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ORIGINAL PAPER

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Echocardiographic Findings of Covid-19 Patients in Canton Sarajevo During the Third Wave of the Covid-19 Pandemic

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ABSTRACT

Background: Increasing evidence indicates that COVID-19 may result in cardiac issues in certain individuals, such as myocarditis, arrhythmias, and heart failure. Ongoing research on echocardiographic manifestations is still limited.

Objective: To investigate the incidence and patterns of left and right ventricular dysfunction in COVID-19 patients. **Methods:** This study retrospectively observed COVID-19 patients admitted to the Clinical Center of University of Sarajevo during the third wave, with a particular focus on cardiac evaluations. **Results.** Our patients, predominantly male 155 (72.4%), with a mean age of 66.2±11.4, having hypertension 86 (40.1%), diabetes mellitus 61 (28.5%), hyperlipidemia 144 (67.3%), were active smokers 87 (40.6%), had family history of cardiovascular diseases 123 (57.5%) and were COVID-19 positive 95 (44.4%), presented because of chest pain 78 (36.4%), dyspnea 103 (48.1%), palpitations 67 (31.3%), fatigue 106 (49.5%) and peripheral oedema 30 (14.0%). COVID-19 patients reported much higher symptoms of dyspnea (65 (68.4%) vs 38 (31.9%)) and fatigue (73 (76.8%) vs 33 (27.7%)) than COVID-19 negative patients. On the initial laboratory report, COVID-19 patients had a significantly ($p<0.05$) higher mean score of C-reactive protein (24.0±4.8 vs. 6.0±2.1), D-dimer (1.6±2.5 vs 0.8±0.6), ALT (94.8±17.2 vs 36.5±19.9) and creatinine (128.0±80.8 vs. 93.4±40.1) when compared to COVID-19 negative patients. COVID-19 patients had enlarged left atrium diametes (31.6±5.6 vs 27.5±5.3), enlarged left ventricular diameter both in systole (27.9±18.1 vs 23.3±16.3) and diastole

(39.3±24.1 vs 34.9±22.7), reduced left ventricular ejection fraction (53.5±9.2 vs 59.8±4.3) and elevated right ventricular systolic pressure (37.0±16.4 vs 35.1±8.6). **Conclusion.** COVID-19 patients had enlarged left atrium, enlarged systolic and diastolic left ventricular diameter, reduced left ventricular ejection fraction and elevated right ventricular systolic pressure.

Keywords. COVID-19, cardiac injury, echocardiography, ventricular function, heart diseases.

1. BACKGROUND

COVID-19, caused by SARS-CoV-2, was first identified in December 2019 in Wuhan City (1), China, and has since spread rapidly, resulting in a global pandemic with over 400 million confirmed cases. The disease can present with a spectrum of symptoms ranging from mild flu-like symptoms such as anosmia, dysgeusia, fever, sore throat, cough, dyspnea, headache, abdominal pain and diarrhea (2) to severe manifestations such as acute respiratory syndrome (ARDS), septic shock, metabolic acidosis, coagulation dysfunction, multiorgan failure or even death (3). It is important to note that some patients with COVID-19 may remain asymptomatic, making early detection and effective control of the disease challenging. (2,4)

There is a dearth of information regarding the impact of COVID-19 on cardiac function (5) and echocardiographic presentations in critically ill patients, thereby rendering the management of such patients challenging.

Although echocardiographic findings (6,7) have been reported in non-critically ill COVID-19 patients, their quantitative evaluation remains inadequate. In light of the high mortality rate associated with severe COVID-19 cases, a comprehensive understanding of the disease is imperative, necessitating the acquisition of data on the subject.

One study (6) showed that nearly one third of critically ill COVID-19 patients manifested with aberrant systolic function in either left or right ventricle during the initial echocardiographic assessment, with left ventricular systolic dysfunction resembling as septic cardiomyopathy and right ventricular systolic dysfunction associated with pressure overload attributed to positive pressure ventilation, hypercapnia and pulmonary embolism. An additional study (8) revealed that COVID-19 infection led to a diverse array of cardiac conditions, including acute myocardial infarction, Takotsubo cardiomyopathy, myocarditis, arrhythmogenic and thrombotic manifestations, as well as potential drug-related effects. Nearly 80% of patients exhibited localized left ventricular wall motion abnormalities, while approximately 60% of patients had a left ventricular ejection fraction lower than 50%. (8) While some COVID-19 patients may not initially exhibit cardiac symptoms, a more thorough echocardiographic analysis, including speckle tracing and deformation patterns, revealed that the majority of COVID-19 patients displayed anomalous left ventricular deformation, particularly in the basal segments, indicative of a basal “Takotsubo-like syndrome” (9). Changes were recorded even in patients with mild to moderate disease.

