Coronavirus disease 2019 infection and the cardiovascular system
Francesco Romeo\textsuperscript{a}, Giuseppe Calcaterra\textsuperscript{b}, Francesco Barilla\textsuperscript{c} and Jawahar L. Mehta\textsuperscript{d}

In early December 2019, an outbreak of pneumonia, a mysterious illness, initially of unknown origin was detected in Wuhan city, capital of Hubei province, China and reported to the WHO Country Office on 31 December.\textsuperscript{1} By 7 January 2020 the cause of this disease was confirmed to be a new coronavirus (CoV) by the Chinese scientists.\textsuperscript{2} The infection which caused severe acute respiratory syndrome spread rapidly throughout China and then soon around the world and the WHO announced it a pandemic on 11 March 2020.

This virus, initially called SARS-CoV-2 because of some similarities with SARS-CoV that produced an outbreak of SARS in 2003, was officially termed COVID-19 (CoV disease 2019) has a much stronger transmission capacity than SARS-CoV, and is now considered a public health emergency of international concern.

On 30 January, the first case of COVID-19 appeared in Italy. A couple of Chinese tourists coming from Wuhan via Beijing were admitted to Spallanzani Hospital in Rome because of respiratory distress. New cases were detected in another group of Italians who were repatriated from the Wuhan area in Lombardy region. Several of these patients developed severe respiratory distress in the next few days. Because of very large number COVID-19-positive patients and a large number of deaths, Europe is now considered epicentre of this pandemic.

CoVs are a large family of enveloped, positive-sense, single-stranded RNA viruses that are extensively found in bats but can be found in many other birds and mammals including humans.

The CoV genome encodes four major structural proteins: the spike (S) protein, nucleocapsid (N) protein, membrane (M) protein, and the envelope (E) protein. The ‘spikes’ glycoprotein is responsible for facilitating entry of the CoV into the target cell; this tiny molecular key helps the virus to enter host cells by fusing the virus with the structure of the angiotensin-converting enzyme 2 (ACE2) receptor protein, which is on the surfaces of respiratory cell membrane. The structure of the spike protein of SARS-CoV-2 that\textsuperscript{3} causes the current outbreak of COVID-19 has been determined by cryogenic electron microscopy.

COVID-19 also has pathogenicity similar to the Middle East Respiratory Coronavirus.\textsuperscript{4}

The clinical spectrum of COVID-19 infection is diverse, varying from asymptomatic state, mild upper respiratory tract illness, to severe pneumonia with respiratory failure and even death. Although the clinical manifestations of COVID-19 are dominated by respiratory symptoms, some patients experience severe myocarditis and heart failure. COVID-19 infection, like any other viral infection, can affect the heart by direct migration from the lungs to the adjacent cardiac structures. Myocardial injury may also be a result of a cytokine storm during respiratory dysfunction and hypoxaemia caused by COVID-19 triggered by an imbalanced response of type 1 and type 2 T-helper cells and resulting in damage to myocardial cells, that is myocarditis.\textsuperscript{1,2,7}

Myocardial injury associated with the COVID-19 occurred in some of the first 41 patients diagnosed with COVID-19 in Wuhan, which mainly manifested as an increase in high-sensitivity cardiac troponin I levels (>28 pg/ml), which indicates the serious nature of the myocardial injury in patients with COVID-19.\textsuperscript{1} Recently, there was report of a patient in China who developed severe infection with COVID-19, had ECG manifestation of acute coronary event (TnT $\rightarrow$ 1000 pg/ml), had normal coronary angiogram and recovered following treatment with corticosteroids and immunoglobin.\textsuperscript{5} Cardiac involvement in COVID-19 infection may be transient, or severe enough to require intensive care and in result death.\textsuperscript{6}

Myocardial damage caused by infection with CoVs undoubtedly increases the difficulty and complexity of patient treatment. Generally speaking, patients with
underlying cardiovascular disease (CVD) who develop COVID-2 infection have increased risk of death. Of special note, patients with acute coronary syndrome and others with preexisting CVD who are infected with COVID-19 may have a poor prognosis. Therefore, understanding the damage caused by COVID-19 to the CV system is of great importance, so that treatment of these patients can be timely and effective.

There is always a question of how to treat patients with COVID-19 infection who present with STEMI-like picture. Since primary percutaneous coronary intervention is the state-of-the-art therapy, current recommendations ACC’s Interventional Council and SCAI are that appropriate personal protective equipment (PPE) should be worn including gown, gloves, goggles (or shields), and a N95 mask, especially given the limited ability to take a history from the patient as well as the potential for clinical deterioration in STEMI cases. The use of Powered Air Purifying Respirator (PAPR) systems may also be reasonable, especially for patients who may be vomiting (e.g. inferior STEMI), or those who may require CPR and/or intubation. It seems that COVID-19 was nearly tailor-made for the human body. Although it seems to have emerged from bats or species that bats feed on, current thinking is that there are a number of these ‘SARS-like’ viruses present in bat communities that use ACE2 receptors to invade cells. The receptors exist in multiple species, including humans, and are ubiquitous and present in the heart, lung, kidney and intestine.

ACE is a pivotal component of the renin–angiotensin system, mediating numerous systemic and local effects on the CV system. ACE is produced in the endothelium of somatic tissues as a transmembrane protein containing two active domains, both of which are inhibited by ACE inhibitors.

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ACE2 has been identified as a functional receptor for CoVs, including SARS-CoV and COVID-19. COVID-19

![Diagram](image-url)
infection is triggered by binding of the spike protein of the virus to ACE2, which is highly expressed in the heart and lungs. COVID-19 mainly invades alveolar epithelial cells, resulting in respiratory symptoms perhaps by binding to ACE2 receptors (Fig. 2). It has been postulated that symptoms of COVID-19 infection are more severe and subsequent mortality is higher in patients with CVD, perhaps because of increased expression of ACE2.

The expression of ACE2 is increased in patients with diabetes, especially those treated with ACE inhibitors and angiotensin II type-I receptor blockers (ARBs). Treatment with ACE inhibitors and ARBs results in an upregulation of ACE2. ACE2 can also be increased by treatment with ibuprofen. Thus, it has been hypothesized that patients with diabetes and hypertension treated with ACE2-stimulating drugs may result in severe and fatal COVID-19. This has been addressed in scientific and lay media. However, there is no clinical evidence that use of ACE inhibitors or ARBs should be curtailed in patients with COVID-19 infection. Similarly, at this time there is no concrete evidence to limit the use of ibuprofen.

COVID-19 infection has spread farther and faster than SARS, and it has somewhat different clinical characteristics. For instance, unlike the SARS outbreak in the early 2000s, when viral shedding began days after symptoms emerged, viral shedding of COVID-19 can start 24–48 h before symptoms appear. COVID-19 infection may be five to 35 times more deadly than seasonal influenza.

COVID-19 is thought to infect host lung cells through binding to ACE2 receptors, but it can cause damage to the heart, although the specific mechanisms are uncertain. Patients with underlying CVD and COVID-19 infection have an adverse prognosis. Therefore, particular attention should be given to cardiovascular protection during treatment for COVID-19.

At the moment, there are no specific therapeutics for patients who develop cardiac manifestations of COVID-19 infection. Thus, the management includes patient isolation, and supportive intensive medical care.

Acknowledgements
Conflicts of interest
None declared.

References

Schematic design of angiotensin-converting enzyme 2 is the host cell receptor thought to be a mediator of pathology caused by coronavirus disease 2019 infection. Antibodies directed at angiotensin-converting enzyme 2 thereby may be useful as therapeutic measure.