

## Editorial



# Beyond COVID-19 Infection: Long-Term Risks of Cardiovascular Sequelae

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Coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had devastating effects on global health. Although the lungs are the most commonly affected organs by SARS-CoV-2, the involvement of other organ systems, especially the heart, is common.<sup>1)</sup> The mechanisms of cardiovascular injury have not been fully understood but include direct cardiac injury mediated by the combination of SARS-CoV-2 and angiotensin-converting enzyme 2, hypoxic injury, hyperinflammation with cytokine release, endothelial dysfunction, and hypercoagulable state.<sup>2)3)</sup>

It is not uncommon to have prolonged symptom such as fatigue, shortness of breath, and cognitive dysfunction after typical recovery period of COVID-19, known as long COVID.<sup>4)5)</sup> While the relationship has not been fully established between COVID-19 and major long term cardiovascular risk, several epidemiologic data suggest that patients who had COVID-19 might have the increased risk of cardiovascular diseases (CVDs) than those who did not experience COVID-19.<sup>6)7)</sup> In a study of more than 150,000 United States veterans who experienced COVID-19 illness, patients with COVID-19 are at increased risks and burden of incident CVD, including cerebrovascular diseases, arrhythmias, ischemic heart diseases, heart failure, myocarditis, pericarditis, thromboembolic disorders, and other cardiac diseases when compared with controls who did not have COVID-19.<sup>6)</sup> While the risk and one-year burdens revealed a graded increase according to the severity of acute COVID-19 infection, the risks were evident even in people without previous history of CVD.

In this issue of *Journal of Cardiovascular Imaging*, Yim et al.<sup>8)</sup> explore the impact of COVID-19 on cardiac injury with comprehensive echocardiographic evaluation including speckle tracking echocardiography at 4–18 weeks with a median of 80 days after COVID-19 diagnosis. Whereas the most patients showed preserved left ventricular (LV) ejection fraction in 127 patients, 53% patients demonstrated abnormal LV global longitudinal strain defined as < 18% among 74 patients available for speckle tracking assessment. Even in patients without prior history of CVD, the values of LV global longitudinal strain were abnormal in 46%. This subtle LV dysfunction may be attributed to both direct cardiotoxicity and secondary effects from systemic inflammation and hypercoagulable state. In another study of 100 patients recently recovered from COVID-19, cardiac magnetic resonance imaging performed at a median of 71 days after COVID-19 also revealed cardiac involvement in 78% of patients

and ongoing myocardial inflammation in 60% of patients, which was independent of preexisting conditions, severity and overall course of acute illness, and the time from the original diagnosis.<sup>9)</sup> Late gadolinium enhancement was observed in 32% of patients and myocardial native T1 and T2 signals were increased in 73% and 60% of patients, respectively.

However, these intriguing results of current study need to be interpreted in the context of several limitations. First, longitudinal assessment was not available in this study. Since few patients had an echocardiographic examination before COVID-19, it remains uncertain whether this abnormal finding may have already existed and therefore be unlinked to COVID-19. Second, 79% of the patients had serious complications, including 76% pneumonia, 37% intensive care unit admission, and 21% intubation. Therefore, it would limit the generalizability of this dataset to asymptomatic or mildly symptomatic COVID-19 patients. Indeed, another study has shown no considerable and persistent cardiac sequelae 6 months following mild COVID-19 compared with matched control.<sup>10)</sup> Selection bias can occur due to inclusion of COVID-19 patients who underwent echocardiographic assessment over the follow-up visit. Lastly, since the study was performed before COVID vaccine era, vaccination may influence the relationship of this subtle LV dysfunction. Also, type of variants may affect this link differently.

Nevertheless, the evidence raises concerns about the potential long-term effects of COVID-19 on cardiovascular system after recovery of acute COVID-19 infection.<sup>11)12)</sup> Further research would be needed to elucidate better a long-term cardiovascular outcome beyond years. Meanwhile, clinicians may have to consider a history of COVID-19 as one of CVD risks and pay more attention to individuals who experienced COVID-19 for their possible burdens.

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#### Conflict of Interest

The author has no financial conflicts of interest.

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