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ORIGINAL ARTICLE

Echocardiogram in Critically ill Patients with COVID-19: ECOVID Study

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Abstract

Background: Literature is scarce on echocardiographic characteristics of COVID-19 patients admitted to the intensive care unit (ICU).

Objectives: To describe echocardiographic characteristics of ICU COVID-19 patients and associate them with clinical signals/symptoms, laboratory findings and outcomes.

Methods: Patients with RT-PCR-confirmed COVID-19, admitted to the ICU, who underwent echocardiography were included. Clinical characteristics associated with an abnormal echocardiogram (systolic ventricular dysfunction of any degree — left and/or right ventricle — and/or high filling pressures and/or moderate to severe pericardial effusion) were analyzed. Groups were compared using the Student's t-test, chi-square, and logistic regression. A $p < 0.05$ was considered statistically significant.

Results: A total of 140 patients met inclusion criteria, and 74 (52.9%) had an abnormal echocardiogram. A low number of left and right ventricular systolic dysfunction was observed, and 35% of the population had a normal diastolic function. In the univariate analysis, characteristics associated with abnormal echocardiogram were age, chronic kidney disease, elevated troponin, previous heart failure, and simplified acute physiology score 3 (SAPS 3). In the regression model, troponin and SAPS3 score were independent markers of abnormal echocardiogram. An abnormal echocardiogram was associated with a higher prevalence of in-hospital death (RR 2.10; 95% CI 1.04-4.24) and orotracheal intubation (RR 2.3; 95% CI 1.14-4.78).

Conclusions: COVID-19 has little effect on ventricular function, but it is common to find increased filling pressures. Elevated serum troponin level and SAPS3 score were the independent markers of an abnormal echocardiogram. In addition, the prevalence of in-hospital death and need for mechanical ventilation were higher in patients with abnormal echocardiogram.

Keywords: COVID-19, Critical Care; Troponin/therapeutic use; Echocardiography/methods; Diagnostic, Imaging.

Introduction

Cardiovascular risk factors are common in hospitalized patients with COVID-19, particularly hypertension and diabetes. In a Chinese study, the prevalence of coronary artery disease and cerebrovascular disease was 6.0% and 2.3%, respectively.[1] Myocardial injury (22.2%), shock (30.6%), and arrhythmias (44.4%) are also frequent, especially in patients admitted to an intensive care unit (ICU).[2] In addition, cardiovascular disease and myocardial injury are associated with a higher mortality rate from COVID-19.[3]

Cardiovascular complications are more common in critically ill patients. Wei et al.,[4] demonstrated that myocardial injury was present in 15.8% of patients and, in half of them, troponin levels were elevated more than five times the upper limit of normal. In this study, the increase in troponin was associated with higher mortality.[4]

Echocardiography is a cardiovascular imaging method widely available in ICUs that can provide valuable information on cardiac function in patients with COVID-19. Dweck et al.,[5] found that 55% of COVID-19 patients had an abnormal echocardiogram using only ventricular dysfunction as a criterion. However, despite being a valuable method, echocardiographic assessment was associated with an increased risk of contamination of healthcare workers.[6,7]

The objective of our study was to describe echocardiographic characteristics in patients admitted to an ICU for COVID-19 and to identify clinical, laboratory findings and outcomes associated with an abnormal echocardiogram, to better identify patients who would most benefit from this method.

Methods

This was a retrospective study that used a convenience sample that included all patients hospitalized in an adult ICU of a private tertiary hospital, who had a RT-PCR-confirmed COVID-19 and underwent transthoracic echocardiography (TTE) during hospitalization. The criteria for admission in this unit were based on institutional protocols and clinical judgment. Echocardiography was ordered at the discretion of the medical team. For patients who underwent more than one exam, the first exam was considered for analysis. Patients with dementia, advanced and terminal illnesses, patients in palliative treatment, and those less than 48 hours in ICU were excluded.

TTE was performed at bedside within 48 hours of hospitalization. The following characteristics were evaluated according to the recommendations of the American Society of Echocardiography:[8] systolic function, ejection fraction, diastolic function, right ventricular function, pulmonary artery systolic pressure (PASP), left atrial size, E/e' ratio, pericardial effusion and right atrial pressure (RAP) estimated by inferior vena cava analysis.

