ORIGINAL ARTICLE

CLINICAL FEATURES AND OUTCOMES OF COVID-19 PATIENTS WITH CARDIOVASCULAR DISEASE: SINGLE CENTER EXPERIENCE

Kardiyovasküler Hastalığı Olan COVID-19 Hastalarının Klinik Özellikleri ve Sonlanımları: Tek Merkez Deneyimi

Aysegul ULGEN KUNAK[1], Tolga KUNAK[2]

[1]Sağlık Bilimleri Üniversitesi,
Antalya Eğitim ve Araştırma Hastanesi,
Kardiyoloji Kliniği,
Antalya,
Türkiye.
[2]Akdeniz Üniversitesi,
Tıp Fakültesi,
Kardiyoloji Anabilim Dalı,
Türkiye.

Ayşegül ÜLGEN KUNAK, Dr.
(0000 0002 8930 3651)
Tolga KUNAK, Dr.
(0000-0002-0838-2037)

İletişim:
Dr. Ayşegül ÜLGEN KUNAK
Sağlık Bilimleri Üniversitesi, Antalya Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, Antalya, Türkiye.

Geliş tarihi/Received: 10.12.2024
Kabul tarihi/Accepted: 21.02.2025
DOI: 10.16919/bozoktip.1598931

Bozok Tıp Derg 2025;15(1):70-76
Bozok Med J 2025;15(1):70-76

ABSTRACT

Objective: The COVID-19 pandemic has highlighted the increased vulnerability of individuals with pre-existing cardiovascular disease (CVD) to severe outcomes. This study aimed to examine the clinical characteristics and outcomes of COVID-19 patients with and without CVD at Kepez State Hospital, Antalya, Türkiye.

Material and Methods: Between March 15 and June 1, 2020, 92 adult patients with confirmed COVID-19 were enrolled. Demographic data, laboratory results, CT findings, treatments, and outcomes were collected and compared between those with and without CVD to explore the relationship between cardiac comorbidities and COVID-19 severity.

Results: Patients with CVD were older, had higher rates of comorbidities like diabetes, hypertension, and dyslipidemia, and presented with more severe symptoms, including shortness of breath. These patients showed higher levels of inflammatory markers (CRP, D-dimer, and troponin T). CVD patients required more oxygen supplementation, non-invasive ventilation, and intubation, leading to higher ICU admission rates and longer hospital stays. Complications such as sepsis, ARDS, and thromboembolism were more common in the CVD group, with all three deaths occurring in this population.

Conclusion: WCOVID-19 patients with pre-existing CVD are at a significantly higher risk of severe outcomes, underscoring the need for targeted risk assessment and management strategies to improve care and reduce morbidity and mortality in this high-risk group.

Keywords: COVID-19; Cardiovascular Disease; Clinical Characteristics; Disease Progression; Outcomes

ÖZET

Amaç: COVID-19 pandemisi, kardiyovasküler hastalığı (KVH) olan bireylerin ciddi sonuçlara karşı daha duyarlı olduğunu göstermiştir. Bu çalışma, Antalya Kepez Devlet Hastanesi'nde KVH'lı ve KVH'sız COVID-19 hastalarının klinik özelliklerini ve sonuçlarını incelemeyi amaçlamıştır.

Gereç ve Yöntemler: 15 Mart ile 1 Haziran 2020 tarihleri arasında COVID-19 testi pozitif 92 yetişkin hasta çalışmaya dahil edilmiştir. Demografik veriler, laboratuvar sonuçları, BT bulguları, tedaviler ve sonuçlar toplanmış ve KVH'lı ve KVH'sız hastalar arasında karşılaştırmalar yapılmıştır.

Bulgular: KVH'lı hastalar daha yaşlıydı, diyabet, hipertansiyon ve dislipidemi gibi daha yüksek oranda eşlik eden hastalıklara sahipti ve daha şiddetli semptomlar (özellikle nefes darlığı) gösteriyorlardı. Ayrıca bu hastalarda inflamatuar belirteçler (CRP, D-dimer ve troponin T) daha yüksekti. KVH'lı hastalar daha fazla oksijen desteği, non-invaziv ventilasyon ve entübasyona ihtiyaç duydu, bu da daha yüksek bir Yoğun Bakım Ünitesi (YBÜ) yatış oranı ve daha uzun hastanede kalış sürelerine yol açtı. Sepsis, ARDS ve tromboembolizm gibi komplikasyonlar KVH'lı hastalarda daha yaygın olup, ölen üç hastanın tamamı KVH'lıydı.

