

## Myocardial Injury in Coronavirus Disease 2019 (COVID-19) Patients

The COVID-19 infection which started at the end of December 2019 in Wuhan, China, has now spread to almost 213 countries, infecting more than two and half million individuals and killing over 182,000.<sup>[1]</sup> It is caused by a novel coronavirus (CoV), currently known as the severe acute respiratory syndrome-CoV-2 (SARS-CoV-2). SARS-CoV-2 is the seventh CoV known to infect humans. Beside SARS-CoV-2, four CoVs are known to cause mild common cold symptoms. The other two viruses, namely SARS-CoV (emerged in 2002–2003) and Middle East respiratory syndrome (MERS-CoV) (emerged in 2012 and is still circulating), have resulted in significant respiratory infections.<sup>[2,3]</sup>

Cardiovascular disease (CVD) is a common comorbidity among those with COVID-19. In a study of 191 patients, any comorbidity was found in 48% of COVID-19 patients (67% of nonsurvivors), hypertension (HTN) in 30% (48% of deceased), diabetes mellitus in 19% (31% of deaths), and coronary artery disease (CAD) in 8% (13% of nonsurvivors).<sup>[4]</sup> The cause of the increased vulnerability of patients with CVD to severe COVID-19 presentation is uncertain at present.

SARS-CoV-2 invades Type II alveolar cells<sup>[5]</sup> through the angiotensin-converting enzyme 2 (ACE2) receptor. Although ACE2 receptor acts as the predominant portal of entry for infection, the role of ACE inhibitors or angiotensin receptor blockers (ARB) is still unclear. The general advice for those who are on ARB or ACE inhibitors is to continue their medications for the time being. ACE2 is highly expressed in the heart as well, offsetting the effects of angiotensin II in states with excessive activation of the renin–angiotensin–aldosterone system such as HTN, congestive heart failure (CHF), and atherosclerosis.<sup>[6]</sup>

Myocardial injury, supported by elevated high-sensitivity cardiac Troponin I or elevated cardiac Troponin-T (cTnT) levels, or new electrocardiogram

or echocardiographic abnormalities, has been described in 7.2% of COVID-19 patients overall, and 22% of the critically ill.<sup>[7]</sup> Elevated cTnT levels, a biomarker of myocardial injury, have been reported in acute respiratory distress syndrome (ARDS), which is evident by significant myocardial strain.<sup>[8]</sup> The exact mechanism of myocardial injury in COVID-19 is still not clear. The rise in myocardial injury biomarkers along with other inflammatory biomarkers, such as D-dimer, ferritin, interleukin-6, and lactate dehydrogenase, could raise the possibility that this echoes a cytokine storm or secondary hemophagocytic lymphohistiocytosis more than isolated myocardial injury.<sup>[7]</sup> Inflammation in COVID-19 may be the possible mechanism for myocardial damage. Guo *et al.* reported that myocardial injury is drastically associated with the fatal outcome of COVID-19, while the prognosis in those with underlying CVD but without myocardial injury is relatively promising. Furthermore, Guo *et al.* have linked Troponin-T (TnT) levels with C-reactive protein and N-terminal pro-B type natriuretic peptide (proBNP), which connected the myocardial injury to the severity of inflammation, myocardial dysfunction, and arrhythmias.<sup>[9]</sup> During hospitalization, their data also showed progressive serial increases in both TnT and proBNP levels in those with significant deterioration of their clinical course toward death, whereas in those with mild illness, low levels of these biomarkers had better prognosis that ended with hospital discharge.<sup>[9]</sup>

The reports of patients presenting with predominantly cardiac symptoms could propose a different pattern, potentially viral myocarditis or stress cardiomyopathy. One potential mechanism is direct cardiomyocyte involvement mediated through ACE2. The SARS-CoV-2 RNA was identified in 35% of autopsied hearts.<sup>[10]</sup> Other suggested mechanisms of COVID-19-related cardiac involvement include a cytokine storm, mediated by an imbalanced

response among the subtypes of T helper cells,<sup>[4]</sup> and hypoxia-induced excessive intracellular calcium leading to cardiomyocyte apoptosis.<sup>[11]</sup>

COVID-19 clinical presentation varies from a mild common cold to a severe lower respiratory tract infection leading to ARDS, with fatal outcome. Myocardial injury is one independent risk factor for in-hospital mortality with an incidence of 19.7% of patients during hospitalization.<sup>[12]</sup> It has been reported that patients with established CVD are susceptible to the most adverse complications of COVID-19, including death.<sup>[13-15]</sup> Furthermore, those without any comorbid conditions have a fatality rate of 0.9%, whereas those with the comorbid CVDs have severe illness and much higher mortality rate, 10.5% for those with CAD and CHF and 6% for those with HTN.<sup>[16]</sup>

Affected patients at high risk of serious illness who are in need for intensive care and those at the greatest risk of mortality are older people, particularly those with underlying comorbid disease, with CVD.<sup>[13-15]</sup> Patients with chronic CAD and CVD risk factors for atherosclerosis have a high risk for developing acute coronary syndrome at the time of acute infections similar to previous seasonal influenza infections and increased CVD mortality.<sup>[17]</sup> Those patients, especially the elderly with CHF and acute/fulminant myocarditis, are more prone to hemodynamic decompensation during the severe and aggressive inflammatory responses to COVID-19 infection. They are having similar pathogenicity as in patients with MERS-CoV, so they are expected to have higher risks of adverse effects and mortality compared with healthy younger population. Of note, a study conducted on 87 heart-transplanted recipients showed no higher risk of infection with SARS-CoV-2 if standard preventive processes were applied.<sup>[18]</sup>

In summary, available data linking myocardial injury with high case fatality rate in those with COVID-19 infection are believed as universal for the time being. There is no evidence supporting the idea of withholding the ARB or ACE inhibitors during the pandemic COVID-19. There is also no indication of postponing the cardiac transplantation during this pandemic COVID-19 as long as both the donor and

the recipient are free from COVID19 infection and tested negative. Basic recommendations of strict hand hygiene, physical distancing, and enhanced COVID-19 testing are the mainstay of prevention.

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Equal contribution.

#### Compliance with ethical principles

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**Elhadi H. Aburawi<sup>1</sup>, Ahmed R. Alsuwaidi<sup>1</sup>**

<sup>1</sup>Department of Pediatrics, CMHS, UAE University, Al Ain, Abu Dhabi, UAE

**Address for correspondence:** Prof. Elhadi H. Aburawi,  
Department of Pediatrics, CMHS, UAE University, Al Ain, Abu Dhabi, UAE.  
E-mail: e.aburawi@uaeu.ac.ae


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**Editors:**  
Elmahdi A Elkhammas (Columbus, OH, USA)  
Salem A Beshyah (Abu Dhabi, UAE)