

# Clinical characteristics and outcomes of COVID-19 patients with a history of cardiovascular disease

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## Abstract

New emerging severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) primarily affects the lungs, but the virus may cause cardiovascular disease (CVD), and a history of CVD is usually associated with comorbidities, which could increase the severity of infections. In this study, we collected demographic and clinical characteristics data from 123 patients with a history of CVD, who were confirmed to have SARS-CoV-2 infection by polymerase chain reaction (PCR) test in Razi Hospital, Rasht, Iran, from March 2021 to June 2021. Chi-Square and Fisher's Exact test with a significance level of  $P$  less than 0.05 was performed. All statistical analysis was performed with SPSS software version 26.0. Among the studied patients, 99 patients were discharged and 24 of them died. 62 (50.4%) of the study population were female and 61 (49.6%) were male, and there is no significant association between gender and the outcome of patients ( $P = 0.159$ ). The total mean age of patients was  $68.35 \pm 12.41$ . Statistical analysis has represented a significant relation of death outcomes in CVD patients with age 60 years and older ( $P = 0.001$ ), in comparison with patients younger than 60 years. In this present study, no significant relation between underlying disease and mortality rate was reported, but in COVID-19 patients with a history of CVD and age upper than 60 years, death outcome was more probable.

**Keywords:** COVID-19, SARS-CoV-2, Cardiovascular disease, Clinical characteristic, Underlying disease

## 1. Introduction

A mysterious outbreak of new coronavirus in 2019, December, which was named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was identified in Wuhan, China [1, 2]. The most common symptom of this virus appears as mild to severe complications such as cough, fever, myalgia,

renal failure, hypoxemia, coagulopathy, gastrointestinal, and cardiovascular complications [3-6]. SARS-CoV-2 has affected more than 238 million individuals worldwide till April 13, 2021, which was confirmed by World Health Organization (WHO). SARS-CoV-2 infection is triggered by the binding of the viral surface spike protein to the human

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angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is highly expressed in various cell lines and organs including the intestine, lung, and heart as well, which results in some complications including hypertension, atherosclerosis, and congestive heart failure [7-9]. Although much of the concentration has been on pulmonary injury, emergency clinicians need to be aware of the cardiovascular disease (CVD), which can be a noteworthy contributor to the mortality of SARS-CoV-2 infection [10-12]. COVID-19 patients with a history of CVD (coronary heart disease, hypertension) presented more severe clinical outcomes and higher mortalities [12]. Several studies have confirmed raises in cardiac enzymes and alterations in electrocardiogram (ECG) and echocardiography suggestive of acute myocardial complications in COVID-19 patients [13]. Furthermore, a cross-sectional study has suggested lower vascular function weeks after SARS-CoV-2 infection in young adults [14].

In this present study, we investigate the association of demographic data, clinical characteristics, and underlying disease with mortality in COVID-19 patients with a history of CVD.

## 2. Materials and Methods

A total number of 123 patients with a history of CVD were selected through the census method, who was admitted to Razi Hospital, Rasht, Iran, from March 2021 to June 2021. Confirmation of SARS-CoV-2 infection was done via polymerase chain reaction (PCR) on the nasopharyngeal and oropharyngeal swap sample, by Roche RNA extraction kit and Pishtaz master-mix. Exclude criteria were patients with negative PCR test results for SARS-CoV-2 and inadequate medical records. This survey was in agreement with the declaration of Helsinki, and the Ethics Committee of the Guilan University of Medical Sciences has approved the study design [IR.GUMS.REC.1399.022]. Written informed consent was waived by the local Ethics Committee due to the use of medical recodes of patients only. Gender, age, history of smoking and opium, clinical symptoms included: fever, cough, myalgia, respiratory distress, impaired consciousness, hyposmia/anosmia, ageusia, anorexia, intubation needed, O<sub>2</sub> saturation, computed tomography (CT) scan result, *length of stay* (LOS), history of underlying disease including cancer, asthma, diabetes, blood pressure disorder, chronic

liver disease (CLD), chronic blood disease, autoimmune disease, chronic kidney disease (CKD), chronic pulmonary disease (CPD), chronic neuropathy, and the outcome of patients were recorded as the variables for our study. The Shapiro-Wilk test was used to test the normality of data distribution. The categorical variables were presented as count and percentage. Chi-Square with a significance level of P less than 0.05 was performed. All statistical analysis was performed with SPSS software version 26.0.