Besides, we evaluated clinical characteristics (age, gender, history of heart failure, hypertension, diabetes, renal failure, obesity, and atrial fibrillation) and laboratory data (ultrasensitive troponin and d-dimer serum levels) of the patients.

The echocardiogram was defined as abnormal when it demonstrated systolic ventricular dysfunction of any degree (left and/or right ventricle) and/or high filling pressures (E/E' ratio> 16; PASP> 40mmHg, RAP> 15mmHg or diastolic dysfunction ≥ grade 2) and/or moderate to severe pericardial effusion (Figure 1).

Statistical Analysis

Continuous variables were described as mean and standard deviation (when there was a normal distribution) or median and interquartile range (when there was not a normal distribution). The normality test used was the Kolmogorov-Smirnov test. Categorical variables were expressed as percentage.

Echocardiographic characteristics were assessed in the entire population and subgroups (hypertensive, diabetic, patients with elevated troponin, and mechanic ventilated patients). For continuous variables, we used the unpaired Student's t-test and for categorical variables, the chi-square test. We also analyzed patients' clinical characteristics associated with an abnormal echocardiogram.

Clinical variables were also assessed using the classification tree,[9] a machine learning statistical technique, to identify variables that could predict an abnormal echocardiogram. Finally, binary logistic regression was performed with variables that showed $p<0.01$ in the univariate analysis (Student's t-test or chi-square test). $P<0.05$ was considered significant. For statistical analysis, the SPSS version 26 program was used.

Results

During the study period, 272 admissions to ICU for COVID-19 were identified. Of these, 159 patients underwent echocardiography (58.5%) and 19 were excluded because they had incomplete demographic data (Figure 2).

We found 74 abnormal echocardiograms (52.9%) according to pre-established criteria. The median time to perform echocardiography was one day after admission. Characteristics of the study population are summarized in Table 1.

Echocardiographic parameters were assessed in the entire population and pre-defined subgroups. The results are shown in Table 2.

