Original Article

Echocardiographic Findings of ICU-Admitted COVID-19 Patients: a Multicenter Retrospective Study

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has left many victims and caused many problems for the healthcare systems of different countries. Many COVID-19 patients have cardiovascular complications, which are detectable using echocardiography. This study aimed to determine the echocardiographic findings and their association with mortality in an intensive care unit (ICU)-admitted COVID-19 patients.

Materials and Methods: In this retrospective study, COVID-19 patients admitted to the ICU of four hospitals in Tehran, Iran, from April 2020 to March 2021 were recruited. Data were collected by the census method. We reviewed the medical records regarding demographic features, clinical history, laboratory results, and echocardiographic findings. Finally, variables were compared regarding disease outcomes at the end of hospitalization. We used the Chi-square test, Fisher׳s exact test, independent-samples t-test, and logistic regression model to analyze the data.

Results: This study showed that the mean age of 629 COVID-19 patients was 66.42±14.53 years. Overall, 56.8% of the patients were male. Multivariate regression analysis showed that age (OR=1.03; 95% CI: 1.01-1.05), left ventricular ejection fraction (OR=0.95; 95% CI: 0.92-0.98), and systolic pulmonary arterial pressure (OR=1.12; 95% CI: 1.06-1.18) were predictors of mortality.

Conclusion: Cardiovascular involvement is prevalent among critically ill COVID-19 patients. Among echocardiographic findings, EF and s-PAP were significantly associated with the disease outcomes.

Keywords: COVID-19, Cardiovascular disease, Echocardiography, Mortality, SARS-CoV-2

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Introduction

In early December 2019, numerous cases of pneumonia were diagnosed in Wuhan, Hubei Province, China. The etiology of this disease was a novel coronavirus called SARS-CoV-2. This virus spread around the world within only a few weeks, posing severe challenges to the healthcare systems of different countries. On March 11, 2020, the World Health Organization (WHO) officially declared

coronavirus disease 2019 (COVID-19) as a pandemic with millions of victims until now[1].

The clinical manifestations of COVID-19 range from mild cases with a flu-like syndrome to severe cases requiring intensive care. The prevalence of cardiovascular complications is relatively high in severe and critical COVID-19 patients. These complications include the development or exacerbation of myocarditis, arrhythmia, thrombosis, acute coronary syndrome, and heart failure[2, 3]. Some previous studies have reported an association between cardiovascular disease (preexisting or new-onset) and the outcomes of COVID-19 patients[4, 5]. In contrast, some studies have shown no association between cardiovascular involvement and patient outcomes[6].

This study aimed to determine the echocardiographic findings and their association with mortality in ICU-admitted COVID-19 patients.

Methods

Study setting and design: This retrospective study studied COVID-19 patients admitted to the intensive care unit (ICU) of four hospitals between April 2020 and March 2021. The study was performed in Imam Hossein, Loghman Hakim, Modarres, and Taleghani hospitals; all of them were affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran,

Patients: The inclusion criteria in this study were as follows: 1) definitive diagnosis of COVID-19, confirmed by real-time polymerase chain reaction (RT-PCR); 2) severe or critical cases of COVID-19 (blood oxygen saturation≤94%, respiratory rate>30/minute, and lung infiltration>50%)[7] who admitted to the intensive care unit (ICU) during the hospitalization; 3) age of at least 18 years; 4) complete transthoracic echocardiographic reports available in the patient's medical record, and 5) death (if reported) due to COVID-19. We also did not exclude any of the included patients.

Data collection: Data were collected by the census method. We reviewed the patients' medical records regarding clinical characteristics and paraclinical findings. The clinical characteristics included demographic features, underlying diseases, symptoms, and outcomes (alive versus expired) at the end of hospitalization. The above data was obtained by history taking. The paraclinical findings included the laboratory, electrocardiographic, and transthoracic echocardiographic results. Expert cardiologists performed transthoracic echocardiography by personal protection protocols recommended for healthcare staff[8]. 2-dimensional and color Doppler echocardiography was performed based on the American Society of Echocardiography[9].

Statistical analysis: We processed the collected data in SPSS version 18.0. Data were described as frequency, percentage, mean, and standard deviation (SD). We used the Chi-square test, Fisher's exact test, independent-samples *t*-test, and logistic regression model to analyze the data. Also, a p-value <0.05 was considered significant.

Ethical considerations: The Ethics Committee of the School of Public Health and Neuroscience Research Center of Shahid Beheshti University of Medical Sciences approved this study (ID: IR.SBMU.PHNS.REC.1400.001).

