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The Prognostic Value of Echocardiographic Findings in Prediction of In-Hospital Mortality of COVID-19 Patients

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Abstract

Introduction: The correlation between echocardiographic findings and the outcome of COVID-19 patients is still under debate.

Objective: In the present study it has been endeavored to evaluate the cardiovascular condition of COVID-19 patients using echocardiography and to assess the association of these findings with in-hospital mortality.

Methods: In this retrospective cohort study, hospitalized COVID-19 patients from February to July 2020 with at least one echocardiogram were included. Data were extracted from patients' medical records and the association between echocardiographic findings and in-hospital mortality was assessed using a multivariate model. The findings were reported as relative risk (RR) and 95% confidence interval (95% CI).

Results: Data from 102 COVID-19 hospitalized patients were encompassed in the present study (63.7±15.7 mean age; 60.8% male). Thirty patients (29.4%) died during hospitalization. Tricuspid regurgitation (89.2%), mitral valve regurgitation (89.2%), left ventricular (LV) diastolic dysfunction (67.6%), pulmonary valve insufficiency (PI) (45.1%) and LV systolic dysfunction (41.2%) were the most common findings on patients' echocardiogram. The analyses of data showed that LV systolic (p=0.242) and diastolic (p=0.085) dysfunction was not associated with in-hospital mortality of COVID-19 patients, while the presence of PI (RR=1.85; 95% CI: 1.02 to 3.33; p=0.042) and patients' age (RR=1.03; 95% CI: 1.01 to 1.08; p=0.009) were the two independent prognostic factors of in-hospital mortality.

Conclusions: It seems that LV systolic and diastolic dysfunction was not associated with in-hospital mortality of COVID-19 patients. However, presence and PI and old age are possible prognostic factors of COVID-19 in-hospital mortality. Therefore, using echocardiography might be useful in management of COVID-19.

Key words: Echocardiography; Mortality; Outcome; SARS-CoV-2

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is the name of a novel coronavirus spread from Wuhan, China in December 2019. Since the declaration of COVID-19 pandemic in March 2020, until November 2020 more than 58 million people have contracted the disease and there have been more than a million deaths, subsequently (1). Although, COVID-19 symptoms are mostly related to the lower respiratory tract infection, the disease expresses symptoms of many other organs' involvement; such as the heart, brain, kidneys and the gastrointestinal tract. In addition to fever, dyspnea, cough and fatigue being the main symptoms, headache, nausea, vomiting, diarrhea and anosmia are also common symptoms of COVID-19 (2-4).

Since, there are several paper that showed troponin I levels in severe COVID-19 patients are much higher than non-severe cases, it seems that COVID-19 could affect cardiac muscle directly and cause cardiovascular disorders (5). Likewise, according to many different reports, vascular involvement such as pulmonary thromboembolism and stroke is also observed in COVID-19. Clinical assessment of patients shows that from every 5 admitted patients, one has cardiac manifestations (6). This cardiac involvement could occur even without symptoms of pulmonary pneumonia (7). Existing literature on cardiovascular complications show that in 55% of COVID-19 patients undergoing

echocardiography, evidence of cardiovascular involvement is present. The most common findings on echocardiogram are right and left ventricular abnormalities, evidence of myocardial infarction and myocarditis. Nearly 15% of the patients had severe left-sided heart failure or tamponade (8); However, there are other studies suggesting different results. For example, in a study conducted on 74 COVID-19 patients it was found that right ventricular enlargement and right ventricular dysfunction were the most common abnormalities in the echocardiogram. Left ventricular function was normal or hyperdynamic in most of the patients (9).

Therefore, it appears that in the setting of COVID-19, abnormal findings on echocardiogram are relatively common. Regarding the life-threatening consequences of cardiovascular complications, it seems that performing echocardiography and examining its relationship with the outcome of the disease, could provide a better view of the disease prognosis.

However, it is yet unclear which echocardiographic findings could be able to predict the outcome of the disease. In the present study an attempt was made to evaluate the most common echocardiography abnormalities of COVID-19 patients and to assess the relationship between the abnormalities and In-hospital mortality.

Methods

Study design

The present retrospective cohort study was performed on the records of COVID-19 patients who were admitted to Imam-Hossein Hospital in Tehran, Iran between March and June 2020. This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences and the researchers adhered to the principles of the Helsinki declaration.