A low occurrence of left and right ventricular systolic dysfunction was observed, and 35.0% of the population had a normal diastolic function. In the subgroup analysis, we found a lower proportion of normal left ventricular systolic function, normal diastolic function, and left atrial enlargement in patients with elevated troponin (above the 99th percentile). There was also a lower prevalence of
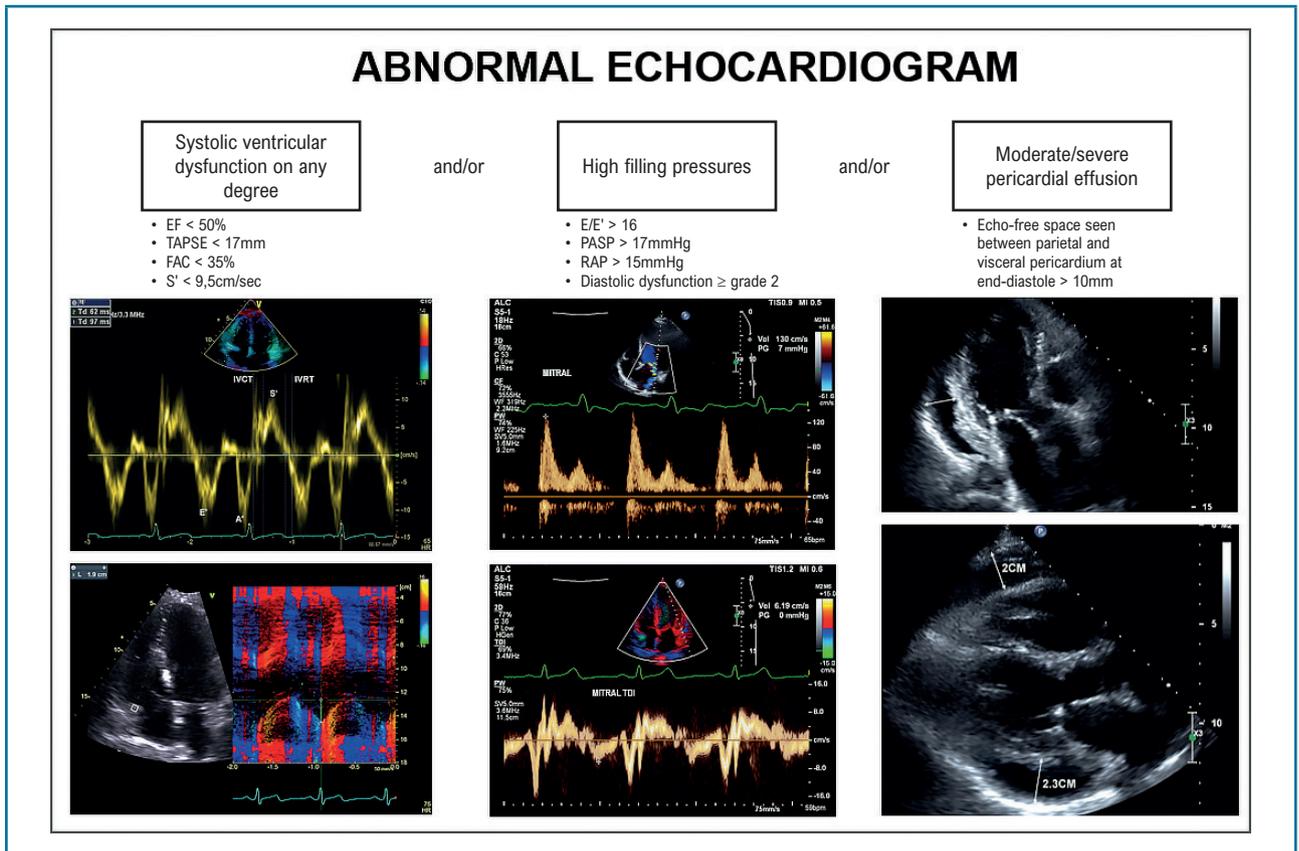
Figure 1 – Criteria for abnormal echocardiogram.
TAPSE: tricuspid annular plane systolic excursion; FAC: fractional area change; PASP: pulmonary artery systolic pressure; RAP: right atrial pressure; EF: ejection fraction.
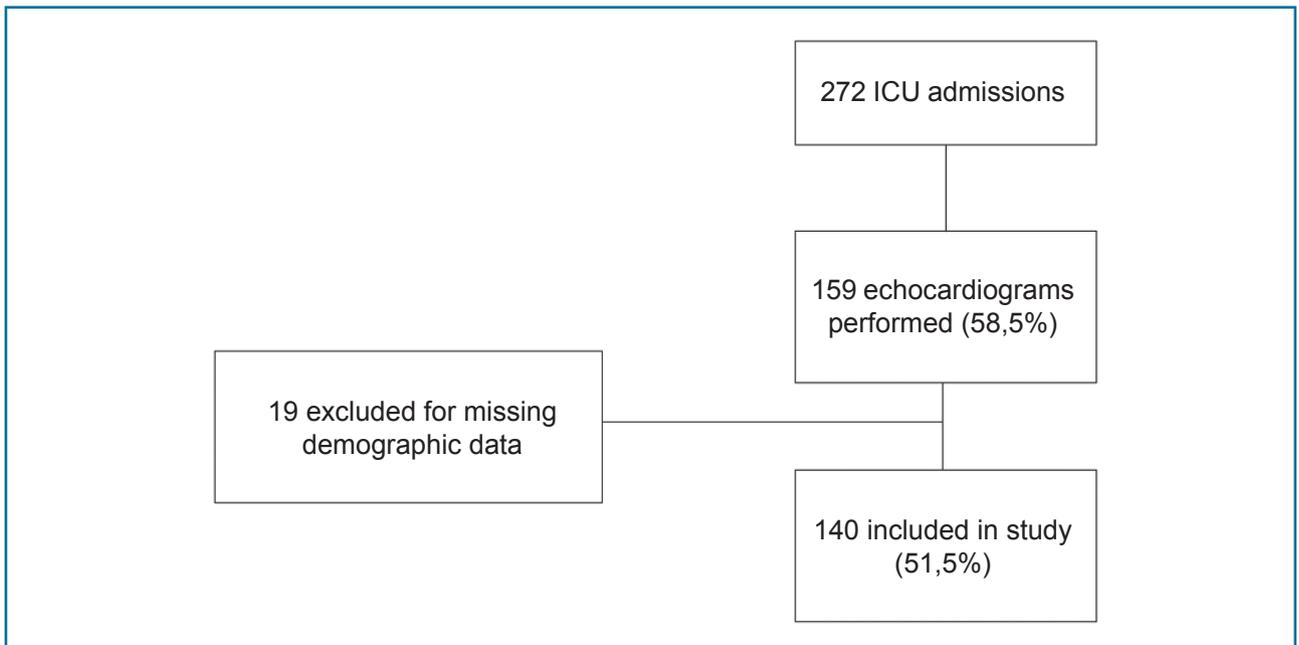

Figure 2 – Flowchart of inclusion of patients in the study.
ICU: intensive care unit.