Results

Baseline characteristics: The mean age of 629 patients included in this study was 66.42±14.53 years (21-99 years), and 56.8% were male. The mean age of the expired patients was higher than those who survived (P<0.001). In terms of the body mass index (BMI), 39.3%, 45.3%, and 15.4% of the patients were normal-weight, overweight, and obese. There was a significant association between BMI and disease outcomes (P=0.041). 66.9% of the patients expired at the end of hospitalization, while 33.1% survived. Table 1 shows detailed demographic and clinical features of the patients.

Hypertension (53.1%) was the most common underlying disease, followed by diabetes mellitus (38.8%) and cardiovascular disease (34.3%). The patient outcomes were significantly associated with chronic kidney disease (CKD) (P=0.012), asthma and chronic obstructive pulmonary disease (COPD) (P=0.010), and malignancies (P=0.002). Dyspnea (73.4%) was more frequent than other clinical manifestations. Also, loss of consciousness was significantly more common among expired patients (P=0.001).

Table 1: Comparison of demographic and clinical features between survivors and non-survivors.

Variables	Survivors (n=208)	Non-survivors (n=421)	Total (n=629)	P-value
Demographic features				
Age	61.15±14.28	69.03±13.89	66.42±14.53	<0.001[c]
Gender (Male: Female)	125:83	232:189	357:272	0.235[a]
BMI (kg/m2)	27.41±5.16	26.24±4.39	26.62±4.67	0.041[c]
Underlying diseases				
Hypertension	106(51.1)	228(54.3)	334(53.1)	0.450[a]
Diabetes mellitus	79(38.0)	165(39.2)	244(38.8)	0.769[a]
Cardiovascular disease	68(23.7)	148(35.2)	216(34.3)	0.541[a]
Chronic kidney disease (CKD)	18(8.7)	67(15.9)	85(13.5)	0.012[a]
Asthma and COPD	30(14.4)	33(7.8)	63(10.0)	0.010[a]
Malignancies (under treatment)	5(2.4)	39(9.3)	44(7.0)	0.002[a]
Cerebrovascular accident	12(5.8)	28(6.7)	40(6.4)	0.670[a]
Symptoms				
Dyspnea	155(74.5)	307(72.9)	462(73.4)	0.669[a]
Cough	132(63.5)	268(63.7)	400(63.6)	0.962[a]
Fever	125(60.1)	235(55.8)	360(57.2)	0.308[a]
Malaise	98(47.1)	220(52.3)	318(50.6)	0.225[a]
Myalgia	82(39.4)	176(41.8)	258(41.0)	0.568[a]
Anorexia	67(32.2)	166(39.4)	233(37.0)	0.078[a]
Nausea	43(20.7)	85(20.2)	128(20.3)	0.887[a]
Vomiting	34(17.8)	67(15.9)	104(16.5)	0.552[a]
Diarrhea	38(18.3)	55(13.1)	93(14.8)	0.084[a]
Loss of consciousness	15(7.2)	73(17.3)	88(14.0)	0.001[a]
Headache	30(14.4)	44(10.5)	74(11.8)	0.146[a]
Chest pain	20(9.6)	43(10.2)	63(10.0)	0.814[a]

Values are expressed as n (%) or mean±SD.
[a]Chi-square test, [b]Fisher's exact test, [c]Independent-samples *t*-test

Laboratory findings: Table 2 shows the laboratory tests of the patients. The hemoglobin level (P=0.004) and platelet count (P<0.001) were lower in the expired group compared to the survivor group; however, the level of N-terminal pro-brain natriuretic peptide (NT-proBNP) was higher in the non-survivors

Table 2: Comparison of laboratory tests between survivors and non-survivors.

Laboratory tests	Unit	Survivors (n=208)	Non-survivors (n=421)	Total (n=629)	P-value
White blood cell count	$\times10^9$cells/L	8.60±4.14	9.52±10.42	9.26±9.04	0.086[a]
Neutrophil-to-lymphocyte ratio	-	7.96±11.18	8.34±7.03	8.22±8.46	0.081[a]
Hemoglobin level	g/L	12.74±2.18	12.22±2.31	12.53±2.14	0.004[a]
Platelet count	$\times10^9$cells/L	225.90±95.60	197.22±98.90	199.06±94.98	<0.001[a]
Erythrocyte sedimentation rate (ESR)	mm/h	46.39±32.46	49.45±28.88		0.250[a]
Troponin	ng/dL	0.03±1.04	0.06±4.28	0.05±3.63	0.550[a]
Creatine kinase-MB (CK-MB)	U/L	18.81±22.36	21.51±44.96	20.65±39.46	0.125[a]
Creatine phosphokinase (CPK)	IU/L	119.62±303.93	180.29±331.98	160.42±323.72	0.440[a]
NT-proBNP	ng/dL	719.85±4609.25	2410.39±7926.15	1953.55±7228.16	<0.001[a]
C-reactive protein (CRP)					0.020[b]
Normal		23(3.7)	21(3.4)	44(7.2)	
+1		41(6.7)	71(11.6)	112(18.2)	
+2		75(12.2)	171(27.9)	246(40.1)	
+3		63(10.3)	149(24.3)	212(34.5)	

