



Prevalence of Cardiovascular Involvement in Patients With COVID-19 Disease

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Abstract

Background: Coronaviruses are a huge family of viruses that lead to various diseases from a common cold to more unadorned illnesses for example SARS-CoV and MERS-CoV. Common symptoms of this infection include respiratory symptoms. In addition, this disease can also manifest with an acute cardiovascular (CV) syndrome. The aim of this study was to determine the frequency of CV involvement in patients with COVID-19 disease admitted to Afzalipour Hospital in Kerman.

Methods: In this study, all patients who were diagnosed with COVID-19 disease and were hospitalized and monitored due to disease conditions were eligible to enter the study. At the beginning of the patient's hospitalization, the patients' vital signs were recorded and the first 12-lead electrocardiography was taken. Then, patients underwent cardiac monitoring and echocardiography at the beginning of hospitalization and afterwards during the course of disease. Preliminary tests including biochemistry, blood cell count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and troponin were also performed for patients.

Results: The mean age of patients with COVID-19 was 55.63 years and 20.2% of them had a history of heart disease. More than half of these patients were men. Ejection fraction was normal in 87.8% of patients. There was a significant relationship between diastolic dysfunction grade and the history of heart disease ($P=0.02$).

Conclusion: Since the incidence of underlying diseases such as diabetes, hypertension and cardiac disorders can raise the risk of corona viruses' disease and also increase the mortality rate of this disease in these people, it is suggested that more attention be paid to the observance of health protocols for people with underlying diseases, and that people with underlying diseases be given priority in vaccinating against this disease.

Keywords: COVID-19, Mortality, Morbidity, Cardiovascular disorders

Citation: Aliramezany M, Mahdavi A, Ghanbarnejad M, Zarrabi M, Ebrahimi SS, Jafari M. Prevalence of cardiovascular involvement in patients with COVID-19 disease. *Journal of Kerman University of Medical Sciences*. 2023;30(6):333-338. doi:10.34172/jkmu.2023.56

Received: June 7, 2023, **Accepted:** October 1, 2023, **ePublished:** December 29, 2023

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a human beta coronavirus, observed in Wuhan, China for the first time, in December 2019, and lead to the coronavirus disease 2019 (COVID-19) (1). This signifies a public health emergency of pandemic proportions, being accountable for increasing rates of global morbidity and mortality (2). COVID-19 has a wide range of clinical manifestations, extending from asymptomatic respiratory failure to multi-organ failure and death. Most of patients with this infection has mild symptoms, but approximately one-fifth need hospitalization and may be affected by a severe disease. Generally, common clinical presentation of SARS-CoV-2 is pneumonia but this virus, may affect all organs, and hurried a variation of systemic involvements such as kidneys, gut, and cardiovascular (CV) apparatus involvements (3).

This virus may worsen the clinical condition of patients

with underlying cardiac and non-cardiac diseases, reported in approximately 20% of the patients, and cause de novo CV problems. Several forms of CV complication have been defined including myocardial injury, pericardial diseases, acute coronary syndrome (ACS), arrhythmias, exacerbation of heart failure (HF), myocarditis-like syndrome, takotsubo syndrome, and arterial and venous atherothrombotic and thromboembolic events (4-6).

Several mechanisms have been postulated for these conditions such as oxygen supply/demand disparity because of the hypoxic state, inflammatory response in form of local and systemic with cytokine-mediated injury, virus-mediated cellular damage, endothelial injury, plaque instability, and prothrombotic status. These situations may be accountable for sequelae and CV hostile proceedings after the infection resolve, and affect patients' consequences in the short and long term. Indeed, as the COVID-19 pandemic has proceeded, some



patients with persistent symptoms or organ involvement after the end of the acute phase of the infection have been reported (7,8).

In a recent Italian study by Carfi et al, in patients who had recovered from COVID-19, 87.4% reported persistence of at least one symptom, particularly fatigue and dyspnea. Patients with community-acquired pneumonia can also have persistent symptoms, suggesting that these findings may not be exclusive to COVID-19. Clinicians and researchers have focused on the acute phase of COVID-19, but continued monitoring after discharge for long-lasting effects is needed (9).

