

Original article

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sST2 and morphofunctional parameters of the left ventricle in patients with coronary artery disease and chronic heart failure after COVID-19

Sergey S. Fateev¹ , Ivan M. Ryzhkov² , Vladimir K. Fedulov¹ ,
Elena V. Kovalenko² , Ludmila I. Markova² , Olga L. Belaya²  
 olgabelaya64@gmail.com

¹Central Military Clinical Hospital, Moscow, Russia

²Moscow State University of Medicine and Dentistry, Moscow, Russia

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Abstract:

Objective: to assess the concentration of the sST2 biomarker and its relationship with the morphological and functional parameters of the LV myocardium in patients with coronary artery disease (CAD) and functional class (FC) I–III chronic heart failure (CHF), who survived COVID-19 or did not experience it.

Materials and Methods. We examined 100 patients (66 males) of median (Me) age of 65 [63; 67] years with stable CAD and FC I–III CHF (sensu New York Heart Association), distributed among two groups depending on the presence of COVID-19 in their anamneses. Along with the conventional clinical examination, the concentration of serum sST2 was determined via ELISA.

Results. We revealed that in patients surviving COVID-19 (Group 1), the sST2 level was 38.4 [35.5; 44.8] ng/mL, while in the comparison group (Group 2), it amounted to 29.63 [27.9; 32.7] ng/mL ($p < 0.001$). In Group 1, the end-diastolic volume and the end-systolic volume of the left ventricle (LV) significantly exceeded values of these parameters in Group 2 ($p = 0.004$ and $p = 0.02$, respectively) and amounted to 118.2 [107.5; 166.5] mL and 44.1 [35.0; 58.1] mL, correspondingly, in Group 1 and 107.5 [92.4; 129.5] mL and 37.9 [29.5; 47.4] mL in Group 2. The number of patients with grade 2 diastolic dysfunction (DD) in Group 1 (18–33.9%) significantly exceeded that in the comparison group (7%–14.9%). Changes in global longitudinal strain (GLS) of the LV in Group 1 (–15.6 [–20.8; –13.8] %) were more pronounced than in the comparison group (–19.9 [–21.5; –16.3] %), $p = 0.018$.

Conclusion. CAD patients with FC I–III CHF, who survived COVID-19, had statistically significantly higher serum sST2 concentration, more pronounced LV DD, and greater LV GLS.

Keywords: coronary artery disease, chronic heart failure, COVID-19, sST2.

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Introduction

COVID-19 still remains an important global issue, especially for patients with severe comorbidities [1]. Chronic heart failure (CHF) is among the most common comorbidities of COVID-19. According to the International registry “Dynamic Analysis of Comorbidities in SARS-CoV-2 Survivors (AKTIV SARS-CoV-2)” and the Cochrane Database of Systematic Reviews (CDSR), CHF is detected in 6.5–16.3% of patients hospitalized with COVID-19 [2, 3].

Recent data suggested that cardiac damage in COVID-19 is often accompanied by diastolic dysfunction (DD) [4]. Heart failure with preserved ejection fraction (HFpEF) is common among individuals hospitalized with COVID-19. Patients with arterial hypertension (AH), type 2 diabetes mellitus (T2DM), obesity, chronic kidney disease (CKD), left ventricular hypertrophy (LVH) and DD, even in the absence of obvious clinical signs of HFpEF, tend to experience a more severe course of COVID-19, and their prognosis is aggravated due to the development of adverse cardiovascular events.

In the case of COVID-19, inflammation is among the key mechanisms for the development of HFpEF [5]. SARS-CoV-2 can cause HFpEF and aggravate the condition of patients with subclinical DD, both as a result of direct damage by the virus and due to disorders in immune mechanisms and functioning of cytokines. The systemic proinflammatory condition generated by the cytokine storm ultimately leads to more frequent left ventricle (LV) remodeling and the development of HFpEF [6].