Subjects

In the current study, all patients with COVID-19 who had at least one echocardiogram during their hospital stay were included. COVID-19 infection was confirmed by a positive RT-PCR (polymerase chain reaction) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a nasopharyngeal specimen. Exclusion criteria were insufficient information in the medical record, unrecorded outcome or pregnancy. During March and June 2020, 991 COVID-19 patients were admitted to the hospital, of whom 102 underwent echocardiography during hospitalization. The mean age of patients was 63.7 ± 15.7 years (60.8% male).

Sample size calculation was performed based on the odds ratio of right ventricular (RV) dysfunction in echocardiography in prediction of in-hospital mortality. With considering of a odds ratio of 2.88, a 43% prevalence of RV dysfunction, with a power of 0.9 and an alpha of 0.05, the estimated sample size was achieved 77 cases.

Data gathering

Baseline and demographic characteristics of the patients were extracted from the hospital's patient registration system and echocardiographic results were also included. At Imam Hossein hospital, echocardiography is performed by cardiologists who have at least 5 years of experience with echocardiography. Echocardiography was performed by a portable device (GE Vivid S5, USA) with a 6 MHz transducer. Patient echocardiogram results were reinterpreted by a cardiac specialist. Echocardiographic findings were left ventricular (LV) systolic dysfunction, right ventricular (RV) systolic dysfunction, LV diastolic dysfunction, RV diastolic dysfunction, left atrial enlargement, LV enlargement, right atrial enlargement, RV enlargement, dilated ascending aorta, aortic valve abnormality, pulmonary valve insufficiency (PI), tricuspid valve abnormality, mitral valve abnormalities, regional wall motion abnormality (RWMA), pulmonary artery pressure (PAP), LV hypertrophy, pericardial effusion, inferior vena cava size, inferior vena cava respiratory variation and ejection fraction. Finally, in-hospital mortality was recorded.

Statistical analysis

Continuous variables were described by mean ± standard deviation (SD), and Categorical variables were expressed as counts (percentage). Kolmogorov-Simonov test was used for checking normality assumption of data. Comparisons of means in normal data were done by T-test. Besides, for evaluating the association between categorical variables The Chi-square test and fisher exact test were used. In addition, a multivariate log binomial regression model was performed for investigating the association of death with echocardiogram factors (10). To avoid over-fitting in the multivariate model, just the factors which lead to p-values less than 0.1 in univariate analysis, were selected for multivariate model. Final model was selected according to backward Wald. Findings were reported as relative risk ratio (RR) and its 95% confidence interval (95% CI). Two-side P-value less than 0.05 was considered statistically significant. Analyzing were done using the STATA 14.0 Package.

RESULTS

Data of 102 patients were included. Thirty patients (29.4%) died during hospitalization. The deceased had a significantly higher mean age (p = 0.009), but the sex distribution (p = 0.320) and body mass index (p = 0.473) of the two groups were similar (Table 1).

Echocardiographic findings in the studied patients were tricuspid regurgitation (89.2%), mitral valve regurgitation (89.2%), LV diastolic dysfunction (67.6%), PI (45.1%), LV systolic dysfunction (41.2%), RWMA (39.2%), abnormal PAP (36.3%), AI (35.3%), LV hypertrophy (17.6%), left atrial enlargement (16.7%), right atrial enlargement (16.7%), RV enlargement (14.7%), RV systolic dysfunction (12.7%), LV enlargement (11.8%) and pericardial effusion (11.8%).

Univariate analyses showed that there was a significant relationship between age (p = 0.009) and aortic valve insufficiency (p = 0.045) with patient mortality. In addition, the relationship between patient mortality and PI (p = 0.051) was close to a significant level. While, LV systolic (p=0.242) and diastolic (p=0.085) dysfunction, RV systolic dysfunction (p=0.171), Left atrial enlargement (p=0.560), Left ventricular enlargement (p=0.744), Right atrial enlargement (p=0.244), right ventricular enlargement (p>0.999), dilated ascending aorta (p>0.999), thickened aortic valve (p=0.383), calcified aortic valve (p=0.751), aortic valve stenosis (p=0.294), tricuspid valve regurgitation (p=0.168), thickened mitral valve (p>0.999), calcified mitral valve (p=0.294), mitral valve regurgitation (0.727), RWMA (p=0.582), abnormal PAP (p=0.958), LV hypertrophy (p=0.123), pericardial effusion (p=0.329) and Inferior vena cava size (p=0.329) (Table 2).

