

Transthoracic Echocardiography Findings of Hospitalized Patients with COVID-19: Results from the Brazilian Echocardiography Registry During the COVID-19 Pandemic (ECOVID)

Achados ao Ecocardiograma Transtorácico em Pacientes Hospitalizados com COVID-19: Resultados do Registro Brasileiro de Ecocardiografia durante a Pandemia de COVID-19 (ECOVID)

Silvio Henrique Barberato,¹ Rafael Borsoi,² Fabio Roston,³ Hudson Laerte Machado Miranda,⁴ Pedro Patriota,⁵ Maria Estefânia Bosco Otto,^{6,7} Adenvalva Lima de Souza Beck,^{7,8} Anderson da Costa Armstrong,⁵ João Marcos Bemfica Barbosa,⁹ Ana Cristina Camarozano Wermellinger,¹⁰ Letícia Braga Paciello da Silva,¹¹ Marcos Valério Coimbra Resende,¹¹ Marcelo Luiz Campos Vieira,¹¹ Marcelo Miglioranza,¹² Miguel Morita Fernandes da Silva²
CardioEco - Centro de Diagnóstico Cardiovascular, Curitiba;¹ Hospital de Clínicas da Universidade Federal do Paraná (UFPR), Curitiba;² Hospital Universitário da Universidade Estadual de Londrina (HU-UEL), Londrina;³ Hospital Samel, Manaus;⁴ Hospital Universitário da Universidade Federal do Vale do São Francisco (HU - UNIVASF), Petrolina;⁵ Hospital Sirio Libanês, Brasília;⁶ Instituto de Cardiologia do Distrito Federal (ICDF), Brasília;⁷ Hospital Santa Lúcia, Brasília;⁸ Hospital Universitário Getúlio Vargas - Universidade Federal do Estado do Amazonas (UFAM), Manaus;⁹ Hospital Nossa Senhora das Graças, Curitiba;¹⁰ Hospital Samaritano, São Paulo;¹¹ Hospital Mãe de Deus, Porto Alegre.¹²

Abstract

Background: Transthoracic echocardiography (TTE) may play a crucial role in the evaluation of cardiac manifestations of coronavirus disease 2019 (COVID-19).

Objective: We aimed to report the prevalence of the main echocardiographic abnormalities of hospitalized COVID-19 patients.

Methods: We performed a prospective multicenter observational study in patients with COVID-19 who underwent TTE during hospitalization. Patients with pre-existing heart failure, coronary artery disease, or atrial fibrillation were categorized as having previous cardiovascular disease (CVD). Clinical and echocardiographic data about cardiac structure and function were collected.

Results: We evaluated 310 patients with COVID-19 (mean age, 62±16 years; 61% men; 53% with arterial hypertension; 33% with diabetes; and 23% with previous CVD). Overall, 65% of the patients required intensive care unit support. The most prevalent echocardiographic abnormalities were LV hypertrophy (29%), pulmonary hypertension (25%), left ventricular (LV) systolic dysfunction (16.5%), right ventricular (RV) systolic dysfunction (15.9%), grade II/III LV diastolic dysfunction (11%), and LV regional wall motion abnormality (11%). Pericardial effusion was uncommon (7% of cases). LV hypertrophy (25% vs. 45%, $p=0.001$), LV systolic dysfunction (11% vs. 36%, $p<0.001$), regional wall motion abnormalities (6% vs. 29%, $p<0.001$), grade II/III LV diastolic dysfunction (9% vs. 19%, $p=0.03$), and pulmonary hypertension (22% vs. 36%, $p=0.019$) were less common in patients without previous CVD. RV systolic dysfunction occurred at similar frequencies in patients with versus without previous CVD (13% vs. 25%, $p=0.07$).

Conclusions: Among patients hospitalized with COVID-19, abnormal echocardiographic findings were common, but less so among those without previous CVD. RV systolic dysfunction appeared to affect similar proportions of patients with versus without previous CVD.

Keywords: Cardiac function; Cardiovascular disease; COVID-19; Echocardiography; SARS-CoV-2

Resumo

Fundamento: A ecocardiografia transtorácica (ETT) pode desempenhar um papel crucial na avaliação das manifestações cardíacas da COVID-19.

Objetivo: Nosso objetivo foi relatar a prevalência das principais anormalidades ecocardiográficas em pacientes hospitalizados com COVID-19.

Mailing Address: Silvio Henrique Barberato •

Avenida República Argentina, 1336, sala 215, CEP 80620-010, Curitiba, Paraná, Brazil.

