the normal range in both groups (Table 3).

Thus, on Day  $17 \pm 1.8$ , patients of Group B 17 had a larger volume of ground glass opacity –  $15.8 [9.8; 24.4] \%$  versus  $3.9 [1.2; 10.9] \%$  in Group A17 ( $p = 0.001$ ) and more severe COVID-19 associated pneumonia – 2 [2; 2] versus 2 [1; 2] in Group A17 ( $p = 0.021$ ).

The comparison of the echocardiographic parameters showed that patients of both groups had preserved LVEF ( $p = 0.456$ ). The assessment of the structural parameters showed that in Group B17 patients had smaller middle segment of the RV –  $3.1 \pm 0.4$  cm versus  $3.5 \pm 0.5$  cm ( $p = 0.006$ ). As for the hemodynamic parameters, patients of Group B17 had higher PASP –  $30 \pm 5$  mm Hg versus  $22.9 \pm 4.2$  mm Hg, but the differences were not significant ( $p = 0.058$ ). The evaluation of the functional parameters demonstrated a significantly lower E/A ratio in Group B17 –  $1.0 [0.98; 1.2]$  versus  $1.4 [1.18; 1.5]$  in Group A17 ( $p = 0.015$ ) and RV  $e'/a'$  –  $0.66 [0.58; 0.85]$

in Group B17 versus  $0.95 [0.79; 1.12]$  in Group A17 ( $p = 0.010$ ). In Groups B17 patients continued to have a higher peak velocity  $s'$  of the tricuspid annulus –  $0.16 [0.14; 0.18]$  m/s versus  $0.13 [0.12; 0.13]$  m/s in Group A17 ( $p < 0.001$ ). There were no significant differences in GLS RV between the groups; it was within the normal range ( $p = 0.801$ ; Table 4).

The relationship between the indicators of RV diastolic function and the findings of laboratory test and clinical examinations on Day  $17 \pm 1.8$  of the disease was of interest. A moderate inverse correlation of the E/A and  $e'/a'$  ratios and the levels of total LDH was identified ( $r = -0.452$ ,  $p = 0.006$  and  $r = -0.334$ ,  $p = 0.050$ , respectively).

**Table 1. Clinical characteristics of patients with COVID-19 associated pneumonia on Day  $10 \pm 2.5$  of the disease**

| Parameter                       | Group A10<br>(n=15)  | Group B10<br>(n=26) | P       |
|---------------------------------|----------------------|---------------------|---------|
| Male, n (%)                     | 13 (86.6)            | 15 (57.7)           | 0.030   |
| Age, years                      | $48 \pm 10$          | $58 \pm 11$         | 0.004   |
| NEWS2 score                     | 3 [3; 3]             | 4 [3; 5]            | 0.002   |
| SHOCS-COVID score               | 7 [7; 8]             | 12 [11; 13]         | < 0.001 |
| Body temperature, °C            | $37.2 \pm 0.5$       | $37.9 \pm 0.7$      | 0.003   |
| SaO <sub>2</sub> , %            | $94 \pm 2$           | $90 \pm 3$          | < 0.001 |
| <b>Laboratory data</b>          |                      |                     |         |
| Leukocytes, 10 <sup>9</sup> /L  | 5.5 [3.5; 9.7]       | 4.8 [4.0; 7.6]      | 0.924   |
| Lymphocytes, 10 <sup>9</sup> /L | $0.9 \pm 0.3$        | $1.0 \pm 0.4$       | 0.597   |
| Platelets, 10 <sup>9</sup> /L   | $218 \pm 65$         | $198 \pm 50$        | 0.288   |
| CRP, mg/L                       | $63.85 \pm 47.5$     | $111.38 \pm 52.5$   | 0.006   |
| LDH, U/L                        | 278.0 [239.1; 334.6] | 355.8 [318; 396.6]  | 0.005   |
| Ferritin, g/L                   | $636 \pm 323$        | $822 \pm 505$       | 0.243   |
| Procalcitonin, ng/mL            | 0.17 [0.12; 0.23]    | 0.09 [0.05; 0.14]   | 0.196   |
| NT-proBNP, ng/mL                | 115 [56; 189]        | 155 [82; 415]       | 0.166   |
| Fibrinogen, g/L                 | $7.2 \pm 1.6$        | $6.8 \pm 1.3$       | 0.328   |
| D-dimer, ng/mL                  | 168 [136; 203]       | 274 [182; 493]      | 0.096   |
| Troponin I, ng/mL               | < 0.02               | < 0.02              | > 0.05  |
| <b>Lung damage</b>              |                      |                     |         |
| Stage on CT                     | 2 [1; 2]             | 2 [2; 3]            | < 0.001 |
| Healthy tissue, %               | 83.2 [75.5; 88.1]    | 49.1 [38.5; 64.4]   | < 0.001 |
| Ground glass opacity, %         | $15.6 \pm 10.1$      | $38.3 \pm 9.6$      | < 0.001 |
| Dense ground glass opacity, %   | 2.1 [1.1; 4.1]       | 3.3 [1.7; 7.9]      | 0.136   |
| Consolidations, %               | 0.2 [0.2; 0.6]       | 0.7 [0.2; 2.6]      | 0.043   |
| Vessels                         | $6.4 \pm 1.1$        | $6.0 \pm 1.7$       | 0.653   |