Along with the clinical picture and objective examination results, echocardiography (EchoCG) data and natriuretic peptide biomarkers are employed to more accurately assess the presence, severity and treatment tactics of CHF, especially in the case of HFpEF. In the last decade, the role of new biomarkers, in particular the tumorigenicity suppressor ST2, has been studied in patients with coronary artery disease (CAD) complicated by CHF. The soluble form of ST2, sST2, reflects the process of ventricular remodeling and myocardial fibrosis. As a member of the interleukin family, it is a dual cardiac inflammation marker for diagnostic and

prognostic assessment in patients with CHF and COVID-19. It is capable of detecting subclinical HF at an early stage of the disease [7].

Objective: to assess the concentration of the sST2 biomarker and its relationship with the morphofunctional parameters of the LV myocardium in patients with CAD and CHF of functional classes (FC) I-III after COVID-19 vs. those who did not experience COVID-19.

Materials and Methods

The study was approved by the interuniversity Ethics Committee on November 25, 2021 (protocol No. 10-21). Prior to the inclusion in the study, written informed consent was obtained from all participants. We examined 100 patients (66 men, 34 women) aged from 45 to 70 years; median (Me) age of 65 [63; 67] years. All participants had CAD (angina pectoris/postinfarction cardiosclerosis), CHF of FC I-III sensu New York Heart Association (NYHA). Their either survived COVID-19 3–6 months ago or did not experience it. The diagnoses of CAD and CHF were established on the basis of the clinical recommendations by the Russian Federation Ministry of Healthcare valid at the time of the examination. Exclusion criteria were acute myocardial infarction, acute cerebrovascular accident, acute thrombosis of any location less than 6 months before the onset of the study, and the presence of malignant neoplasms. Patients who refused to continue the examination were excluded from the study. All study subjects were distributed among two groups depending on the presence of a history of COVID-19. Group 1 included 53 patients (32 men, 21 women) who survived COVID-19; Me age of 65 [61; 68] years. Group 2 (comparison group) comprised 47 patients (34 men, 13 women), who did not experience COVID-19; Me age of 66 [64; 67] years. A group of 20 apparently healthy individuals (10 men and 10 women) with values of sST2 indicative of their healthy status and Me age of 61 [57; 64] years constituted the control for our study. The patients received basic treatment in accordance with current clinical recommendations.

Patients of both study groups did not differ significantly from each other in terms of main clinical and demographic indicators: 22.6% of patients in Group 1 vs. 14.9% in Group 2 ($p=0.324$) smoked; 9.4% and 6.4%, respectively, suffered from FC I angina pectoris ($p=0.575$); 58.5% and 68.1%, correspondingly, were diagnosed with FC II angina pectoris ($p=0.321$); 5.7% vs. 8.5% of patients, respectively, had FC III angina pectoris ($p=0.577$); 34 and 29.8% ($p=0.655$) suffered acute myocardial infarction, and 7.5 and 6.4% ($p=0.820$) from acute cerebrovascular accident. A history of angioplasty was present in 39.6% and 38.3% ($p=0.892$), coronary artery bypass grafting in 7.5% and 2.1% ($p=0.214$), atrial fibrillation in 37.7% and 29.8% ($p=0.402$) of patients in Groups 1 and 2, respectively. AH was characteristic of 98% of patients in Group 1 and 100% of patients in Group 2 ($p=0.344$). T2DM was present in 62.3% and 68.1% ($I=0.542$), chronic kidney disease in 64% and 68% ($p=0.678$), obesity in 47% and 34% ($p=0.182$) of patients in Groups 1 and 2, correspondingly. FC I CHF was diagnosed in 37.7% and 38.3% ($p=0.954$), FC II CHF in 43.4% and 48.9% ($p=0.579$), FC III CHF in 18.9% and 12.8% ($p=0.577$) in Groups 1 and 2, respectively.