## 3. Result

The statistical analysis of demographic and clinical characteristics of a total of 123 patients with a history of CVD that was confirmed as COVID-19 patients, has been shown in (Tables 1 and 2). 99 patients were discharged and 24 of them died. 62 (50.4%) of the study population were female and 61 (49.6%) were male, and there is no significant association between gender and the outcome of patients ( $P = 0.159$ ). The total mean age of patients was  $68.35 \pm 12.41$ . Statistical analysis has represented a significant relation of death outcomes in CVD patients with age 60 and older ( $P = 0.001$ ), in comparison with patients younger than 60 years. Approximately, none of the patients with death outcome outcomes were under 60 years. Also, between the history of smoking and using opium with death outcome, no association was reported ( $P = 0.381$  and  $P = 0.959$ ), respectively. The most common reported symptom was fever, cough, myalgia, respiratory distress, decreased O<sub>2</sub> saturation, and CT scan positive result ( $P = 0.756$ ,  $P = 0.133$ ,  $P = 0.211$ ,  $P = 0.309$ ,  $P = 0.087$ ,  $P = 0.054$ ), respectively. Also, some other symptoms such as hyposmia/anosmia, ageusia, and intubation needed, which were less reported in these patients, represented no significant association between the presence of these symptoms and death outcome, ( $P = 0.509$ ,  $P = 0.605$ ,  $P = 0.605$ ,  $P = 0.857$ ), respectively. While impaired consciousness and anorexia were rarely reported in patients, statistical analysis revealed remarkable relation between these signs and death outcomes in CVD patients ( $P < 0.001$  and  $P = 0.004$ ). The most-reported underlying disease was diabetes (47.15%), and blood pressure disorder (47.96%). The statistical analysis represented no significant association between any reported underlying diseases and death outcomes, including cancer, asthma,

Table 1. Demographic and clinical characteristics data of COVID-19 patients with a history of CVD

<b>Demographic</b>		<b>Discharge No. (%)</b>	<b>Death No. (%)</b>	<b>P value</b>
Gender	Female	53 (53.5)	9 (37.5)	0.159
	Male	46 (46.5)	15 (62.5)	
Age	<60	32 (32.2)	0	0.001
	>60	67 (67.7)	24 (100)	
Smoking history	Yes	4 (4)	2 (8.3)	0.381
	No	95 (96)	22 (91.7)	
Opium	Yes	12 (13.1)	3 (12.5)	0.959
	No	87 (87.9)	21 (87.5)	
<b>Clinical symptoms</b>				
Fever	Yes	53 (53.5)	12 (50%)	0.756
	No	46 (46.5)	12 (50)	
Cough	Yes	62 (62.6)	11 (45.8)	0.133
	No	37 (37.4)	13 (54.2)	
Myalgia	Yes	47 (47.5)	8 (33.3)	0.211
	No	52 (52.5)	16 (66.7)	
Respiratory distress	Yes	59 (59.6)	17 (70.8)	0.309
	No	40 (40.4)	7 (29.2)	
Impaired consciousness	Yes	7 (7.1)	8 (33.3)	0.000
	No	92 (92.9)	16 (66.7)	
Hyposmia/Anosmia	Yes	8 (8.1)	1 (4.2)	0.509
	No	91 (91.9)	23 (95.8)	
Ageusia	Yes	7 (7.1)	1 (4.2)	0.605
	No	92 (92.9)	23 (95.8)	
Anorexia	Yes	0	2 (8.3)	0.004
	No	100 (100)	22 (91.7)	
Intubation	Yes	5 (5.1)	1 (4.2)	0.857
	No	94 (94.9)	23 (95.8)	
O <sub>2</sub> Saturation	<93%	24 (24.2)	10 (41.7)	0.087
	>93%	75 (75.8)	14 (58.3)	
CT scan result	Positive	70 (70.7)	12 (50)	0.054
	Negative	29 (29.3)	12 (50)	
LOS	<5 day	46 (46.5)	13 (54.2)	0.219
	5-10 day	38 (38.4)	5 (20.8)	
	>10 day	15 (15.2)	6 (25)	

Table 2. Comorbid underlying disease in COVID-19 with a history of CVD

Underlying disease	Demographic	Discharge n (%)	Death n (%)	P value
Cancer	Yes	4 (3.3)	0	0.317
	No	95 (96)	24 (100)	
Asthma	Yes	11 (11.1)	3 (12.5)	0.848
	No	88 (88.9)	21 (87.5)	
Diabetes	Yes	49 (49.5)	9 (37.5)	0.291
	No	50 (50.5)	15 (62.5)	
Blood pressure disorder	Yes	49 (49.5)	10 (41.7)	0.491
	No	50 (50.5)	14 (58.3)	
Chronic liver disease	Yes	1 (1)	1 (4.2)	0.273
	No	98 (99)	23 (95.8)	
Chronic blood disorder	Yes	4 (4)	1 (4.2)	0.978
	No	95 (96)	23 (95.8)	
Autoimmune disorder	Yes	1 (1)	0	0.621
	No	98 (99)	24 (100)	
Chronic kidney disease	Yes	9 (9.1)	3 (12.5)	0.614
	No	90 (90.9)	21 (87.5)	
Chronic pulmonary disease	Yes	2 (2)	1 (4.2)	0.541
	No	97 (98)	23 (95.8)	
Chronic neuropathy	Yes	2 (2)	2 (8.3)	0.118
	No	97 (98)	22 (99.7)	

