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Article

At the Heart of the Matter: What do a cardiologist need to know about COVID19?

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Abstract: After the outbreak of the coronavirus disease in late 2019 (COVID-19), an infectious disease caused by a newly discovered coronavirus SARS-CoV-2, the number of confirmed cases worldwide has reached more than 4.2 million, resulting in a death toll of more than 293 thousand (as of May 13, 2020). Common symptoms associated with COVID-19 include fever, cough, loss of appetite, fatigue, short of breath and muscle aches. Loss or disturbances in taste and smell have also been reported in some cases. While most of the focus on COVID-19 has been on its pulmonary complications like pneumonia and acute respiratory distress syndrome (ARDS), emerging evidence suggests that cardiovascular (CV) complications, resulting either from SARS-CoV-2 infection or from adverse effects of pharmacologic therapeutics, could contribute significantly to the mortality associated with COVID-19. This article briefly summarized recent reports on the cardiovascular complications linked to COVID-19 that every cardiologist should be aware of when treating these patients.

Keywords: COVID-19, cardiovascular complications

1. Pathophysiology and clinical features of COVID-19

COVID-19 is caused by acute infection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an enveloped, single-stranded positive-sense RNA virus [1,2]. SARS-CoV-2 accesses host cells using its spike protein, a special surface glycoprotein that binds to its receptor, angiotensin-converting enzyme 2 (ACE2). ACE2 is most abundant in type 2 pneumocytes and enterocytes, and hence lungs and GI tract have been proposed as the primary entry sites for SARS-CoV-2 [3].

Although SARS-CoV-2 has a tropism for ACE2-expressing cells, many of the clinical features of COVID-19 are linked to systemic hyperinflammation or so-called "cytokine release syndrome (CRS)" caused by SARS-CoV-2 infection. Elevation of multiple inflammatory cytokines including IL-2, IL6, IL-7, GM-CSF, MCP-1 and TNF in COVID-19 patients can result in acute lung injury, ARDS, multi-organ failure and death.1 The disruption of immune system, increased metabolic demand and hypercoagulable state likely lead to increased risk of cardiovascular complications [1,4]. Recent evidence also suggest that SARS-CoV-2 could also infect and damage human heart directly through binding at ACE2 receptors expressed in the cardiac tissue [5].

Although the prevalence of cardiovascular complications in COVID-19 patients remains unclear, pre-existing cardiovascular diseases (CVD) have been reported to be associated with increased severity and mortality of COVID-19 [6,7], highlighting the importance of cardiovascular monitoring and early

intervention in these patients to improve the outcomes of COVID-19 patients. This article briefly summarized recent information on CV complications linked to COVID-19 (Figure.1).