Previous clinical studies on patients with pneumonia have documented a two- to eight-fold increase in the risk of CV diseases within the first 30 days from hospitalization; this risk remained high even up to 10 years (10). The highest probability to develop adverse CV events was observed during the first years, independently of the severity of the respiratory infection (11).

These data, along with the uncertainty about the course of the disease, emphasize the importance of close monitoring of patients who recovered, either partially or completely, from COVID-19. To date, the need of long-term outcome data remains unaddressed, and the type and real incidence of CV sequelae after COVID-19 is poorly known. The aim of this study was to determine the frequency of CV involvement in patients with COVID-19 disease admitted to Afzalipour Hospital in Kerman.

Methods

The present study was a descriptive cross-sectional study. The statistical population of this study consisted of patients with COVID-19 who were admitted to Afzalipour Hospital in Kerman during the epidemic period. Confirmation of COVID-19 disease was based on national guidelines and definitive case definition was based on positive PCR test or lung CT scan findings. In this study, all patients who were diagnosed with COVID-19 disease and were hospitalized and monitored due to the disease conditions were eligible to enter the study. Other patients receiving home care for any reason were not included in the study. A total of 163 patients were enrolled through convenience sampling method.

At the beginning of patient's hospitalization, vital signs were recorded and the first 12-lead electrocardiography (ECG) was taken and all patients underwent echocardiography for the detection of pericardial effusion, myocarditis, systolic-diastolic function and valvular involvement. Otherwise, the same echocardiography was performed in the course of the disease. Also, initial tests including biochemistry, blood cell count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were performed for the patients.

Demographic variables in this study included age, sex, heart disease status and other underlying diseases.

Hemodynamic findings (blood pressure, heart rate, respiration rate) of patients were also collected. To collect information, a data collection form was used, which is organized in 3 main sections. The first part included demographic information, the second part included vital signs, and the third part included patients' final outcome, length of hospital stays, and hospitalization in the intensive care unit (ICU). Finally, the obtained information was analyzed using descriptive and analytical statistics.

In this study, the ratio estimation formula was used to calculate the sample size according to the frequency of CV complications in a similar study (12). Considering the error rate of 7%, 95% confidence interval and 23% prevalence of CV complication in COVID-19 patients who were hospitalized, the study volume in this study was 145 patients and to increase the study capacity, 163 patients were investigated.

Statistical analysis

All collected data were coded and entered into SPSS software (version 22) and mean, standard deviation, frequency and percentage were used to describe the data using tables and graphs. For quantitative data analysis, the normal distribution of data was first measured using the Kolmogorov-Smirnov test. Mann-Whitney U test and t-test were used for compare quantitative data between two groups of patients based on their coronary artery disease status such as age, length of hospital stay and hemodynamic indices. Chi-square test and Fisher's exact test were used to compare qualitative variables between the two groups of patients such as gender, underlying disease, arrhythmia, ischemia, myocarditis and thrombosis. Finally, Cox regression was used to determine the attenuation risk. All statistical analyzes were performed in SPSS statistical software version 23. Significance level for double range tests was considered 0.05.

Ethics statement

Prior to the study, the necessary permits were obtained from the ethics committee of Kerman University of Medical Sciences. Conscious consent was obtained from patients for diagnostic interventions.

Also, the information of patients who were eligible for inclusion in the study was kept confidential. Participation in the study was completely optional and patients could cancel the study at any time.

Results

In our study, 163 patients with COVID-19 were studied. The mean and standard deviation of the age of patients with COVID-19 was 55.63 ± 17.93 years. More than half of these patients were men (55.8%) and 65% of them had underlying diseases including hypertension, diabetes and

CV disease (Table 1).

Mean and standard deviation of systolic and diastolic blood pressure in patients were 126.88 ± 22.5 and 78.46 ± 14.39 mm/Hg, respectively. Also, the mean duration of hospitalization for patients with COVID-19 was 11.83 ± 7.91 days and 31.3% of patients were hospitalized in ICU. Also, 17.8% of patients with COVID-19 died (Table 2) and in 74.2% of patients, the ECG was abnormal.