Sonuç: COVID-19, KVH'sı olan hastalar için ciddi sonuçlar açısından daha yüksek bir risk oluşturduğundan, bu yüksek riskli grup için özel risk değerlendirmesi ve tedavi stratejileri gereklidir.

Anahtar Kelimeler: *COVID-19; Hastalık Progresyonu; Kardiyovasküler Hastalıklar; Klinik Özellikler; Sonlanımlar*

INTRODUCTION

The COVID-19 pandemic has revealed significant vulnerabilities in patients with pre-existing cardiovascular diseases (CVD). As a novel respiratory virus, SARS-CoV-2 not only affects the lungs but also has a profound impact on the cardiovascular system, often exacerbating underlying conditions and complicating clinical outcomes. Individuals with CVD are at a higher risk of severe illness and mortality, highlighting the intricate interplay between viral infections and cardiovascular health. This article delves into the clinical features, disease progression, and outcomes of COVID-19 in patients with cardiovascular comorbidities, aiming to provide a comprehensive understanding of how these factors contribute to the overall prognosis and management of this high-risk population.

MATERIALS AND METHODS

This retrospective single-center study included 92 patients over 18 years old who were admitted to Kepez State Hospital in Antalya, Türkiye between March 15 and June 1, 2020, with suspected COVID-19 infection and who were followed PCR diagnosed a COVID-19 test positivity. The COVID-19 patients, who were subsequently scanned through the hospital records system and chart review, were divided into two groups based on whether they had cardiovascular disease or not.

Demographic data, laboratory test results, chest computed tomography findings, in-hospital treatment, and in-hospital outcomes for patients with and without CVD were collected. If the data from the records were missing or needed to be verified, the data were obtained through direct contact with the physicians and other health care providers. All data were reviewed by two physicians. Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition (1). Acute Respiratory Distress Syndrome (ARDS) was defined according to the interim guidance of WHO for novel coronavirus. Whether there is a difference between the groups in terms of disease progression and prognosis was retrospectively evaluated.

Data analysis was conducted separately for patients with and without cardiovascular disease. Continuous variables are presented as either the mean (standard deviation) or the median (interquartile range), depending on the distribution. Categorical variables were analyzed using the chi-square test, with the Fisher exact test applied to categories with smaller sample sizes. Comparisons of continuous variables were made using the Mann-Whitney U test. All statistical analyses were performed using SPSS software version 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) and a significance level of $P<0.05$ was considered statistically significant.

The study was approved by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (KAEK-409, 12.06.2020).

RESULTS

The mean patient age was 49.8 years, with a slight predominance of men (52%). Coronary heart disease was the most common heart disease (Table 1). Typical symptoms were cough, fatigue, fever, shortness of breath and myalgia, while arthralgia, headache, nausea and vomiting occurred less frequently (Table 2). Patients with CVD were significantly older and had higher comorbidity rates of diabetes, hypertension, and dyslipidemia. Shortness of breath was significantly more common in the CVD group. There were no significant differences in gender, concomitant asthma or chronic obstructive pulmonary disease, or other underlying symptoms. Patients with CVD were more likely to receive chronic therapy with ACEi, ARB, ARNI, anti-aggregants, anticoagulants and statins. At admission, vital signs were similar between groups, except for significantly lower ambient air oxygen saturation and higher respiratory rate in CVD patients (Table 3). The laboratory parameters are listed in Table 4. Compared to non CVD patients, the CVD group had significantly lower haemoglobin, lymphocyte count, serum calcium and albumin levels. Importantly, lactate dehydrogenase, baseline and peak CRP, high-sensitivity troponin T and D-dimer levels were increased in the CVD group. Chest CT findings were essentially similar, with air bronchogram frequency being the only significant difference between groups. Table 5 provides data in hospital management. CVD patients showed higher rates of nasal oxygen and oxygen mask use. Five patients required intubation, and the intubation

Bozok Tıp Derg 2025;15(1):70-76
Bozok Med J 2025;15(1):70-76

rate was increased in the CVD group. Non-invasive ventilation was used in 4.5% of patients. ICU admission was significantly higher in CVD patients (53.3% vs. 6.5%, p<0.001). Total hospital stay was longer in the CVD group, although ICU length of stay was comparable. Complications primarily included sepsis or septic shock, ARDS, and arterial/venous thromboembolism. All three deaths occurred in the CVD group (Table 6).

