Therapeutics and Clinical Risk Management

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Cardiovascular Considerations in COVID19: A Comprehensive Review

This article was published in the following Dove Press journal:
Therapeutics and Clinical Risk Management

Faeze Keihanian[1,2]
Leila Bigdelu[1,3]

[1]Cardiovascular Department, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [2]Pharmaceutical Research Center, Booali Research Center, Mashhad University of Medical Sciences, Mashhad, Iran; [3]Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Therapeutics and Clinical Risk Management downloaded from https://www.dovepress.com/
For personal use only.

Abstract: Coronavirus disease 2019 (COVID19) is spreading rapidly and there is now much concern regarding different aspects of public health. Underlying disorders like cardiovascular diseases can increase the mortality rate. Understanding cardiovascular complications, manifestations and management in COVID19 is a necessary need. In this comprehensive review, we evaluated different aspects of cardiovascular disorders or complications related to COVID19 infection.

Keywords: SARS-CoV-2, COVID-19, cardiovascular diseases, complication

Background

Since December 2019, the new coronavirus (COVID19) outbreak has been a great concern in the public health worldwide.[1] Acute coronary syndrome and cerebrovascular events might be triggered by some pathogens.[2,3] Respiratory and urinary tract infections have been correlated with a short-term incremental rate of myocardial infarction and ischemic stroke.[4] In the recent two decades, coronaviruses and influenza viruses presented as outbreaks several times, leading to a great mortality and financial burden.

The SARS outbreak led to 916 mortalities in 29 countries in 2002. Thereafter, in 2012, the Middle East respiratory syndrome coronavirus (MERS) led to 800 mortalities in about 27 nations.[5] The exact mechanisms that increase the higher risk due to such infections is not well understood yet; however, it may be due to higher cardiovascular stress in the underlying infection, lowering oxygenation in underlying pulmonary disorders, or systemic inflammation with plaque disruption which can precipitate thrombosis.[3]

Acute respiratory distress syndrome with cytokine storm may be the reason for increased mortality in COVID19.[6] In more than 15% of infected patients, an interstitial pneumonia occurs that might proceed to acute respiratory distress syndrome (ARDS) or multiple organ failure and eventually death.[7]

Patients with coronary artery disorder and heart failure are at increased risk of acute events or exacerbation. Viral infections can potentially destabilize coronary plaques through several mechanisms including systemic inflammatory responses recently documented with COVID19.[8]

Despite the higher infectivity and lower mortality of COVID19 than severe acute respiratory syndrome (SARS) and MERS, many uncertainties, including the route of transmission, viral evolution, epidemic dynamics, appropriate anti-viral treatment and strategies for disease control remain.[9] Although the mortality rate

Correspondence: Leila Bigdelu
Tel +98 5138400000
Fax +98 5138453239
Email BigdeluL@mums.ac.ir

submit your manuscript | www.dovepress.com
DovePress
http://doi.org/10.2147/TCRM.S264377

© 2020 Keihanian and Bigdelu. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v3.0) License (http://creativecommons.org/licenses/by-nc/3.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

remains low at 2.3% based on some Chinese reports, it would be 6% in patients with hypertension, 7.3% in those with diabetes, 10.5% in patients with cardiovascular disease (CVD) and 14.8% in those ≥ 80 years.[10] It is demonstrated that comorbidity, age, lymphocyte and lactate dehydrogenase which was considered as CALL score in a study, as a simple index had diagnostic value in forecasting prognosis.[11] There are some different risk factors in mortality prognosis such as age of more than sixty-five years, CD3 to CD8 ratio lesser than 75, cardiac troponin I more than 0.05 and history of CVD.[12] The prevalence of comorbidities with COVID19 patients is likely to vary greatly between countries depending on the background population at risk and preventive measures taken. This review focused on cardiovascular manifestations, challenges and considerations for patients with COVID19 infection.

Here, we assessed various aspects of cardiovascular-related mechanism in clinical investigations of COVID19. We explored different studies in EMBASE, Science Citation Index, TRIP, Database of Abstracts of Reviews of Effectiveness (DARE), MEDLINE, Cochrane Library, NHS and Social Science Citation Index.