The standard examination included an assessment of the clinical condition of a patient with CHF, clinical and biochemical blood tests, and a urine test. Serum sST2

concentrations were quantified by enzyme-linked immunosorbent assay (ELISA) using the Presage® ST2 Assay Kit. Electrocardiography (ECG), a 6-minute walk test, and EchoCG were performed to determine the main structural and functional parameters of the heart and the severity of DD. Global longitudinal strain (GLS) of the LV was identified by the speckle tracking method. The studies were carried out in the laboratory and Department of Functional Diagnostics at the Central Military Clinical Hospital.

Statistical processing of the obtained results was carried out using IBM SPSS Statistics v. 12 software. Data were presented as median (Me) and interquartile range (Q25 - Q75). To test statistical hypotheses when analyzing quantitative indicators, the Mann–Whitney U test was employed. When analyzing qualitative characteristics by contingency tables, Pearson's chi-squared test was used. Searching for relationships between variables, we applied the correlation analysis to calculate Spearman's rank correlation coefficients. The significance of differences was assumed at $p<0.05$.

Results

The main parameters of clinical and laboratory examination of patients included in the study are presented in *Table 1*. It is clear that in patients surviving COVID-19, the levels of sST2 biomarker, N-terminal fragment of the brain natriuretic peptide precursor (NT-proBNP), glucose, and creatinine were significantly higher (while the results of the 6-minute walk and glomerular filtration rate were lower) than those in the comparison group.

To assess the structural and functional parameters of the LV myocardium, EchoCG was performed, the results of which are shown in *Table 2*: between the group of patients who had COVID-19 and the comparison group, we detected significant differences in the indicators of left atrium volume (LAV), LA volume index (LAVI), end-diastolic and end-systolic volumes (EDV and ESV) of the LV, end-diastolic and end-systolic diameters (EDD and ESD) of the LV (*Table 2*). Patients who survived COVID-19 had exhibited higher values of LV volumetric parameters. Impaired LV diastolic function was observed in every patient of both groups, and the number of patients with grade 2 DD in Group 1 ($n=18$) significantly exceeded that in the comparison group ($n=7$). The differences between E, E/A, E/e', and GLS were also statistically significant.

Correlation analysis yielded close relationships between the level of sST2 biomarker, NT-proBNP and various EchoCG indicators (*Table 3*). Statistically significant correlations of moderate strength were identified in both study groups between sST2, NT-proBNP and volumetric characteristics of the LV myocardium, in particular LAV, LAVI, LV ESV, LV EDV, as well as left ventricular mass index (LVMI) and left ventricular ejection fraction (LVEF). It is noteworthy that the Spearman's rank correlation coefficients in the group of patients who survived COVID-19 had somewhat higher values. When assessing the relationship of biomarkers with the severity of LV DD, we noted that sST2 correlated more closely with E, E/A and E/e' than with NT-proBNP in all patients included in the study. In Group 1 (COVID-19 survivors), a medium strength relationship was revealed between sST2 and E/e'. There was a direct correlation

between GLS, sST2 and NT-proBNP parameters, which was stronger in the group of COVID-19 survivors (Table 3).

Table 1. Clinical and laboratory parameters of patients included in the study, Me [Q25; Q75]

Parameter	Group		P-value
	1 (CAD+CHF+COV ID-19) (n=53)	2 (CAD+CHF) (n=47)	
Scale for assessing the clinical condition of a patient with CHF, points	5 [3; 6]	5 [3; 6]	0.870
6-minute walk test, m	385 [310; 430]	410 [380; 440]	0.049
sST2, ng/mL	38.4 [35.5; 44.8]	29.6 [27.9; 32.7]	0.001
NT-proBNP, pg/mL	680 [470; 1050]	430 [320; 680]	0.001
Galectin-3, ng/mL	19.9 [12.1; 28.4]	15.8 [11.7; 22.3]	0.035
Low-density lipoprotein cholesterol, mmol/L	2.4 [1.7; 3.3]	2.5 [1.9; 3.2]	0.365
Glucose, mmol/L	6.3 [5.8; 6.8]	6.1 [5.3; 6.4]	0.007
Creatinine, μ mol/L	98.5 [90; 126]	90.3 [79.8; 108]	0.038
Glomerular filtration rate (CKD-EPI), mL/min/1.73 m ²	61.4 [48.5; 72.6]	67.1 [54.5; 83.1]	0.037