DISCUSSION

Our study aimed to assess the outcomes of COVID-19 patients with pre-existing cardiovascular disease and determine the extent to which these patients experienced elevated risks for adverse outcomes,

Table 1. Baseline characteristics of the study group

	Total (N: 92)	Patients with cardiac disease (N:15)	Patients without cardiac disease (N:77)	p-value
Demographics				
Age, years	49.8±18.4	72.5± 15.8	45.4±15.4	<0.001
Sex (male), n (%)	52 (56.5)	11 (73.3)	41 (53.2)	0.169
Clinical history, n (%)				
Hypertension	26 (28.3)	12 (80)	14 (18.2)	<0.001
Diabetes	16 (17.4)	7 (46.7)	9 (11.7)	0.004
Smoker	19 (20.7)	4 (26.7)	15 (19.5)	0.503
Dyslipidaemia	11 (12)	7(46.7)	4 (5.2)	<0.001
Heart Failure	6 (6.5)	6 (40)	0 (0)	<0.001
Atrial Fibrillation	7 (7.6)	7 (46.7)	0 (0)	<0.001
Coronary Artery Disease	10 (10.9)	10 (66.7)	0 (0)	<0.001
Valvular heart disease	6 (6.5)	6 (40)	0 (0)	<0.001
Chronic Obstructive Pulmonary Disease	9 (9.8)	3 (20)	6 (7.8)	0.160
Asthma	10 (10.9)	0 (0)	10 (13)	0.358
Prior ACEi/ARB/ARNI therapy	18 (19.6)	8 (53.3)	10 (13)	0.001
Prior anticoagulant therapy	5 (5.4)	4 (26.7)	1 (1.3)	0.002
Prior antiaggregant therapy	13 (14.1)	8 (53.3)	5 (6.5)	<0.001
Prior statin therapy	8 (8.7)	7 (46.7)	1 (1.3)	<0.001

ACEi: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, ARNI: Angiotensin receptor neprilysin inhibitor

Table 2. Symptoms on admission

	Total (N: 92)	Patients with cardiac disease (N:15)	Patients without cardiac disease (N:77)	P-value
Symptoms on admission, n (%)				
Cough	70 (76.1)	12 (80)	58 (75.3)	0.69
Fatigue	51 (55.4)	11 (73.3)	40 (51.9)	0.127
Fever	47 (51.1)	11 (73.3)	36 (46.8)	0.06
Short of breath	47 (51.1)	12 (80)	35 (45.5)	0.014
Myalgia	40 (43.5)	8 (53.3)	32 (41.6)	0.400
Arthralgia	26 (28.3)	5 (33.3)	21 (27.3)	0.755
Headache	23 (25)	1 (6.7)	22 (28.6)	0.104
Nausea or Vomiting	13 (14.1)	3 (20)	10 (13)	0.476

Bozok Tıp Derg 2025;15(1):70-76
Bozok Med J 2025;15(1):70-76

Table 3. Vital signs on admission

Vital signs on admission	Total N:92	Patients with cardiac disease N:15	Patients without cardiac disease N:77	P-value
Temperature , C	37.03±0.7	37.4±0.8	36.9±0.7	0.078
Systolic blood pressure, mmHg	115.9±13.7	117.3±16.6	115.6±13.2	0.57
Diastolic blood pressure, mmHg	71.1±8.8	70.7±11.6	71.2±8.2	0.93
Heart rate, b.p.m	88.5±17	96.7±29	86.9±13.2	0.39
Oxygen saturation (ambient air), %	95.9±3.6	92.2±5.7	96.7±2.5	<0.001
Respiratory rate, per minute	17±3	19.6±3	16.4±3	0.001