E-mail: silviohb@cardiol.br

Manuscript received 9/30/2021; revised 10/7/2021; accepted 10/14/2021

DOI: 10.47593/2675-312X/20213404eabc256



Original article

Métodos: Realizou-se estudo observacional multicêntrico prospectivo com pacientes com COVID-19 submetidos a ETT durante a internação. Pacientes com insuficiência cardíaca prévia, doença arterial coronariana ou fibrilação atrial foram classificados como portadores de doença cardiovascular (DCV) prévia. Foram coletados dados clínicos e ecocardiográficos da estrutura e da função cardíaca.

Resultados: Avaliamos 310 pacientes com COVID-19, com 62 ± 16 anos de idade, 61% homens, 53% com hipertensão arterial, 33% com diabetes e 23% com DCV prévia. No total, 65% dos pacientes necessitaram de suporte em unidade de terapia intensiva. As alterações ecocardiográficas mais prevalentes foram hipertrofia do ventrículo esquerdo (VE) (29%), hipertensão pulmonar (25%), disfunção sistólica do VE (16,5%), disfunção sistólica do ventrículo direito (VD) (15,9%), disfunção diastólica do VE grau II/III (11%) e alteração da contratilidade regional do VE (11%). Derrame pericárdico foi incomum (7%). Hipertrofia do VE (25 vs. 45%, $p=0,001$), disfunção sistólica do VE (11 vs. 36%, $p<0,001$), alterações da contratilidade regional (6 vs. 29%, $p<0,001$), disfunção diastólica do VE grau II/III (9 vs. 19%, $p=0,03$) e hipertensão pulmonar (22 vs. 36%, $p=0,019$) foram menos comuns nos pacientes sem do que com DCV prévia. A disfunção sistólica do VD mostrou-se semelhante em pacientes sem e com DCV prévia (13 vs. 25%, $p=0,07$).

Conclusões: Entre os pacientes hospitalizados com COVID-19, os achados ecocardiográficos anormais foram comuns, porém menos encontrados naqueles sem DCV. A disfunção sistólica do VD pareceu afetar de forma semelhante pacientes com e sem DCV prévia.

Palavras-chave: COVID-19; SARS-CoV-2; Função cardíaca; Ecocardiografia; Doença cardiovascular.

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may result in severe respiratory distress and acute cardiac injury. Impaired cardiac function and prior cardiovascular disease (CVD) in patients with COVID-19 are associated with a worse prognosis.¹ Transthoracic echocardiography (TTE) plays a central role in the management of patients with new or worsening cardiovascular symptoms, hemodynamic instability, and increased biomarker levels since it provides crucial information about cardiac structure and function.² On the other hand, the use of echocardiography should be based on the critical consideration of the benefits for patients versus the risk of contamination for healthcare workers.³

TTE findings among COVID-19 patients have been conflicting. While some studies reported a high prevalence of left ventricular (LV) systolic dysfunction,^{4,5} others suggested that it is less common, with LV diastolic dysfunction and right ventricular (RV) dysfunction being more prevalent.^{6,7} Referral bias, definitions of abnormal TTE findings, and differences in population characteristics such as the proportion of patients with previous cardiovascular disease (CVD) may partly explain these differences. However, it remains unclear in what ways and how often COVID-19 affects cardiac function.

Therefore, here we aimed to determine the prevalence of the main abnormal echocardiographic findings of hospitalized patients with COVID-19 and compare them between those with and without a history of previous CVD through a real-world, multicenter collaborative study (Brazilian Echocardiography Registry during COVID-19 pandemic [ECOVID]).

Methods

ECOVID is a prospective multicenter national observational study of hospitalized patients with suspected or confirmed COVID-19. The registry started in Brazil on April 4, 2020, with the purpose of collecting epidemiological clinical data and echocardiographic findings from centers of all five macro-regions of the country.

Population

We included consecutive patients older than 18 years of age with COVID-19 who were referred for TTE during hospitalization. Patients with clinical symptoms of COVID-19 and positive real-time polymerase chain reaction (RT-PCR) test results were classified as confirmed cases. Patients with clinical signs and symptoms of COVID-19 and compatible findings on chest computed tomography (bilateral ground-glass opacity) but without a positive RT-PCR test result were considered highly probable cases. This study was approved by the ethics committee of the coordinating center (# 4.033.139) and local ethics committee of each respective site. To reduce the risk of SARS-CoV-2 cross-infection between healthcare workers and patients, the ethics committee waived the requirement to obtain informed consent and approved the entry of unidentified patient information into the study database.