CAD, coronary artery disease; CHF, chronic heart failure; sST2, soluble interleukin 1 receptor-like 1; NT-proBNP, N-terminal fragment of the brain natriuretic peptide precursor.

Table 2. Echocardiography parameters of patients included in the study, Me [Q25; Q75]

Parameter	Group 1 (n=53)	Group 2 (n=47)	P-value
LAV, mL	67 [56; 78]	58 [48; 70]	0.02*
LAVI, mL/m ²	32 [29.2; 34.6]	29.2 [24.2; 34.2]	0.04*
IVS, cm	1.2 [1.2; 1.4]	1.4 [1.3; 1.5]	0.09
PLVW, cm	1.2 [1.1; 1.3]	1.2 [1.1; 1.4]	0.58
LV EDD, cm	5.0 [4.8; 5.8]	4.8 [4.5; 5.4]	0.02
LV ESD, cm	3.3 [3.0; 3.7]	3.4 [3.0; 3.7]	0.02
LV EDV, mL	118.2 [107.5; 166.6]	107.5 [92.5; 129.5]	0.004
LV ESV, mL	44.1 [35.0; 58.1]	35.0 [23.0; 52.0]	0.02
LVMI, g/m ²	153.7 [126.7; 169.8]	133.5 [116.3; 178.9]	0.32
LVEF, %	55 [46; 57]	55.5 [52; 58]	0.14
Peak E-wave velocity, cm/s	68 [59.9; 88.4]	59.9 [52.3; 68.4]	0.001
Peak A-wave velocity, cm/s	79.4 [77.0; 87.6]	74.4 [67.0; 81.0]	0.001
E/A	0.78 [0.7; 1.2]	0.8 [0.7; 1.1]	0.01
E/E'	9.8 [8.2; 13.9]	8.6 [7.5; 10.3]	0.01
GLS, %	-15.6 [-20.8; -13.8]	-19.9 [-21.5; -18.3]	0.018

LAV, left atrium volume; LAVI, left atrium volume index; IVS, interventricular septum thickness; PLVW, posterior left ventricular wall thickness; LV EDD, left ventricular end-diastolic diameter; LV ESD, left ventricular end-systolic diameter; LV EDV, left ventricular end-diastolic volume; LV ESV, left ventricular end-systolic volume; LVMI, left ventricular mass index; LVEF, left ventricular ejection fraction; E/A, ratio of peak E-wave velocity to peak A-wave velocity; E/E', ratio of mitral to myocardial early velocities; GLS, global longitudinal strain of the LV; *p<0.05.

Table 3. Correlation between the levels of sST2, NT-proBNP and echocardiography parameters in the study groups