In the present study, left ventricle (LV) ejection fraction (EF) was unchanged in 6.91% of patients, while 4.8% of patients with normal cardiac function had decreased EF. The most common positive echocardiographic findings were related to diastolic dysfunction (70.6%), right ventricle enlargement (25.8%), and right ventricle dysfunction (15.3%). Other variables such as pericardial effusion, regional wall motion abnormalities (RWMA), abnormal EF and global hypokinesia were reported to be less than ten percent positive (Table 3). diastolic dysfunction grade 1 has been reported in 2.3% of people without a history of heart disease and in 13.3% of people with a history of positive CV disease. There was a significant relationship between diastolic dysfunction grade and history of CV disease ($P=0.02$). In patients with a history of CV disease, variables such as EF (80%), right ventricular enlargement (23.3%) and diastolic dysfunction (100%) were reported to be positive. diastolic dysfunction was significantly associated with a history of CV disease ($P<0.001$). Other variables were less than

20% positive in people with a history of CV disease. These variables had no significant relationship with the history of CV disease ($P<0.05$, Table 4). In patients with COVID-19 disease, 5.5% ischemia, 0.6% endocarditis, 2.5% pericardial effusion, 3.1% myocarditis, 62.5% arrhythmias, and 1.8% embolism were seen (Table 5).

Ischemia (5.6%), endocarditis (1.4%), pericardial effusion (4.2%) and pulmonary emboli (2.8%) were more frequent in women and myocarditis (3.3%) and arrhythmia (64.8%) were more common in men. As it has been shown in Table 6, there was no significant relationship between sex and variables of ischemia ($P<0.99$), endocarditis ($P=0.44$), pericardial effusion ($P=0.32$), myocarditis ($P<0.99$), arrhythmia ($P=0.5$) and pulmonary emboli ($P=0.58$).

In patients with a history of CV disease, 76% ischemia, 3.3% pericardial effusion and 56.7% arrhythmia were

Table 1. Demographic characteristics of patients

Clinical presentation	Value
Blood pressure	
Systolic blood pressure	126.88 ± 22.5
Diastolic blood pressure	78.46 ± 14.39
Length of hospital stay(day)	11.83 ± 7.91
Admitted in ICU	
Yes	51 (31.3%)
No	112 (68.7%)
ICU stay(day)	12.78 ± 9.72
Renal function	
Normal	134 (82.2%)
Abnormal	29 (17.8%)
Troponin level	
Normal	154 (94.5%)
Abnormal	9 (5.5%)
Liver function	
Normal	152 (93.3%)
Abnormal	11 (6.7%)
Final outcome	
Discharge	134 (82.2%)
Death	29 (17.8%)

Table 2. Primary clinical presentation in patients with COVID-19 disease

Variables	Total number of patients = 163	
Mean age \pm SD	55.63 ± 17.93	
Gender	Male	91 (55.8%)
	Female	72 (44.2%)
Underlying diseases		
Hypertension	Yes	59 (36.2%)
	No	104 (63.8%)
Diabetes mellitus	Yes	123 (75.5%)
	No	40 (24.5%)
Cardiovascular disease	Yes	134 (82.2%)
	No	29 (17.8%)

Table 3. Determining the frequency distribution of echocardiographic findings

Variable	Number (%)	
Ejection fraction	Normal	143 (87.8%)
	Mild dysfunction	9 (5.5%)
	Moderate dysfunction	3 (1.8)
	Severe dysfunction	8 (4.9)
Pericardial effusion	Negative	158 (96.9%)
	Positive	5 (3.1%)
Right ventricle enlargement	Negative	121 (74.2%)
	Mild	37 (22.7%)
	Severe	5 (3.1%)
Right ventricle dysfunction	Negative	138 (84.7%)
	Positive	25 (15.3%)
RWMA	Negative	159 (97.5%)
	Positive	4 (2.5%)
Global hypokinesia	Negative	155 (95.1%)
	Positive	8 (4.9%)
Diastolic dysfunction	Negative	48 (29.4%)
	Positive	115 (70.6%)