Data collection

At each participant center, cardiologists completed a case report form after the TTE. The protocol definitions in the case report form were discussed with each investigator, who was asked to follow the same standard protocol to improve consistency across sites. Data were entered online and submitted to the coordinating center via a secure website. The study coordinating center assigned a unique identification number to each patient to avoid duplicate entries and certify the security of their protected health information.

Clinical and demographic data

Each investigator reviewed the medical charts and interviewed the patients or relatives to obtain their clinical and demographic data including age, sex, weight, height, and history of arterial hypertension, diabetes mellitus, obesity, smoking, coronary artery disease (prior myocardial infarction, percutaneous coronary intervention, and/or coronary artery bypass graft), heart failure, atrial fibrillation, chronic obstructive pulmonary disease, cerebrovascular stroke, chronic kidney disease (serum creatinine level ≥ 1.5 mg/dL), and cancer. Previous CVD was defined as a history of coronary computed tomography angiography or coronary angiography showing an obstruction $\geq 50\%$ in any major coronary artery, percutaneous

or surgical coronary revascularization, myocardial infarction, heart failure, or atrial fibrillation. COVID-19-related signs and symptoms and the need for supportive measures for critically ill patients (non-invasive ventilation, mechanical ventilation, and use of vasoactive drugs) were also collected.

Echocardiographic data

A focused protocol was used in the majority of the scans to mitigate the risk to healthcare professionals.^{3,8,9} Imaging acquisition and interpretation were performed by certified physicians according to international guidelines.^{10,11} All procedures followed the respective institutional protocol regarding the use of personal protective equipment and the cleaning of equipment after each scan. LV ejection fraction (LVEF) was assessed by visual estimation and/or the modified Simpson's biplane method. LV systolic dysfunction was defined as an LVEF < 50% (mild, 40–49%; moderate, 30–39%; and severe, <30%). The LV diastolic function analysis included measurements of peak early filling (E-wave) and late diastolic filling (A-wave) velocities, E/A ratio, early diastolic mitral septal and lateral annular velocities (e'), and E/e' ratio. Patients were classified as having normal (E/A 0.8–2.0, E/e' < 10) or abnormal (grade I: E/A ≤ 0.8, E/e' < 10; grade II: E/A 0.8–2.0, E/e' 10–14; or grade III: E/A ≥ 2; E/e' > 14) diastolic dysfunction.¹² The diastolic function grade was considered "unknown" when it was judged as indeterminate or when the data were not collected. RV systolic dysfunction was determined by visual estimation and/or semi-quantitatively (tricuspid annular plane systolic excursion (TAPSE) < 17 mm and/or tissue Doppler of the free lateral wall [S'] < 9.5 cm/s indicated RV dysfunction).¹³ Valvular regurgitation was assessed according to American Heart Association/American College of Cardiology guidelines.¹⁴ Pulmonary artery systolic pressure (PASP) was estimated from the peak tricuspid regurgitation velocity obtained using continuous-wave Doppler echocardiography, while the right atrial pressure was estimated by inferior vena cava size.¹⁵ Pulmonary hypertension was defined as a PASP ≥ 36 mmHg (mild, 36–45 mmHg; severe, ≥60 mmHg).

Statistical analysis

Continuous variables were assessed for Gaussian distribution and are presented as mean ± standard deviation or median (25th percentile, 75th percentile). Clinical, demographic, and echocardiographic parameters were compared between groups based on the history of CVD using Student's t-test or the chi-squared test. For some patients, data were missing on days since symptom onset, fever, cough, dyspnea, myalgia, sore throat, diarrhea, headache, anosmia, and chest pain. We used multiple imputations to account for missing data under a missing at random assumption. Data were imputed using a data augmentation algorithm, a Markov Chain Monte Carlo procedure, assuming a joint multivariate normal distribution for the entered variables.¹⁶ The imputation of 20 datasets was performed using age, sex, body mass index (BMI), and site center as predictors. Linear regression was then applied to the multiple-imputed data to combine the 20 datasets as previously described for comparison between patients with and those without previous CVD.¹⁷ We considered values of p < 0.05 as statistically significant. The statistical analyses were performed using Stata version 15.1 (Stata Corp, College Station, TX, USA).