Therefore, by fitting a multivariate model, it was determined that the presence of PI (RR = 1.85; 95% CI: 1.02 to 3.33; p = 0.042) and the age of patients (RR = 1.03; 95% CI: 1.01 to 1.08; p = 0.009) are

Table 1: Baseline characteristics of study COVID-19 patients

Characteristics	Alive (n=72)	Dead (n=30)	P
Age (year)	61.1±15.9	69.9±13.6	0.009
Gender			
Female	26 (36.1)	14 (46.7)	0.320
Male	46 (63.9)	16 (53.3)	
Body mass index			
Underweight	1 (1.4)	1 (3.3)	
Normal	34 (47.2)	11 (36.7)	0.473
Overweight	27 (37.5)	11 (38.7)	
Obese	10 (13.9)	7 (23.3)	

Table 2: Echocardiography findings of study COVID-19 patients according the survival

Characteristics	Alive (n=72)	Dead (n=30)	P
Left ventricular systolic dysfunction*			
No	45 (62.5)	15 (50.0)	0.242
Yes	27 (37.5)	15 (50.0)	
Right ventricular systolic dysfunction			
No	65 (90.3)	24 (80.0)	0.171
Mild to moderate	7 (9.7)	6 (20.0)	
Left ventricular diastolic dysfunction			
No	27 (37.5)	6 (20.0)	0.085
Mild to severe	45 (62.5)	24 (80.0)	
Left atrial enlargement			
No	59 (81.9)	26 (86.7)	0.560
Mild to severe	13 (18.1)	4 (13.3)	
Left ventricular enlargement			
No	64 (88.9)	26 (86.7)	0.744[a]
Mild to severe	8 (11.1)	4 (13.3)	
Right atrial enlargement			
No	58 (80.6)	27 (90.0)	0.244
Mild to moderate	14 (19.4)	3 (10.0)	
Right ventricular enlargement			
No	61 (84.7)	26 (86.7)	>0.999[a]
Mild to severe	11 (15.3)	4 (13.3)	
Dilated ascending aorta			
No	69 (95.8)	29 (96.7)	>0.999[a]
Mild to severe	3 (4.2)	1 (3.3)	
Thickened aortic valve			
No	59 (81.9)	27 (90.0)	0.383[a]
Yes	13 (18.1)	3 (10.0)	
Calcified aortic valve			
No	62 (86.1)	27 (90.0)	0.751[a]
Yes	10 (13.9)	3 (10.0)	
Aortic valve insufficiency			
No	51 (70.8)	15 (50.0)	0.045
Mild to moderate	21 (29.2)	15 (50.0)	
Aortic valve stenosis			
No	72 (100.0)	29 (96.7)	0.294[a]
Severe	0 (0.0)	1 (3.3)	
Pulmonary valve insufficiency			
No	44 (61.1)	12 (40.0)	0.051
Mild to moderate	28 (38.9)	18 (60.0)	
TR (Tricuspid valve regurgitation)			
No	10 (13.9)	1 (3.3)	0.168[a]
Mild to severe	62 (86.1)	29 (96.7)	
Thickened mitral valve			
No	70 (97.2)	29 (96.7)	>0.999[a]
Yes	2 (2.8)	1 (3.3)	
Calcified mitral valve			
No	72 (100.0)	29 (96.7)	0.294[a]
Yes	0 (0.0)	1 (3.3)	
Mitral valve regurgitation			
No	7 (9.7)	4 (13.3)	0.727[a]
Mild to severe	65 (90.3)	26 (86.7)	
Regional wall motion abnormality			
No	45 (62.5)	17 (56.7)	0.582
Yes	27 (37.5)	13 (43.3)	
Hypokinesia			
No	46 (64.8)	18 (62.1)	0.797
Yes	25 (35.2)	11 (37.9)	

*Defined as ejection fraction with cut off of 50%.

[a] Based on Fisher's exact test.

Table 2 (in continue): Echocardiography findings of study COVID-19 patients according the survival

Characteristics	Alive (n=72)	Dead (n=30)	P
Akinesia			
No	65 (91.5)	28 (96.6)	0.670[a]
Yes	6 (8.5)	1 (3.3)	
Dyskinesia			
No	71 (100.0)	28 (96.6)	0.290[a]
Yes	0 (0.0)	1 (3.4)	
Pulmonary artery pressure*			
Normal	46 (63.9)	19 (63.3)	0.958
Abnorma	26 (36.1)	11 (36.7)	
Left ventricular hypertrophy			
No	62 (86.1)	22 (73.3)	0.123
Mild to severe	10 (13.9)	8 (26.7)	
Pericardial effusion			
No	65 (72.2)	25 (27.8)	0.329[a]
Normal or mild	7 (58.3)	5 (41.7)	

* Pulmonary artery pressure <30 mmHg was considered as normal, and value >30 mmHg was considered as abnormal.
[a] Based on Fisher's exact test

Table 3: Multiple logistic regression of prognostic factors of echocardiography in prediction of mortality in study COVID-19 patients

Variable	Relative risk	95% CI	P
Pulmonary valve insufficiency	1.85	1.02-3.33	0.042
Age	1.03	1.01-1.04	0.009

CI: confidence interval

independent prognostic factors of in-hospital mortality (Table 3).

