

# COVID-19 and its Cardiovascular Complications: A Review of the Literature

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## Abstract

The Novel Coronavirus Disease 19 (COVID-19) is a clinical syndrome caused by SARS-CoV-2. While the most regarded severe complication of COVID-19 is acute respiratory distress syndrome, the virus could have multiple impacts in other areas of the body, including the cardiovascular system. In this review, we will look at the cardiovascular manifestations of COVID-19, as described in the current literature.

**Keywords:** COVID-19; Syndrome; Cardiovascular complications; Myocardial injury

## Introduction

The year 2020 has proven to be a challenging year for those devastated by the pandemic caused by SARS-CoV-2 (COVID-19). The virus has impacted the entire world and has left many baffled by its persistent reach. An estimated 185 countries are affected with over 3 million cases accounted for worldwide as of April 28, 2020 [1]. While the virus' most feared complication is severe respiratory failure, it has proven to cause complications in other organs, namely the heart. While the cardiovascular manifestations of SARS-CoV-2 are yet to be fully elucidated, it is important to anticipate and build awareness of the various cardiac issues that may arise while taking care of a patient infected with SARS-CoV-2. The literature has shown that these patients may suffer from myocardial injury, arrhythmogenic disturbances, ischemic events and thrombotic events that are attributable, if not, related to infection by SARS-CoV-2 [2]. In this review, we will take a closer look at what we know thus far about the cardiovascular complications of COVID-19.

## Overview of Cardiovascular Complications

Based on data mainly from China, where the pandemic originated, cardiac injury has shown to be a salient feature of this disease, occurring in up to 30% of hospitalized patients with COVID-19 [3]. SARS-CoV-2 infection is associated with various inflammatory mediators that are implicated in cardiac injury, according to recent data [4]. Of the hospitalized patients with COVID-19 with myocardial injury, they had an overall worse prognosis and increased overall mortality. Multiple studies have shown an increase in cardiac biomarkers, mainly troponins I and T, in patients with severe disease [1]. The exact mechanism of myocardial injury is still not fully understood; whether it be from direct damage to cardiac myocytes and/or from systemic inflammation from overwhelming cytokine proliferation is still being considered. During hospitalization, patients with elevated troponin levels more frequently developed acute respiratory distress syndrome, acute kidney

injury, and increased thrombotic complications according to a study by Guo et al. [5].

As a preponderance of data has shown, COVID-19 may predispose patients to increased risk for venous and arterial thromboembolism due largely to an increased inflammatory state. In a study of 184 ICU patients with COVID-19 pneumonia, 31% had thrombotic events, including pulmonary embolism (PE), deep vein thrombosis or stroke, with PE being the most common among them [6]. Some estimate that 40% of hospitalized patients with COVID-19 were found to have cardiovascular or cerebrovascular disease [7]. The high incidence of these thromboembolic events suggests an important role of SARS-CoV-2 in the development of increased coagulability. Furthermore, patients with preexisting cardiovascular disease are at higher risk of developing thromboembolic events and have been treated with subsequent anti-coagulation. Studies point to an increase in coagulation laboratory abnormalities in patients with severe COVID-19, including increased D-dimer; a small study of 25 patients found that D-dimer was elevated in all of them (median of 6.06 mcg/ml) and 10 of them had pulmonary embolism (PE) found on CT-Angiography (CTPA). Patients with PE showed a median D-dimer level of 11.07 mcg/ml and levels above 1 mcg/ml were correlated with increased risk of death during that hospitalization. Thus, a study found the possibility of reduced mortality in severe COVID-19 on anti-coagulation with low molecule weight heparin [8,9].

Along with increased thromboembolic events, it is generally recognized that patients with underlying coronary artery disease are at increased risk of acute coronary events in the face of an infection and/or other inflammatory condition [10]. It is postulated that this susceptibility to coronary events is due to increased myocardial demand that is triggered by these infections. In turn, it is the preponderance of inflammation that leads to atherosclerotic plaque instability and ultimately rupture. This pathogenicity is not dissimilar to the proposed mechanism of myocardial injury seen in viral myocarditis from SARS-CoV-2 as noted above and it is recognized that increased inflammation in COVID-19 could increase risk for plaque rupture. The diagnosis of Acute Coronary Syndrome (ACS), however, in a patient with COVID-19 could be challenging, given the range of causes for elevated troponin and other cardiac biomarkers. Furthermore, the symptoms of

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COVID-19 are not dissimilar to typical presentations of ACS, including chest pain, shortness of breath and worsening exercise intolerance [11].