The data are presented as  $M \pm SD$  or  $Me [Q1; Q3]$  depending on the type of distribution. NEWS2, the National Early Warning Score; SHOCS-COVID, Symptomatic Hospital and Outpatient Clinical Score for COVID-19; SaO<sub>2</sub>, oxygen saturation of the blood; CRP, C-reactive protein; LDH, lactate dehydrogenase; NT-proBNP, N-terminal pro-brain natriuretic peptide; CT, computed tomography.

**Table 2. Echocardiographic characteristics of patients with COVID-19 associated pneumonia on Day 10±2.5 of the disease**

| Parameter                          | Group A10<br>(n=15) | Group B10<br>(n=26) | p     |
|------------------------------------|---------------------|---------------------|-------|
| LVEF, %                            | 62 [60; 65]         | 60 [57; 64]         | 0.178 |
| RV, parasternal view, mm           | 3.0±0.4             | 2.9±0.3             | 0.293 |
| Basal RV segment, apical view, mm  | 3.8±0.5             | 3.8±0.4             | 0.809 |
| Middle RV segment, apical view, mm | 3.1±0.3             | 3.1±0.5             | 0.998 |
| RV length, apical view, cm         | 7.1±1.1             | 7.0±1.1             | 0.764 |
| RV free wall thickness, cm         | 0.6 [0.5; 0.7]      | 0.5 [0.5; 0.6]      | 0.287 |
| Maximum PA gradient, m/s           | 2.1 [1.8; 2.9]      | 2.0 [1.8; 2.7]      | 0.807 |
| PASP, mm Hg                        | 31.3 [29.5; 32.3]   | 30.3 [26; 32.6]     | 0.535 |
| mPAP, mm Hg                        | 14.8 [10.2; 22.2]   | 16.2 [12.2; 23.3]   | 0.342 |
| TAPSE, cm                          | 2.6±0.4             | 2.4±0.3             | 0.130 |
| RV ESA ind., mm <sup>2</sup>       | 5.4 [4.2; 6.1]      | 5.6 [4.2; 6.2]      | 0.811 |
| RV EDA ind., mm <sup>2</sup>       | 10.4 [8.7; 11.8]    | 10.5 [9.0; 11.1]    | 0.870 |
| RV FAC, %                          | 44.4±6.1            | 47.7±9.3            | 0.244 |
| RV e', m/s                         | 0.13±0.02           | 0.14±0.03           | 0.326 |
| RV a', m/s                         | 0.15±0.03           | 0.16±0.04           | 0.209 |
| RV s', m/s                         | 0.14 [0.14; 0.15]   | 0.15 [0.12; 0.16]   | 0.485 |
| RV E, m/s                          | 0.53±0.13           | 0.55±0.10           | 0.717 |
| RV A, m/s                          | 0.49±0.09           | 0.47±0.10           | 0.533 |
| RV E/A                             | 1.12±0.32           | 1.19±0.3            | 0.490 |
| RV E/e'                            | 4.07±0.75           | 3.99±0.91           | 0.776 |
| RV DT, m/s                         | 196.4±40.1          | 201±55              | 0.775 |
| Tei (PW)                           | 0.18±0.08           | 0.22±0.08           | 0.235 |
| Tei (TDI)                          | 0.31±0.09           | 0.31±0.13           | 0.990 |
| RV e'/a'                           | 0.8 [0.76; 1.05]    | 0.8 [0.7; 0.95]     | 0.308 |
| RV GLS, %                          | 19.9±3.5            | 23.2±4.8            | 0.048 |
| RA GLS, %                          | 24.0 [22.1; 35.7]   | 33.4 [24.2; 38.2]   | 0.268 |

