

## Original Article

# Long-Term Electrocardiogram and Echocardiography Findings of Patients with Severe COVID-19

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## Abstract

**Background:** Coronavirus disease 2019 (COVID-19) was a pandemic that can involve the cardiopulmonary system. Long-term cardiac involvement evaluations were less studied in the literatures. In the present study, we aimed to investigate long-term electrocardiographic and echocardiographic findings of patients with severe COVID-19 after a year of follow-up.

**Materials and Methods:** This retrospective cohort study was performed on patients admitted to one of the university hospitals in Tehran, Iran, from the beginning of February 2021 to February 2022. Echocardiography and electrocardiogram were done for all patients at admission and after one year of discharge. Patients' demographics, medical history, echocardiographic, and electrocardiographic information were recorded and analyzed.

**Results:** Sixty patients were enrolled in the study. The mean age of patients was 53.63±12.50 years, and 58.33% were male. After assessing electrocardiography changes and echocardiography results, it was observed that QRS abnormality and inverted T-wave after one year were significantly more than during hospitalization (P<0.05). The pulmonary arterial pressure had increased after one year (24.30±4.79 mmHg to 26.50±7.69 mmHg, p-value=0.026).

**Conclusion:** New cardiac problems in patients with severe COVID-19 disease may appear after one year, and these patients should be evaluated periodically.

**Keywords:** COVID-19, Echocardiography, Electrocardiogram, Myocardial injury, Pulmonary artery pressure

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## Introduction

The coronavirus disease 2019 (COVID-19) firstly was seen in China. Myocardial involvement predicts poor prognosis in COVID-19 patients<sup>1</sup>. Different hypotheses exist for myocardial participation, but the exact etiology is unclear. It is mentioned that some of these etiologies are stress-cardiomyopathy, cytokine

storm or injury, myocarditis, and hypoxemia<sup>2,3</sup>. On the other hand, pulmonary involvement is one of the main manifestations of COVID-19, and this involvement in patients with a history of cardiac injury can worsen or exacerbate cardiac involvement<sup>4</sup>. Systemic inflammation, as the physiological mechanism of COVID-19, can cause cardiac injury. Endothelial cell damage and hypoxemia-related myocardial cell injury

are the causes of cardiac involvement due to systemic inflammation, and it occurs following up-regulation of angiotensin-converting enzyme 2 (ACE 2) in the pulmonary and heart<sup>5-7</sup>.

It is reported that cardiac involvement is prevalent. In a study conducted by Guo et al., it was mentioned that the prevalence of cardiac involvement is about 25% in patients with COVID-19<sup>3</sup>. Cardiac problems in these patients are associated with increased mortality<sup>3</sup>. The prevalence of acute cardiac injury and arrhythmia was reported in 16.7% and 7.2% of the patients<sup>8</sup>.

The mortality rate in COVID-19 patients with cardiac involvement varies from 1/100,000 to 100/100,000. Some factors are associated with increased morbidity and mortality rates, including underlying diseases and comorbidities, higher age, male gender, and obesity<sup>9-11</sup>. A study by Lalani et al. found that age, acute kidney injury, and severity of COVID-19 correlated to a higher mortality rate in COVID-19 patients with cardiac involvement<sup>12</sup>.

The electrocardiogram (ECG) and echocardiography can represent cardiac involvement and its adverse presentations. Arrhythmia, myocarditis, and myocardial ischemia can be seen in these tests<sup>13,14</sup>. In this study, we aimed to investigate long-term electrocardiographic and echocardiographic findings in patients with severe COVID-19 in a tertiary hospital.

## Methods

**Study design and participants:** In this retrospective cohort study, patients with severe covid-19 who were admitted to a university hospital during a period of three months (from the beginning of February 2021 to February 2022) were included in the study. This study was approved by review board and research ethics committees of school of medicine, Shahid-Beheshti university of Medical Sciences (IR.SBMU.MSP.REC.1401.204).

Inclusion criteria were hospitalization due to severe covid-19 according to the following criteria: rapid development of respiratory symptoms, the incidence of dyspnea and tachypnea, SPO<sub>2</sub> <90 (RR>30 per minute) with FiO<sub>2</sub>/PaO<sub>2</sub> <300mmHg, and increased gradient a-A with an increase of more than 50% of the lung involvement in the CT scan.

