Editorial

Persistence of coronavirus in the cardiac tissue in patients following recovery from COVID-19

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It is well known that coronavirus disease 2019 (COVID-19) patients present with symptoms involving multiple organs, in addition to its original manifestation of respiratory symptoms. Studies have reported that the coronavirus affects extrapulmonary organs including cardiovascular system (1-5). The cardiac injury associated with COVID-19 includes development of acute myocardial injury, cardiac arrhythmia and other cardiac complications which worsen the prognosis (6-8). Early reports during the pandemic outbreak in 2020 showed that about 12% of COVID-19 patients suffered from acute heart injuries (9), and 5–25% of hospitalised COVID-19 patients had elevations in cardiac troponin which is a biomarker of myocardial injury (9-11). While acute cardiac injury is well recognised and reported in the literature with clear definition, chronic cardiovascular damage associated with COVID-19 patients remains uncertain due to variable clinical manifestations in long-COVID patients. Chronic or long-COVID phase is defined as the situation that signs and symptoms of COVID-19 can last for more than 3 months from the onset of the symptoms (12).

Cardiovascular manifestations of long-COVID are due to multiple cardiac and extracardiac pathological sequelae, which include chest pain, atrial fibrillation, pulmonary hypertension, ventricular dysfunction, postural tachycardia syndrome, etc. Furthermore, studies have reported cardiac complications in patients affected by long-COVID, with frequency ranging from <1% to 27.5% in long-COVID patients requiring hospitalisation (13,14). These complications (relatively high prevalence compared to other less common complications) include chronic myocarditis/pericarditis, myocardial oedema, left ventricle thrombosis, coronary microvascular disease, pulmonary hypertension, and right ventricle systolic dysfunction (12,15). Since long-COVID will lead to increased health care burden in addition to the cost of acute COVID-19 medical expenditure, it is clinically important to improve the diagnosis and treatment of long-COVID patients, specifically, in these with cardiovascular symptoms and complications.

While more evidence is needed to improve our understanding of the underlying mechanisms of cardiovascular long-COVID manifestations, a recent study by Yu *et al.* has provided findings to prove the persistence of coronavirus in the cardiac tissue (16). This is a prospective cohort study and the aim is to investigate the long-term persistence of coronavirus within cardiac tissue in patients who recovered from COVID-19.

Authors prospectively enrolled 41 patients from a single clinical centre who underwent open heart surgery. The

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inclusion criteria are those receiving both left mitral valve replacement and left atrial volume reduction surgery, over 18 years old, negative polymerase chain reaction (PCR) test with no infection symptoms for at least 6 months following recovery from COVID-19 during the Omicron wave with further two negative COVID-19 antigen tests detected prior to surgery. Of 41 patients, 28 underwent mitral valve heart surgery, and nine of them met the selection criteria for inclusion in the study. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA genomes were detected within the surgically resected left atrial tissue in four patients, while in the remaining five patients, SARS-CoV-2 RNA genomes were not detected. There were no significant differences in patient's age, gender, body mass index, or other demographic or clinical characteristics between cardiac tissue SARS-CoV-2 positive and negative groups (P>0.05 for all comparisons) (16). Further analysis of inflammatory factors in the cardiac tissue showed that among the four SARS-Cov-2 positive cases, interleukin (IL)-6 and IL-1β levels were significantly higher in two positive patients than those negative patients without viral colonization within the cardiac tissue. No significant differences were found between the two groups in terms of perioperative and postoperative outcomes, with all patients discharged from the hospital with complete recovery after 3 months of follow-up.

The main contribution of this study by Yu and colleagues lies in providing further evidence about the long-term persistence of coronavirus within cardiac tissue as the patients included in their study exceeded 4 months of recovery period after COVID infection. Previous studies reported the cardiac involvement in individual COVID-19 cases with SARS-CoV-2 RNA even detected in the myocardium 5 months after COVID-19 (8,17-19). It remains unclear regarding the exact timing of viral colonization in recovered or asymptomatic patients following COVID infection, and Yu *et al.* proved the presence of SARS-CoV-2 within the cardiac tissues in 44% (4/9) of patients. The cardiac damage is most likely due to inflammatory injury caused by the coronavirus as indicated by the elevation of inflammatory cytokines (IL-6 and IL-1β). A recent study has reported the capillary paralysis could be persistent for up to 18 months in COVID-19 patients, although whether the damage being reversible remains unclear (20). Therefore, it is imperative to improve our understanding of the mechanisms in long-COVID patients, especially those with damage to the cardiovascular system.

In summary, Yu *et al.* reported the presence of coronavirus within the cardiac tissue in recovered COVID-19 patients even after 6 months of COVID infection. Despite a small number of cases included in this study, findings suggest the colonization of SARS-CoV-2 in the myocardium may induce further inflammatory changes resulting in cardiac damage. Cardiovascular complications will significantly increase the mortality of COVID patients, which includes conditions from acute myocardial injury to fulminant myocarditis, venous thromboembolism and life-threatening arrhythmias. The study findings highlight the importance of paying more attention to long-COVID patients with chronic conditions, especially with cardiac disease.

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