Values are expressed as mean±SD or n (%).
[a]Independent-samples *t*-test, [b]Chi-square test

compared to the survivors (P<0.001). Besides, the C-reactive protein (CRP) level was significantly associated with patient outcomes (P=0.020).

Electrocardiographic findings: In 83.6% of the patients, a normal sinus rhythm was observed. The most common arrhythmia was atrial fibrillation (12.6%), followed by sinus tachycardia (2.5%), atrial flutter (1.0%), and sinus bradycardia (0.3%).

Echocardiographic findings: Table 3 shows the echocardiographic results of the patients based on the outcomes. The mean left ventricular (LV) ejection fraction (LVEF) was 43.69±8.92%. The LVEF was significantly lower in the expired group than in the survivors (P<0.001). The mean systolic pulmonary artery pressure (s-PAP) was 32.35±9.91 mmHg; it was significantly higher in the expired group compared to the survivors (P<0.001). However, there was no significant association between other echocardiographic findings and patient outcomes.

Predictors of death: Multivariate logistic regression analysis showed that age (OR=1.03; 95% CI: 1.01-1.05), left ventricular ejection fraction (OR=0.95; 95%

Table 3: Comparison of the echocardiographic findings between survivors and non-survivors.

Variables	Survivors (n=208)	Non-survivors (n=421)	Total (n=629)	P-value
LV enlargement	8(3.8)	16(3.8)	24(3.8)	0.978[a]
LVEF (%)	45.72±9.25	42.70±8.60	43.69±8.92	<0.001[b]
LV diastolic dysfunction	14(6.7)	23(5.5)	37(5.9)	0.525[a]
LA dilatation	9(4.3)	14(3.3)	23(3.7)	0.529[a]
RV enlargement	18(8.7)	42(10.0)	60(9.5)	0.595[a]
RV systolic dysfunction	40(19.2)	84(20.0)	124(19.7)	0.831[a]
Mitral regurgitation	45(21.6)	72(17.1)	117(18.4)	0.169[a]
Mitral stenosis	2(1.0)	3(0.7)	5(0.8)	0.741[a]
Mitral valve prolapse	4(1.9)	4(1.0)	8(1.3)	0.306[a]
Aortic valve insufficiency	17(8.2)	22(5.2)	39(6.2)	0.149[a]
Pulmonary valve insufficiency	3(1.4)	4(1.0)	7(1.1)	0.580[a]
Tricuspid valve regurgitation	50(24.0)	95(22.6)	145(23.1)	0.680[a]
s-PAP (mmHg)	28.16±6.75	34.41±10.56	32.35±9.91	<0.001[b]
Pericardial effusion	21(10.1)	30(7.1)	51(8.1)	0.199[a]

Values are expressed as n (%) or mean±SD.
LV: Left ventricle, RV: Right ventricle, s-PAP: Systolic pulmonary arterial pressure.
No patients had pulmonary valve stenosis, aortic valve stenosis, or tricuspid valve stenosis.
[a]Chi-square test, [b]Independent-samples *t*-test

CI: 0.92-0.98), and systolic pulmonary arterial pressure (OR=1.12; 95% CI: 1.06-1.18) were predictors of mortality (Table 4).

Discussion

Based on the findings, the mean LVEF of ICU-admitted COVID-19 patients was below normal; it was lower in deceased patients than the survivors. Besides, the mean s-PAP of these patients was above normal range; it was higher in expired patients than in the survivors. Some of our findings were consistent with previous studies, while some were inconsistent.

Some previous studies have shown an association between cardiovascular involvement and mortality in COVID-19 patients. SARS-CoV-2 can directly affect the heart tissue. The precise mechanism of cardiac damage caused by COVID-19 is unknown, though several explanations exist. First, cardiomyocytes have angiotensin-converting enzyme 2 (ACE-2) receptors; therefore, the virus may enter myocytes in interaction with these receptors and cause cell damage. Second, tumor necrosis factor-α (TNF-α), produced by systemic inflammation in response to viruses, can cause damage to myocytes. This systemic inflammation is associated with an increase in serum CRP levels. Third, hypercoagulopathy, thrombosis, and hypoxia can cause significant damage to myocytes[10].

