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Cardiovascular complications in patients hospitalized with COVID-19: A cross-sectional study

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Abstract

This study aimed to evaluate the cardiovascular complications in patients hospitalized with COVID-19. An analytical cross-sectional study was conducted to investigate the prevalence of cardiovascular disorders among patients infected with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The study focused on individuals admitted to Shahid Beheshti Hospital in Kashan throughout 2018-2019. A comprehensive questionnaire was administered to collect demographic information, vital signs upon admission, symptoms experienced, underlying medical conditions, cardiovascular risk factors, duration of hospitalization, discharge status, and laboratory test results. The data encompassed a wide range of variables including age, sex, race, vital signs, symptoms, comorbidities, cardiovascular risk factors, hospitalization duration, discharge outcome, and laboratory parameters. The study encompassed a total of 440 patients diagnosed with COVID-19. The average age of the participants was 61.28 (SD=18.97) years. The presence of a cardiac disorder exhibits a statistically significant correlation with admission to the intensive care unit (ICU) (P=0.004). Furthermore, the findings indicate that gender, age, decreased level of consciousness, pulse rate (PR), respiratory rate (RR), oxygen saturation (SPO_2), and various laboratory parameters (excluding white blood cell (WBC), erythrocyte sedimentation rate (ESR), Mg, Troponin, pH, PaO_2, and $PaCO_2$), alongside ICU hospitalization and mechanical ventilation, significantly associated with patient mortality (P<0.05). SARS-CoV-2 has the potential to exacerbate conditions in individuals with pre-existing cardiovascular diseases, necessitating meticulous planning of treatment strategies. Additionally, SARS-CoV-2 can induce cardiovascular disorders in affected individuals, underscoring the importance of vigilant monitoring and management of resultant cardiac complications during the treatment of SARS-CoV-2.

Keywords: SARS-CoV-2, COVID-19, Nursing, Secondary Complications, Cardiovascular Disorder.

1 | Introduction

In December 2019, an unidentified pneumonia case was reported in Wuhan, China [1]. The World Health Organization provisionally named the novel coronavirus as COVID-19 on January 21, 2020. The virus was later classified as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is an enveloped, non-segmented, positive-sense single-stranded RNA virus from the Coronaviridae family [2].

The pathogenesis of SARS-CoV-2 and the inflammation it induces may result in long-term secondary complications such as cardiovascular disorders [3]. It not only precipitates acute respiratory distress syndrome but also leads to multi-organ dysfunction

necessitating intensive care and potentially resulting in mortality [4].

The cytokine storm associated with SARS-CoV-2 infection produces pro-inflammatory cytokines and chemokines including Tumor Necrosis Factor-α (TNFα), IL-1β, and IL-6, which contribute to secondary complications and multi-organ damage [5]. Risk factors for severe COVID-19 have been identified as male sex, advanced age, chronic lung, kidney, and cardiovascular disease, diabetes, and obesity. Observational data suggest that approximately 1% to 2% of patients with SARS-CoV-2 infection experience myocardial infarctions (MIs), while 25% to 33% of patients with cardiac conditions are infected with SARS-CoV-2 [6].

SARS-CoV-2 can cause myocardial damage, MI, thrombosis or blood clots in the vessels, and cardiac arrhythmias. From a molecular perspective, it appears that SARS-CoV-2 affects the cardiovascular system by activating the immune and coagulation systems. Furthermore, inflammation can cause significant damage to the heart and blood vessels [7].

A substantial proportion of hospitalized SARS-CoV-2 patients experience myocardial damage, which is associated with an increased mortality risk. Clinical reports from China, Italy, and the United States have noted an association of SARS-CoV-2 with the prominent occurrence of cardiovascular complications including myocarditis, acute MI, and congestive heart failure, similar to observations made during the SARS and Middle East respiratory syndrome (MERS) epidemics [8].

Given the wide range of clinical symptoms and the various complications caused by SARS-CoV-2 in different organs of the human body, particularly the cardiovascular system, there is an increased mortality associated with SARS [9]. Therefore, understanding the biological features of SARS-CoV-2 infections and identifying the frequency of cardiovascular disorders among affected patients will contribute to the development of appropriate treatment plans, diagnostic tests, vaccines, and pharmacological therapies. This study aimed to investigate the frequency of cardiovascular disorders in patients with SARS-CoV-2.