Table 1 – Characteristics of the study population (n=140).

Characteristics	
Age (mean ± SD)	65.6 ± 16.1 years
Age ≥ 65 years	55.7%
Male gender	66.4%
Obesity	20.7%
Previous heart failure	6.4%
Chronic kidney disease	7.9%
Systemic arterial hypertension	60.7%
Diabetes	35.7%
Previous myocardial infarction	7.9%
Previous atrial fibrillation	4.3%
Previous stroke	5.0%
Mechanically ventilated patients	49.2%
Use of vasopressors	39.8%
Renal replacement therapy	18.0%
Troponin elevation	46.4%
Mean SAPS3	46.6±14.2
Length of stay (median – IQR) (days)	7 [5 ;19]
In-hospital mortality	37.9%

SAPS: Simplified acute physiology score; SD: standard deviation; IQR: interquartile range.

diastolic dysfunction among hypertensive and diabetic patients, and a higher prevalence of left atrial enlargement in hypertensive patients. Furthermore, we found three cases of Takotsubo cardiomyopathy that showed complete recovery after 10 days (Figure 3).

Univariate analysis of the clinical characteristics and outcomes associated with an abnormal echocardiogram are available in Table 3.

In the univariate analysis, characteristics associated with an abnormal echocardiogram were age, elevated troponin, chronic kidney disease, previous heart failure, mechanical ventilation and SAPS3 score. In the binary logistic regression model, variables with p<0.01 were included, except for previous heart failure, since all patients with this previous condition had an abnormal echocardiogram. The regression model is shown in Table 4.

In this regression model, troponin elevation and SAPS3 score were independent markers of abnormal echocardiogram in patients admitted to the ICU for COVID19. In the classification tree, elevated troponin was the main marker of abnormal echocardiogram (Figure 4).

Regarding the outcomes, the abnormal echocardiogram was associated with a higher prevalence of in-hospital death (RR 2.10; 95% CI 1.04-4.24) and orotracheal intubation (RR 2.3; 95% CI 1.14-4.78).

Table 2 – Echocardiographic characteristics of the study population and subgroups.

	All (n=140)	Arterial hypertension (n=85)			Diabetes (n=50)			Elevated troponin (n=65)			MVP (n=63)		
		Yes	No	p	Yes	No	p	Yes	No	p	Yes	No	p
Normal LVSF	89.3%	89.4%	89.1%	0.581	88.0%	90.0%	0.459	83.1%	94.7%	0.026	85.7%	90.8%	0.270
LVEF	65±12	64±12	67±12	0.196	65±13	66±12	0.644	63±13	67±11	0.108	64±13	66±13	0.551
Normal LVDF	35.0%	24.7%	50.9%	0.001	22.0%	42.2%	0.012	18.5%	49.3%	0.001	28.6%	40.0%	0.120
Normal RVSF	98.6%	96.4%	100%	0.153	100%	97.8%	0.412	96.9%	100%	0.214	98.4%	98.5%	0.744
PASP	40±12	41±12	39±15	0.591	41±14	40±11	0.660	41±11	39±12	0.532	41±10	44±12	0.412
LAE	22.1%	28.2%	12.7%	0.024	28.0%	18.9%	0.151	29.2%	16.0%	0.047	22.2%	26.2%	0.378
E/e'	10±4	10±4	9±3	0.208	11±4	9±4	0.222	10±4	9±3	0.153	10±4	10±4	0.825
PEf	6.4%	7.1%	5.4%	0.326	10.0%	4.4%	0.206	4.6%	8.0%	0.558	4.8%	7.7%	0.574
RAP > 15	32.4%	33.3%	30.9%	0.627	32.0%	32.6%	0.773	42.2%	24.0%	0.061	45.2%	24.6%	0.051