At first, the list of COVID-19 patients who were

discharged and had echocardiography on the first visit (from the beginning of February 2021 to February 2022) was obtained from the medical information source. Then they were selected according to the file of COVID-19-positive patients admitted to the hospital due to severe COVID-19 at the mentioned time. After one year from discharge, selected patients, with their personal consent, were recalled for cardiac evaluation.

**Data collecting and extraction:** The selected patients were contacted by phone, informed consent was obtained to perform clinical examinations, and they were invited to the hospital to collect information. Echocardiography and electrocardiography were performed for the patients after one year. The information related to the first visit, including demographic characteristics, clinical manifestations, severity of the disease, and the recorded results of electrocardiography and echocardiography during the initial admission, were extracted from the patient's file using a researcher-made checklist by a cardiologist.

The electrocardiographic evaluation evaluated heart rhythm, T-ST disturbances, Q wave and QT interval, and any occurrence of heart block. Also, in the echocardiographic evaluation, changes in the diameter of the heart chambers, changes in the atrium and ventricular wall thickness, valvular disorders, ventricular dysfunction (based on LVEF), and pulmonary artery pressure were recorded.

**Sampling method and sample size:** The sampling method was non-probability convenience sampling. We considered 0.5 a medium effect size based on Cohen's d benchmark (14), 80% power, and 5% attrition rate. The sample size was calculated as 60 patients using G\*power version 3.1.9.4.

**Statistical analysis:** At first, the normality of quantitative variables was evaluated using the Kolmogorov-Smirnov test and Q-Q plot. Mean, and standard deviation (SD) were used to describe quantitative variables, and frequency and percentage (%) were used to describe qualitative variables.

Due to the non-normal distribution of continuous variables, the Mann-Whitney U test was used to compare the mean of continuous variables between gender groups. Fisher's exact test compared the frequency of categorized variables between gender groups. In addition, due to the non-normally distribution of data, Wilcoxon signed-rank test was

used to compare the mean of paired continuous variables in initial and one-year visits. Also, McNamara's test was used for comparing paired two-group variables, and the marginal homogeneity test was used to compare more than two groups paired nominal data. Statistical analysis at a significance level of less than 0.05 has been done two-way using STATA version 14 software.

## Results

This study was performed on patients with severe COVID-19, 60 patients were evaluated, and the mean age was  $53.63 \pm 12.50$  years. Thirty-five patients were male (58.33%), and 25 were female (41.67%). General and medical data of patients between gender groups showed in Table 1.

All patients were evaluated by echocardiography after one year, and it was observed that only the pulmonary arterial pressure increased significantly ( $24.30 \pm 4.79$  Vs.  $26.50 \pm 7.69$  mmHg p-value= 0.026) and other parameters of echocardiography didn't show significant change after one-year. The echocardiographic findings of patients with a history of covid-19 at the beginning and after one year are listed in Table 2.

The patients were also assessed by ECG after one-year. It was observed that the manifestations of T-wave inversion and QRS abnormality significantly increased after one year in patients with severe COVID-19 involvement (p-value<0.05). There were no significant changes in other ECG parameters in the patients after one year (p-value>0.05). The related data showed in Table 3. It should be considered that T wave inversion is negative T wave  $\geq 2$  mm in at least two leads from V1 -V6 or inferior-lateral leads, and QRS abnormality means any abnormality in duration ( $\geq 110$ -120 msec) or voltage. Low voltage was as amplitude  $\leq 5$  mm in limb leads and/ or  $\leq 10$  mm in precordial leads. High voltage is determined according to romhilt voltage criteria. Pathologic Q wave means any Q wave in V1-V3, abnormally wide Q wave ( $\geq 0/03$  msec), or abnormally deep ( $\geq 0/1$  mv).

## Discussion

In this retrospective cohort study that was conducted on patients who were involved with severe COVID-19 to evaluate the ECG and echocardiographic changes after one year, it was observed that T-wave inversion and QRS abnormality significantly increased after one year. Also, the pulmonary arterial pressure increased significantly after one year.

It was mentioned that preexisting cardiovascular disorder is associated with severe forms of COVID-19<sup>17, 18</sup>. In the present study, there was no association between previous cardiovascular disorders and the occurrence of cardiovascular diseases after one year in patients with severe COVID-19. This issue may come from the low statistical population of our study. More studies should be done in the future about this issue.