2 │ Methods

2.1 │ Study design and subjects

An analytical cross-sectional study was formulated to examine the prevalence of cardiovascular disorders among SARS-CoV-2 patients. These patients were admitted to Shahid Beheshti Hospital, located in Kashan, from 2018 to 2019. The study encompassed a total of 440 Iranian patients diagnosed with SARS-CoV-2. The criteria for inclusion in this study were as follows: patients who were admitted to the hospital with a confirmed diagnosis of SARS-CoV-2 and had comprehensive data in their medical records. The exclusion criteria encompassed patients with incomplete medical records, the absence of electrocardiogram data and those who were hospitalized for less than three days.

2.2 │ Ethics consideration

The research protocol received approval from the Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.MEDNT.REC.1399.155). Throughout the study, stringent measures were taken to safeguard all patient-related information, and data extraction was performed anonymously. In instances where it was deemed necessary, patients were contacted and their informed consent was duly obtained.

2.3 │ Sample size

The sample size was determined using a specific formula, resulting in an initial calculation of 400 cases. This was based on an estimated prevalence of cardiovascular disorders at 7%, as per the study conducted by Wang et al., (2020) [10]. The desired precision and confidence levels were set at 2.5% and 95% respectively. To account for potential missing data, the sample size was further increased by 10%, leading to a final total of 440 cases.

$$n = \frac{(z_{1-\alpha/2})^2 p(1-p)}{d^2}$$

2.4 │ Data collection

A comprehensive questionnaire was developed to gather pertinent information. This included demographic details such as age, sex, and race, as well as vital signs upon admission (temperature, blood pressure, respiratory rate (RR), pulse rate (PR), presence of fever, and weakness). Symptoms such as fatigue, chills, dry cough, productive cough, dyspnea, anorexia, myalgia, sore throat, diarrhea, vomiting, nausea, headache, dizziness, abdominal pain, rhinorrhea, chest pain, seizures, olfactory and gustatory disorders, and altered consciousness were also recorded. Underlying conditions were taken into account, including cardiovascular disease, diabetes, hypertension, chronic obstructive pulmonary disease, renal disease, neurological disorders, obesity, hepatic disease, endocrine disorders, hematological disorders, and active malignancy. Cardiovascular risk factors such as hypertension, obesity, diabetes, smoking, hyperlipidemia, family history of heart disease, history of heart disease, and type of heart

disease (congestive heart failure, cardiac arrest, arrhythmia, coronary artery occlusion, history of open-heart surgery, valvular diseases) were also noted. Additional data collected included the total duration of hospitalization, discharge status (partial recovery, full recovery), and results of laboratory tests such as electrolyte levels, hematological parameters, biochemical tests, coagulation function, and blood gas analysis.

2.5 | Statistical analysis

Statistical analyses were conducted using SPSS version 20 software (SPSS Inc., Chicago, IL). The normality of data distribution was assessed using the Kolmogorov-Smirnov and Levene tests. Results were expressed as median (minimum-maximum values) or mean ± standard deviation (SD), and percentages where appropriate. Univariate analysis (Mann-Whitney test, Fisher's exact test) was employed to identify cardiovascular disorders associated with COVID-19. Simple logistic regression and simple linear regression models were utilized to analyze the relationship between individual variables and outcomes such as mortality rate, duration of hospitalization, and clinical outcomes. In multivariate analyses, multiple logistic regression models (adjusted odds ratio) and multiple linear regression were used to control for confounding factors and to identify factors associated with qualitative and quantitative clinical outcomes. A $P<0.05$ was considered statistically significant.

3 | Results

3.1 | Participants' characteristics

As delineated in Table 1, the study encompassed a total of 440 patients diagnosed with COVID-19. The average age of the participants was 61.28 (SD=18.97) years. A significant proportion of the sample, 58.9%, were female. The study also revealed that 5.2% of the participants had a history of smoking, 4.1% were identified as drug users, and 0.2% reported a history of alcohol consumption. Furthermore, 37.5% of the participants were diagnosed with hypertension, and 12.1% had experienced blood clots. This data provides a comprehensive overview of the demographic and health characteristics of the participants involved in the study.

3.2 | Correlation of heart disorder with the outcome of patients

The study found a significant correlation between the presence of cardiac disorders and hospitalization in the Intensive Care Unit (ICU) ($P=0.004$), with 25.6% of patients with heart conditions requiring ICU admission. However, the presence of cardiac disorders did not show a statistically significant association with the need for ventilation ($P=0.171$), the duration of hospital stays ($P=0.565$), or patient mortality ($P=0.481$). These findings are elaborated in Table 2. This data underscores the complex interplay between cardiac disorders and various clinical outcomes in COVID-19 patients.