MVP: mechanically ventilated patients; LVSF: left ventricular systolic function; LVEF: left ventricular ejection fraction; LVDF: left ventricular diastolic function; RVSF: right ventricular systolic function; PASP: pulmonary artery systolic pressure; LAE: left atrial enlargement; PEf: pericardial effusion; RAP: right atrial pressure.
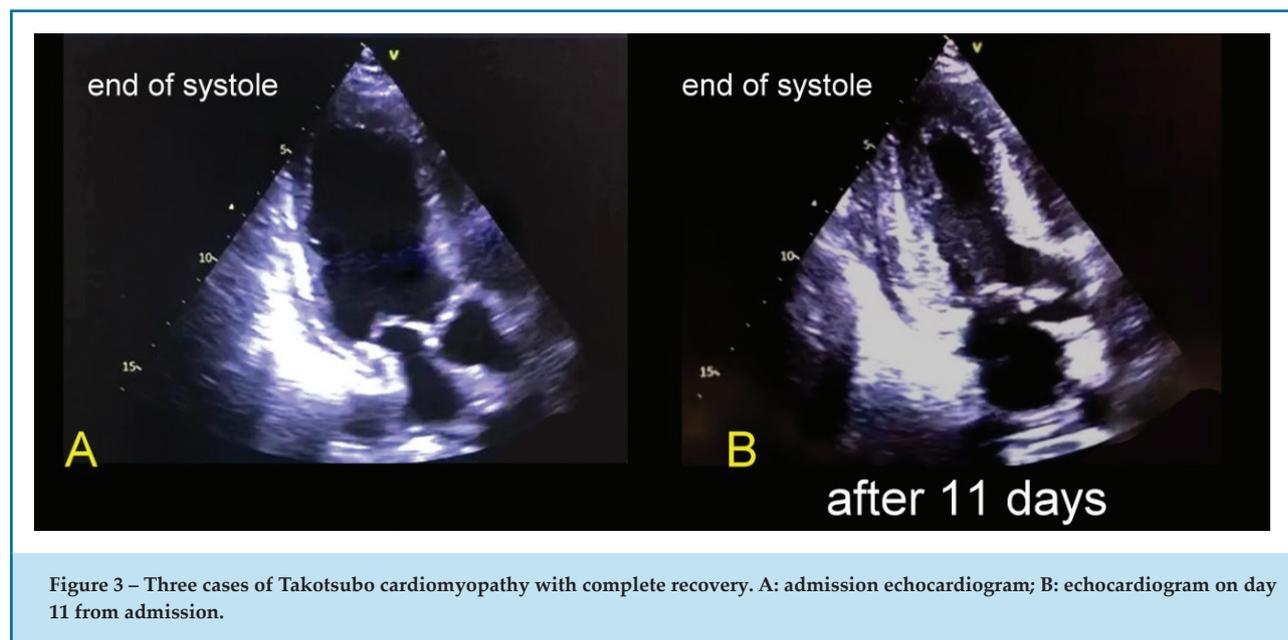
Figure 3 – Three cases of Takotsubo cardiomyopathy with complete recovery. A: admission echocardiogram; B: echocardiogram on day 11 from admission.

Table 3 – Clinical features, laboratory variables and outcomes associated with an abnormal echocardiogram of the study patients.