Probable Mechanisms of Cardiovascular System Injury Due to SARS-CoV-2

Viral infections might lead to decompensation of chronic CVD. It can be due to higher metabolic demand caused by infection and lower cardiac supply. The viral infection along with superimposed pneumonia would affect the cardiovascular system.[8] Varying, subclinical left ventricular (LV) diastolic damage in acute SARS, even in patients with no concurrent cardiac disease, is frequent, similar to the outcome of systemic inflammatory response, and is not exclusive for SARS.[13] Based upon the clinical manifestation and laboratory results of COVID19, and the mechanisms of SARS-CoV, COVID19 might influence the cardiovascular system throughout various mechanisms. Viral infection directly damages cardiomyocytes. This hypothesis is confirmed by detection of viral RNA in 35% of human cardiac specimen autopsy from patients with SARS during the Toronto outbreak in 2003.[14] Second, severe 2019-nCoV pneumonia can cause airway obstruction and affect gas exchange resulting in hypoxemia, which markedly lowers the energy reserve by cellular anabolism and advances anaerobic fermentation followed by intra-cellular acidosis and oxygen free radicals to impair the phospholipid layer of cellular membrane. At the same time, calcium entry induced by hypoxia causes damage and develops the apoptosis of cardiomyocytes.[15] Moreover, high levels of IL-1β, IFN-γ IP-10 and MCP-1 were found in COVID19 infection, which increases Th1 cell responses.[1] The disproportion of types 1 and 2 T helper cell responses can stimulate cytokine storm leading to myocardial injury. Another mechanism of acute myocardial injury due to SARS- CoV-2 might be attributed to angiotensin-converting enzyme 2 (ACE2). The SARS-CoV-2 binds to the zinc peptidase ACE2. ACE2 is extensively expressed in different parts of the body, like the lungs and cardiovascular system and signaling pathways related to ACE2 may also have a role in cardiac injury.[1]

Cardiovascular Complications of SARS-CoV-2

General Cardiovascular Complications and Cardiac Injury

Cardiac disorders and diabetes can duplicate the risk of mortality more than other risk factors.[16] Therefore, evaluation of cardiovascular and metabolic disorders in patients with COVID19 infection seems to be necessary. In one study of cardiovascular complications in 121 patients with SARS,[17] persistent tachycardia was found in 71.9% (including 40% with continued tachycardia during outpatient follow-up), sustained asymptomatic hypotension during hospitalization in 50.4%, transient bradycardia in 14.9%, transient cardiomegaly (without signs or symptoms of heart failure) in 10.7% and transient paroxysmal AF (with spontaneous resolution) in one case. These cardiovascular complications were statistically uncorrelated with oxygen desaturation or intensive care unit (ICU) admission. Earlier researches have demonstrated a link between cardiovascular metabolic disorders and SARS or MERS.[17–19] Besides, it is shown that MERS can lead to acute myocarditis and heart failure.[20]

In a recent study on critically ill patients with COVID19 infection, comorbidities were seen in 86%, with chronic kidney disease and congestive heart failure being the most common. Three patients (of 21 patients) had elevated cardiac troponin-I (cTnI) and the mean BNP level was 4720 pg/mL. Cardiomyopathy developed in seven patients (33%). It is unclear whether the high rate of cardiomyopathy in the study is due to a direct cardiac

complication of COVID19 infection or overwhelming critical illness.[21]

In a study of 41 patients with COVID19 infection, myocardial injury was reported in five in Wuhan accompanied by a rise in hs-CRP and TnI. Eighty percent of patients with myocardial injury need ICU admission and had a higher blood pressure than those who did not need ICU admission.[1]

Findings of a recent meta-analysis showed that assessment of cTnI or cardiac troponin-T (cTnT) might be helpful in predicting the disease severity in patients with COVID19 infection.

According to the results of comparing severe cases with other ones (123 versus 218 patients) in China, cTnI values in severe cases were significantly more than those with mild disease. Therefore, measuring cardiac damage biomarkers at admission of patients with COVID19 infection can help to detect those with cardiac injury and predict its progression.[22] In another study on 120 patients with COVID19 infection, NT-ProBNP and cTnI were elevated in 27.5% and 10%, respectively. It is also demonstrated that the plasma level of IL-6 was markedly increased in patients with COVID19 infection and cardiovascular damage. In addition, mortality rate was correlated with the cardiac damage induced by fulminant myocarditis.[23] Another investigation in Wuhan indicated that the level of myocardial injury in patients admitted to ICUs was significantly higher than those who did not. Biomarker levels (CK-MB, hs-TnI) were also higher in ICU than those who did not with a meaningful difference.

Cardiac damage is a prevalent status in patients admitted with COVID19 and is related to high in-patient mortality rate.[24] This claims that patients with severe COVID19 infection are more prone to adverse events leading to myocardial injury.[25] Cardiovascular adverse events of influenza infection, like myocarditis, acute myocardial infarction and deterioration of heart failure were well-recognized during previous historical epidemics and markedly contributed to mortality.[26] Although, first presentations of some COVID19 positive patients had been cardiovascular symptoms like palpitation or chest pain instead of respiratory symptoms in China in the grey literature. Generally, 11.8% of patients died with no previous history of CVD, there was substantial cardiac damage with elevation of TnI or cardiac arrest during hospitalization.[27] So, cardiovascular symptoms in COVID19 positive patients can be more prevalent, probably due to systemic inflammation and immune system response. Similarly, former coronavirus epidemics have been related to a serious burden of cardiovascular events and adverse effects.[26] It is mentioned that myocardial injury is related to mortality in COVID19, but the prognosis of patients with underlying CVD and with no cardiac injury is better. The cause of this event is due to cardiac dysfunction and arrhythmias and inflammation-related-myocardial infarction. Myocardial cells in subjects with underlying CVD (ie, hypertension, coronary heart disease, and cardiomyopathy) are more prone to be damaged by viral illness. This damage can result from direct injury by the virus, systemic inflammatory responses, destabilized coronary plaque, and aggravated hypoxia.[28]