Table 4. Laboratory findings

Laboratory Findings					
Variable	Reference range	Total N:92	Patients with CVD N:15	Patients without CVD 77	P-value
Haemoglobin, g/dl	(11.9-16.9)	13.5± 1.7	12.1±1.6	13.8±1.5	0.001
White blood cell count, per µL	(3910-10.900)	7131±3015	8094±3042	6939±2993	0.135
Neutrophils, per µL	(1800-6980)	4724±2729	6159±2629	4437±2674	0.021
Lymphocytes, per µL	(1260-3350)	1726±958	1200±937	1831±933	0.009
Platelet count, per µL	(166.000-308.000)	199833±78850	211400±100757	197520±74326	0.697
Blood urea nitrogen, mg/dL	(8.9-20.6)	13.86±8	20.6±16	12.5±4.1	<0.001
Creatinine, mg/dL	(0.72-1.25)	0.85±0.23	1.02±0.42	0.82±0.15	0.023
Sodium, mEq/L	(135-145)	138±2.9	137±2.8	138±2.9	0.115
Potassium, mEq/L	(3.5-5.1)	4.14±0.36	4.27±0.5	4.1±0.3	0.546
Magnesium, mg/dL	(1.6-2.6)	1.93±0.2	1.84±0.21	1.97±0.18	0.09
Calcium, mg/dL	(8.4-10.2)	9.18±0.74	8.7±0.6	9.3±0.7	0.003
Alanine aminotransferase, U/L	(5-55)	42.2±76	38.9±30	42.9±2.7	0.607
Aspartate transaminase, U/L	(5-34)	34.7±34	39.2±27	33.9±35.8	0.413
Total bilirubin, mg/dL	(0.2-1.2)	0.57±0.26	0.65±0.3	0.55±0.26	0.410
Lactate dehydrogenase, U/L	(125-220)	253.7±108	327±105	238±102	0.001
Baseline C-reactive protein, mg/L	(0-5)	37.3±59,8	86.2±80	27.5±50.1	<0.001
Peak C-reactive protein, mg/L	(0-5)	65.6±80.6	156.8±105	47.3±60.7	<0.001
Albumin, g/L	(35-52)	37.7±7.4	34.2±6.6	38.7±7.3	0.007
High sensitivity troponin T, ng/L	(0-14)	27.1±118	151.4±286	5.4±9.1	<0.001
Creatine kinase, U/L	(30-200)	92±91.8	131.8±129	81.3±77.5	0.341
D-Dimer, ng/ml	(0-240)	559.8±1542	1803±3457	319±573	<0.001
Fibrinogen, mg/dL	(200-400)	376.4±177	502±189	359±171	0.08
Ferritin, ng/ml	(22-322)	270.7±326	518±433	240±302	0.09
Prothrombin time, s	(10-13.5	13.8±5.9	14.2±5.1	13.7±6.1	0.368
Activated partial thromboplastin times	(25.1-36.5)	29.7±5.1	29.1±5.6	29.8±5	0.625
International Normalized Ratio (INR)	(0.8-1.2)	1.21±0.5	1.26±0.46	1.2±0.5	0.193

Table 5. In-hospital management of study group

In hospital management of the patients	Total N: 88	Patients with CVD N:15	Patients without CVD N:73	P-value
Needed ventilatory support				
Nasal oxygen 2-4 L/min, n (%)	25 (28.4)	8 (53.3)	17 (23.3)	0.023
Oxygen with mask, n (%)	6 (6.8)	4 (26.7)	2 (2.7)	0.006
Non-invasive ventilation, n (%)	4 (4.5)	2 (13.3)	2 (2.7)	0.123
Intubation, n (%)	5 (5.7)	4 (26.7)	1 (1.4)	0.002

CVD: Cardiovascular Disease

Table 6. In-hospital outcomes of study group.