Results

We included 310 hospitalized patients between April 4 and September 9, 2020, of whom 186 (88.4%) had RT-PCR-confirmed COVID-19, and 36 (11.6%) had highly probable COVID-19. Table 1 summarizes the demographics, clinical characteristics, and comorbidities of the study population. Overall, the mean age of the population was 62 ± 16 years old (range 19–94 years), 61% were men, and the mean BMI was 28 ± 8 (range 17.6–48.4) kg/m². The most prevalent cardiovascular risk factors were hypertension (53%), diabetes mellitus (33%), and obesity (30%). Sixty-five percent of the patients were in intensive care units (ICUs), 46% required invasive mechanical ventilation, and 19% required vasopressor drugs. Twenty-three percent of patients had a history of CVD, including coronary artery disease (14%), heart failure (8%), and atrial fibrillation (5%). Patients without previous CVD were younger, had a lower prevalence of cardiovascular risk factors such as hypertension, diabetes, and smoking, and were less likely to have chronic obstructive pulmonary disease and chronic kidney disease than patients with previous CVD (Table 1). COVID-19-related symptoms and supportive measures were similar between patients with and without previous CVD (Table 2). The main clinical indications for referral for TTE were suspected heart failure (50%), suspected acute coronary syndrome (chest pain, electrocardiography abnormalities, and

Table 1 - Demographics and comorbidities according to history of previous cardiovascular disease.

	All patients n=310	No previous CVD n=240	Previous CVD n=70	P value
Age, years	62±16	59±16	69±14	< 0.001
Male sex, n (%)	189 (61.0%)	146 (60.8%)	43 (61.4%)	0.93
BMI, kg/m ²	28.2±7.9	28.1±5.5	28.6±13.1	0.63
Obesity, n (%)	94 (30.3%)	76 (31.7%)	18 (25.7%)	0.34
Hypertension, n (%)	164 (52.9%)	113 (47.1%)	51 (72.9%)	< 0.001
Diabetes mellitus, n (%)	104 (33.5%)	67 (27.9%)	37 (52.9%)	< 0.001
Smoking, n (%)	39 (12.6%)	24 (10.0%)	15 (21.4%)	0.011
Previous CAD, n (%)	44 (14.2%)	0 (0.0%)	44 (62.9%)	< 0.001
Previous HF, n (%)	25 (8.1%)	0 (0.0%)	25 (35.7%)	< 0.001
Previous AF, n (%)	17 (5.5%)	0 (0.0%)	17 (24.3%)	< 0.001
Pulmonary disease, n (%)	30 (9.7%)	17 (7.1%)	13 (18.6%)	0.004
Chronic kidney disease, n (%)	36 (11.6%)	21 (8.8%)	15 (21.4%)	0.004
Dialysis, n (%)	3 (1.0%)	3 (1.2%)	0 (0.0%)	0.35
Cerebrovascular disease, n (%)	15 (4.8%)	9 (3.8%)	6 (8.6%)	0.10
Cancer, n (%)	10 (3.2%)	7 (2.9%)	3 (4.3%)	0.57

AF, atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; HF, heart failure.

Original article

Table 2 - COVID-19-related symptoms and supportive measures according to history of previous cardiovascular disease*.

	All patients n=310	No previous CVD n=240	Previous CVD n=70	P value
Days since symptom onset	11.9±9.3	11.97±8.65	11.62±11.44	0.79
Fever, n (%)	160 (58.2%)	126 (59.4%)	34 (54.0%)	0.44
Cough, n (%)	167 (60.7%)	133 (62.7%)	34 (54.0%)	0.21
Dyspnea, n (%)	195 (70.9%)	155 (73.1%)	40 (63.5%)	0.14
Myalgia, n (%)	70 (25.5%)	58 (27.4%)	12 (19.0%)	0.18
Sore throat, n (%)	17 (6.2%)	12 (5.7%)	5 (7.9%)	0.51
Diarrhea, n (%)	29 (10.5%)	24 (11.3%)	5 (7.9%)	0.44
Headache, n (%)	35 (12.7%)	29 (13.7%)	6 (9.5%)	0.38
Anosmia, n (%)	10 (3.6%)	10 (4.7%)	0 (0.0%)	0.08
Chest pain, n (%)	19 (6.9%)	15 (7.1%)	4 (6.3%)	0.84
Intensive care, n (%)	202 (65.2%)	158 (65.8%)	44(62.9%)	0.65
NIV, n (%)	51 (16.5%)	34(14.2%)	17(24.3%)	0.045
Intubated, n (%)	142 (45.8%)	116 (48.3%)	26(37.1%)	0.10
Vasopressor drug, n (%)	60 (19.4%)	46(19.2%)	14(20.0%)	0.88

CVD, cardiovascular disease; NIV, non-invasive mechanical ventilation.