diabetes, blood pressure disorder, CLD, CPD, autoimmune disease, CKD, CPD, and chronic neuropathy ( $P = 0.317$ ,  $P = 0.848$ ,  $P = 0.291$ ,  $P = 0.491$ ,  $P = 0.273$ ,  $P = 0.978$ ,  $P = 0.621$ ,  $P = 0.614$ ,  $P = 0.541$ ,  $P = 0.118$ ), respectively. Although the outcome of patients, either discharged or dead, showed no association with LOS ( $P = 0.219$ ), among patients with higher LOS for more than 10 days, the mortality rate was increased.

#### 4. Discussion

SARS-CoV-2 is a critical life-threatening issue, attracts worldwide attention, and causes lots of health and social expenses [3]. Due to the susceptibility of CVD patients to severe conditions of SARS-CoV-2 infection, specific attention should be given to cardiovascular protection during treatment for COVID-19 [15]. According to a meta-analysis study on hospitalized patients with COVID-19, hypertension, CVD, diabetes, CKD, and Chronic obstructive pulmonary diseases (COPD) were the most prevalent underlying diseases, while CVD had the highest prevalence among diseases that put patients at higher risk of SARS-CoV-2 threats [16]. Some studies illustrated hypertension and CVD as the most common related mortality factor in patients with CVD who were infected by respiratory viruses (Middle East respiratory syndrome (MERS-CoV) and influenza) [17-20]. It has been reported that elderly people with comorbidities of hypertension, CVD, or diabetes, are more susceptible to severe symptoms of SARS-CoV-2 infection [21]. Consequently, patients with a history of CVD consider a high-risk group with death determination [22-25]. Similar to our report, COVID-19 patients aged older than 60 years with underlying CVD can aggravate symptoms and result in death outcomes [26, 27]. Although, in our study, there was no statistically significant relationship between the comorbid underlying disease with death outcome in COVID-9 patients with CVD, all mentioned diseases, separately, were reported as a risk factor to worsen the condition and lead to death in these patients [28-32]. Among demographical and clinical characteristics, male gender, elderly age, and fever are associated with a greater risk of development of acute respiratory syndrome, severe condition, and death [31, 33].

Lack of access to consumption of blood pressure and heart medications data, the impact of unwanted side effects of these medications on the worsening

COVID-19 condition, as well as incomplete information about the treatment methods used for these patients are some of the limitations of this study.

Various comorbidities like CVD, CPD, hypertension, and diabetes are risk factors for poor clinical outcomes among patients infected with SARS-CoV-2. Patients with a history of CVD had a broad range of severe conditions that led to a higher risk of development of critical or fatal COVID-19 disease. According to our study, older age, anorexia, and impaired consciousness are the risk factors for COVID-19 patients with a history of CVD, which could result in death outcomes.

#### Authors' contributions

Concept and Study design: TY, AA, SM, MSD; Methods, data collection, and experimental work: VSH, SN, MK, CHT, SHA, SM, NF; Results analysis and conclusions: VSH, SN, SM, NF; Manuscript preparation and editing: TY, MK, CHT, SHA, AA, SM, MSD, NF. All authors read and approved the final version of manuscript.

#### Conflict of interests

No potential conflict of interest was reported by the authors.

#### Ethical declarations

All subjects gave their informed consent to participate in the study, which was approved by the ethical committee at the Guilan University of Medical Science [IR.GUMS.REC.1399.022].

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#### References

1. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect.* 2020; 9(1):221-36.
2. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol.* 2020; 92(4):401-2.
3. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020; 395(10223):507-13.