3.3 | The relationship of various clinical factors with the death of patients

An investigation into the factors associated with the mortality of COVID-19 patients with cardiovascular diseases revealed that the nationality of the patients, smoking habits, pre-existing conditions, and a range of clinical symptoms (including fever, weakness and fatigue, cough, anorexia, muscle pain, shortness of breath, sore throat, diarrhea, vomiting, nausea, headache, dizziness, abdominal pain, runny nose, chest pain, seizures, and decreased level of consciousness) did not exhibit a significant correlation with patient mortality ($P\geq0.05$). Further details regarding the relationship between clinical and laboratory findings and patient mortality are presented in Table 3. The analysis indicated that variables such as gender, age, pulse rate (PR), RR, oxygen saturation (SPO_2), certain laboratory findings (excluding white blood cell (WBC), erythrocyte sedimentation rate (ESR), Mg, Troponin, PH, PaO_2, and $PaCO_2$), ICU admission, and the need for ventilation were significantly associated with patient mortality ($P<0.05$). It is noteworthy that the Multiple Imputation method was employed to address missing data about laboratory findings.

To validate the findings, the Omnibus test was conducted. The results of the Omnibus test indicated that the model's fit was both acceptable and statistically significant, with an error level of ≤0.001. Furthermore, out of the variables that demonstrated a significant correlation with patient mortality in Table 3, ten variables - namely, age, PR, respiratory rate (RR), Neutrophil count, platelet count (PLT), partial thromboplastin time (PTT), blood urea nitrogen (BUN), sodium levels (Na), ICU admission, and the requirement for ventilation were retained in the regression model. According to the coefficient of determination (Pseudo R-square), these remaining variables were capable of explaining between 28.4% and 45.7% of the variation's inpatient mortality. This underscores the multifactorial nature of patient outcomes in the context of COVID-19 (Table 4).

Table 1. Demographic data and Clinical characteristics in study (N=440).

	Frequency (%) or Mean (SD)
Demographic characteristics	
Age	61.28 (SD=18.97)
18-30	24 (5.5)
31-60	90 (20.45)
>60	326 (74.09)
Gender	
Male	181 (41.1)
Female	259 (58.9)
Clinical characteristics	
Smoking	
Yes	23 (5.2)
No	417 (94.8)
Drug abuse	
Yes	18 (4.1)
No	422 (95.9)
Alcohol	
Yes	1 (0.2)
No	439 (99.8)
Underlying condition	
Diabetes	122 (27.7)
Cardiovascular disease	91 (20.7)
High blood pressure	165 (37.5)
Hyperlipidemia	44 (10.0)
Pulmonary disease	27 (6.1)
Kidney disease	23 (5.2)
Hepatic disease	4 (0.9)
Neurology	41 (9.3)
Hematic	6 (1.4)
Cancer	7 (1.6)
Type of cardiovascular disease	
Congestive heart failure	8 (8.8)
Infarction	2 (2.2)
Coronary artery occlusion	11 (12.1)
Valvular disease	4 (4.4)
CABG	6 (6.6)
IHD	60 (65.9)

Values are given as Mean (SD) for continuous variables and frequency (%) for categorical variables.

Table 2. Correlation of heart disorder with patient's outcome (N=440).

Outcome	Cardiovascular disorder		P-value
	Yes	No	
Hospitalization in the ICU	75 (25.6)	20 (13.6)	0.004*
Connection to Ventilation	39 (13.3)	13 (8.8)	0.171*
Hospitalization Period	7.43 (SD=5.03)	7.14 (SD=4.92)	0.565**
Death	58 (19.8)	25 (17)	0.481*

Values are given as Mean (SD) for continuous variables and frequency (%) for categorical variables.
*P-value was obtained with Fisher exact test.
**P-value was obtained with Mann-Whitney U-test.

4 | Discussion

Cardiovascular diseases are globally recognized as the leading cause of mortality and disability. Previous studies have reported the prevalence of cardiovascular diseases in 13% and 33% of patients with SARS and MERS, respectively [11]. Preliminary reports from China have identified cardiovascular disease and its associated risk factors, such as hypertension and diabetes, as prevalent comorbidities in patients with SARS-CoV-2 [12]. The findings of the current study suggest that obesity may play a significant role in the requirement for ventilation and the duration of hospitalization. Additionally, hyperlipidemia may significantly influence survival rates. An initial report from Wuhan, which included 41 hospitalized SARS-CoV-2 patients, indicated a 32% prevalence of any underlying diseases, with diabetes, hypertension, and other cardiovascular diseases being the most common [13]. Furthermore, a study involving 1099 SARS-CoV-2 patients revealed that 25% of the patients had comorbidities, including

hypertension, diabetes, and coronary heart disease [14]. Thus, it can be inferred that cardiovascular disease is one of the underlying conditions that exacerbate the condition in SARS-CoV-2 patients. However, the mechanisms remain elusive; a potential explanation could be that cardiovascular diseases in older patients lead to a weakened immune system function and an increased level of ACE2, making these individuals more susceptible to SARS-CoV-2 infection [15].

