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Epicardial adipose tissue: fuel for COVID-19-induced cardiac injury?

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This Commentary referes to 'Does epicardial fat contribute to COVID-19 myocardial inflammation?', by E.A. Malavazos *et al.*, doi:10.1093/eurheartj/ehaa471.

With coronavirus disease 2019 (COVID-19), cardiac injury has attracted attention owing to the risk of mortality and morbidity. The incidence of cardiac injury associated with COVID-19 reaches 7–31%, depending on the patient population and definitions. Possible mechanisms of the cardiac injury are angiotensin-converting enzyme 2- (ACE2) mediated direct myocardial injury, hypoxia-induced injury, microvascular damage, and systemic inflammatory response syndrome. There are cases of acute myocarditis as a cardiac

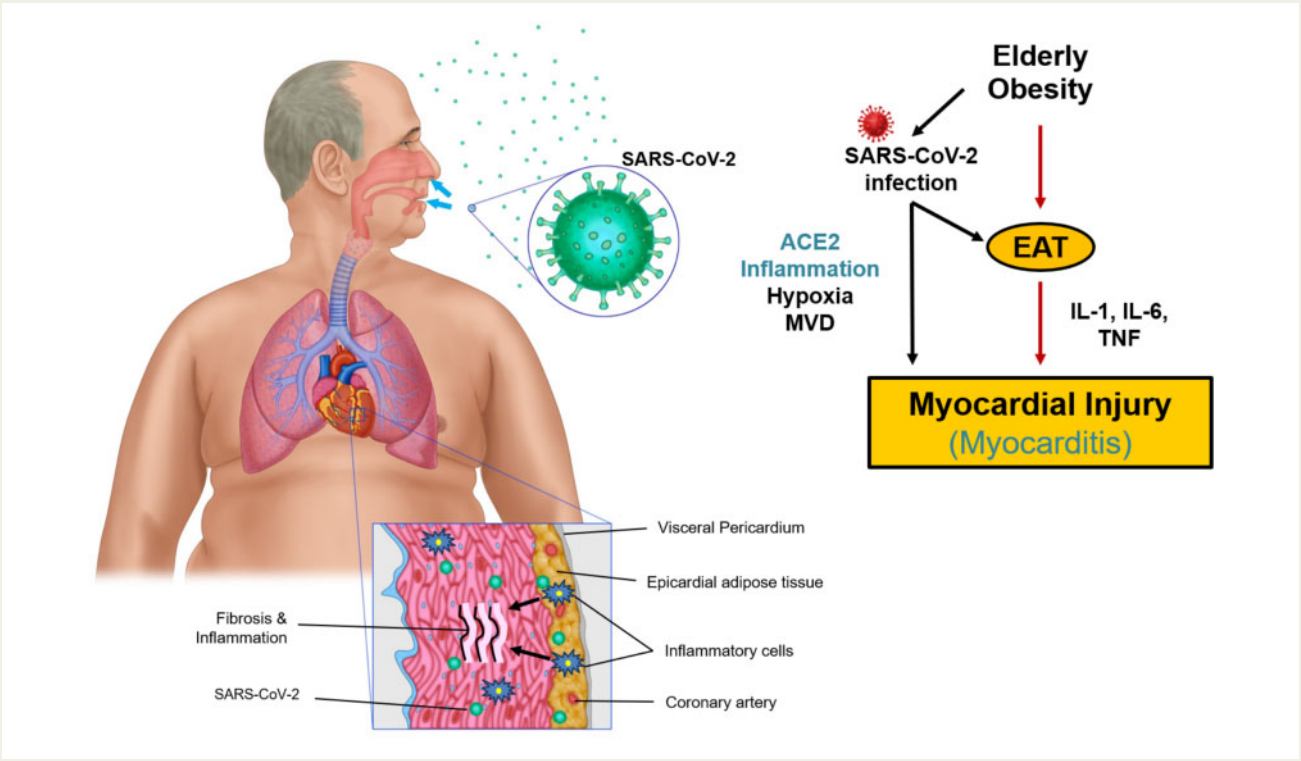

Figure 1 Cardiac injury associated with SARS-CoV-2 and the role of epicardial adipose tissue. EAT, epicardial adipose tissue; ACE2, angiotensin-converting enzyme 2; MVD, microvascular damage; TNF, tumour necrosis factor; IL, interleukin.

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manifestation in COVID-19. Among the possible mechanisms of cardiac injury, ACE2-mediated direct myocardial injury and inflammation are specifically suggested as significant contributors to myocarditis associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections.[1,2]

Epicardial adipose tissue (EAT), located between the myocardium and visceral pericardium, is a unique fat depot with multifaceted features such as local and systemic physiological effects.[3] This tissue has the highest rates of lipogenesis and fatty acid metabolism among the visceral fat depots and displays metabolic, thermogenic, and mechanical properties. Metabolic syndrome, visceral adiposity, and cardiac abnormalities such as coronary artery disease are associated with increased amounts of EAT.[3]

Malavazos *et al.* raised an interesting issue regarding EAT and the incidence of myocardial injury in COVID-19. Since they share similar risk factors and mechanisms related to cardiac inflammation, it can be assumed that patients with cardiac injury would have a higher level of EAT.

The SARS-CoV-2 infection is triggered by binding of the spike protein of the virus to ACE2, which is highly expressed in the heart and lungs. From a previous experiment, ACE2 and the inflammatory cytokines tumour necrosis factor- (TNF) α and interleukin-6 (IL-6) have been demonstrated to be expressed at higher levels in EAT in heart explants removed from obese patients. We may infer that EAT would act as a major contributor for the SARS-CoV-2 entry into the heart and promote an augmented inflammatory response in the myocardium and surrounding structures, causing myocardial complications such as myocarditis and cardiac dysfunction, providing an inflammatory environment by stimulation of inflammatory cells, adipokines, and cytokines.[4] The cascade of inflammatory factors such as TNF-α and IL-6 has been linked to a diminished inotropic effect and decreased cardiac function, resulting in aggravation of hypoxia and a systemic myocardial inflammatory response.[3,4]

Being elderly and being obese are common contributors to EAT and there is an increased chance of SARS-CoV-2 infections in these subjects.[5] The higher prevalence of cardiac injury associated with COVID-19 in these specific populations may be linked to EAT acting as a 'fuel for cardiac inflammation' (*Figure 1*).

From the evidence that EAT plays an essential role as a reservoir for SARS-CoV-2 and the related immune amplification, it is plausible to hypothesize that the amount of EAT is associated with the degree of myocardial damage. However, whether there is a direct association between the amount of EAT measured by echocardiography or computed tomography and the severity of the SARS-CoV-2-related cardiac injury has never been investigated. We need to speculate on the role of EAT in the cardiac manifestations related to COVID-19 with utilization of big data from the accumulating global experience.

Conflict of interest: none declared.

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