The data are presented as M±SD or Me [Q1; Q3] depending on the type of distribution. LVEF, left ventricular ejection fraction; RV, right ventricle; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; mPAP, mean pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; ind., index; ESA, end-systolic area; EDA, end-diastolic area; FAC, fractional area change; PW – pulse-wave Doppler; TDI, tissue Doppler imaging; GLS, global longitudinal strain; RA, right atrium.

The levels of total LDH were correlated with the volume of ground glass opacity ( $r=0.361$ ;  $p=0.002$ ) and dense ground glass opacity ( $r=0.361$ ;  $p=0.002$ ). The data obtained allow discussing the possible formation of RV diastolic dysfunction in patients with a large volume of damaged pulmonary parenchyma.

On Day 17±1.8 of the disease, the SIR intensity regressed in both groups. There was a positive trend in lung damage in both groups. Group B17 patients continued to have a larger volume of damaged

pulmonary parenchyma and moderate respiratory failure. According to echocardiography, LVEF remained normal. There was a significant decrease in a number of indicators characterizing the formation of RV diastolic dysfunction [7].

## Discussion

Following the study objective, the condition of the right heart was assessed in patients with COVID-19 associated pneumonia of varying severity on Day 10±2.5 and Day 17±1.8 during regression of SIR intensity. At each stage of the study, patients of both groups differed in the severity and volume of pulmonary

**Table 3. Clinical characteristics of patients with COVID-19 associated pneumonia on Day 17±1.8 of the disease**

| Parameter                       | Group A17<br>(n=15)  | Group B17<br>(n=26)  | p       |
|---------------------------------|----------------------|----------------------|---------|
| <b>Clinical status</b>          |                      |                      |         |
| NEWS2 score                     | 1 [1; 1]             | 1 [1; 2]             | 0.210   |
| SHOCS-COVID, score              | 1 [1; 2]             | 2 [2; 5]             | 0.002   |
| SaO <sub>2</sub> , %            | 96 [95; 96]          | 94 [93; 95]          | < 0.001 |
| <b>Laboratory data</b>          |                      |                      |         |
| Leukocytes, 10 <sup>9</sup> /L  | 8.6±3.3              | 8.7±4.3              | 0.950   |
| Lymphocytes, 10 <sup>9</sup> /L | 1.8 [1.1; 2.5]       | 1.8 [0.9; 2.2]       | 0.179   |
| Platelets, 10 <sup>9</sup> /L   | 273 [250; 326]       | 267 [211; 337]       | 0.867   |
| CRP, mg/L                       | 3.8±2.6              | 2.7±1.8              | 0.094   |
| LDH, U/L                        | 251.4 [207.9; 304.4] | 271.1 [235.9; 356.8] | 0.102   |
| Ferritin, g/L                   | 685 [487; 914]       | 632 [457; 1012]      | 0.988   |
| NT-proBNP, ng/mL                | 84 [30; 107]         | 147 [92; 271]        | 0.024   |
| Fibrinogen, g/L                 | 4.2±1.0              | 3.1±0.9              | < 0.001 |
| D-dimer, ng/mL                  | 179 [156; 210]       | 173 [115; 510]       | 0.920   |
| Troponin I, ng/mL               | < 0.2                | < 0.2                | > 0.05  |
| <b>Lung damage</b>              |                      |                      |         |
| Stage on CT                     | 2 [1; 2]             | 2 [2; 2]             | 0.021   |
| Healthy tissue, %               | 95.6 [84.0; 97.9]    | 83 [72.9; 88.8]      | 0.002   |
| Ground glass opacity, %         | 3.9 [1.2; 10.9]      | 15.8 [9.8; 24.4]     | 0.001   |
| Dense ground glass opacity, %   | 0.2 [0.1; 0.9]       | 1.0 [0.2; 2.2]       | 0.082   |
| Consolidations, %               | 0.1 [0.1; 0.2]       | 0.2 [0.1; 0.6]       | 0.273   |
| Vessels                         | 6.0 [5.6; 6.5]       | 6.7 [5.6; 7.7]       | 0.162   |