Discussion

This study showed that valvular disorders, LV diastolic dysfunction and LV systolic dysfunction are the most common disorders found in the electrocardiogram of patients with COVID-19, respectively. The analysis showed that LV systolic and diastolic dysfunction and RV dysfunction were not associated with COVID-19 related in-hospital mortality, while age and the presence of PI were found to be two independent predictors of in-hospital mortality. Due to indistinct mechanism of cardiovascular damage by SARS-CoV-2, by direct attack to myocytes or secondary to hemodynamic and immunological consequences of the infection, such as volume overload in sepsis or cytokine storm, any abnormalities in accordance with patients' mortality should be given special attention. Pulmonary valve insufficiency is generally associated with arrhythmias, right-sided heart dysfunction, and ultimately left heart damage. Ventricular arrhythmias or heart failure due to progressive ventricular defects can cause sudden cardiac death (11). The results of the present study are in line with the results of similar studies showing that the presence of abnormalities in the echocardiogram is associated with an increased risk of in-hospital mortality in COVID-19 patients (12). COVID -19 infection can cause cardiac involvement even without pulmonary involvement (7). Through fever, increased activity of cytokines in the immune system, or ARDS in patients with pulmonary involvement, this infection could increase the pressure on the pulmonary circulation, putting additional burden on the cardiovascular system (13). Pulmonary valve insufficiency, especially in increased myocardial activity, increases the right ventricular diastolic pressure, thus impairing the left ventricular function. Left ventricular diastolic dysfunction is an independent cause of death in patients with normal ejection fraction (14). As a result, it can be concluded that even a small amount of pulmonary valve insufficiency - with mechanisms not fully understood - could create a setting for arrhythmia and reduced cardiac output due to the left and right ventricular dysfunctions.

In the present study, it was found that the majority of patients with COVID-19 have echocardiographic abnormalities. In accordance with the present study, Dweck et al examined 1216 patients with COVID-19 and showed that in 55% of patients who undergo echocardiography, there is evidence of cardiac dysfunction. In this study, the most common abnormal echocardiographic findings were left ventricular dysfunction (39%) and right ventricular dysfunction (33%). In addition, it was found that about 15% of patients had severe ventricular dysfunction or tamponade (8). On the other hand, a study on 74 patients showed that right ventricular enlargement and right ventricular dysfunction are the most important abnormalities observed in the echocardiogram of COVID-19 patients (9). Bursi et al. also studied 49 COVID-19 patients with coronary artery disease, and concluded that the right ventricular failure is the most common abnormality observed in patients' echocardiograms and it is an independent prognostic factor of mortality in these patients(15). As it can be seen, the findings of studies on echocardiographic abnormalities in COVID-19 patients differ considerably. The reason for this difference can be attributed to the unknown pathogenicity of SARS-CoV-2. Due to the fact that the receptor for this virus (angiotensin-converting enzyme 2) is widely distributed in various tissues of the body (16), it may cause a wide range of

disarrays, leading to significant differences in the study findings. But what is certain is that the majority of patients with COVID-19 have abnormal findings on echocardiography.

Limitations

Like many retrospective studies, this study has had limitations. The number of patients undergoing echocardiography was limited. Performing echocardiography on patients is indicated based on clinical evidence, such as increased shortness of breath, which point to a more severe form of the disease or a deterioration in patient status, increasing the likelihood of finding abnormal data in the samples. Also, due to the lack of patients' echocardiogram prior to COVID-19 infection, it is not fully clear whether the observed abnormalities throughout the disease are acute, already present and have become more severe, or remained unchanged. Finally, the uncertainty of when to perform echocardiography in the course of the disease is a major limitation; this is because echocardiography may have been performed in the early stages of the disease and the patient may have developed symptoms of cardiac involvement later, or it may have been done too late with transient abnormalities gone away.

Conclusions

The findings of the present study showed that valvular insufficiency, LV diastolic dysfunction and LV systolic dysfunction are the most common abnormalities found in the electrocardiogram of patients with COVID-19, respectively. The analysis showed that LV systolic and diastolic dysfunction and RV dysfunction were not associated with COVID-19 related in-hospital mortality, while age and the presence of PI were found to be two independent prognostic factor ofCOVID-19 in-hospital mortality.

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Authors' contribution

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest

None declared.

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