The mechanisms of COVID-19 that make cardiovascular involvement have not been fully found. SARS-CoV-2 can involve cardiomyocytes and develop myocarditis. In pathologic evaluations, virus particles were seen in cardiomyocyte specimens<sup>19</sup>. During post-COVID-19 involvement, over-infiltration of cytokines may develop vascular inflammation and myocardial inflammation, which leads to further myocardial infarction (MI) or heart failure (HF)<sup>20, 21</sup>. COVID-19 causes systemic complications such as sepsis and disseminated intravascular coagulation, which may evolve into cardiac complications<sup>22, 23</sup>.

In a study conducted on COVID-19 patients to evaluate the ECG and echocardiographic findings, 142 patients were evaluated. The mean age of patients was  $60.69 \pm 15.70$  years. Age, dyslipidemia, diabetes, RV size, ejection fraction, O2 saturation, and systolic blood pressure increased mortality. They found that COVID-19 could cause ventricular dysfunction. We found that PAP, QRS abnormality, and T-wave inversion were increased in patients with COVID-19 after one year. We also observed that the prevalence of underlying disorders was not high in our cases. This difference between the two studies may come from the difference in the method of the two studies. In the current study, we evaluated patients with severe COVID-19 after one year, but Keihanian et al., all patients with COVID-19 were evaluated. Based on these two studies, prolonged cardiac involvement in patients with severe COVID-19 is high and associated

**Table 1.** The general and medical information on patients with a history of COVID-19.

Variables	Female (n=25, 41.67%)	Male (n=35, 58.33%)	Total (n=60, 100%)	p-value
Age (years)	51.68 ± 12.25	55.02 ± 12.67	53.63 ± 12.50	0.272
<b>Current smoker</b>				
No	25 (100.00)	28 (80.00)	53 (88.33)	<b>0.035*</b>
Yes	0 (0.00)	7 (20.00)	7 (11.67)	
<b>Diabetes Mellitus</b>				
No	21 (84.00)	26 (74.29)	47 (78.33)	0.527
Yes	4 (16.00)	9 (25.71)	13 (21.67)	
<b>Hypertension</b>				
No	21 (84.00)	27 (77.14)	48 (80.00)	0.745
Yes	4 (16.00)	8 (22.86)	12 (20.00)	
<b>Dyslipidemia</b>				
No	20 (80.00)	32 (91.43)	52 (86.67)	0.259
Yes	5 (20.00)	3 (8.57)	8 (13.38)	
<b>Ischemic Heart Disease (IHD)</b>				
No	24 (96.00)	33 (94.29)	57 (95.00)	1.000
Yes	1 (4.00)	2 (5.71)	3 (5.00)	
<b>Another comorbidity <sup>1</sup></b>				
No	22 (88.00)	32 (91.43)	54 (90.00)	0.686
Yes	3 (12.00)	3 (8.57)	6 (10.00)	
<b>Family history of IHD</b>				
No	22 (88.00)	25 (71.43)	47 (78.33)	0.204
Yes	3 (12.00)	10 (28.57)	13 (21.67)	
<b>Medication history</b>				
<b>Cardiac drugs</b>				
No	24 (96.00)	31 (88.57)	55 (91.67)	0.390
Yes	1 (4.00)	4 (11.34)	5 (8.33)	
<b>Anti-hypertensive drugs</b>				
No	24 (96.00)	30 (85.71)	54 (90.00)	0.386
Yes	1 (4.00)	5 (14.29)	6 (10.00)	
<b>Anti-diabetic agents</b>				
No	22 (88.00)	32 (91.43)	54 (90.00)	0.686
Yes	3 (12.00)	3 (8.57)	6 (10.00)	
<b>Antilipemic agents</b>				
No	24 (96.00)	33 (94.29)	57 (95.00)	1.000
Yes	1 (4.00)	2 (5.71)	3 (5.00)	
<b>Anti-inflammatory drugs</b>				
No	23 (92.00)	31 (88.57)	54 (90.00)	1.000
Yes	2 (8.00)	4 (11.43)	6 (10.00)	
<b>Drug therapy for chronic kidney disease</b>				
No	25 (100.00)	34 (97.14)	59 (98.33)	1.000
Yes	0 (0.00)	1 (2.86)	1 (1.67)	
<b>Covid-19 related symptoms at a one-year follow-up visit</b>				
No symptom	24 (96.00)	32 (91.43)	56 (93.33)	0.634
Dyspnea	1 (4.00)	3 (8.57)	4 (6.67)	

Data describes as n (%) or mean ± standard deviation. \* Statistically significant, p-value < 0.05. N/A means not applicable. <sup>1</sup>Other comorbidity means hypothyroid disorder, cancer, lupus, and/ or End Stage Renal Disease (ESRD).