4. Chen Q, Xu L, Zhu W, Ge J. Cardiovascular manifestations in severe and critical patients with COVID-19. *Clin Cardiol.* 2020; 43(10):1054.
5. Kunutsor SK, Laukkanen JA. Renal complications in COVID-19: a systematic review and meta-analysis. *Ann Med.* 2020; 52(7):345-53.
6. Zhang X, Yang X, Jiao H, Liu X. Coagulopathy in patients with COVID-19: a systematic review and meta-analysis. *Aging (Albany NY).* 2020; 12(24):24535-51.
7. Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zuo W. Single-Cell RNA Expression Profiling of ACE2, the Receptor of SARS-CoV-2. *Am J Respir Crit Care Med.* 2020; 202(5):756-9.
8. Tikellis C, Thomas MC. Angiotensin-Converting Enzyme 2 (ACE2) Is a Key Modulator of the Renin Angiotensin System in Health and Disease. *Int J Pept.* 2012; 2012:256294.
9. Djomkam ALZ, Olwal CO, Sala TB, Paemka L. Commentary: SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Front Oncol.* 2020; 10:1448.
10. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. *J Am Coll Cardiol.* 2020; 75(18):2352-71.
11. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020; 395(10223):497-506.
12. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med.* 2020; 46(5):846-8.
13. Doyen D, Mocerri P, Ducreux D, Dellamonica J. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. *Lancet.* 2020; 395(10235):1516.
14. Ratchford SM, Stickford JL, Province VM, Stute N, Augenreich MA, Koontz LK, et al. Vascular alterations among young adults with SARS-CoV-2. *Am J Physiol Heart Circ Physiol.* 2021; 320(1):H404-h10.
15. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol.* 2020; 17(5):259-60.
16. Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of Underlying Diseases in Hospitalized Patients with COVID-19: a Systematic Review and Meta-Analysis. *Arch Acad Emerg Med.* 2020; 8(1):e35.
17. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *Lancet Infect Dis.* 2013; 13(9):752-61.
18. Noorwali AA, Turkistani AM, Asiri SI, Trabulsi FA, Alwafi OM, Alzahrani SH, et al. Descriptive epidemiology and characteristics of confirmed cases of Middle East respiratory syndrome coronavirus infection in the Makkah Region of Saudi Arabia, March to June 2014. *Ann Saudi Med.* 2015; 35(3):203-9.
19. Wang R, Hozumi Y, Zheng YH, Yin C, Wei GW. Host Immune Response Driving SARS-CoV-2 Evolution. *Viruses.* 2020; 12(10).
20. Mertz D, Kim TH, Johnstone J, Lam PP, Science M, Kuster SP, et al. Populations at risk for severe or complicated influenza illness: systematic review and meta-analysis. *Bmj.* 2013; 347:f5061.
21. de Almeida-Pititto B, Dualib PM, Zajdenverg L, Dantas JR, de Souza FD, Rodacki M, et al. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *Diabetol Metab Syndr.* 2020; 12:75.
22. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *Jama.* 2020; 323(11):1061-9.
23. Peng YD, Meng K, Guan HQ, Leng L, Zhu RR, Wang BY, et al. [Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV]. *Zhonghua Xin Xue Guan Bing Za Zhi.* 2020; 48(6):450-5.
24. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020; 395(10229):1054-62.
25. Alshaikh MK, Alotair H, Alnajjar F, Sharaf H, Alhafi B, Alashgar L, et al. Cardiovascular Risk Factors Among Patients Infected with COVID-19 in Saudi Arabia. *Vasc Health Risk Manag.* 2021; 17:161-8.
26. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020; 395(10223):514-23.
27. Bonow RO, Fonarow GC, O'Gara PT, Yancy CW. Association of Coronavirus Disease 2019 (COVID-19) With Myocardial Injury and Mortality. *JAMA Cardiol.* 2020; 5(7):751-3.
28. Shi Q, Zhang X, Jiang F, Zhang X, Hu N, Bimu C, et al. Clinical Characteristics and Risk Factors for Mortality of COVID-19 Patients With Diabetes in Wuhan, China: A Two-Center, Retrospective Study. *Diabetes Care.* 2020; 43(7):1382-91.
29. Mubarik S, Liu X, Eshak ES, Liu K, Liu Q, Wang F, et al. The Association of Hypertension With the Severity of and Mortality From the COVID-19 in the Early Stage of the Epidemic in Wuhan, China: A Multicenter Retrospective Cohort Study. *Front Med (Lausanne).* 2021; 8:623608.
30. Choudhary NS, Dhampalwar S, Saraf N, Soin AS. Outcomes of COVID-19 in Patients with Cirrhosis or Liver Transplantation. *J Clin Exp Hepatol.* 2021; 11(6):713-9.
31. Cai R, Zhang J, Zhu Y, Liu L, Liu Y, He Q. Mortality in chronic kidney disease patients with COVID-19: a systematic review and meta-analysis. *Int Urol Nephrol.* 2021; 53(8):1623-9.
32. Meza D, Khuder B, Bailey JI, Rosenberg SR, Kalhan R, Reyfman PA. Mortality from COVID-19 in Patients with

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COPD: A US Study in the N3C Data Enclave. *Int J Chron Obstruct Pulmon Dis.* 2021; 16:2323-6.

33. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med.* 2020; 180(7):934-43.