Parameter	Spearman's rank correlation coefficient					
	sST2			NT-proBNP		
	Group		All patients (n=100)	Group		All patients (n=100)
	1 (n=53)	2 (n=47)		1 (n=53)	2 (n=47)	
LAV, mL	0.54*	0.41*	0.50*	0.46*	0.34*	0.46*
LAVI, mL/m ²	0.45*	0.34*	0.42*	0.4*	0.30*	0.39*
IVS, cm	0.14	0.21	0.005	0.16	0.39*	0.16
PLVW, cm	0.16	0.25	0.11	0.17	0.4	0.24*
LV EDD, cm	0.44*	0.29*	0.46*	0.34*	0.3*	0.39*
LV ESD, cm	0.44*	0.38*	0.45*	0.34*	0.36*	0.4*
LV EDV, mL	0.45*	0.29*	0.46*	0.34*	0.3*	0.39*
LV ESV, mL	0.43*	0.38*	0.45*	0.34*	0.36*	0.40*
LVMI, g/m ²	0.39*	0.30*	0.32*	0.34*	0.36*	0.36*
LVEF, %	-0.55*	-0.43*	-0.43*	-0.52*	-0.37*	-0.47*
Peak E-wave velocity, cm/s	0.35*	0.07	0.41*	0.3*	-0.002	0.27*
Peak A-wave velocity, cm/s	-0.1	-0.25	-0.09	0.08	-0.15	0.001
E/A	0.25	0.16	0.32*	0.14	0.06	0.16
E/E'	0.31*	0.27	0.38*	0.22	0.13	0.26*
GLS	0.71*	0.42*	0.55*	0.68*	0.42*	0.59*

sST2, soluble interleukin 1 receptor-like 1; NT-proBNP, N-terminal fragment of the brain natriuretic peptide precursor; LAV, left atrium volume; LAVI, left atrium volume index; IVS, interventricular septum thickness; PLVW, posterior left ventricular wall thickness; LV EDD, left ventricular end-diastolic diameter; LV ESD, left ventricular end-systolic diameter; LV EDV, left ventricular end-diastolic volume; LV ESV, left ventricular end-systolic volume; LVMI, left ventricular mass index; LVEF, left ventricular ejection fraction; E/A, ratio of peak E-wave velocity to peak A-wave velocity; E/E', ratio of mitral to myocardial early velocities; GLS, global longitudinal strain of the LV; *p<0.05.

Discussion

High incidence of cardiovascular complications in patients who survived COVID-19 implies the importance of diagnosing CHF and LV DD, especially in the presence of chronic HFpEF, which requires improvement of research methods, particularly assessment of EchoCG parameters and biomarker confirmation of myocardial involvement. When performing EchoCG in patients hospitalized with COVID-19, it is often possible to detect LV DD. The latter was observed in all patients included in this study. LV DD was more pronounced in the group of patients with a history of COVID-19. Grade 1 DD was diagnosed in 34% of patients in Group 1 and in 44.9% of patients in the comparison group. D. Brito et al. showed that patients with symptomatic COVID-19 had significantly lower septal e' and mean e' velocities compared with asymptomatic patients [8]. The identification of such structural and functional abnormalities typical of diastolic HF has raised concerns that COVID-19 survivors may develop HFpEF in the long term. E. Goerlich et al. also found DD in patients hospitalized with COVID-19. An increase in LV filling pressure (E/e' ratio) was observed in 25% of patients [9]. According to our data, E/e' was elevated in 12 (22.6%)

patients who had COVID-19 and in 2 (4.3%) patients in the comparison group.

The consequences of myocardial damage may persist even after convalescence of COVID-19. Longitudinal myocardial function is most sensitive to early structural changes, and therefore LV GLS is the gold standard for quantifying myocardial fibrosis. GLS is higher in patients with LV DD, which is associated with increased LV filling pressure (E/e' ratio). Besides, GLS measured via two-dimensional speckle tracking EchoCG is more sensitive than LVEF in terms of assessing LV systolic function and is often reduced in patients with HFpEF [10]. Determination of GLS allows for more accurate identification of a group of patients with asymptomatic changes in the LV, especially in the presence of normal EF.

In some patients, even with a mild form of COVID-19 without concomitant pathology, myocardial dysfunction occurred after their recovery. D. Brito et al. showed that in a cohort of young athletes who recovered after COVID-19, 11% had a decrease in GLS. In the ECHOCVID-19 study, LVEF was similar in all study groups, and LV GLS was significantly reduced in patients with COVID-19. In our study, LVEF did not exhibit significant differences between groups (Table 2). More severe impairment of LV and right ventricular GLS were more common in patients with severe COVID-19 and were independent predictors of mortality [8]. Our data indicated that in patients of Group 1, changes in LV GLS were more pronounced and significantly different from those in the comparison group (without COVID-19 in their anamneses) (Table 2). For instance, GLS values above -18 were observed in 32 subjects (60.4%) in the group of patients surviving COVID-19 and in 16 (34%) patients of the comparison group.