The data are presented as M±SD or Me [Q1; Q3] depending on the type of distribution. NEWS2, the National Early Warning Score; SHOCS-COVID, Symptomatic Hospital and Outpatient Clinical Score for COVID-19; SaO<sub>2</sub>, oxygen saturation of the blood; CRP, C-reactive protein; LDH, lactate dehydrogenase; NT-proBNP, N-terminal pro-brain natriuretic peptide; CT, computed tomography.

parenchyma damage: in Group B10 and Group B17, patients had a larger volume of ground glass opacity, dense ground glass opacity, and consolidations. The comparative analysis of the structural and hemodynamic parameters of the right heart showed no significant differences on Day 10 $\pm$ 2.5 of the disease with high SIR intensity. However, RV GLS was higher in patients with more severe COVID-19associated pneumonia, which we considered consistent with RV hyperfunction during high SIR intensity.

On Day 17 $\pm$ 1.8 of the disease, as the general condition of patients improved, SIR intensity regressed, and a positive trend was observed on CT, changes in structural and functional indicators were identified during the analysis of echocardiographic parameters: in patients of Group B17, the mean RV diameter decreased, there was a trend to RV diastolic dysfunction, and RV GLS was normal and did not significantly differ between the groups.

According to the Russian registry ACTIV (n=2,256), which included patients with the history of COVID-19, new cases of chronic heart failure were registered in 0.8% of patients in the first 3 months of follow-up and 1.3% within 4–6 months of follow-up [8]. Thus, it is important to monitor the state of the cardiovascular system in patients both during the maximum intensity of SIR and later during its regression.

Günay et al. (2021) [9] obtained interesting findings in a comparative analysis of echocardiographic parameters in patients with the history of moderate-to-severe COVID-19 (n=51) 30 days after the discharge from hospital. Healthy volunteers were included in the study as controls (n=32). Patients with the history of COVID-19 had significantly higher RV EDA and ESA, basal and mean RV diameters compared to the control group (p<0.001). The authors focused on such functional indicators as lower RV GLS in the discharged patients – 15.7 [–12.6; –18.7] % versus –18.1 [–14.8; –21] % in the control group (p=0.011). There was a positive correlation between the main SIR marker CRP and RV GLS (r=0.612; p<0.001), but the SIR markers were within normal range. The examination of RV diastolic function showed higher rate of late diastolic tricuspid flow A in patients with the history of COVID-19–58 $\pm$ 11 versus 44 $\pm$ 10 in the controls (p<0.001). Thus, in the above study, the authors focused on changes in the indicators of the structural, hemodynamic, and functional parameters of the right heart 30 days after COVID-19associated pneumonia.