*Multiple imputation was used for 32 patients for whom data were missing for days since symptom onset, fever, cough, dyspnea, myalgia, sore throat, diarrhea, headache, anosmia, and chest pain (please see Methods for details). **Described as mean ± standard error.

troponin elevation) (20%), hemodynamic instability (18%), suspected myocarditis (16%), suspected pulmonary embolism (6%), clinically relevant arrhythmias (5%), and others (e.g., suspected pericardial effusion, endocarditis, syncope, and cardioembolic source of brain stroke) (5%).

Table 3 shows the main TTE findings of the hospitalized patients with COVID-19 according to history of previous CVD. The most prevalent echocardiographic abnormalities were LV hypertrophy (29%), pulmonary hypertension (25%), LV systolic dysfunction (16.5%), RV systolic dysfunction (15.9%), grade II/III LV diastolic dysfunction (11%), and LV regional wall motion abnormality (11%). Pericardial effusion (7%) and moderate to severe valvular regurgitation (9%) were less common. None of the patients had evidence of wall motion abnormalities suggestive of stress-induced cardiomyopathy.

As expected, patients without CVD were less likely to present TTE findings suggestive of abnormal LV structure and/or function, including LV hypertrophy (25% vs. 45%, $p=0.001$), LV systolic dysfunction (13% vs. 36%, $p<0.001$), regional wall motion abnormalities (6% vs. 29%, $p<0.001$), grade II or III LV diastolic dysfunction (9% vs. 29%, $p=0.03$), and pulmonary hypertension (22% vs. 36%, $p=0.019$), but only 52% displayed a normal TTE findings. The frequency of RV systolic dysfunction (13% vs. 25%, $p=0.07$) was similar between patients with and those without previous CVD.

When we analyzed only patients without previous pulmonary disease, the frequency of RV systolic dysfunction was also similar for patients with and those without previous CVD (15% vs. 20%, respectively, $p=0.45$). Echocardiography results changed clinical management in 25% of cases, mostly triggering the initiation of therapy for heart failure, prescription of anticoagulants, or referral for catheterization.

Discussion

In this multicenter registry, we found that abnormal findings on TTE were relatively common among hospitalized patients with COVID-19, even those without previous CVD. Although individuals without CVD were less likely to present echocardiographic findings suggestive of abnormal LV structure and/or function compared to those with previous CVD, roughly half of them displayed at least one abnormal finding. LV hypertrophy and pulmonary hypertension were the most prevalent abnormalities in the group without previous CVD, followed by RV systolic dysfunction and LV systolic dysfunction. In contrast, only 1 in 13 patients without previous CVD had severe echocardiographic abnormalities.

Previous studies described echocardiographic findings in patients with COVID-19, but the results have been considerably heterogeneous. The prevalence of LV systolic dysfunction, RV dysfunction, and RV dilation have ranged from 5.4%¹⁸ to 37.4%,⁵ 3.6%¹⁸ to 33%,¹⁹ and 0%²⁰ to 46.9%,²¹ respectively. While most studies have identified RV dysfunction and/or dilation as the most frequent echocardiographic change,^{6,7,22,23} others reported that LV systolic dysfunction was more prevalent.^{18, 20} The contradictory results regarding the prevalence and consequences of echocardiographic changes among patients with COVID-19 have several caveats. Relatively small samples, referral bias, differences in TTE protocols, inaccurate definitions of echocardiographic abnormalities, and differences in population characteristics, such as the proportion of patients with previous CVD, may have led to the wide-ranging conclusions about the cardiac manifestations of COVID-19. Our study sheds light on the contribution of previous CVD to the prevalence of echocardiographic findings in patients hospitalized with COVID-19.

To mitigate referral bias, Szekely et al. systematically performed TTE in 100 consecutive patients hospitalized for COVID-19, 43% of whom had prior CVD. They found that the most frequent abnormality was RV dysfunction/dilation, while only a minority of patients (10%) presented with LV systolic dysfunction.⁶ In addition, COVID-19 patients with myocardial injury or a worse clinical condition did not demonstrate a significantly higher prevalence in LV systolic function, but they had worse RV function than patients without myocardial injury or with a better clinical condition.⁶ The high prevalence of RV dysfunction and small proportion of LV dysfunction were also reported in other smaller studies.^{7,22,23} Although these studies did not analyze differences according to the presence or absence of previous CVD, our findings expand their research by confirming that RV involvement is common and seems to affect patients with versus without previous CVD similarly. As expected, LV hypertrophy, systolic dysfunction, and diastolic dysfunction

Table 3 - Echocardiographic findings of hospitalized patients with COVID-19 according to history of previous cardiovascular disease.