In response to structural and functional changes (strain, stretching of the heart walls), as well as pathomorphological changes in the myocardium (local and systemic inflammation), the circulation of the sST2 biomarker in the blood may increase, which reflects the process of fibrosis in the myocardium. After infection of the body and activation of the cytokine system, levels of sST2, which is a ligand for interleukin-33, can increase sharply. High concentrations of sST2 in the blood may influence the antihypertrophic and antiapoptotic role of the interleukin-33 and ST2 system in the heart, promoting myocardial remodeling and leading to adverse outcomes in patients suffering from cardiovascular diseases [11]. Indeed, in the group of patients who survived COVID-19, the concentration of sST2 was significantly higher than that in the comparison group (Table 1).

Our data on the association of sST2 with structural and functional parameters of the LV were supported by the results of a study by V. Agrawal et al., in which sST2 levels exhibited a statistically significant direct correlation with E/e', peak velocity of tricuspid regurgitation, LAVI and E/A [12]. It was demonstrated that the mean level of sST2 was significantly higher in patients with grade III DD and FC IV CHF. The authors noted that sST2 assessment added important information to support the diagnosis of LV DD and, accordingly, could be a good predictor of DD in patients with HFpEF [12]. The PARAMOUNT study revealed that sST2 levels were higher in HFpEF than reference values in matched control groups and that aggravation of DD, as

measured by increases in E/e' and LAV, was associated with increases in sST2 values during follow-up [13].

Hence, in patients with CAD and FC I-III CHF who survived COVID-19, we revealed significantly higher levels of the serum biomarker sST2 than in the comparison group, and their closer relationship with LV DD and volumetric indicators of the LV. These findings imply the necessity to determine the threshold values of this biomarker when assessing the risk of adverse cardiovascular events.

Conclusion

The serum concentrations of the biomarker of myocardial remodeling and fibrosis (sST2), LV DD, volumetric LV parameters, and GLS in patients with stable CAD and FC I-III CHF, who survived COVID-19, were significantly higher than in the group of patients who did not experience it. Further study of the relationship between these indicators, their dynamics and assessment of prognosis in the course of a long-term follow-up after COVID-19 will help improving the efficacy of the prevention and diagnosis of CHF in patients suffering from CAD.

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Conflict of interest: the authors declare no conflicts of interest.

References

1. Ferrara P, Albano L. COVID-19 and healthcare systems: What should we do next? *Public Health*. 2020; (185): 1-2. <https://www.doi.org/10.1016/j.puhe.2020.05.014>
2. Arutyunov GP, Tarlovskaya EI, Arutyunov AG, et al. International registry "Dynamic Analysis of Comorbidities in SARS-CoV-2 Survivors (AKTIV SARS-CoV-2)": Analysis of 1,000 patients. *Russ J Cardiol*. 2020; 25 (11): 4165. (In Russ.). <https://www.doi.org/10.15829/1560-4071-2020-4165>
3. Pierpaolo P, Doolub G, Wong ChM, et al. COVID-19 and its cardiovascular effects: A systematic review of prevalence studies. *Cochrane Database Syst Rev*. 2021; 3 (3): CD013879. <https://www.doi.org/10.1002/14651858.CD013879>
4. Mehra MR, Ruschitzka F. COVID-19 Illness and heart failure: A missing link? *JACC Heart Fail*. 2020; 8 (6): 512-4. <https://www.doi.org/10.1016/j.jchf.2020.03.004>
5. Glezeva N, Baugh JA. Role of inflammation in the pathogenesis of heart failure with preserved ejection fraction and its potential as a therapeutic target. *Heart Fail Rev*. 2014; 19 (5): 681-94. <https://www.doi.org/10.1007/s10741-013-9405-8>
6. Mehta P, McAuley DF, Brown M, et al. HLH Across Specialty Collaboration, UK. COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020; 395 (10229): 1033-4. [https://www.doi.org/10.1016/S0140-6736\(20\)30628-0](https://www.doi.org/10.1016/S0140-6736(20)30628-0)
7. Zeng Z, Hong XY, Li Y, et al. Serum-soluble ST2 as a novel biomarker reflecting inflammatory status and illness severity in patients with COVID-19. *Biomark Med*. 2020; 14 (17): 1619-29. <https://www.doi.org/10.2217/bmm-2020-0410>
8. Brito D, Meester S, Yanamala N, et al. High prevalence of pericardial involvement in college student athletes recovering from COVID-19. *JACC Cardiovasc Imaging*. 2021; 14 (3): 541-55. <https://www.doi.org/10.1016/j.jcmg.2020.10.023>