Damage to cardiomyocytes results in increased serum levels of troponin and NT-proBNP, higher in critically ill COVID-19 patients than in non-critically ill

Table 4: Logistic regression analysis for determining independent predictors of mortality.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.04 (1.02-1.05)	<0.001	1.03 (1.01-1.05)	**0.008**
BMI	0.94 (0.91-0.99)	0.015	0.98 (0.92-1.05)	0.713
Malignancy	4.14 (1.60-10.68)	0.003	NA	NA
CKD	1.99 (1.15-3.46)	0.014	0.69 (0.25-1.87)	0.468
Asthma & COPD	0.50 (0.29-0.85)	0.011	1.09 (0.31-3.78)	0.889
Hemoglobin level	0.90 (0.83-0.97)	0.003	1.08 (0.93-1.26)	0.298
Platelet count	0.997 (0.995-0.999)	<0.001	0.99 (0.98-1.01)	0.152
NT-proBNP	1.00 (1.00-1.00)	0.002	1.00 (1.00-1.00)	0.101
LVEF	0.95 (0.93-0.97)	<0.001	0.95 (0.92-0.98)	**<0.001**
s-PAP	1.11 (1.08-1.15)	<0.001	1.12 (1.06-1.18)	**<0.001**

OR: odds ratio, CI: confidence interval, NA: not applicable

patients[11]. Myocardial injury can be detected on echocardiography as hypokinesia, EF reduction, and left atrial dilatation[12]. Some previous studies have shown an association between reduced EF and mortality, which is in line with the present study[13, 14]. On the other hand, no significant association was found between these two parameters[15, 16].

Cardiac complications of COVID-19 can be secondary to pulmonary involvement. Pulmonary artery hypertension has been reported in many COVID-19 hospitalized patients[17]. The RV enlargement, RA dilatation, RV systolic dysfunction, tricuspid regurgitation, and high s-PAP are indicators of RV involvement in the echocardiography of COVID-19 patients[18, 19]. Similarly, in our study, many patients had the abovementioned manifestations. Most studies have shown an association between RV involvement and disease outcomes. In a survey by D' Alto et al., tricuspid annular plane systolic excursion (TAPSE), PAP, and inferior vena cava (IVC) diameter represent, all representing RV dysfunctions, were significantly higher in deceased COVID-19 patients compared to the surviving patients[20].

In previous studies, RV dysfunction was associated with mortality[21], which is inconsistent with our results. The majority of patients in our study underwent echocardiography in the first days of hospitalization. Due to the pulmonary involvement caused by COVID-19, their s-PAPs were higher than normal range, which may later have caused RV dysfunction. So in the last days before death (or discharge), they had RV dysfunction, for which echocardiography has not been available since.

In another study by Jain et al., the prevalence of pulmonary artery hypertension and RV enlargement was higher in expired patients than in the survivors; however, other parameters indicating RV dysfunction were not different between the two groups[22]. Based on our results, s-PAP was higher in the expired group than in the survivors, which is in line with previous studies. However, unlike previous studies, other parameters indicating RV dysfunction were not significantly different between the two groups. This contradiction can be explained by the involvement of confounding factors, such as underlying diseases.

Patients diagnosed with COVID-19 are prone to coagulopathy and thrombosis. These conditions can

lead to acute coronary syndrome, pulmonary embolism, cerebrovascular accidents, and deep vein thrombosis[23]. These diseases can cause cardiovascular complications, increasing mortality risk[24].

Each demographic feature and underlying disease can play a potential role in the mortality of COVID-19 patients. In this regard, a study by Shi et al. showed significant differences in terms of sex, age, cardiovascular disease, hypertension, chronic kidney disease, and cerebrovascular disease between the expired and survivor groups[25]. However, further analytical studies are needed to determine the definite role of each possible risk factor in mortality.

Our study had some limitations. First, this was a retrospective study in which some of the laboratory tests were missing. Besides, laboratory kits were not the same, leading to bias. Second, this study was performed on only ICU-admitted COVID-19 patients to reduce bias; this might have affected the generalizability of our findings. Third, we had no control over the confounding variables according to the study method.

Conclusion

Among ICU-admitted COVID-19 patients, different RV and LV dysfunctions are common and significantly associated with the patient outcomes. Therefore, echocardiographic findings, significantly reduced EF and high s-PAP, can help predict the mortality of patients.

Acknowledgment

Conflict of interest

The authors further declare that they have no conflict of interest.

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