Parameter	All patients n=310	No previous CVD n=240	Previous CVD n=70	P value
LV hypertrophy, n (%)	91 (29.5%)	60(25.1%)	31(44.9%)	0.001
LV dilation, n (%)	38 (12.4%)	15(6.3%)	23(33.8%)	< 0.001
LV systolic dysfunction, n (%)				< 0.001
None	257 (83.4%)	213 (89.1%)	44(63.8%)	
Mild	14 (4.5%)	8 (3.3%)	6 (8.7%)	
Moderate	17 (5.5%)	8 (3.3%)	9 (13.0%)	
Severe	20 (6.5%)	10(4.2%)	10(14.5%)	
LV diastolic dysfunction, n (%)				< 0.001
None	127 (41.0%)	116 (48.3%)	11(15.7%)	
Mild	130 (41.9%)	93(38.8%)	37(52.9%)	
Moderate	32 (10.3%)	21(8.8%)	11(15.7%)	
Severe	3 (1.0%)	1 (0.4%)	2 (2.9%)	
Unknown	18 (5.8%)	9 (3.8%)	9 (12.9%)	
LV regional wall motion abnormality, n (%)	35 (11.4%)	15(6.3%)	20(29.0%)	< 0.001
RV systolic dysfunction, n (%)				0.07
None	259 (84.1%)	207 (86.6%)	52(75.4%)	
Mild	24 (7.8%)	17(7.1%)	7 (10.1%)	
Moderate	13 (4.2%)	9 (3.8%)	4 (5.8%)	
Severe	12 (3.9%)	6 (2.5%)	6 (8.7%)	
Pulmonary hypertension				0.019
None	229 (75.1%)	185 (78.4%)	44(63.8%)	
Mild	44 (14.4%)	33(14.0%)	11(15.9%)	
Moderate	28 (9.2%)	16(6.8%)	12(17.4%)	
Severe	4 (1.3%)	2 (0.8%)	2 (2.9%)	
Moderate to severe valve regurgitation, n (%)				
Aortic	4 (1.3%)	1 (0.4%)	3 (4.4%)	0.011
Mitral	13 (4.3%)	6 (2.5%)	7 (10.3%)	0.005
Tricuspid	11 (3.6%)	5 (2.1%)	6 (8.8%)	0.009
Pericardial effusion, n (%)	22 (7.1%)	16 (6.7%)	6 (8.6%)	

CVD, cardiovascular disease; LV, left ventricular; RV, right ventricular.

were more common in patients with previous CVD, partially reflecting the higher prevalence of cardiovascular risk factors and pre-existing cardiovascular conditions. In contrast, nearly 11% of patients without CVD presented LV systolic dysfunction, which may reflect a COVID-19-related *de novo* LV impairment. Echocardiographic parameters that identify myocardial damage earlier and more accurately than the traditional parameters, such as two-dimensional LV or RV global longitudinal strain, have been less used in the context of COVID-19 due to the recommendations for the use of focused examination protocols that minimize the healthcare worker exposure time to infection. Studies that assessed LV systolic function with global longitudinal strain detected a higher proportion of patients with LV dysfunction than those that used LVEF.²⁴

Pulmonary hypertension was less common in patients without CVD than in those with prior CVD, but the frequency of RV systolic dysfunction was similar between the two groups. Interestingly, when only patients without previous pulmonary disease were evaluated, the frequency of RV

systolic dysfunction was also similar for patients with versus without previous CVD. In addition, RV systolic dysfunction appeared to be more frequent than LV systolic dysfunction in patients without previous CVD. The development of RV-related changes in COVID-19 may be the consequence of a myriad of phenomena that affect the lungs, such as hypoxia, inflammation, acute respiratory distress syndrome, pulmonary microvascular thrombosis, pulmonary thromboembolism, and mechanical ventilation.