9. Goerlich E, Metkus TS, Gilotra NA, et al. Prevalence and clinical correlates of echo-estimated right and left heart filling pressures in hospitalized patients with coronavirus disease 2019. *Crit Care Explor.* 2020; 2 (10): e0227. <https://www.doi.org/10.1097/CCE.0000000000000227>
10. Kraigher-Krainer E, Shah AM, Gupta DK, et al. Impaired systolic function by strain imaging in heart failure with preserved ejection fraction. *J Am Coll Cardiol.* 2014; 63 (5): 447-56. <https://www.doi.org/10.1016/j.jacc.2013.09.052>
11. Miftode R-S, Petris AO, Aursulesei VO, et al. The novel perspectives opened by ST2 in the pandemic: A review of its role in the diagnosis and prognosis of patients with heart failure and COVID-19. *Diagnostics (Basel).* 2021; 11 (2): 175. <https://www.doi.org/10.3390/diagnostics11020175>
12. Agrawal V, Hardas S, Gujar H, Phalgune DS. Correlation of serum ST2 levels with severity of diastolic dysfunction on echocardiography and findings on cardiac MRI in patients with heart failure with preserved ejection fraction. *Indian Heart J.* 2022; 74 (3): 229-34. <https://www.doi.org/10.1016/j.ihj.2022.03.001>
13. Zile MR, Jhund PS, Baicu CF, et al. Plasma biomarkers reflecting profibrotic processes in heart failure with a preserved ejection fraction: Data from the prospective comparison of ARNI with ARB on management of heart failure with preserved ejection fraction study. *Circ Heart Fail.* 2016; 9 (1): e002551. <https://www.doi.org/10.1161/CIRCHEARTFAILURE.115.002551>

Authors:

Sergey S. Fateev – PhD, Director of the Central Military Clinical Hospital, Moscow, Russia, <https://orcid.org/0009-0005-3039-9504>;

Ivan M. Ryzhkov – Graduate Student, Department of Hospital Therapy No.2, Semashko Higher School of Clinical Medicine, <https://orcid.org/0009-0008-8531-2447>;

Vladimir K. Fedulov – PhD, Cardiologist, <https://orcid.org/0009-0009-6336-1237>;

Elena V. Kovalenko – PhD, Associate Professor, Department of Hospital Therapy No.2, Semashko Higher School of Clinical Medicine, <https://orcid.org/0000-0001-9202-3522>;

Ludmila I. Markova – DSc, Professor, Department of Hospital Therapy No.2, Semashko Higher School of Clinical Medicine, <https://orcid.org/0000-0002-3396-9235>;

Olga L. Belaya – DSc, Professor, Department of Hospital Therapy No.2, Semashko Higher School of Clinical Medicine, <https://orcid.org/0000-0002-5256-350>.