Table 3. Factors related to the death of patients (univariate correlation) (N=440).

	Mortality	Survived	P-value
Gender			
Male	60 (72.3)	199 (55.7)	0.006*
Female	23 (27.7)	158 (44.3)	
Age	69.38 (SD=18.50)	59.40 (SD=18.59)	<0.001**
Clinical finding			
SBP	120.00 (110-130)	120 (110-130)	0.51**
DBP	75.00 (70-80)	80.00 (70-80)	0.16**
T	37.30 (36.8-38)	37.20 (36.9-38)	0.70**
PR	90 (84-99)	84 (80-96)	0.007**
RR	18 (16-22)	18 (16-19)	0.005**
SPO_2	92.00 (87-96)	95.00 (90-97)	0.002**
Laboratory finding			
WBC	7.00 (4.90-11.60)	6.00 (4.66-8.96)	0.80**
Neutrophil	80.25 (74.22-86.02)	73.00 (64.20-80.40)	<0.001**
Lymphocyte	14.30 (8.20-18.7)	20.00 (12.95-27.65)	<0.001**
BS	127 (104-216.5)	113.00 (96.00-157.00)	0.025**
PLT	154 (114-212)	186.00 (145.00-235.00)	0.003**
HB	12.9 (11.30-14.60)	13.70 (12.10-14.90)	0.025**
LDH	783.50 (642.20-1068.50)	569.00 (413.00-790.00)	<0.001**
INR	1.34 (1.20-1.68)	1.21 (1.13-1.34)	<0.001**
PT	14.40 (12.80-17.40)	12.40 (11.60-14.00)	<0.001**
PTT	29.90 (24.42-38.25)	25.00 (23.00-28.00)	<0.001**
ALT	31.50 (39.25-10.10)	22.00 (15.00-31.00)	0.014**
AST	49.00 (22.00-48.00)	28.00 (21.00-37.00)	<0.001**
CPK	214.00 (103.00-473.00)	96.50 (58.00-184.50)	<0.001**
BUN	26.00 (16.00-51.00)	16.00 (12.00-21.00)	<0.001**
Cr	1.31 (1.00-2.30)	1.00 (0.90-1.20)	<0.001**
ESR	32.00 (13.25-49.00)	26.00 (11.00-45.00)	0.228**
CRP	60.50 (38.50-69.00)	35.00 (14.00-61.00)	<0.001**
NA	135.00 (132.00-139.00)	137.00 (134.00-139.00)	0.029**
K	4.30 (4.00-4.70)	4.20 (3.90-4.50)	0.045**
Mg	2.11 (1.90-2.40)	2.02 (1.81-2.28)	0.131**
Troponin	4.00 (3.00-5.00)	4.00 (5.00-3.00)	0.250**
pH	7.35 (7.19-7.46)	7.40 (7.34-7.44)	0.222**
PaO_2	43.00 (33.00-60.50)	49.00 (31.00-76.00)	0.413**
$PaCO_2$	32.00 (25.00-46.50)	37.00 (31.75-44.00)	0.118**
HCO_3	19.00 (13.80-26.90)	22.00 (18.00-26.77)	0.022**
Hospitalization in ICU	43.00 (51.80)	52.00 (14.60)	<0.001*
Connection to ventilation	31.00 (37.30)	21.00 (5.90)	<0.001*
Hospitalization period	8.31 (SD=6.24)	7.11 (SD=4.63)	0.101**

Values are given as Mean (SD) for continuous variables and frequency (%) for categorical variables.
*P-value was obtained with Fisher exact test.
**P-value was obtained with Mann-Whitney U-test.

Moreover, the potential role of SARS-CoV-2 in the onset of myocarditis has been considered. According to studies conducted in China, acute myocardial injury, characterized by elevated levels of cardiac biomarkers or electrocardiogram abnormalities, was observed in 7.2% to 22% of SARS-CoV-2 patients [10]. The National Health Commission of China reported that approximately 12% of patients without known cardiac disease experienced an increase in troponin level or cardiac arrest during hospitalization. Based on the results of these studies, the presence of myocardial damage in patients with SARS-CoV-2 has been associated with a poor prognosis [15]. Our findings indicate that biochemical parameters related to cardiovascular diseases, including variables of gender, age, PR, RR, SPO_2, certain laboratory findings (excluding WBC, ESR, Mg, Troponin, PH, PaO_2, and

$PaCO_2$), ICU admission, and the need for ventilation, have a significant correlation with the severity of COVID-19 and can be crucial factors in survival rates. Additionally, the levels of WBC, lymphocytes, neutrophils, D-dimer, and H_3CO may play a pivotal role in the duration of hospitalization.