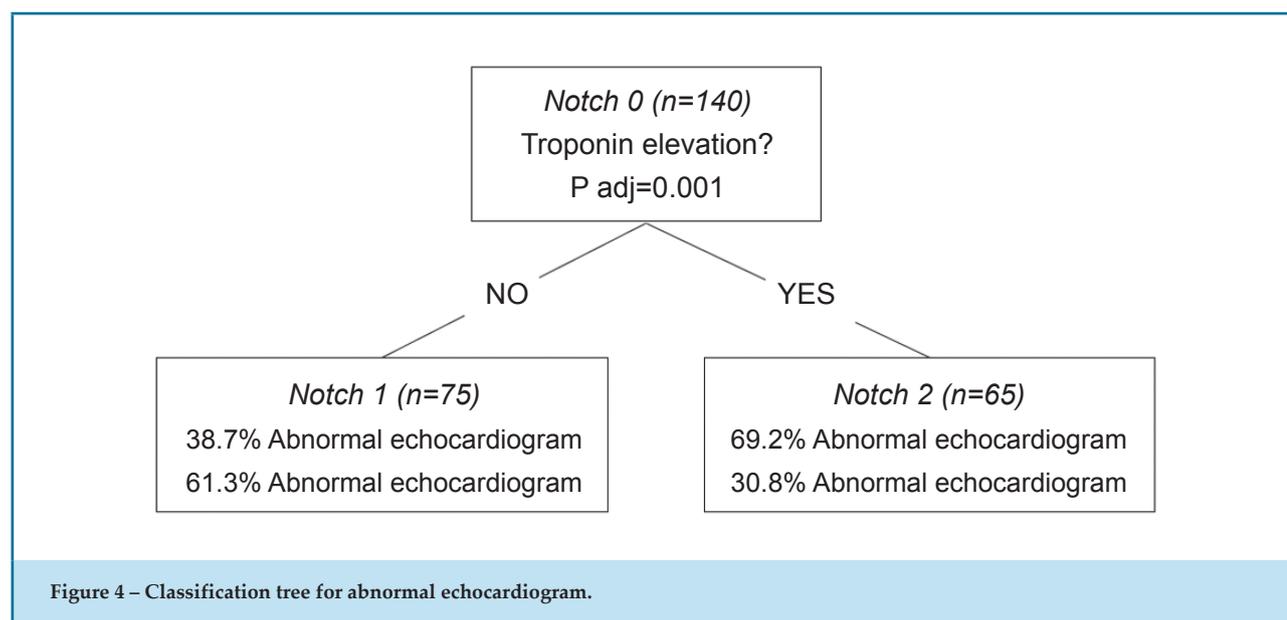|	Normal echocardiogram (n=66)	Abnormal echocardiogram (n=74)	p
Male sex	65.2%	67.6%	0.451
Mean age	**61.5±15.6**	**69.3±15.7**	**0.004**
Age ≥ 65 years	**42.4%**	**67.6%**	**0.002**
SAH	53.0%	67.6%	0.056
DM	30.3%	40.5%	0.139
CKD	**3.0%**	**12.2%**	**0.043**
Previous myocardial infarction	6.1%	9.5%	0.336
Previous HF	**0.0%**	**12.2%**	**0.003**
Previous atrial fibrillation	1.5%	6.8%	0.133
Previous stroke	4.5%	5.4%	0.564
Obesity	19.7%	21.6%	0.472
Troponin elevation	**30.3%**	**60.8%**	**<0.001**
Mean peak D-dimer (ng/mL)	9107±16643	11587±15418	0.362
Mechanic ventilated patients	**37.5%**	**58.3%**	**0.015**
Use of vasopressors	30.4%	47.2%	0.069
Renal replacement therapy	10.7%	23.6%	0.067
Mean SAPS3	**42.0±14.0**	**50.7±13.2**	**<0.001**
In-hospital mortality	**28.8%**	**45.9%**	**0.027**

SAH: arterial hypertension; DM: diabetes mellitus; CKD: chronic kidney disease; HF: heart failure; SAPS: simplified acute physiology score.

Table 4 – Binary logistic regression with clinical variables correlated with an abnormal echocardiogram.			
Variable	OR	95% CI	P
Troponin elevation	**2.76**	**1.32-5.83**	**0.007**
Age	1.01	0.98-1.03	0.561
SAPS3	1.04	1.01-1.07	0.025
SAPS: simplified acute physiology score; CI: confidence interval.			

Figure 4 – Classification tree for abnormal echocardiogram.

Discussion

The new coronavirus disease (COVID-19) is highly transmissible and can cause a severe inflammatory response that affects several organs.[10] Because of this high transmissibility, several measures were taken to reduce the population's exposure to the virus. Healthcare workers demand special care due to the exposure during the care of these patients,[11] and hence strategies to reduce this exposure are welcome.

Echocardiogram is a very useful tool in the ICU that can provide information in several clinical settings, such as hemodynamic instability, ventricular dysfunction, acute coronary syndrome, hypovolemia, acute valve dysfunction, infectious endocarditis, cardiac tamponade, pulmonary embolism, and aortic dissection.[12] Few echocardiographic data of patients admitted by COVID-19, however, are available.