The severity of the primary respiratory involvement and probability of complications is raised in subjects with underlying CVD.[19] Hypotension, tachycardia, bradycardia, arrhythmia, or even sudden cardiac death were prevalent in SARS cases. Echocardiography commonly shows subclinical left ventricular diastolic impairment. Besides, in those with systolic impairment and reduced ejection fraction there is a higher probability of the need for mechanical ventilation.[13,29] Early COVID19 case reports recommended that those with a history of comorbidities are at more risk of adverse events or death. About fifty percent of admitted patients had a chronic medical disorder (40% CVD or cerebrovascular diseases). In the greatest clinical-cohort of COVID19 to date, acute cardiac injury, shock, and arrhythmia were reported in 7.2%, 8.7%, and 16.7% of patients, respectively, with a higher prevalence in those needing intensive care.[25] It has been reported that in patients with complicated COVID19 infection, 58%, 25% and 44% had hypertension, cardiac disease and arrhythmia, respectively.[1] According to recorded mortality statistics in China, 35% of patients with COVID19 infection had a history of hypertension and 17% had a previous coronary heart disease. Moreover, patients older than 60 years had more systemic symptoms and more severe pneumonia than those below 60 years.[30] A meta-analysis indicated that hypertension, cardiovascular or cerebrovascular disorders and diabetes were found in 17.1%, 16.4% and 9.7% of patients, respectively. They compared these statistics with the general population and showed no susceptibility of patients with hypertension and diabetes to COVID19 infection.[31]

Previous CVD are underlying disorders that exacerbate the status of COVID19 infection, which might lead to death.[27] Various antiviral drugs could lead to cardiovascular insufficiency, arrhythmia or other cardiovascular

adverse effects. Therefore, the risk of cardiac toxicity should be assessed carefully.[32]

According to a meta-analysis, about eight percent of patients with COVID19 infection had acute cardiac injury.[33] A patient was reported with no previous history of chronic disorder admitted in ICU and developed severe respiratory failure, heart failure, septicemia and sudden cardiac death in the eleventh day of hospitalization. It can be justified by direct acute cardiac injury due to COVID19 virus infection.[34] In another report, the frequency of myocardial injury in ICU or severe cardiac cases was approximately thirteen folds more compared to non-ICU or cardiac patients. Therefore, patients with COVID19 infection and underlying heart disease can have impaired cardiac supply, poor tolerance to severe pneumonia and are more susceptible to heart failure.[31] Data gathering in this field is bounded because of the low sample size and time restriction until now and most investigations had no comorbidities analysis in patients who died due to COVID19 infection. Therefore, the association between CVD and COVID19-related mortality may not be confirmed. The fact is that patients with hypertension, CVD, cerebrovascular or diabetes are more susceptible to severe infection or ICU admission due to COVID19 infection. The incidence of hypertension was twofold, cardiovascular and cerebrovascular disorders were threefold and diabetes was twofold higher in severe or ICU needing patients than others.[33]

Some patients with severe COVID19 infection might deteriorate quickly due to acute respiratory distress syndrome, which leads to septic shock and finally multiple organ failure and fulminant myocarditis.

Clinicians should consider the rapid increase in the level of cTnI or new-onset arrhythmias. Using mechanical ventilators and circulatory support systems, like IABP, Impella, and ECMO, may be helpful for these patients.[35] In a retrospective study, cardiovascular manifestations and in-hospital outcomes of confirmed COVID19 healthcare workers were evaluated. The mean age of patients and comorbidities were less than the general population. Patients with cardiovascular presentations and those without it accounted for 58.5% and 41.5%, respectively. Patients with cardiovascular manifestations had lower baseline lymphocyte count (990 versus 1550), more positive PCR detection of throat swab (50% versus 11.8%, P = 0.011), and more oxygen support (79.2% and 23.5%, P<0.001) compared to those without it. The incidence of in-hospital complications was markedly more in patients with cardiovascular presentation (75.0% versus 23.5%, P = 0.001). In their multi-variable logistic regression model, concomitant cardiovascular presentation in patients with COVID19 infection was not independently related to in-hospital complications.[36] In another investigation, on 54 patients with COVID19 pneumonia, it was shown that patients with NT-proBNP more than 88.64 pg/mL level had higher risks of in-hospital mortality. NT-proBNP has been shown to be an independent risk factor for in-hospital mortality in patients with severe COVID19 infection.[37]

Thrombosis

Primary studies have demonstrated that there are higher risks of venous thrombo-embolism and acute myocardial infarctions that are probably induced by extreme inflammation, platelet activation, endothelial dysfunction, and stasis.[38]

