COVID-19 and the cardiovascular system

In the current article, Zheng et al (Nat Rev Cardiol 2020;17:259–260, PMID 32139904) provide an up-to-date review of 2019 coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 infects host cells using the host receptor angiotensin-converting enzyme 2 (ACE2). In patients with COVID-19, the incidence of cardiovascular involvement is high, although the specific mechanisms remain uncertain. The mechanism may be related to ACE2, which is expressed not only in the lungs but also in the cardiovascular system; therefore, ACE2-related signaling pathways might also play a role in cardiac injury. Other proposed mechanisms of myocardial injury include a cytokine storm triggered by an imbalanced response by type 1 and type 2 T-helper cells, respiratory dysfunction, and hypoxemia, resulting in damage to myocardial cells. The authors conclude that particular attention should be given to cardiovascular protection during treatment of COVID-19.

A highly conserved cryptic epitope in the receptor binding domains of SARS-CoV-2 and SARS-CoV

In the current study, Yuan et al (Science 2020;368:630, PMID 32245784) investigated the antigenicity of the SARS-CoV-2 virus, which causes COVID-19, by determining the crystal structure of the neutralizing antibody CR3022, isolated from a convalescent SARS patient, in complex with the receptor binding domain (RBD) of the SARS-CoV-2 spike (S) protein at 3.1-Å resolution. CR3022 targets a highly conserved epitope, distal from the receptor binding site, enabling cross-reactive binding between SARS-CoV-2 and SARS-CoV. The investigators further used structural modeling to show that the binding epitope can be accessed by CR3022 only when at least 2 RBDs on the trimeric S protein are in the "up" conformation and slightly rotated. The authors conclude that the availability of conserved epitopes may allow structure-based design not only of a SARS-CoV-2 vaccine but also of cross-protective antibody responses against future coronavirus epidemics and pandemics.

COVID-19, arrhythmic risk, and inflammation: Mind the gap

In the current editorial, Lazzerini et al (Circulation 2020;10.1161/CIRCULATION.120.047293, PMID 32286863) discuss the possible underlying mechanisms for cardiac arrhythmias in patients with COVID-19. An exaggerated host immune response in COVID-19 leads to a cytokine storm and multiorgan dysfunction. High levels of circulating cytokines, particularly interleukin 6 (IL-6), are commonly found in patients with COVID-19 and have been shown to be associated with increased in-hospital mortality. There is a high incidence of cardiac arrhythmias, particularly in patients admitted to the intensive care unit (ICU), with a prevalence of 44%, and malignant ventricular arrhythmias were found in 5.9% of cases. Despite the high incidence of cardiac arrhythmias in ICU patients, only half show evidence of acute cardiac injury, suggesting other factors in addition to myocardial damage in the arrhythmia mechanisms in these patients. Inflammatory cytokines, particularly IL-6, can promote QTc prolongation directly by modulating cardiomyocyte ion channels and indirectly by increasing the bioavailability of concomitant QT-prolonging drugs (via CYP450-3A4 inhibition). The authors conclude that the underlying mechanisms of cardiac arrhythmias in COVID-19 are multifactorial, including cardiac myocyte injury, inflammatory cytokines, and antiviral drugs in combination with other QT-prolonging medications.

Description and proposed management of the acute COVID-19 cardiovascular syndrome

In the current article, Hendren et al (Circulation 2020;doi:10.1161/CIRCULATION.120.047349, PMID 32297796) provide a timely review of acute COVID-19 cardiovascular syndrome (ACoVCS) in a subset of patients with COVID-19. The review summarizes the available data on ACoVCS epidemiology, pathogenesis, diagnosis, and treatment. ACoVCS can manifest as an acute cardiac injury with cardiomyopathy, ventricular arrhythmias, and hemodynamic instability in the absence of obstructive coronary artery disease. Although the etiology remains uncertain, several possible underlying mechanisms include viral myocarditis, microvascular injury, systemic cytokine-mediated injury, or stress-related cardiomyopathy. Systemically elevated cytokines also may be cardiotoxic. The authors conclude that management of ACoVCS should balance the goals of minimizing health care staff exposure during testing that will not change clinical management with early recognition of the syndrome at a time when intervention may be most effective.

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