In our study, echocardiographic changes were present in 52.9% of echocardiograms. The prevalence of ventricular dysfunction was low, and main changes were related to high filling pressures. The prevalence of ventricular dysfunction was similar to that found by Szekely et al.,[13] where 10% of patients had systolic ventricular dysfunction. Also, 20% of these patients had high filling pressures. The high number of patients with dysfunction or enlargement of the right ventricle (39%) in this study[13] was noteworthy. However, the authors do not specify the occurrence of right systolic dysfunction alone. Right ventricular dilation can happen for a variety of conditions, including hypervolemia and mechanical ventilation. In our study, right ventricular dilation was not evaluated, but systolic right ventricular dysfunction was uncommon.

Dweck et al.,[5] studied echocardiographic variables in patients with a presumed diagnosis of COVID-19 using a

questionnaire answered by echocardiographers around the world.[5] In this study, 1,216 patients were included and 61% of these patients had a normal systolic left ventricular function. Of these, 60% required intensive care and 73% had confirmed diagnosis of COVID-19. The prevalence of hypertension in this study was low and may point to a population with lower cardiovascular risk. As its data were obtained through a questionnaire from several countries, we can expect great variability of data since the echocardiogram is an operator-dependent method.

In the analysis of parameters associated with an abnormal echocardiogram, myocardial injury, previous heart failure, mechanic ventilated patients, age, and SAPS3 stood out. Only two studies performed a similar analysis. Szekely et al.,[13] used broader criteria for abnormal echocardiogram (any degree of systolic and/or diastolic dysfunction, valve changes, and right ventricular dilation and dysfunction). Variables that were associated with this outcome in this study were: B-type natriuretic peptide (BNP) > 80pg/mL, C-reactive protein> 5mg/L, and systolic blood pressure. However, patients were less severe, as only 10% of them required mechanical ventilation, and only 3% used vasopressors.

Yuan et al.,[14] analyzed 434 patients hospitalized for COVID-19, who underwent echocardiography within 14 days, aiming to identify the variables related to the presence of an urgent echocardiographic finding (left ventricular ejection fraction ≤35%, wall motion score index ≥1.5, ≥moderate right ventricular dysfunction, ≥moderate pericardial effusion, intracardiac thrombus, PASP> 50mmHg, or ≥moderate-severe valvular disease).[14] In this study,[14] troponin and BNP were associated with urgent echocardiographic findings, data similar to that found in our study. However, in their study, many patients who were not admitted to the ICU were included, resulting in a less severe profile, in addition to using other criteria to define an abnormal echocardiogram. Anyway, the similarity of results brings robustness to our findings.

Troponin is a marker of worse prognosis in several clinical conditions, including in COVID-19. Lala et al.,[15] showed that 36% of patients had elevated troponin levels and this biomarker was associated with higher mortality. Additionally, troponin elevation was more common in patients with cardiovascular disease.[15]

Few studies have evaluated the association of an abnormal echocardiogram with adverse outcomes. In our study, an abnormal echocardiogram was associated with increased hospital mortality and the need for mechanical ventilation. The few studies published on this topic only pointed to the prognostic value of right ventricular dysfunction in patients with COVID-19.[16,17]

The main limitations of our study are the fact that it was a retrospective study, and the echocardiographic analysis was not performed in ideal conditions. All examinations were performed at the bedside in unfavorable scenarios (patients on mechanical ventilation, with multiple devices that made the access for the echocardiographer difficult), in addition to the need for a fast examination to reduce the exposure of the healthcare professional. For this reason, many parameters were assessed subjectively but covering all the main information. Echocardiograms were carried out by examiners fully certified by the Brazilian Cardiology Society. Despite the limitations, no study published to date has exclusively studied patients admitted to intensive care, which brings originality to these data.

Conclusions

In patients admitted to intensive care with COVID-19, the echocardiogram showed a low prevalence of myocardial dysfunction and a high prevalence of increased filling pressures. An elevated serum troponin level was an independent marker of abnormal echocardiogram. An abnormal echocardiogram was associated with increased hospital mortality and the need for mechanical ventilation.

Author contributions

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the IDOR - Instituto D'Or de Pesquisa e Ensino under the protocol number CAAE 33206620.0.0000.5249. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. As this is a retrospective study, the informed consent term was waived by the ethics committee.

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