COVID19 related-coagulopathy,[39,40] may relate to the higher number of arterial ischemic events. Higher levels of D-dimer in the setting of COVID19 have been defined in 3 of the previously described cohort studies.[41–43] It seems that pulmonary thrombosis is frequent in COVID19 pneumonia and makes 2 forms, proximal pulmonary emboli and/or distal thrombosis.[44] The frequency of COVID19-related thrombosis is not recognized well and most of investigations did not consider systematic and comprehensive investigation protocols on this issue. It shows that it is crucial to perceive the stage of disease and location of patient (ward vs ICU). These factors can have an influence on the quantity of anticoagulant a patient needed and can affect later thrombosis. In addition, there is evidence in a majority of studies, that can refer pulmonary embolism (PE) as “in situ” pulmonary thrombosis.[45] Latest investigations suggested that the incidence of thrombotic risk in ICU COVID19 patients (severe cases) was increased.[46,47] The most common thrombotic event was PE.[48] There are three possible mechanisms related to pulmonary thrombosis proposed in COVID19: 1) endothelial inflammation and microvascular thrombosis; 2) disturbing Virchow’s triad inside the lung by changing pulmonary blood flow; 3) transition of deep vein thrombosis to PE.[48]

Drug-Related Complications

Different COVID19 treatment drugs like chloroquine or hydroxychloroquine (alone or with azithromycin) and lopinavir/ritonavir could increase the QTc interval and risk of drug-induced torsade de pointes (DI-TdP) and drug-induced sudden cardiac death (DI-SCD).[49] Ventricular arrhythmias

and mortality is reported by use of hydroxychloroquine alone or with macrolide. Bundle branch block, ventricular tachycardia, and ventricular fibrillation are the other adverse events related to hydroxychloroquine.[50,51] These complications should be considered when patients are under treatment by these drugs and ECG monitoring is required.

Arrhythmia

Another complication induced by COVID19 is arrhythmia. The rate of arrhythmia among 138 patients hospitalized with COVID19-related pneumonia was reported in 17% and more frequent in 44% of patients admitted in an ICU.[52] In an observational study among 700 patients, there were 9 cardiac arrests, 25 atrial fibrillation (AF) events, 9 clinically significant bradyarrhythmias, and 10 non-sustain tachycardia (NSVTs). The important point is that all cardiac arrests happened in ICU admitted patients. Hospitalization in ICU was related to AF and NSVT.[53] The probable processes that could lead to arrhythmia in COVID19 patients are myocarditis, hypoxia, abnormal host immune-response, myocardial strain, myocardial ischemia, electrolyte derangement, intra-vascular volume disturbances and drug adverse effects.[54] Malignant arrhythmias in COVID19 were first reported in 5.9% (11/187), including VT/ventricular fibrillation (VF).[28] Also, it was reported a large-series of subjects died from COVID19, and showed that most etiology of mortality in seven of the eighty-one cases was cardiac arrest (8.64%), acute coronary syndrome (4.94%) and malignant arrhythmias (2.47%), respectively.[55] Despite the perceived association, some case reports have described the phenomenon of sinus bradycardia in text of COVID19 as the most common arrhythmias.[56]

Long-Term Complications

Long-term complications of COVID19 infection should be considered in their follow-ups. The clinical effects of pneumonia and persistent systemic inflammation and procoagulant activity after resolution of infection, have been related with a higher risk of CVD for up to 10-years of follow-up.[57] It is likely that patients infected via respiratory virus outbreaks would experience similar adverse outcomes. Current data on long-term follow-up is based upon other previous types of coronaviruses. In a study performed on 25 cases recovered from SARS-CoV infection, it was shown that 68% had hyperlipidemia, 44% cardiovascular disorder and 60% glucose metabolism disorders after a 12-year follow-up.[58] Analysis of metabolic characteristics indicated that metabolism of lipids was dysregulated in patients with previous SARS infection. In previous SARS cases, the serum level of free fatty acids, lysophosphatidyl choline, lysophosphatidyl ethanolamine and phosphatidyl glycerol were markedly higher than those without a history of SARS.[58] The mechanisms that affect lipid and glucose metabolisms are not understood yet. According to the similar structure of SARS and COVID19 virus agents, COVID19 may lead to chronic cardiovascular complications.

While viral phenotype, base-line clinical features, primary disease severity, and immediate management effect short term survival, extra-pulmonary manifestations mainly determine the long-term prognosis.[9] More long-term studies should be performed in those who recovered from the infection.

Challenges About RAAS Inhibitors

ACE2 is a membrane-bound aminopeptidase with a critical role in the cardiovascular and immune systems.[59] ACE2 is a counter-regulatory enzyme that degrades angiotensin II to angiotensin-(1–7), thereby weakening its impacts on vaso-constriction, sodium retention and fibrosis.[60] ACE2 expression is very tissue-specific, mainly expressed in the cardiovascular, renal and gastrointestinal systems and respiratory tract epithelium, but the circulating levels of soluble ACE2 are low.[61] Therefore, in addition to coronaviruses causing pneumonia through ACE2 receptors in lung epithelial cells, we must consider possible viral effects on myocardial tissue. ACE2 has been identified as a functional receptor for coronaviruses,[59] including SARS-CoV and SARS-CoV-2. SARS-CoV-2 infection is stimulated by the binding of the spike protein of the virus to ACE2, which is highly expressed in heart and lungs.[59] SARS-CoV-2 mainly invades alveolar epithelial cells, resulting in respiratory symptoms. These symptoms are more severe in patients with CVD, which might be associated with the increased expression of ACE2 in these patients compared to healthy ones. There is a hypothesis that ACE2 levels can be increased by the use of renin–angiotensin–aldosterone system inhibitors. Given that ACE2 is a functional receptor for SARS-CoV-2, concerns have been raised regarding the safety and potential effects of antihypertension therapy with ACE inhibitors or angiotensin-receptor blockers in patients with COVID19 infection.[62] There are few human studies to assess the effects of RAAS inhibitors on ACE2 expression and data