Table 4. Factors related to the death of patients (multiple correlation) (N=440).

	B	SE	Wald	P-value	OR (95%CI)
Age	0.017	0.009	3.821	0.051	1.017 (1.035-1.000)
PR	0.019	0.009	4.309	0.038	1.019 (1.037-1.001)
RR	0.072	0.037	3.848	0.050	1.075 (1.155-1.000)
Neutrophil	0.039	0.014	8.226	0.004	1.040 (1.068-1.012)
PLT	0.006	0.002	8.885	0.003	0.994 (0.998-0.989)
PTT	0.036	0.013	7.597	0.006	1.036 (1.063-1.010)
BUN	0.037	0.008	19.674	0.000	1.038 (1.021-1.055)
Na	-0.079	0.032	6.089	0.014	0.924 (0.984-0.868)
Hospitalization in the ICU	0.974	0.464	4.397	0.036	2.648 (6.580-1.066)
Connection to Ventilation	1.37	0.544	6.348	0.012	3.934 (11.415-1.355)

Arrhythmia and sudden cardiac arrest are common manifestations of SARS-CoV-2. It has been reported that palpitations are the primary symptom of SARS-CoV-2 in patients without fever or cough [14]. In a cohort study, cardiac arrhythmia was reported in 17% of SARS-CoV-2 patients, 44% of whom were in the ICU, although the type of arrhythmia was not recorded [10]. In another study involving 187 hospitalized SARS-CoV-2 patients in Wuhan, individuals with elevated troponin T levels were more susceptible to arrhythmias such as ventricular tachycardia and fibrillation compared to individuals with normal troponin levels. Possible mechanisms of acute coronary syndrome induced by SARS-CoV-2 could include plaque rupture, coronary artery spasm, or microthrombi caused by systemic inflammation or cytokine storm [16]. For instance, activated macrophages secrete collagenases that degrade collagen, a major component of the fibrous layer on atherosclerotic plaques, which can lead to plaque rupture [17].

4.1 | Limitations

Cross-sectional studies are capable of identifying associations between variables, yet they cannot inherently establish causality. Consequently, although such a study may uncover a correlation between COVID-19 and cardiovascular complications, it cannot conclusively ascertain that COVID-19 directly causes these complications.

4.2 | Recommendations for future research

Conducting longitudinal investigations is imperative to delineate the temporal association between COVID-19 infection and the onset of cardiovascular complications, thereby facilitating a comprehensive comprehension of the disease's progression and enduring cardiovascular repercussions. Moreover, the development of predictive models or risk stratification tools holds promise in identifying COVID-19 patients predisposed to cardiovascular complications, thus enabling early detection, intervention, and enhanced patient management. Furthermore, fostering interdisciplinary collaboration among cardiologists, infectious disease specialists, pulmonologists, and other pertinent disciplines is essential to holistically explore the intersection of COVID-19 and cardiovascular health, thereby advancing our collective understanding of the disease.

5 | Conclusions

The evidence suggests that SARS-CoV-2 exacerbates the condition of many patients with pre-existing cardiovascular diseases. Consequently, therapeutic strategies for these individuals must be formulated with an increased level of caution. It is also plausible that SARS-CoV-2 could induce cardiac arrhythmias and other cardiovascular complications in infected individuals. Therefore, it is of paramount importance to consider the potential cardiac disorders that may arise in the course of treating SARS-CoV-2. This underscores the need for a comprehensive approach to patient care that takes into account the complex interplay between SARS-CoV-2 and cardiovascular health.

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Authors' contributions

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: AR, MT, FM, FSA, FR, MS; Drafting the work or revising it critically for important intellectual content: AR, MT, FM, FSA, FR, MS; Final approval of the version to be published: AR, MT, FM, FSA, FR, MS; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity

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Ethics approval and consent to participate

The research protocol received approval from the Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.MEDNT.REC.1399.155). Throughout the study, stringent measures were taken to safeguard all patient-related information, and data extraction was performed anonymously. In instances where it was deemed necessary, patients were contacted and their informed consent was duly obtained.

Competing interests

We do not have potential conflicts of interest with respect to the research, authorship, and publication of this article.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on request.

Using artificial intelligent chatbots

None.

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