In hospital outcomes	Total N:88	Patients with CVD N:15	Patients without CVD N:73	P-value
Intensive care unit admission, n (%)	13 (14.1)	8 (53.3)	5 (6.5)	<0.001
Hospital length of stay, days	11.6±10.4	18.4±15.7	10.2±8.5	0.005
Intensive care unit length of stay, days	18±20	16.8±16.8	20±27	0.833
ARDS, n (%)	5 (5.4)	4 (26.7)	1 (1.3)	0.002
Thromboembolic complications, n (%)	2 (2.2)	2 (13.3)	0 (0)	0.025
Septic shock/sepsis, n (%)	6 (6.5)	5 (33.3)	1 (1.3)	<0.001
Death	3 (3.3)	3 (20)	0 (0)	0.004

CVD: Cardiovascular Disease, ARDS: Acute Respiratory Distress Syndrome

including mortality, respiratory failure, and prolonged hospitalization. The findings reveal a significantly higher rate of complications and poorer outcomes among patients with CVD, aligning with prior evidence on the interaction between COVID-19 and cardiovascular comorbidities (2,3).

The presence of pre-existing CVD was associated with a markedly increased risk of severe COVID-19 outcomes, including a higher likelihood of intensive care unit (ICU) admission and use of mechanical ventilation (4). Studies have shown that patients with CVD tend to exhibit increased levels of pro-inflammatory cytokines and endothelial dysfunction, which can exacerbate the cytokine storm and respiratory distress seen in severe COVID-19 cases (5). This heightened inflammatory response may lead to increased cardiac stress and accelerate the progression of acute respiratory failure (6,7). Furthermore, the systemic inflammation triggered by SARS-CoV-2 may aggravate underlying cardiovascular issues, creating a feedback loop that worsens both cardiac and pulmonary function (8).

Our findings showed that patients with CVD had significantly higher mortality rates than those without pre-existing cardiovascular conditions. This elevated mortality risk aligns with prior studies indicating that pre-existing heart conditions make patients more vulnerable to adverse COVID-19 outcomes, particularly in older adults with underlying conditions like hypertension and coronary artery disease (9,10). The ACE2 receptor, utilized by SARS-CoV-2 for cellular entry, is highly expressed in cardiac tissue, which may explain the direct viral impact on the cardiovascular system and increased fatality risk among CVD patients (11).

Studies have also shown that arrhythmias and myocardial injury are common complications in COVID-19 patients with CVD, often manifesting early in the disease course (12). Myocardial injury markers, particularly elevated troponin levels, have been associated with a poorer prognosis and increased mortality in COVID-19, indicating that cardiac complications contribute significantly to the heightened mortality in this group (13). Notably, a retrospective study by Shi et al. found that mortality among COVID-19 patients with elevated troponin levels was markedly higher than in those with normal

levels, underscoring the role of cardiac injury in adverse outcomes (14).

Patients with pre-existing CVD were also more likely to experience prolonged hospitalization and extended ICU stays, likely due to the need for close monitoring and management of both respiratory and cardiac functions (15). Inflammatory processes and endothelial injury associated with COVID-19 may worsen atherosclerosis, resulting in acute coronary syndromes or exacerbation of heart failure (16). Additionally, prolonged hospital stays and ICU admissions expose CVD patients to a higher risk of secondary infections and further complications, such as sepsis or acute kidney injury, which further worsens outcomes (17).

Several studies have examined the impact of cardiovascular medications, particularly ACE inhibitors and angiotensin II receptor blockers (ARBs), on COVID-19 outcomes in patients with CVD. ACE2, the receptor for SARS-CoV-2, is upregulated by ACE inhibitors and ARBs, raising concerns about increased susceptibility to infection among users of these drugs (18). However, evidence remains inconclusive, with some studies suggesting that these medications may confer protective effects by reducing inflammation and preventing cardiovascular complications during COVID-19 infection (19,20). A large meta-analysis by Zhang et al. found no increased risk of adverse outcomes associated with ACE inhibitors or ARBs in COVID-19 patients with hypertension, indicating these drugs may be safely continued (21).

Mechanistically, the interaction between COVID-19 and CVD may be explained by a combination of direct viral injury, heightened inflammatory response, and coagulation abnormalities. The virus can directly infect cardiac cells, while the ensuing inflammatory response leads to myocardial injury and arrhythmias (22). Moreover, SARS-CoV-2 is known to induce a hypercoagulable state, which may cause thrombosis and contribute to ischemic events such as myocardial infarction and stroke, both of which are more common in patients with CVD (23,24). Elevated D-dimer levels and other markers of coagulation have been associated with severe outcomes and may serve as prognostic indicators in COVID-19 patients with CVD (25).