are lacking about the effects of RAAS inhibitors on lung-specific expressions of ACE2. Therefore, this limited data is not enough to support or refute these concerns.[63] On the other hand, a high level of angiotensin II activity may have an important role in organ injury in COVID19 infection.[64,65] In experimental models, exposure to the SARS-CoV-1 spike protein induced acute lung injury, which is limited by RAAS blockade.[66] In another animal study, it was shown that using ACEi and ARB might create a protection against severe lung complications in COVID19 infection.[67]

Based on the current available guidelines and considering the overwhelming evidence of mortality reduction in CVD, ACEi and ARB therapy should be initiated in patients with heart failure, hypertension, or myocardial infarction as tolerated, regardless of SARS-CoV-2.[68] In addition, abrupt withdrawal of RAAS inhibitors in high-risk patients may result in clinical instability and adverse health outcomes.[63]

Some experts have suggested that rigorous use of guideline-directed, plaque stabilizing agents could offer additional protection to patients with COVID19 infection (statins, beta blockers, ACE inhibitors, ASA);[69] however, such therapies should be tailored individually.

Myocardial Infarction

Classic symptoms and manifestations of acute myocardial infarction (AMI) might not present during coronavirus infection, which leads to under-diagnosis.[8] Xu et al evaluated the clinical characteristics and risk factors of patients with COVID19 infection and AMI. They reported cardiac complications in 42 of 53 (79.25%) patients including tachycardia (n = 15), electrocardiography abnormities (n = 11), diastolic dysfunction (n = 20), elevated myocardial enzymes (n = 30) and AMI (n = 6). All the six patients with AMI were aged more than 60 years and five had two or more underlying comorbidities (hypertension, diabetes, CVD, and chronic obstructive pulmonary disease). Novel coronavirus pneumonia (NCP) severity score was higher in patients with AMI than those with non-definite AMI ($p<0.001$). All patients with AMI required care in an intensive care unit and three died and two remained hospitalized. Their analysis showed that CRP levels, NCP severity, and underlying comorbidities were the risk factors for myocardial injury in patients with COVID19 infection.[70]

Due to a delay in the results of PCR and its effects on the time of STEMI emergency reperfusion, it is suggested to isolate patients suspected of SARS-CoV-2 infection and to administer thrombolytic therapy immediately within the reperfusion time.

High-risk patients with contraindications for thrombolysis should be assessed regarding the risk of infection transmission and the benefit of PCI. Meanwhile, performing PCI only for the culprit vessel is recommended.

If patients are admitted within the reperfusion time window (less than 12 hours) and no contraindication for thrombolysis exists, thrombolytic therapy should be performed in an isolation ward. After successful thrombolysis, treatment should be continued in the isolation ward. After the patient recovered from COVID19 pneumonia and PCR findings were twice negative, elective PCI should be considered. Patients within the reperfusion time window with contraindications for thrombolysis or failure of thrombolysis need a comprehensive evaluation of the risks of PCI and infection control.[71]

For most patients with NSTEMI and suspected COVID19 infection, timing should allow for diagnostic testing prior to cardiac catheterization, and allow for a more informed decision regarding infection control. Rapid discharge of patients with primary NSTEMI following revascularization would likely be important in terms of maximizing bed availability and reducing patient exposure within the hospital. It has been suggested that in appropriately selected patients with known COVID19 and NSTEMI (eg, particularly for patients with type 2 MI), conservative therapy may be sufficient based on the patient's risk. Recent reports from China outline a protocol that relies on rapid nucleic acid testing and reliance on fibrinolytic therapy. This is a controversial subject, especially in the United States where primary PCI is routine for patients with STEMI. Furthermore, it is complicated by the fact that access to rapid testing is limited. However, in patients with known COVID19 infection and STEMI, the balance of staff exposure and patient benefit should be weighed carefully. Fibrinolysis can be considered an option for relatively stable patients with STEMI and active COVID19 infection. For elective patients, Case decisions should be individualized, taking into account the risk of COVID19 exposure versus the delay in diagnosis or therapy.[72] Recent reports suggest that acute cardiac injury is present in about 7% of patients with COVID19 infection and may represent either type 2 MI or myocarditis.[73]

Pro-coagulant effects of systemic inflammation[74] may increase the likelihood of stent thrombosis and assessment

of platelet function and intensified anti-platelet therapy should be considered in those with a history of previous coronary intervention.

Conclusion

COVID19 is now a serious pandemic infection with different clinical features. Underlying CVD may lead to adverse clinical outcomes or long-term complications in patients with COVID19 infection. Keeping in mind the cardiovascular presentations, underlying CVD and its adverse events can help the clinician to make better decisions in the management of COVID19 infection. However, there are many gaps in the pathophysiology of direct cardiovascular injuries due to COVID19 infection. Performing large scale and multicentric investigations on cardiovascular complications of COVID19 infection would help CVD control to a great extent.