Table 4. Comparison of echocardiographic findings based on history of heart disease

Variable	History of cardiovascular disease		P value	
	Yes	No		
Ejection fraction	Normal	24 (80%)	119 (89.5%)	0.44
	Mild	3 (10%)	7 (5.2%)	
	Moderate	0 (0%)	1 (0.8%)	
	Severe	3 (10%)	6 (4.5%)	
Pericardial effusion	Negative	29 (96.7%)	129 (97%)	>0.99
	Positive	1 (3.3%)	4 (3%)	
Right ventricle enlargement	Negative	23 (76.7%)	98 (73.7%)	0.92
	Mild	6 (20%)	31 (23.3%)	
	Severe	1 (3.3%)	4 (3%)	
Right ventricle dysfunction	Negative	23 (76.7%)	115 (86.5%)	0.25
	Positive	7 (23.3%)	18 (13.5%)	
Left ventricle enlargement	Negative	30 (100%)	132 (99.2%)	0.63
	Positive	0 (0%)	1 (0.8%)	
RWMA	Negative	29 (96.7%)	130 (97.7%)	>0.99
	Positive	1 (3.3%)	3 (2.3%)	
Global hypokinesia	Negative	27 (90%)	128 (96.2%)	0.16
	Positive	3 (10%)	5 (3.8%)	
Diastolic dysfunction	Negative	0 (0%)	48 (36.1%)	<0.001
	Positive	30 (100%)	85 (63.9%)	

Table 5. Frequency distribution of cardiac involvement

Variable	Number (%)
Ischemia	Negative 154 (94.5%)
	Positive 9 (5.5%)
Endocarditis	Negative 162 (99.4%)
	Positive 1 (0.6%)
Pericardial effusion	Negative 159 (97.5%)
	Positive 4 (2.5%)
Myocarditis	Negative 158 (96.9%)
	Positive 5 (3.1%)
Arrhythmias	Negative 61 (37.4%)
	Positive 102 (62.6%)
Pulmonary emboli	Negative 160 (98.2%)
	Positive 3 (1.8%)

observed.

History of CV disease had no significant relationship with ischemia ($P=0.67$), endocarditis ($P<0.99$), pericardial effusion ($P=0.56$), myocarditis ($P=0.58$), arrhythmia ($P=0.45$) and pulmonary emboli ($P<0.99$) with. The results have been presented in [Table 7](#).

Discussion

In this study, 163 patients with COVID-19 with a mean age of 55.63 ± 17.93 were included. More than half of the patients (55.8%) were men. Also, more than half of the

Table 6. Distribution of cardiac involvement based on gender

Variable	Gender		P value
	Male	Female	
Ischemia	Negative 86 (94.5%)	68 (94.4%)	0.99
	Positive 5 (5.5%)	4 (5.6%)	
Endocarditis	Negative 91 (100%)	71 (98.6%)	0.44
	Positive 0 (0%)	1 (1.4%)	
Pericardial effusion	Negative 90 (98.9%)	69 (95.8%)	0.32
	Positive 1 (1.1%)	3 (4.2%)	
Myocarditis	Negative 88 (96.7%)	70 (97.2%)	0.99
	Positive 3 (3.3%)	2 (2.8%)	
Arrhythmias	Negative 32 (35.2%)	29 (40.3%)	0.52
	Positive 59 (64.8%)	43 (59.7%)	
Pulmonary emboli	Negative 90 (98.9%)	70 (97.2%)	0.58
	Positive 1 (1.1%)	2 (2.8%)	

Table 7. Distribution of cardiac involvement based on history of heart disease

Variable	History of cardiovascular disease		P value
	Yes	No	
Ischemia	Negative 28 (93.3%)	126(94.7%)	0.67
	Positive 2 (6.7%)	7(5.3%)	
Endocarditis	Negative 30 (100%)	132(99.2%)	>0.99
	Positive 0 (0%)	1 (0.8%)	
Pericardial effusion	Negative 29 (96.7%)	130 (97.7%)	0.56
	Positive 1 (3.3%)	3 (2.3%)	
Myocarditis	Negative 30 (100%)	128 (96.2%)	0.58
	Positive 0 (0%)	5 (3.8%)	
Arrhythmias	Negative 13 (43.3%)	48 (36.1%)	0.45
	Positive 17 (56.7%)	85 (63.9%)	
Embolism	Negative 30 (100%)	130 (97.7%)	>0.99
	Positive 0 (0%)	3 (2.3%)	

patients (68%) had an underlying disease.