As major efforts by the scientific community aim to mitigate the severe health consequences of the COVID-19 pandemic, it becomes challenging to balance the use of echocardiography to provide high-quality medical care without excessively increasing the risk of cross-infection between healthcare professionals and patients. There is a relative lack of prospectively collected data regarding the prevalence and extent of cardiac findings in patients with severe COVID-19. Our results increase the understanding of which parameters of cardiac function are most frequently abnormal in patients with severe COVID-19 according

to the history of previous CVD using real-world national registry data. It is important to emphasize that the presence of cardiac dysfunction is independently associated with worse prognosis in patients with severe COVID-19.⁽²⁵⁾ TTE evaluations should be considered in patients with COVID-19 and suspected cardiovascular complications to characterize the underlying cardiac substrate, for risk stratification, and to potentially guide management strategies.²⁵ In patients with acute clinical deterioration, focused (or complete, if necessary) TTE may help in clinical decision-making in a significant proportion of scenarios. On the other hand, its indications should be based on critical consideration of the benefits to patients, contamination risk for healthcare personnel, and use of the limited personal protective equipment.

Our study has some limitations that deserve attention. First, the echocardiographic measurements were performed by local investigators without confirmation by a core lab. Nevertheless, all echocardiograms were performed by experienced physicians who followed international guidelines. Second, abnormal findings may have been overestimated due to referral bias, as the echocardiograms were performed at the discretion of the attending physician. Third, 36 of 310 patients were diagnosed with COVID-19 based on clinical and imaging data, but no RT-PCR testing was performed. All “probable” cases were included at the very beginning of the pandemic in Brazil, at which time many hospitals still did not have sufficient tests. Finally, although we described the TTE findings in patients without previous CVD, we still cannot rule out whether these cardiac abnormalities were pre-existing; thus, our results should be interpreted with caution.

References

1. Costa IBSDS, Bittar CS, Rizk SI, Araújo Filho AE, Santos KAQ, Machado TIV, et al. The Heart and COVID-19: What Cardiologists Need to Know. *Arq Bras Cardiol* 2020;114(5):805-16.
2. Costa IBSDS, Rochitte CE, Campos CM, Barberato SH, Oliveira GMM, Lopes MACQ, et al. Cardiovascular Imaging and Interventional Procedures in Patients with Novel Coronavirus Infection. *Arq Bras Cardiol* 2020;115(1):111-26.
3. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE Statement on Protection of Patients and Echocardiography Service Providers During the 2019 Novel Coronavirus Outbreak: Endorsed by the American College of Cardiology. *J Am Soc Echocardiogr* 2020;33(6):648-53.
4. Sud K, Vogel B, Bohra C, Garg V, Talebi S, Lerakis S, et al. Echocardiographic Findings in Patients with COVID-19 with Significant Myocardial Injury. *J Am Soc Echocardiogr* 2020;33(8):1054-5.
5. Dweck MR, Bularga A, Hahn RT, Bing R, Lee KK, Chapman AR, et al. Global Evaluation of Echocardiography in Patients with COVID-19. *Eur Heart J Cardiovasc Imaging* 2020;21(9):949-58.
6. Szekely Y, Lichter Y, Taieb P, Banai A, Hochstadt A, Merdler I, et al. The Spectrum of Cardiac Manifestations in COVID-19 - A Systematic Echocardiographic Study. *Circulation* 2020;142(4):342-53.
7. Jain SS, Liu Q, Raikhelkar J, Fried J, Elias P, Poterucha TJ, et al. Indications for and Findings on Transthoracic Echocardiography in COVID-19. *J Am Soc Echocardiogr* 2020;33(10):1278-84.
8. Skulstad H, Cosyns B, Popescu BA, Galderisi M, Salvo GD, Donal E, et al.

Conclusions

Among hospitalized patients with COVID-19, echocardiographic findings of abnormal cardiac structure and/or function were less common among those without previous CVD. RV systolic dysfunction appeared to affect patients with and those without previous CVD similarly, even those without previous pulmonary disease. TTE findings were normal in just over half of the patients without previous CVD. If properly indicated, TTE can provide useful information for the clinical management of critically ill patients with COVID-19.

Acknowledgments

We express our gratitude to the following colleagues who assisted with this research: Francisco de Assis Carvalho Santana, Fernando Melo Netto, Simone Ferreira Leite, Bianca Corrêa Rocha de Mello, Dassis Cajuba, Filipe Lima de Menezes, Nathalia Caetano Lobo, Vanessa Guimarães Esmanhoto Andrioli, and Pedro Gabriel Melo de Barros e Silva.

Authors' contributions

Research creation and design: SHB, RB. Data acquisition: RB, FR, HLMM, PP, MEBO, ALSB, ACA, JMBS, ACCW, LBPS, MVCRR, MLCP. Data analysis and interpretation: SHB, RB, MMFS. Statistical analysis: SHB, MMFS. Obtaining financing: SHB. Manuscript writing: SHB, MMFS. Critical revision of the manuscript for important intellectual content: SHB, MMFS.