Abbreviations

ACE2, angiotensin-converting enzyme 2; ACEi, angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; ARDS, acute respiratory distress syndrome; CK-MB, creatine kinase myocardial band; COVID19, coronavirus disease 2019; cTnI, cardiac troponin-I; cTnT, cardiac troponin-T; CVD, cardiovascular disease; ECMO, extracorporeal membrane oxygenation; hs-TnI, hypersensitive troponin-I; IABP, intra-aortic balloon pump; ICU, intensive care unit; IFN-γ IP-10, interferon gamma-induced protein 10; IL-1β, interleukin 1-beta; LV, left ventricular; MCP-1, monocyte chemoattractant protein-1; MERS, Middle East respiratory syndrome coronavirus; NCP, novel coronavirus pneumonia; NSTEMI, non-ST-segment elevation myocardial infarction; NT-ProBNP, N-terminal pro b-type natriuretic peptide; PCI, percutaneous coronary intervention; PCR, polymerase chain reaction; RAAS, renin–angiotensin–aldosterone system; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus type2; STEMI, ST-segment elevation myocardial infarction.

Disclosure

The authors report no conflicts of interest for this work.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395 (10223):497–506. doi:10.1016/S0140-6736(20)30183-5
2. Stöllberger C, Finsterer J. Role of infectious and immune factors in coronary and cerebrovascular arteriosclerosis. *Clin Diagn Lab Immunol*. 2002;9(2):207–215.
3. Elkind MS, Harrington RA, Benjamin IJ. Role of the American heart association in the global COVID19 pandemic. *Circulation*. 2020;141 (15). doi:10.1161/CIRCULATIONAHA.120.046749
4. Davis MM, Taubert K, Benin AL, et al. Influenza vaccination as secondary prevention for cardiovascular disease: a science advisory from the American Heart Association/American College of Cardiology. *J Am Coll Cardiol*. 2006;48(7):1498–1502. doi:10.1016/j.jacc.2006.09.004
5. Song Z, Xu Y, Bao L, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses*. 2019;11(1):59. doi:10.3390/v11010059
6. Rajan R, Jarallah M, Dashti R. Cardiovascular complications of novel Wuhan coronavirus (COVID19)–A 2020 update. *J Cardiol Curr Res*. 2020;13(1):28.
7. Mattiuzzi C, Lippi G. Which lessons shall we learn from the 2019 novel coronavirus outbreak? *Ann Transl Med*. 2020;8(3):48. doi:10.21037/atm.2020.02.06
8. Madjid M, Solomon SD, Vardeny O, Mullen B. Cardiac implications of novel coronavirus (COVID19). *ACC Clin Bull*. 2020.
9. Xiong T-Y, Redwood S, Prendergast B, Chen M. Coronaviruses and the cardiovascular system: acute and long-term implications. *Eur Heart J*. 2020;41(19):1798–1800. doi:10.1093/eurheartj/ehaa231
10. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA*. 2020;323(13):1239. doi:10.1001/jama.2020.2648
11. Ji D, Zhang D, Xu J, et al. Prediction for progression risk in patients with COVID19 Pneumonia: the CALL score. *Clin Infect Dis*. 2020;71(6):1393–1399. doi:10.1093/cid/ciaa414
12. Du R-H, Liang L-R, Yang C-Q, et al. Predictors of mortality for patients with COVID19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J*. 2020;55(5):2000524. doi:10.1183/13993003.00524-2020
13. Li SS-L, Cheng C-W, Fu C-L, et al. Left ventricular performance in patients with severe acute respiratory syndrome: a 30-day echocardiographic follow-up study. *Circulation*. 2003;108(15):1798–1803. doi:10.1161/01.CIR.0000094737.21775.32
14. Oudit G, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. *Eur J Clin Invest*. 2009;39(7):618–625. doi:10.1111/j.1365-2362.2009.02153.x
15. Li F, Li W, Farzan M, Harrison SC. Structure of SARS coronavirus spike receptor-binding domain complexed with receptor. *Science*. 2005;309(5742):1864–1868. doi:10.1126/science.1116480
16. Chan J, Ng C, Chan Y, et al. Short term outcome and risk factors for adverse clinical outcomes in adults with severe acute respiratory syndrome (SARS). *Thorax*. 2003;58(8):686–689. doi:10.1136/thorax.58.8.686
17. Yu C, Wong RS, Wu E, et al. Cardiovascular complications of severe acute respiratory syndrome. *Postgrad Med J*. 2006;82(964):140–144. doi:10.1136/pgmj.2005.037515
18. Yang J, Feng Y, Yuan M, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. *Diabetic Med*. 2006;23(6):623–628. doi:10.1111/j.1464-5491.2006.01861.x
19. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *Int J Infect Dis*. 2016;49:129–133. doi:10.1016/j.ijid.2016.06.015