While this study provides valuable insights into the outcomes of COVID-19 patients with cardiovascular disease (CVD), several limitations must be acknowledged. Firstly, our findings are derived from a hospital-based cohort and may not fully represent outcomes in milder cases of COVID-19 managed in outpatient settings. Furthermore, the limited sample size presents another important limitation. As an observational study, confounding variables may have influenced the associations observed between CVD and COVID-19 outcomes. Future research should focus on longitudinal studies to better understand the long-term effects of COVID-19 on cardiovascular health in this high-risk population.

CONCLUSION

These findings underscore the heightened vulnerability of COVID-19 patients with pre-existing CVD to adverse outcomes, necessitating tailored risk stratification and therapeutic interventions for optimal patient care and mitigation of morbidity and mortality in this high-risk population. Understanding the intricate interplay between COVID-19 and cardiovascular health is imperative for informing evidence-based practices and enhancing clinical management strategies.

Acknowledgments

The authors declare that they have no competing financial interests or personal relationships that might have influenced the work reported in this paper.

REFERENCES

1. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:762–77.

2. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, et al. COVID-19 and Cardiovascular Disease. Circulation. 2020;141(20):1648–55.

3. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17(5):259–60.

4. Bansal M. Cardiovascular disease and COVID-19. Diabetes Metab Syndr. 2020;14(3):247–50.

5. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811–8.

6. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and Thrombotic or Thromboembolic Disease:

Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;75(23):2950-73.

7. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol. 2020;5(7):802–10.

8. 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.

9. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. JAMA Cardiol. 2020;5(7):831–40.

10. Shi S, Qin M, Cai Y, Liu T, Shen B, Yang F, et al. Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019. Eur Heart J. 2020;41(22):2070–9.

11. 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.

12. Tersalvi G, Vicenzi M, Calabretta D, Biasco L, Pedrazzini G, Winterton D. Elevated Troponin in Patients With Coronavirus Disease 2019: Possible Mechanisms. J Card Fail. 2020;26(6):470–5.

13. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020;323(16):1612–4.

14. 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.

15. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020;382(19):1787–99.

16. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020;323(20):2052–9.

17. 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.

18. Zhang P, Zhu L, Cai J, Lei F, Qin JJ, Xie J, et al. Association of Inpatient Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Mortality Among Patients With Hypertension Hospitalized With COVID-19. Circ Res. 2020;126(12):1671–81.

19. Bauer A, Schreinlechner M, Sappler N, Dolejsi T, Tilg H, Aulinger BA, et al. Discontinuation versus continuation of renin-angiotensin-system inhibitors in COVID-19 (ACEI-COVID): a prospective, parallel group, randomised, controlled, open-label trial. Lancet Respir Med. 2021;9(8):863–72.

20. Ma J, Shi X, Yu J, Lv F, Wu J, Sheng X, et al. Association of ACEi/ARB Use and Clinical Outcomes of COVID-19 Patients With Hypertension. Front Cardiovasc Med. 2021;8:577398.

21. Gnanenthiran SR, Borghi C, Burger D, Caramelli B, Charchar F, Chirinos JA, et al. Renin-angiotensin system inhibitors in patients with COVID-19: a meta-analysis of randomized controlled trials led by the International Society of Hypertension. J Am Heart Assoc. 2022 Sep 6;11(17):e026143.

22. Shu H, Wen Z, Li N, Zhang Z, Ceesay BM, Peng Y, et al. COVID-19 and Cardiovascular Diseases: From Cellular Mechanisms to Clinical Manifestations. Aging Dis. 2023;14(6):2071–88.

23. Fox SE, Heide RSV. COVID-19: The Heart of the Matter-Pathological Changes and a Proposed Mechanism. J Cardiovasc Pharmacol Ther. 2021;26(3):217–24.

24. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020 Jun;7(6):e438–40.

25. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020 Apr;18(4):844-7.