Conflict of interest

The authors have declared that they have no conflict of interest.

- COVID-19 Pandemic and Cardiac Imaging: EACVI Recommendations on Precautions, Indications, Prioritization, and Protection for Patients and Healthcare Personnel. *Eur Heart J Cardiovasc Imaging* 2020;21(6):592-8.
9. Beck ALS, Barberato SH, Almeida ALC, Grau CRPC, Lopes MMU, Lima RSL, et al. Position Statement on Indications and the Safe Reintroduction of Cardiovascular Imaging Methods in the COVID-19 Scenario – 2021. *Arq Bras Cardiol* 2021;116(3):659-78.
10. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28(1):1-39.e14.
11. Douglas PS, Carabello BA, Lang RM, Lopez L, Pellikka PA, Picard MH, et al. 2019 ACC/AHA/ASE Key Data Elements and Definitions for Transthoracic Echocardiography: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Data Standards (Writing Committee to Develop Cardiovascular Endpoints Data Standards) and the American Society of Echocardiography. *J Am Coll Cardiol/American Heart Association Task Force on Clinical Data Standards* 2019;74(3):403-69.
12. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography. *Eur J Echocardiogr* 2009;10(2):165-93.
13. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the Echocardiographic

- Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography Endorsed by the European Association of Echocardiography, a Registered Branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;23(7):685-713; quiz 86-8.
14. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2017;70(2):252-89.
 15. Barberato SH, Romano MMD, Beck ALS, Rodrigues ACT, Almeida ALC, Assunção BMBL, et al. Position Statement on Indications of Echocardiography in Adults – 2019. *Arq Bras Cardiol* 2019;113(1):135-81.
 16. Demirtas H, Freels SA, Yucel RM. Plausibility of Multivariate Normality Assumption When Multiply Imputing non-Gaussian Continuous Outcomes: A Simulation Assessment. *J Stat Comput Simul* 2008;78(1):69-84.
 17. Toutenburg H, Rubin, DB: Multiple Imputation for Nonresponse in Surveys. *Stat Pap* 1990;31(1):180-.
 18. Deng Q, Hu B, Zhang Y, Wang H, Zhou X, Hu W, et al. Suspected Myocardial Injury in Patients with COVID-19: Evidence from Front-Line Clinical Observation in Wuhan, China. *Int J Cardiol* 2020;311:116-21.
 19. Li Y, Li H, Zhu S, Xie Y, Wang B, He L, et al. Prognostic Value of Right Ventricular Longitudinal Strain in Patients with COVID-19. *JACC Cardiovasc Imaging* 2020;13(11):2287-99.
 20. van den Heuvel FMA, Vos JL, Koop Y, van Dijk APJ, Duijnhouwer AL, de Mast Q, van de Veerdonk FL, Bosch F, Kok B, Netea MG, Hoogerwerf J, Hoefsloot W, Tjwa ETTL, de Korte CL, van Kimmenade RRJ, Nijveldt R. Cardiac function in relation to myocardial injury in hospitalised patients with COVID-19. *Neth Heart J* 2020;28(7-8):410-7.
 21. Rath D, Petersen-Urbe Á, Avdiu A, Witzel K, Jaeger P, Zdanyte M, et al. Impaired Cardiac Function Is Associated with Mortality in Patients with Acute COVID-19 Infection. *Clin Res Cardiol* 2020;109(12):1491-9.
 22. Argulian E, Sud K, Vogel B, Bohra C, Garg VP, Talebi S, et al. Right Ventricular Dilation in Hospitalized Patients with COVID-19 Infection. *JACC Cardiovasc Imaging* 2020;13(11):2459-61.
 23. Mahmoud-Elsayed HM, Moody WE, Bradlow WM, Khan-Kheil AM, Senior J, Hudsmith LE, et al. Echocardiographic Findings in Patients with COVID-19 Pneumonia. *Can J Cardiol* 2020;36(8):1203-7.
 24. Carrizales-Sepúlveda EF, Vera-Pineda R, Flores-Ramírez R, Hernández-Guajardo DA, Pérez-Contreras E, Lozano-Ibarra MM, et al. Echocardiographic Manifestations in COVID-19: A Review. *Heart Lung Circ* 2021;30(8):1117-29.
 25. Giustino G, Croft LB, Stefanini GC, Bragato R, Silbiger JJ, Vicenzi M, et al. Characterization of Myocardial Injury in Patients with COVID-19. *J Am Coll Cardiol* 2020;76(18):2043-55.