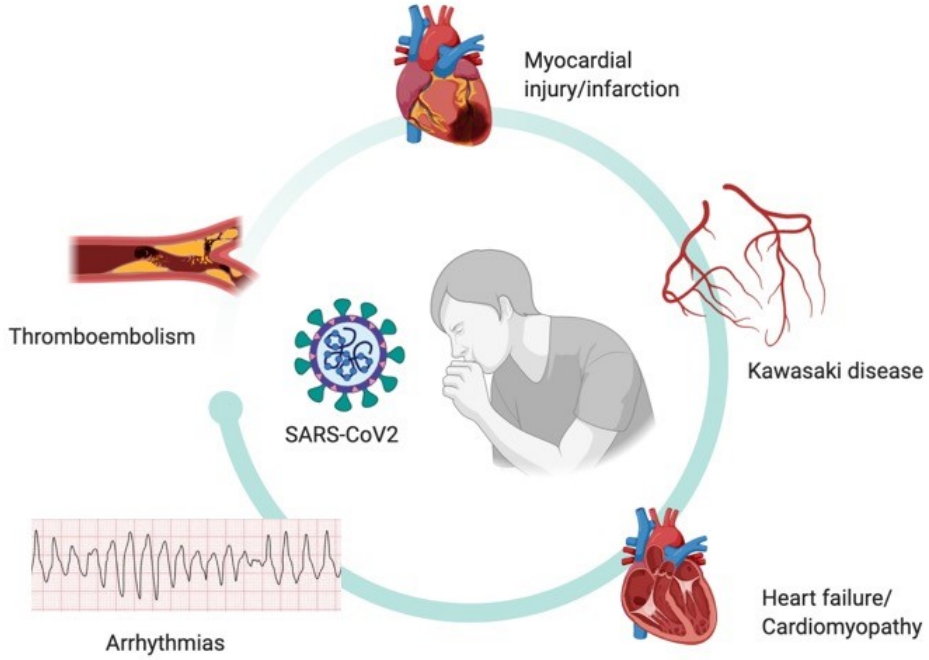

Figure 1. Cardiovascular complications linked to COVID-19

2. Cardiovascular complications associated with COVID-19

2.1. Myocardial injury, myocarditis and myocardial ischemia

Viral infection has been associated with myocardial injury through increased cardiac stress or direct myocardial injury. In a study of 41 COVID-19 patients in Wuhan, 5 (12%) were found to have an increased high-sensitivity troponin 1 level [8]. Another study on 671 severe COVID-19 patients showed that myocardial injury is far more common in those who died of COVID-19 than those who survived (75.8% vs 9.7%, P<0.001). The risk of in-hospital death among severe COVID-19 cases can be predicted by serum markers of myocardial injury, and was significantly associated with age, inflammatory response and co-existing morbidities [9]. High SARS-CoV-2 viral load has been shown to be associated with myocarditis and increased mononuclear infiltrates in autopsy studies on COVID-19 patients [10,11]. It has even been suggested that up to 7% of COVID-19-related death could be owing to myocarditis [12]. Systemic inflammation is known to increase the risk of myocardial ischemia and infarction by provoking plaque disruption in the coronary arteries. The risk of myocardial ischemia and infarction in COVID-19 patients is likely increased owing to systemic inflammation and hypercoagulability [13]. It requires careful clinical assessment to differentiate between post-infection myocardial injury and acute coronary syndrome in COVID-19 as restoration of coronary blood flow could potentially improve the chances of survival in these patients.

2.2. Cardiomyopathy and acute heart failure

Acute heart failure could be one of the primary clinical presentations of COVID-19 patients. One study showed that acute heart failure was the initial presentation of 23% of COVID-19 patients, whereas cardiomyopathy occurred in 33% of cases with COVID-19 [14]. Another study showed that heart failure developed in 24% of COVID-19 cases and was associated with an increased risk of mortality [15]. Up to half of these COVID-19 heart failure cases did not have a known history of hypertension of

pre-existing CVD [15]. It remains unknown if acute heart failure in COVID-19 cases is due to new onset cardiomyopathy or an exacerbation of previously undiagnosed heart failure. Therefore, it is important to be cautious about the potential of acute heart failure in COVID-19 patients when administrating intravenous fluids.

2.3. Thromboembolism

It has been reported that COVID-19 patients are at an increased risk of venous thromboembolism [16,17], which can be attributed to systemic inflammation and multiorgan dysfunction that predispose to a hypercoagulable state. Studies revealed a significant proportion of COVID-19 patients develop coagulopathy, typically with a marked elevation of D-dimer, a modest decrease in platelet count, and a prolongation of the prothrombin time [8,14,16,17]. Coagulopathy in COVID-19 patients is associated with increased risks of death and one report showed that prophylactic heparin in severe COVID-19 patients with coagulopathy was associated with a lower mortality [17,18].

In one way the hypercoagulability observed in severe COVID-19 cases mimics other systemic coagulopathies associated with severe infections, such as thrombotic microangiopathy or disseminated intravascular coagulation, but coagulopathy associated with COVID-19 has distinct features. In sepsis, thrombocytopenia is often more profound, and D-dimer concentrations do not reach the high values seen in COVID-19 patients. In addition, post-mortem studies in COVID-19 patients showed typical microvascular platelet-rich thrombotic deposition in small vessels of the lungs and other organs. However, no signs of hemolysis or schistocytes in the blood smear and the platelet count tends to be higher than would be expected in case of thrombotic microangiopathy. Therefore, patients with severe COVID-19 might need thromboprophylaxis owing to their hypercoagulable state. Currently multiple randomized controlled trials are underway to test this hypothesis.

2.4. Arrhythmias

It has been reported that palpitation presents in > 7% of COVID-19 patients [19]. One study showed that arrhythmias were present in 17% of hospitalized and 44% of ICU patients with COVID-19 [20]. Arrhythmias developed with viral illness could be due to hypoxia, inflammatory stress and metabolic abnormalities. Importantly, many of the medications used in COVID-19 patients are associated with QT prolongation and increased risk of ventricular arrhythmias. For example, antimalarials (chloroquine and hydroxychloroquine), azithromycin, protease inhibitor lopinavir/ritonavir are known to prolong QT intervals. The broad off-label use of hydroxychloroquine and azithromycin in COVID-19 patients raised a great concern about the potential risk of QT prolongation and torsade de pointes, especially in the presence of electrolyte and metabolic imbalance in severe COVID-19 cases.

2.5. Kawasaki disease

Although children have been relatively less affected by COVID-19, increasing number of Kawasaki disease were reported in young children tested positive for SARS-CoV-2 infection [21]. Kawasaki disease is a rare acute pediatric vasculitis, with coronary artery aneurysms as its main complication. In a recent report in Italy, ten cases of a Kawasaki-like disease occurred in Bergamo, Italy, at the peak of the pandemic (Feb 18 to Apr 20, 2020), a monthly incidence 30-fold higher than observed for Kawasaki disease over the previous 5 years (Verdoni L et al, the Lancet 2020, May 13 online). It is believed that this could be a Kawasaki-like disease caused specifically by SARS-CoV-2. It requires further studies to understand the pathophysiology of this emerging pediatric coronary vasculitis associated with COVID-19.

Conflicts of Interest:
The authors declare no conflict of interest.

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