There is a notable scarcity of current data regarding cardiac involvement in COVID-19 patients in Bosnia and Herzegovina, as well as the broader region. Information and research specific to the impact of COVID-19 on the cardiovascular system in this area are limited, highlighting a gap in our understanding of the extent and nature of cardiac manifestations among individuals affected by the virus. The absence of such data underscores the importance of ongoing research to inform medical practices, treatment strategies, and public health initiatives in the face of the COVID-19 pandemic.

2. OBJECTIVE

This study addresses the knowledge gap in cardiac involvement among COVID-19 patients by examining the incidence and patterns of left and right ventricular dysfunction, providing insights into the impact of COVID-19 on the cardiovascular system in Bosnia and Herzegovina.

3. MATERIAL AND METHODS

This retrospective observational study involving patients admitted to the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo was conducted during the third wave of COVID-19. The study was approved by the Bioethical Committee of Clinical Center of University of Sarajevo and done in accordance with all amendments of Helsinki declaration.

Subjects

Subjects included in the study setting were patients

referred to the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo during the third wave of COVID-19 in the country for cardiac echocardiographic imaging. Inclusion criteria were (i) patients who weren't admitted because of pPCI, preoperative preparation, valve replacement or CABG and (ii) patients who weren't in acute coronary syndrome, acute heart failure and other cardiovascular urgencies. All subjects were informed about the objectives of the study, their voluntary participation, including informed consent and details what data were obtained for the study purposes.

Study instruments and data collection

All patients underwent transthoracic echocardiography using a GE Vivid™ S70 ultrasound machine. All studies were recorded and analyzed by multiple experts to prevent subjectiveness in the analysis. Common echocardiography parameters for left ventricular (LV) function and hemodynamic status were collected. These include left atrium diameter (LA), left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVEDS), interventricular septum diastolic diameter (IVSD), interventricular septum systolic diameter (IVSS), right ventricular systolic pressure (RVSP), mitral valve regurgitation (MR), aortic valve regurgitation (AR), tricuspid valve regurgitation (TR), mitral valve stenosis (MS), aortic valve stenosis (AS), left ventricular ejection fraction (LVEF) and the presence of pericardial effusion.

Statistical analysis

Collected data were summarized and descriptive statistics were run. Normal distributed data were displayed in frequencies and percentage (mean±standard deviation), while data with not-normal distribution were presented with median (25th, 75th percentile). To assess various variables in association with certain phenomena independent samples t test, Mann Whitney U test or χ^2 test as appropriate were conducted. Statistical significance level was set at $p < 0.05$ (two-sided).

4. RESULTS

In total 214 patients from the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of

		COVID-19 positive N=95	COVID-19 negative N=119
Sex (No, %)	Male	63 (66.3%)	92 (77.3%)
	Female	32 (33.7%)	27 (22.7%)
Age (mean±SD)		68.5±11.4	64.0±11.5
Risk factors (No, %)	HTA	19 (20.0%)	67 (56.3%)
	DM	26 (27.3%)	35 (29.4%)
	HLP	57 (60.0%)	87 (73.1%)
	Smoking	32 (33.7%)	55 (46.2%)
	Family history	54 (56.8%)	69 (57.9%)

Table 1. Sex, age and cardiovascular associated risk factors such as hypertension, diabetes mellitus, hyperlipidemia, smoking status and positive family history of cardiovascular disease among COVID-19 positive and COVID-19 negative patients admitted at the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo. HTA-hypertension, DM-diabetes mellitus, HLP-hyperlipidemia,