Mean systolic and diastolic blood pressures in patients were 126.88 ± 22.5 and 78.46 ± 14.39 mm Hg, respectively. Also, the mean duration of hospitalization for patients with COVID-19 was 11.83 ± 7.91 days and 31.3% of patients were hospitalized in ICU and 17.8% of patients died. Li et al in China examined the daily changes in blood pressure of 79 patients with COVID-19 admitted to the hospital. The mean blood pressure in hospitalized patients was 131.3/75.2 mm Hg and in discharged patients was 125.4/77.3 mm Hg, which is consistent with the present study. Also, in the mentioned study, 3.80% of patients were admitted to the ICU and 3.80% of patients died (13). The difference in the values of the above study with the current study can be due to differences in sample size and geographical area.

In this study, 4.8% of patients with normal heart function had a decreased Ejection Fraction. The

most common positive echocardiographic findings were diastolic dysfunction (70.6%), right ventricular enlargement (25.8%) and right ventricle dysfunction (15.3%). In our study, there was a significant association between diastolic dysfunction and history of CV disease. Hani M Mahmoud-Elsayed et al. (2020) in the United Kingdom evaluated echocardiographic findings in patients with COVID-19 pneumonia in a sample size of 74 patients and reported the main disorders of right ventricular (RV) dilatation (41%) and RV dysfunction (27%). RV disorder was associated with increased levels of D-dimer protein and CRP. In contrast, left ventricular function was hyperdynamic or normal in most patients (89%). Again, the difference in the results of this study with the current study may be due to differences in sample size and location of the study (14). Szekely et al examined the spectrum of cardiac manifestations in COVID-19 patients on a sample size of 112 patients and reported that in COVID-19 infection, left ventricular systolic function in most patients survived, but left ventricular diastolic function and right ventricular function were impaired. High troponin and poorer clinical grade are associated with worse right ventricular function. Acute right ventricular dysfunction with or without deep vein thrombosis is more common in patients presenting with clinical worsening follow-up; But acute left ventricular systolic dysfunction was observed more in 20%. The differences in the results of the mentioned study and the current study can be due to the difference in the sample size of the two studies (15).

In this study, 5.5% ischemia, 0.6% endocarditis, 2.5% pericardial effusion, 3.1% myocarditis, 62.6% arrhythmia and 1.8% pulmonary emboli were seen among the patients. There was no statistically significant relationship between these problems and history of heart disease. Abi Nassif et al in Lebanon examined cardiac appearances in COVID-19 patients and focused on the pediatric population. They concluded that COVID-19 may affect the cardiac system at different stages and can lead to myocardial ischemia, arrhythmia, HF, myocarditis and multisystem inflammatory syndrome in children. The frequency of cardiac complications differs among these patients (16).

Conclusion

The results of this study showed a significant relationship between sinus tachycardia and a history of CV disease. The underlying diseases such as diabetes, hypertension and CV disorders can increase the risk of corona viruses' disease, and also increase the mortality rate from these diseases. Therefore, it is suggested that more attention be paid to the observance of health protocols for people with underlying diseases, and that people with underlying diseases be given priority in vaccinating against this disease. Special consideration should also be rewarded

to the CV support of these high-risk patients and special diagnostic and therapeutic protocols should be developed to prevent CV complications, as along with the treatment of patients with COVID-19. It is highly desirable that future studies in this area be directed to studying and describing the prevalence, mechanisms and consequences of different CV events during the course of the disease and to the therapeutic and challenges arising from the concurrence of these two diseases.

Authors' Contribution

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Competing Interests

The authors declared that there is no conflict of interest.

Funding

None.

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