20. Alhogbani T. Acute myocarditis associated with novel Middle East respiratory syndrome coronavirus. *Ann Saudi Med*. 2016;36 (1):78–80. doi:10.5144/0256-4947.2016.78
21. Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID19 in Washington State. *JAMA*. 2020;323(16):1612. doi:10.1001/jama.2020.4326
22. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID19): evidence from a meta-analysis. *Prog Cardiovasc Dis*. 2020;63(3):390–391. doi:10.1016/j.pcad.2020.03.001
23. Chen C, Zhou Y, Wang DW. SARS-CoV-2: a potential novel etiology of fulminant myocarditis. *Herz*. 2020;1–3.
24. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID19 in Wuhan, China. *JAMA Cardiol*. 2020;5(7):802–810. doi:10.1001/jamacardio.2020.0950
25. Cai J, Xu J, Lin D, et al. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clin Infect Dis*. 2020.
26. Nguyen JL, Yang W, Ito K, Matte TD, Shaman J, Kinney PL. Seasonal influenza infections and cardiovascular disease mortality. *JAMA Cardiol*. 2016;1(3):274–281. doi:10.1001/jamacardio.2016.0433
27. Zheng -Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID19 and the cardiovascular system. *Nat Rev Cardiol*. 2020;1–2.
28. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID19). *JAMA Cardiol*. 2020;5(7):811–818. doi:10.1001/jamacardio.2020.1017
29. Harris JE, Shah PJ, Korimilli V, Win H. Frequency of troponin elevations in patients with influenza infection during the 2017–2018 influenza season. *IJC Heart Vascul*. 2019;22:145–147. doi:10.1016/j.ijcha.2018.12.013
30. Chan JF-W, Yuan S, Kok K-H, 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):514–523. doi:10.1016/S0140-6736(20)30154-9
31. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID19 in China. *Clin Res Cardiol*. 2020;1–8.
32. Sakabe M, Yoshioka R, Fujiki A. Sick sinus syndrome induced by interferon and ribavirin therapy in a patient with chronic hepatitis C. *J Cardiol Cases*. 2013;8(6):173–175. doi:10.1016/j.jccase.2013.08.002
33. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID19 in China. *Clin Res Cardiol*. 2020;109(5):531–538. doi:10.1007/s00392-020-01626-9
34. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395 (10223):507–513. doi:10.1016/S0140-6736(20)30211-7
35. Chen C, Zhou Y, Wang DW. SARS-CoV-2: a potential novel etiology of fulminant myocarditis. *Herz*. 2020;45(3):230–232. doi:10.1007/s00059-020-04909-z
36. Liu R, Ming X, Zhu H, et al. Association of cardiovascular manifestations with in-hospital outcomes in patients with COVID19: a hospital staff data. *medRxiv*. 2020.
37. Gao L, Jiang D, Wen X, et al. Prognostic value of NT-proBNP in patients with severe COVID19. *medRxiv*. 2020.
38. Chen S, Huang B, Luo D, et al. Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases. *Zhonghua Bing Li Xue Za Zhi*. 2020;49: E005–E.
39. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–1062. doi:10.1016/S0140-6736(20)30566-3
40. Zhang Y, Cao W, Xiao M, et al. Clinical and coagulation characteristics in 7 patients with critical COVID-2019 pneumonia and acro-ischemia. *Zhonghua Xue Ye Xue Za Zhi= Zhonghua Xueyexue Zazhi*. 2020;41(4):302–307.
41. Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. *Intensive Care Med*. 2020;1–10.
42. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res*. 2020;191:9–14. doi:10.1016/j.thromres.2020.04.024
43. Bellosta R, Luzzani L, Natalini G, et al. Acute limb ischemia in patients with COVID19 pneumonia. *J Vasc Surg*. 2020. doi:10.1016/j.jvs.2020.04.483
44. Price LC, McCabe C, Garfield B, Wort SJ. Thrombosis and COVID19 pneumonia: the clot thickens! *Eur Respir J*. 2020;56 (1):2001608. doi:10.1183/13993003.01608-2020
45. Wang T, Chen R, Liu C, et al. Attention should be paid to venous thromboembolism prophylaxis in the management of COVID19. *Lancet Haematolo*. 2020;7(5):e362–e3. doi:10.1016/S2352-3026(20)30109-5
46. Klok FA, Kruip M, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID19. *Thromb Res*. 2020;191:145–147. doi:10.1016/j.thromres.2020.04.013
47. Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemostas*. 2020.
48. Klok FA, Kruip M, Van Der Meer N, et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID19: an updated analysis. *Thromb Res*. 2020.
49. Giudicessi JR, Noseworthy PA, Friedman PA, et al., editors. Urgent guidance for navigating and circumventing the QTc-prolonging and torsadogenic potential of possible pharmacotherapies for coronavirus disease 19 (COVID19). *Mayo Clin Proc*. 2020;95(6):1213–1221. doi:10.1016/j.mayocp.2020.03.024.
50. Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID19 pandemic. *J Am Coll Cardiol*. 2020;75 (18):2352–2371. doi:10.1016/j.jacc.2020.03.031
51. Talasaz AH, Kakavand H, Van Tassell B, et al. Cardiovascular complications of COVID19: pharmacotherapy perspective. *Cardiovasc Drugs Ther*. 2020. doi:10.1007/s10557-020-07037-2
52. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585
53. Bhatla A, Mayer MM, Adusumalli S, et al. COVID19 and cardiac arrhythmias. *Heart Rhythm*. 2020;17(9):1439–1444. doi:10.1016/j.hrthm.2020.06.016
54. Dherange P, Lang J, Qian P, et al. Arrhythmias and COVID19: a review. *JACC: Clin Electrophysiol*. 2020.
55. Du Y, Tu L, Zhu P, et al. Clinical features of 85 fatal cases of COVID19 from Wuhan. a retrospective observational study. *Am J Respir Crit Care Med*. 2020;201(11):1372–1379. doi:10.1164/rccm.202003-0543OC
56. Kir D, Mohan C, Sancassani R. Heart brake: an unusual cardiac manifestation of COVID19. *JACC: Case Rep*. 2020;2(9):1252–1255.
57. Corrales-Medina VF, Alvarez KN, Weissfeld LA, et al. Association between hospitalization for pneumonia and subsequent risk of cardiovascular disease. *JAMA*. 2015;313(3):264–274. doi:10.1001/jama.2014.18229
58. Wu Q, Zhou L, Sun X, et al. Altered lipid metabolism in recovered sars patients twelve years after infection. *Sci Rep*. 2017;7(1):1–12.
59. Turner AJ, Hiscox JA, Hooper NM. ACE2: from vasopeptidase to SARS virus receptor. *Trends Pharmacol Sci*. 2004;25(6):291–294. doi:10.1016/j.tips.2004.04.001