Acute decompensated heart failure (ADHF) may be the primary presentation in a patient with COVID-19. The literature shows that ADHF may present in 23% of patients in their initial presentation, with cardiomyopathy occurring in over 30% of them, whether it be from myocarditis, ischemia, or non-ischemic etiologies for ADHF [12]. The rate of preexisting CHF and the development of ADHF in patients with COVID-19 is currently unknown but it is not unreasonable to assume most patient presenting with ADHF had a propensity for the development of ADHF if not already compromised heart function. Despite this, nearly half the patients that presented with ADHF did not have a known history of hypertension or known cardiovascular disease [13].

Among the most common patient presentations with COVID-19, palpitations have been an initial symptom in just over 5% of patients [14]. The incidence of new arrhythmias in patients infected with SARS-CoV-2 is well accounted for in several hospitals around the world and the cause of which has been largely due to myocarditis, pro-inflammatory effects and/or concurrent use of arrhythmogenic medications, such as Hydroxychloroquine (known to cause QT prolongation by blocking Kv11.1 (HERG)) [15]. A range of dysrhythmias has been encountered in patients with COVID-19, most frequently being sinus tachycardia, which can be due to fever, pain, hypoxia, anxiety, hypoperfusion or other inciting factors. One study found that arrhythmias were found in 17% of hospitalized patients and 44% of ICU patients [16]. Despite incidental arrhythmogenic disturbances, a malignant arrhythmia in the setting of elevated cardiac biomarkers should raise suspicion for viral myocarditis if not acute myocardial infarction as part of the differential diagnosis [17]. In addition to these considerations, atrial tachycardia has been accounted for in patients with severe COVID-19, including atrial fibrillation (AF) with rapid ventricular response. AF is a known complication of acute illness and can be triggered or worsened by sepsis or an increased inflammatory state, such as the cytokine storm seen in severe COVID-19 infection. Increased sympathetic activity (SNS) can put a patient into rapid ventricular response [8]. Worsening AF can also predispose patients to compromised left ventricular filling and thus ADHF.

## Discussion

The COVID-19 pandemic has various cardiovascular manifestations that have burdened many across the world. Most of what is known about these manifestations, originally, were from data from previous pandemics including MERS and SARS in the early 21st century. While there are some similarities between these pandemics and COVID-19, there are also some stark differences, namely the increased incidence of thrombotic complications with SARS-CoV-2. While the COVID-19 pandemic has proven to be more persistent and have a farther reach, its rate of death has proven to be lower compared to MERS and SARS, while having a dramatically higher number of overall deaths. The occurrence of cardiovascular complications as noted above, has raised concerns about the spread of this virus among patients with preexisting cardiovascular disease. It has been a point of concern that patients with preexisting cardiovascular conditions are at increased risk of mortality and overall have poorer prognosis. Through a mechanism likely related to Angiotensin Converting Enzyme 2 (ACE-2) receptor, the virus affects the cardiovascular system by causing direct myocardial injury and through an increased inflammatory state creates a pro-thrombotic environment conducive to pulmonary embolisms and devastating cerebrovascular events.

Based on our knowledge from MERS-CoV pandemic in early 21st century, we saw that patients developed myocardial injury as expressed by myocardial edema and injury to apical and lateral walls of the left ventricle. This injury is possibly from direct viral infection through the ACE-2 receptor that is a human cell receptor with strong affinity to the spike protein on SARS-CoV-2. Furthermore, these ACE-2 receptors are highly expressed in

the heart which begs the question (18). However, interestingly, a recent pathology study did not find profound mononuclear inflammatory infiltrates in heart tissue and no profound myocardial damage, suggesting that COVID-19 may not directly affect the heart. However, there are limitations to this study given lack of MRI and echocardiographic imaging findings done.

Although our understanding of the cardiovascular complications of COVID-19 are still being developed, we have made significant strides in our knowledge of this virus' effects on the heart and its devastating effects on a patient with COVID-19 pneumonia. Cardiovascular complications seem to be intertwined with the severity of COVID-19 pneumonia and seem to afflict those with increased propensity, whether it be preexisting cardiovascular disease, diabetes, elderly or prior respiratory disease. Elevated biomarkers, regardless of a clear understanding of increased myocardial demand or ischemia has portended a worse prognosis and a higher rate of mortality. It seems clear, however, that in-depth biologic and pathologic studies are needed to clearly elucidate the pathophysiology of cardiac complications of SARS-CoV-2, to develop better therapies and treatments to manage patients with severe COVID-19 pneumonia.

## Conclusion

The Novel Coronavirus Disease 19 (COVID-19) is a clinical syndrome caused by SARS-CoV-2. While the most regarded severe complication of COVID-19 is severe respiratory distress syndrome, the virus could have multiple impacts in other areas of the body, including the cardiovascular system. Recent studies have shown a wealth of knowledge in our understanding of the cardiac complications from COVID-19 pneumonia, yet more in-depth biologic and pathologic studies must be done to elucidate why this occurs, in order to provide better therapies for patients afflicted with this devastating and unprecedented disease.

## Conflicts of Interest

Author have no conflict of interest to declare.

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