**Table 2.** Echocardiographic findings of patients with a history of COVID-19 at the beginning and after one year.

Factors	At first (n=60)	One-year later (n=60)	Pairwise comparison p-value
<b>LV Ejection Fraction (%)</b>	53.50 ± 2.31	53.30 ± 2.82	0.406
<b>Diastolic Dysfunction</b>			
Normal	9 (15.00)	13 (21.67)	0.125
Mild	51 (85.00)	47 (78.33)	
<b>RV Function</b>			
Normal	54 (90.00)	53 (88.33)	0.179
Mild	6 (10.00)	5 (8.33)	
Moderate	0 (0.00)	2 (3.33)	
<b>Mitral Regurgitation</b>			
Normal	3 (5.00)	7 (11.67)	0.572
Mild	56 (93.33)	50 (83.33)	
Mild to Moderate	1 (1.67)	1 (1.67)	
Moderate	0 (0.00)	2 (3.33)	
<b>Tricuspid Regurgitation</b>			
Normal	1 (1.67)	3 (5.00)	0.235
Mild	58 (96.67)	51 (85.00)	
Mild to Moderate	0 (0.00)	1 (1.67)	
Moderate	1 (1.67)	4 (6.67)	
Severe	0 (0.00)	1 (1.67)	
<b>Aortic Insufficiency</b>			
Normal	55 (91.67)	53 (88.33)	0.083
Mild	2 (3.33)	4 (6.67)	
Mild to Moderate	2 (3.33)	1 (1.67)	
Moderate	1 (1.67)	2 (3.33)	
<b>Pulmonary Insufficiency</b>			
Normal	56 (93.33)	57 (95.00)	1.000
Mild	4 (6.67)	2 (3.33)	
Moderate	0 (0.00)	1 (1.67)	
<b>Mitral Stenosis</b>			
Normal	60 (100.00)	60 (100.00)	N/A
<b>Tricuspid Stenosis</b>			
Normal	60 (100.00)	60 (100.00)	N/A
<b>Aortic Stenosis</b>			
Normal	60 (100.00)	60 (100.00)	N/A
<b>Pulmonary Stenosis</b>			
Normal	60 (100.00)	59 (98.33)	1.000
Mild	0 (0.00)	1 (1.67)	
<b>Pulmonary Regurgitation</b>			
Normal	60 (100.00)	60 (100.00)	N/A
<b>LA size</b>			
Normal	60 (100.00)	59 (98.33)	1.000
Mild enlargement	0 (0.00)	1 (1.67)	
<b>LV size</b>			
Normal	60 (100.00)	60 (100.00)	N/A
<b>RV size</b>			
Normal	56 (93.33)	55 (91.67)	0.157
Mild enlargement	4 (6.67)	3 (5.00)	
Moderate enlargement	0 (0.00)	2 (3.33)	
<b>RA size</b>			
Normal	60 (100.00)	58 (96.67)	0.157
Mild enlargement	0 (0.00)	1 (1.67)	
Moderate enlargement	0 (0.00)	1 (1.67)	
<b>Pulmonary artery pressure</b>	24.30 ± 4.79	26.50 ± 7.69	<b>0.026*</b>

Data describes as n (%) or mean ± standard deviation, \* statistically significant, P\_value < 0.05.