		COVID-19 positive N=95	COVID-19 negative N=119	p value
Symptoms (No, %)	Chest pain	35 (36.8%)	43 (36.1%)	N/A
	Dyspnea	65 (68.4%)	38 (31.9%)	N/A
	Palpitations	25 (26.3%)	42 (35.3%)	N/A
	Fatigue	73 (76.8%)	33 (27.7%)	N/A
	Peripheral oedema	12 (12.6%)	18 (15.1%)	N/A
Laboratory findings (mean±SD)	C-reactive protein	24.0±4.8	6.0±2.1	<0.05
	D-dimer	1.6±2.5	0.8±0.6	<0.05
	AST	66.5±6.2	47.0±5.3	>0.05
	ALT	94.8±17.2	36.5±19.9	<0.05
	CK	84.5±8.7	54.6±11.2	>0.05
	CKMB	21.04±8.1	15.2±5.3	>0.05
	LDH	451.6±32.0	342.3±23.8	>0.05
	Urea	10.9±9.5	8.3±6.5	>0.05
Creatinine	128.0±80.8	93.4±40.1	<0.05	

Table 2. Symptoms and laboratory findings among COVID-19 positive and COVID-19 negative patients admitted at the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo. AST- aspartate transaminase, ALT- alanine transaminase, CK-creatin kinase, CKMB- creatine kinase fraction MB, LDH-lactate dehydrogenase

		COVID-19 positive N=95	COVID-19 neg- ative N=119	p value
Echo find- ings	LA	31.6±5.6	27.5±5.3	<0.05
	LVEDD	34.9±22.7	39.3±24.1	<0.05
	LVEDS	23.3±16.3	27.9±18.1	<0.05
	IVSD	8.7±5.0	9.5±4.8	>0.05
	IVSS	11.3±4.9	11.6±5.1	>0.05
	RVSP	35.1±8.6	37.0±16.4	<0.05
	MR	43	44	N/A
	AR	54	40	N/A
	TR	19	34	N/A
	MS	0	2	N/A
	AS	6	3	N/A
	LVEF	53.5±9.2	59.8±4.3	<0.05
Pericardial effusion	15	4	N/A	

Table 3. 2D echocardiography findings among COVID-19 positive and COVID-19 negative patients admitted at the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo. LA-left atrium diameter, LVEDD-Left ventricular end diastolic diameter, LVEDS-left ventricular end systolic diameter, IVSD-interventricular septum diastolic diameter, IVSS-interventricular septum systolic diameter, RVSP-right ventricular systolic pressure, MR-mitral valve regurgitation, AR- aortic valve regurgitation, TR-tricuspid valve regurgitation, MS-mitral valve stenosis, AS- aortic valve stenosis, LVEF- left ventricular ejection fraction

University of Sarajevo were included in the study. Our patients were predominantly male 155 (72.4%), with a mean age of 66.2±11.4, having hypertension 86 (40.1%), diabetes mellitus 61 (28.5%), hyperlipidemia 144 (67.3%), were active smokers 87 (40.6%) and had family history of cardiovascular diseases 123 (57.5%). The sample included 95 (44.4%) COVID-19 positive patients and 119 (55.6%) COVID-19 negative patients. No statistical difference (p>0.05) regarding sex, age and cardiovascular risk factors between COVID-19 positive and COVID-19 negative patients was observed. All other demographic data (sex, age) and cardiovascular associated risk factors are presented in Table 1.

Patients were admitted to the Clinic for Heart, Blood

Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo because of chest pain 78 (36.4%), dyspnea 103 (48.1%), palpitations 67 (31.3%), fatigue 106 (49.5%) and peripheral oedema 30 (14.0%). COVID-19 patients reported much higher symptoms of dyspnea (65 (68.4%) vs 38 (31.9%)) and fatigue (73 (76.8%) vs 33 (27.7%)) than COVID-19 negative patients. On the initial laboratory report, COVID-19 patients had a significantly (p<0.05) higher mean score of C-reactive protein (24.0±4.8 vs. 6.0±2.1), D-dimer (1.6±2.5 vs 0.8±0.6), ALT (94.8±17.2 vs 36.5±19.9) and creatinine (128.0±80.8 vs. 93.4±40.1) when compared to COVID-19 negative patients. All symptoms

and other laboratory report data between COVID-19 positive and COVID-19 negative patients are presented in Table 2.

All patients admitted to the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo have undergone echocardiographical examination. All 2D echocardiography findings among COVID-19 positive and COVID-19 negative patients admitted at the clinic are presented in Table 3. COVID-19 patients had enlarged left atrium diameters (31.6±5.6 vs 27.5±5.3), enlarged left ventricular diameter both in systole (27.9±18.1 vs 23.3±16.3) and diastole (39.3±24.1 vs 34.9±22.7), reduced overall left ventricular ejection fraction (53.5±9.2 vs 59.8±4.3) and elevated right ventricular systolic pressure (37.0±16.4 vs 35.1±8.6).