The results of this study also showed that RV diastolic function changed during SIR regression. At the same

**Table 4.** Echocardiographic characteristics of patients with COVID-19associated pneumonia on Day 17 $\pm$ 1.8 of the disease

| Parameter                          | Group A17<br>(n=15) | Group B17<br>(n=26) | p       |
|------------------------------------|---------------------|---------------------|---------|
| LVEF, %                            | 61 [59; 63]         | 60 [59; 62]         | 0.456   |
| RV, parasternal view, cm           | 3.0 $\pm$ 0.4       | 2.8 $\pm$ 0.3       | 0.153   |
| Basal RV segment, apical view, cm  | 3.9 $\pm$ 0.3       | 3.7 $\pm$ 0.3       | 0.369   |
| Middle RV segment, apical view, cm | 3.5 $\pm$ 0.5       | 3.1 $\pm$ 0.4       | 0.006   |
| RV length, apical view, cm         | 6.9 $\pm$ 0.8       | 6.8 $\pm$ 0.7       | 0.738   |
| RV free wall thickness, cm         | 0.5 [0.5; 0.6]      | 0.6 [0.6; 0.6]      | 0.105   |
| Maximum PA gradient, m/s           | 2.3 $\pm$ 0.6       | 2.7 $\pm$ 0.8       | 0.131   |
| PASP, mm Hg                        | 22.9 $\pm$ 4.2      | 30 $\pm$ 5          | 0.058   |
| mPAP, mm Hg                        | 15.7 [10.7; 17.2]   | 16.9 [12.1; 20.0]   | 0.155   |
| TAPSE, cm                          | 2.2 $\pm$ 0.5       | 2.4 $\pm$ 0.4       | 0.216   |
| RV ESA ind., mm <sup>2</sup>       | 5.5 [4.4; 6.4]      | 5.2 [4.6; 5.6]      | 0.495   |
| RV EDA ind., mm <sup>2</sup>       | 11.2 [8.7; 13.0]    | 9.8 [8.7; 10.9]     | 0.420   |
| RV FAC, %                          | 44.1 $\pm$ 7.3      | 45.7 $\pm$ 9.0      | 0.620   |
| RV e', m/s                         | 0.11 [0.10; 0.13]   | 0.12 [0.11; 0.13]   | 0.505   |
| RV a', m/s                         | 0.13 [0.12; 0.14]   | 0.17 [0.15; 0.17]   | < 0.001 |
| RV s', m/s                         | 0.13 [0.12; 0.13]   | 0.16 [0.14; 0.18]   | < 0.001 |
| RV E, m/s                          | 0.55 $\pm$ 0.12     | 0.50 $\pm$ 0.06     | 0.208   |
| RV A, m/s                          | 0.41 $\pm$ 0.07     | 0.47 $\pm$ 0.09     | 0.039   |
| RV E/A                             | 1.4 [1.18; 1.5]     | 1.0 [0.98; 1.2]     | 0.015   |
| RV E/e'                            | 4.1 [3.5; 4.9]      | 4.2 [3.8; 5.0]      | 0.817   |
| RV DT, m/s                         | 200 [176; 225]      | 215 [171; 268]      | 0.531   |
| Tei (PW)                           | 0.20 $\pm$ 0.09     | 0.21 $\pm$ 0.09     | 0.772   |
| Tei (TDI)                          | 0.30 [0.27; 0.34]   | 0.30 [0.20; 0.39]   | 0.528   |
| RV e'/a'                           | 0.95 [0.79; 1.12]   | 0.66 [0.58; 0.85]   | 0.010   |
| RV GLS, %                          | 22.4 $\pm$ 3.6      | 22.9 $\pm$ 4.2      | 0.801   |
| RA GLS, %                          | 32.7 $\pm$ 6.0      | 33.5 $\pm$ 6.0      | 0.784   |

The data are presented as M $\pm$ SD or Me [Q1; Q3] depending on the type of distribution. LVEF, left ventricular ejection fraction; RV, right ventricle; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; mPAP, mean pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; ind., index; ESA, end-systolic area; EDA, end-diastolic area; FAC, fractional area change; PW – pulse-wave Doppler; TDI, tissue Doppler imaging; GLS, global longitudinal strain; RA, right atrium.

time, the indicators of RV diastolic function and total LDH were correlated in patients with COVID-19associated pneumonia: the indicators of RV diastolic function worsened as with the volume of damaged pulmonary parenchyma increased. In our previous study [3], the correlation between the SIR markers and RV GLS was shown, but the levels of SIR markers and

RV GLS were investigated at the time of maximum SIR intensity.