60. Vickers C, Hales P, Kaushik V, et al. Hydrolysis of biological peptides by human angiotensin-converting enzyme-related carboxypeptidase. *J Biol Chem*. 2002;277(17):14838–14843. doi:10.1074/jbc.M200581200
61. Serfozo P, Wysocki J, Gulua G, et al. Ang II (Angiotensin II) conversion to angiotensin-(1-7) in the circulation is POP (Prolyloligopeptidase)-dependent and ACE2 (angiotensin-converting enzyme 2)-independent. *Hypertension (Dallas, Tex: 1979)*. 2020;75(1):173–182. doi:10.1161/HYPERTENSIONAHA.119.14071
62. Zheng -Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID19 and the cardiovascular system. *Nat Rev Cardiol*. 2020;17(5):259–260. doi:10.1038/s41569-020-0360-5
63. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin–angiotensin–aldosterone system inhibitors in patients with COVID19. *N Engl J Med*. 2020;382(17):1653–1659. doi:10.1056/NEJMsr2005760
64. Gurwitz D. Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. *Drug Dev Res*. 2020;81(5):537–540. doi:10.1002/ddr.21656
65. Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci*. 2020;63(3):364–374. doi:10.1007/s11427-020-1643-8
66. Kuba K, Imai Y, Rao S, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. *Nat Med*. 2005;11(8):875–879. doi:10.1038/nm1267
67. Cardiology ESo. Position statement of the ESC Council on Hypertension on ACE-inhibitors and angiotensin receptor blockers. *ESC*. 2020.
68. Kuster GM, Pfister O, Burkard T, et al. SARS-CoV2: should inhibitors of the renin–angiotensin system be withdrawn in patients with COVID19? *Eur Heart J*. 2020;41(19):1801–1803. doi:10.1093/eurheartj/ehaa235
69. Madjid M, Casscells SW. Of birds and men: cardiologists' role in influenza pandemics. *Lancet*. 2004;364(9442):1309. doi:10.1016/S0140-6736(04)17176-6
70. Xu H, Hou K, Xu H, et al. Acute myocardial injury of patients with coronavirus disease 2019. *medRxiv*. 2020.
71. Zeng J, Huang J, Pan L. How to balance acute myocardial infarction and COVID19: the protocols from Sichuan Provincial People's Hospital. *Intensive Care Med*. 2020;1–3.
72. Welt FG, Shah PB, Aronow HD, et al. Catheterization laboratory considerations during the coronavirus (COVID19) pandemic: from ACC's interventional council and SCAI. *J Am Coll Cardiol*. 2020;75(18):2372–2375. doi:10.1016/j.jacc.2020.03.021
73. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID19. *JAMA*. 2020;323(14):1406. doi:10.1001/jama.2020.2565
74. Libby P, Simon DI. Inflammation and thrombosis: the clot thickens. *Am Heart Assoc*. 2001.

Therapeutics and Clinical Risk Management Dovepress

Publish your work in this journal

Therapeutics and Clinical Risk Management is an international, peer-reviewed journal of clinical therapeutics and risk management, focusing on concise rapid reporting of clinical studies in all therapeutic areas, outcomes, safety, and programs for the effective, safe, and sustained use of medicines. This journal is indexed on PubMed Central, CAS, EMBase, Scopus and the Elsevier Bibliographic databases. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/therapeutics-and-clinical-risk-management-journal