5. DISCUSSION

To the readers knowledge, this is the first study in region of West Balkan that is assessing COVID-19 infection effects on cardiovascular health from an echocardiographic aspect. Our patients were predominantly male having cardiovascular risk factors such as hypertension, diabetes mellitus, hyperlipidemia; were active smokers and with a family history of cardiovascular diseases. COVID-19 patients had enlarged left atrium diameters, enlarged left ventricular diameter both in systole and diastole, reduced left ventricular ejection fraction and elevated right ventricular systolic pressure.

When compared to similar study conducted in Turkey (7), our study showed similar results regarding the decrease in left ventricular function and enlargement of the left ventricle due to COVID-19 infection. This finding could be attributed to myocardial injury (10, 11) which has been shown to be associated with COVID-19 due to hypoxic damage, respiratory distress and inflammation (12). Myocarditis or myopericarditis associated with COVID-19 is another factor contributing to reduced left

ventricular function (13), as indicated indirectly by post-mortem findings showing cardiac lymphocyte infiltrates and a macrophagic response (14). Another researcher (15) associates alterations in left ventricular systolic function with both typical and atypical Takotsubo syndrome, potentially induced by emotional and physical stress from the infection itself. This is characterized by typical apical ballooning and the presence of possible adverse findings.

Even though some patients didn't show clinical and 2D echocardiographic signs of left heart failure, a thorough left ventricular examination with strain and strain rate modalities could give us an information of the subclinical left ventricular impairment. Some studies (16) already explained such findings at a large scale reaching almost one third of the recovered COVID-19 patients. Stobe (9) demonstrated that, despite having a normal left ventricular ejection fraction, individuals with mild to severe COVID-19 symptoms exhibited abnormal deformation imaging. Specifically, a reduced longitudinal strain was observed in more than one basal segment, suggesting a potential subepimyocardial involvement of SARS-CoV-2-induced myocarditis. Additionally, the left ventricular global longitudinal strain was altered in the majority of hospitalized COVID-19 patients (9).

The aforementioned Turkish study (7) revealed that COVID-19 infection can have a detrimental effect on the function of the right ventricle of the heart, as well. Our study shows higher right ventricular systolic pressure among COVID-19 patients which could be attributed to the aforementioned factors. This occurs as a result of damage to the alveoli, which are responsible for gas exchange in the lungs, as well as damage to the pulmonary capillaries. Furthermore, the inflammation, hypoxia, and hypercapnia that occur in the lungs due to COVID-19 can increase pulmonary vascular resistance, thereby affecting the function of the right ventricle (17). Additionally, individuals affected by COVID-19 manifest a prothrombotic condition, heightening their susceptibility to thromboembolic incidents, encompassing deep vein thrombosis and pulmonary embolism (18, 19).

Our study had several limitations. Firstly, the study type as cross-sectional limits us to infer causality. Secondly, the study has a small sample size. Thirdly, this study only included those patients who had some cardiovascular symptoms thus they were referred to an echocardiographic examination. The study limits asymptomatic patients who may have echo findings, but due to good compensation mechanism they are asymptomatic. Future studies should investigate prospectively on a large multicentric sample the effect of COVID-19 infection on the cardiovascular health, especially on asymptomatic patients.

6. CONCLUSION

In conclusion, Bosnia and Herzegovina COVID-19 patients who were admitted to the Clinic for Heart, Blood Vessels and Rheumatic Diseases of Clinical Center of University of Sarajevo had enlarged left atrium diameters, enlarged left ventricular diameter both in systole and

diastole, reduced left ventricular ejection fraction and elevated right ventricular systolic pressure. COVID-19 patients showed impaired left ventricular function which is possibly attributed to the myocardial injury, hypoxia and the inflammation due to the infection. A follow up of these patients and a detailed echocardiographic examination including strain and strain rate is needed for further investigation of this cardiovascular healthcare entity.

- **Author's contribution:** Every author participated in every stage of preparing this article. Data sampling was conducted by A.S., L.B., I.S. and I.D. Data processing, coding and initial descriptive data analysis was done by A.A., L.R., M.A., A.M.. The statistical analysis was done by A.S. and I.S.. The postprocessing of echo images was done by A.S., L.B.. The initial draft was written by I.D. and A.A.. Critical revision was conducted by L.R., M.A and A.M. The final proof-reading was approved by all authors.
- **Conflict of interests:** None to declare.
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