Yaroslavskaia et al. (2022) [10] studied changes in the echocardiographic parameters of LV and RV in patients with the history of COVID-19-associated pneumonia (n=116) 3 and 12 months after the discharge from hospital. When studying several parameters of the right heart, the authors revealed multidirectional changes in RV geometry – RV length and anteroposterior dimensions decreased, but basal RV diameter increased, which increased RV sphericity index. Thickness of RV free wall increased but did not reach the values corresponding to hypertrophy. Hemodynamic parameters worsened: PA diameter and PASP increased. As for the functional indicators, TAPSE and RV FAC normalized. The data obtained confirmed hemodynamic changes in the right heart in the long term after COVID-19.

We studied RV parameters at an earlier stage of the disease. Characteristic features of RV geometry were observed in patients with severe COVID-19-associated pneumonia in the early stages of the disease – smaller mean RV diameter (significant differences), smaller basal RV diameter and length, thicker RV free wall (insignificant differences).

On the one hand, significant changes in the RV diastolic function during SIR regression, the identified correlation of these indicators with the volume of lung damage allow discussing the findings as the debut of RV

diastolic dysfunction in patients with severe COVID-19-associated pneumonia. On the other hand, it is premature to interpret the obtained changes in terms of the formation of persistent diastolic dysfunction, since the indicators were at the lower threshold of normal range.

Our study had some limitations. They included a small sample of patients, short follow-up period, and inability to conduct advanced echocardiography of the right heart in patients transferred to the intensive care unit (lack of equipment).

## Conclusion

Changes in the indicators reflecting the formation of right ventricular diastolic dysfunction were observed in patients with severe COVID-19-associated pneumonia during the regression of the systemic inflammatory response intensity. Attention should be paid to evaluating right ventricular diastolic function in patients with COVID-19-associated pneumonia over time as early as during hospital stay.