**Table 3.** ECG findings of patients with a history of COVID-19 at the beginning and after one year.

Factors	At first (n=60)	One-year later (n=60)	Pairwise comparison p-value
Heart rate (per minute)	80.10 ± 12.02	81.75 ± 14.43	0.619
<b>Rhythm</b>			
Sinus	57 (95.00)	53 (88.33)	0.361
Sinus-tachycardia	3 (5.00)	4 (6.67)	
Sinus / PAC	0 (0.00)	2 (3.33)	
PVC bigeminy	0 (0.00)	1 (1.67)	
<b>Axis</b>			
Normal	59 (98.33)	59 (98.33)	1.000
LAD	1 (1.67)	1 (1.67)	
<b>P-wave</b>			
Normal	60 (100.00)	60 (100.00)	N/A
<b>T-wave inversion</b>			
No	55 (91.67)	45 (75.00)	0.006*
Yes	5 (8.33)	15 (25.00)	
<b>ST-segment</b>			
Normal	56 (93.33)	53 (88.33)	0.375
Depression	4 (6.67)	7 (11.67)	
Elevation	0 (0.00)	0 (0.00)	
<b>QRS</b>			
Normal	59 (98.33)	50 (83.33)	0.004*
Abnormal	1 (1.67)	10 (16.67)	
<b>QT-interval</b>			
Normal	60 (100.00)	60 (100.00)	N/A

Data describes as n (%) or mean ± standard deviation. \*Statistically significant, p-value < 0.05.

N/A means not applicable.

with Increased PAP and, but RV abnormality is seen in all patients with COVID-19. Demographic and medical history may be important in cardiac involvement in all patients with COVID-19. However, based on the before-after design of our study, the effect of these factors was not considered. However, this issue should be evaluated in further studies<sup>24</sup>.

In a study performed by Kaliyaperumal et al., it was observed that abnormal ECG was detected among patients admitted due to COVID-19 in 255 (81%) patients. Abnormalities in rhythm were seen in 9 patients (2.9%), the rate in 115 patients (36.5%), short QRS complex in 8.3%, prolonged PR interval in 2.9%, and prolonged QT interval in 8.3%<sup>25</sup>. In the current study, abnormalities in rhythm and QRS were seen in 7 (11.67) and 10 (16.67), respectively. The recent

study's findings differed from those of Kaliyaperumal et al. These differences may come from differences in understudied populations and research methodology.

In a study by Chen et al., it was found that ST-T abnormalities (34.3%) were the most common ECG presentation, and atrial arrhythmias with rapid rhythms (8.5%) and sinus tachycardia (13.3%) were the most prevalent arrhythmias in patients hospitalized for COVID-19. The current study observed that T-wave inversion was the most common ECG abnormality (8.33) at admission and after one year. Mild MR and TR were the most frequent abnormalities in echocardiography at admission time and after one year. Our study's findings differed from Chen et al.' study. These differences should be evaluated in further studies. Also, Chen et al. found that in severe COVID-

19, ST-T abnormalities, sinus tachycardia, and atrial arrhythmias were significantly more common<sup>26</sup>. In the present study, we found that T-wave inversion, QRS abnormality, and pulmonary arterial pressure were significantly increased after one year from severe COVID-19.

Su et al. found that myocardial injuries were higher in COVID-19 patients with T-wave inversion, and T-wave inversion is associated with a higher mortality rate<sup>27</sup>. The current study found that T-wave inversion significantly increased during one year of severe COVID-19. T-wave inversion seems to be a poor prognostic value for patients with COVID-19 because this finding can increase the mortality rate based on Su et al.'s study. We found that this finding significantly increased after one year. T-wave inversion is associated with myocardial infarction (MI) or injuries<sup>28</sup>. This manifestation develops ST-elevation MI<sup>29</sup>. So, in patients who were involved with severe COVID-19, the presence of an inverted T-wave should be a concern for the occurrence of MI in the future.

In the current study, we observed that the patients experienced significantly increased PAP after one year. Mamzer et al. found that annual recognition of pulmonary hypertension increased in patients with COVID-19, and COVID-19 is a risk for pulmonary hypertension<sup>30</sup>. The finding of this study was similar to the current research. The limitation of this study was the small sample size, and it is recommended to do more studies with more significant sample sizes in the future.

## Conclusion

Patients with severe COVID-19 are at risk of cardiac involvement in the future. Periodic cardiac assessment of these patients is essential. Echocardiography and ECG should be done in these patients for follow-ups. Inverted T-wave and QRS abnormality in ECG and increased PAP in echocardiography are important findings in patients with a history of COVID-19 involvement. They can prone the patients to further cardiac injuries or myocardial involvement.

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## Conflict of interest

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

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