## Funding

*No funding was received for this study.*

*No conflict of interest is reported.*

**The article was received on 10/04/2022**

## REFERENCES

1. Ammirati E, Wang DW. SARS-CoV-2 inflames the heart. The importance of awareness of myocardial injury in COVID-19 patients. *International Journal of Cardiology*. 2020;311:122–3. DOI: 10.1016/j.ijcard.2020.03.086
2. Dweck MR, Bularga A, Hahn RT, Bing R, Lee KK, Chapman AR и др. Global evaluation of echocardiography in patients with COVID-19. *European Heart Journal Cardiovascular Imaging*. 2020;21(9):949–58. DOI: 10.1093/ehjci/jeaa178
3. Poteshkina N.G., Krylova N.S., Karasev A.A., Nikitina T.A., Svanadze A.M., Beloglazova I.P. и др. Right heart condition in patients with COVID-19 pneumonia. *Russian Journal of Cardiology*. 2021;26(11):66–72. [Russian: Потешкина Н.Г., Крылова Н.С., Карасев А.А., Никитина Т.А., Сванадзе А.М., Белоглазова И.П. и др. Состояние правых отделов сердца у пациентов с COVID-19-ассоциированной пневмонией. *Российский кардиологический журнал*. 2021;26(11):66–72]. DOI: 10.15829/1560-4071-2021-4733
4. Carr E, Bendayan R, Bean D, Stammers M, Wang W, Zhang H и др. Evaluation and improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study. *BMC Medicine*. 2021;19(1):23. DOI: 10.1186/s12916-020-01893-3
5. Mareev V.Yu., Begrambekova Yu.L., Mareev Yu.V. How evaluate results of treatment in patients with COVID-19? Symptomatic Hospital and Outpatient Clinical Scale for COVID-19 (SHOCS-COVID). *Kardiologiia*. 2020;60(11):35–41. [Russian: Мареев В.Ю., Бергамбекова Ю.Л., Мареев Ю.В. Как оценивать результаты лечения больных с новой коронавирусной инфекцией (COVID-19)? Шкала Оценки Клинического Состояния (ШОКС–КОВИД). *Кардиология*. 2020;60(11):35–41]. DOI: 10.18087/cardio.2020.11.n1439
6. Ministry of Health of Russian Federation. Temporary methodical recommendations. Prevention, diagnosis and treatment of new coronavirus infection (COVID-2019). Version 9 (26.10.2020). Av. at: [https://static-0.minzdrav.gov.ru/system/attachments/attaches/000/052/548/original/%D0%9C%D0%A0\\_COVID-19\\_%28v.9%29.pdf?1603730062](https://static-0.minzdrav.gov.ru/system/attachments/attaches/000/052/548/original/%D0%9C%D0%A0_COVID-19_%28v.9%29.pdf?1603730062). 2020 г. [Russian: Министерство здравоохранения РФ. Временные методические рекомендации «Профилактика, диагностика и лечение новой коронавирусной инфекции (COVID-19)». Версия 9 (26.10.2020). Доступно на: [https://static-0.minzdrav.gov.ru/system/attachments/attaches/000/052/548/original/%D0%9C%D0%A0\\_COVID-19\\_%28v.9%29.pdf?1603730062](https://static-0.minzdrav.gov.ru/system/attachments/attaches/000/052/548/original/%D0%9C%D0%A0_COVID-19_%28v.9%29.pdf?1603730062)]
7. Zaidi A, Knight DS, Augustine DX, Harkness A, Oxborough D, Pearce K и др. Echocardiographic Assessment of the Right Heart in Adults: A Practical Guideline from the British Society of Echocardiography. *Echo Research & Practice*. 2020;7(1):G19–41. DOI: 10.1530/ERP-19-0051
8. Arutyunov G.P., Tarlovskaya E.I., Arutyunov A.G., Belenkov Yu.N., Konradi A.O., Lopatin Yu.M. и др. Clinical features of post-COVID-19 period. Results of the international register “Dynamic analysis of comorbidities in SARS-CoV-2 survivors (AKTIV SARS-CoV-2)”. Data from 6-month follow-up. *Russian Journal of Cardiology*. 2021;26(10):86–98. [Russian: Арутюнов Г.П., Тарловская Е.И., Арутюнов А.Г., Беленков Ю.Н., Конради А.О., Лопатин Ю.М. и др. Клинические особенности постковидного периода. Ре-

- зультаты международного регистра «Анализ динамики коморбидных заболеваний у пациентов, перенесших инфицирование SARS-CoV-2 (АКТИВ SARSCoV-2)». Предварительные данные (6 месяцев наблюдения). Российский кардиологический журнал. 2021;26(10):86-98]. DOI: 10.15829/1560-4071-2021-4708
9. Günay N, Demiröz Ö, Kahyaoglu M, Başlılar Ş, Aydın M, Özer MÇ и др. The effect of moderate and severe COVID-19 pneumonia on short-term right ventricular functions: a prospective observational single pandemic center analysis. *The International Journal of Cardiovascular Imaging*. 2021;37(6):1883–90. DOI: 10.1007/s10554-021-02171-w
  10. Yaroslavskaia E.I., Krinochkin D.V., Shirokov N.E., Gorbatenko E.A., Krinochkina I.R., Gulyaeva E.P. и др. Comparison of clinical and echocardiographic parameters of patients with COVID-19 pneumonia three months and one year after discharge. *Kardiologiia*. 2022;62(1):13–23. [Russian: Ярославская Е.И., Криночкин Д.В., Широков Н.Е., Горбатенко Е.А., Криночкина И.Р., Гульяева Е.П. и др. Сравнение клинических и эхокардиографических показателей пациентов, перенесших пневмонию COVID-19, через три месяца и через год после выписки. *Кардиология*. 2022;62(1):13-23]. DOI: 10.18087/cardio.2022.1.n1859