EDITORIAL

COVID-19 and cardiovascular disease

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INTRODUCTION

In December 2019, a cluster of patients with pneumonia of unknown cause was linked to a seafood wholesale market in Wuhan, China. A previously unknown betacoronavirus was discovered through unbiased sequencing in samples from patients with pneumonia. Human airway epithelial cells were used to isolate a novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or 2019-nCoV for short (Figure 1). SARS-CoV-2 formed a clade within the subgenus sarbecovirus, subfamily Orthocoronavirinae. Different from both MERS-CoV and SARS-CoV, 2019-nCoV is the seventh member of the family of coronaviruses that infect humans. Coronavirus disease (COVID-19) is the clinical infectious disease syndrome caused by SARS-CoV-2.[1] SARS-CoV-2 infects host cells through the angiotensin-converting enzyme type 2 (ACE2) receptors, leading to COVID-19-related pneumonia and multiorgan dysfunction, while also causing acute myocardial injury and chronic damage to the cardiovascular system.

The most common symptoms of COVID-19 are fever, breathlessness, fatigue and dry cough. Some patients may have muscular aches and pains, nasal congestion, runny nose, sore throat or diarrhoea. Symptoms are usually mild and begin gradually. Many people become infected but remain asymptomatic. Over 80% will recover from the disease without needing special treatment. Around 1 out of every 6 people who gets COVID-19 becomes seriously ill and develops difficulty breathing. Older people, and those with underlying medical problems like high blood pressure, cardiovascular disease (CVD), lung disease, cancer or diabetes, are more likely to develop serious illness.

COVID-19 is transmitted from those who have been infected by SARS-CoV-2. The disease can spread from person to person through small droplets from the nose or mouth, which are spread when a person with COVID-19 coughs or exhales. These droplets land on objects and surfaces around the person. The virus may remain viable on hard surfaces for days. Other people then catch COVID-19 by touching these objects or surfaces, then touching their eyes, nose or mouth. Individuals

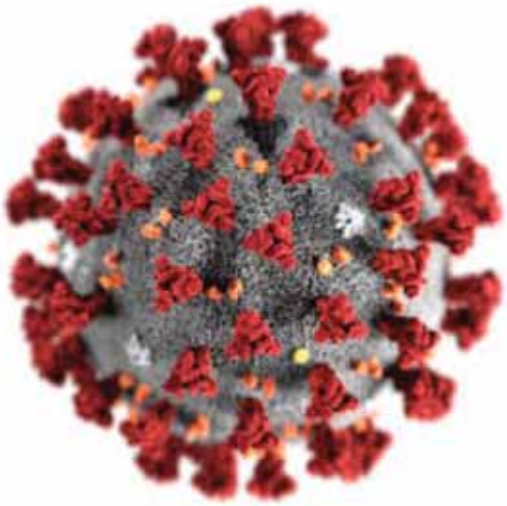

FIGURE 1: Illustration of 2019-nCoV.
Credit: US Centres for Disease Control and Prevention.

also catch COVID-19 if they breathe in droplets from a person with COVID-19 who coughs out or exhales droplets. Hence the primacy of physical distancing as a fundamental public health concept: staying more than 1.5 metres away from a person who is sick to prevent transmission. The incubation period refers to the time between catching the virus and beginning to have symptoms of the disease. Most estimates of the incubation period for COVID-19 range from 1 - 14 days, but most commonly it is around 5 days. Asymptomatic individuals are still capable of transmitting the virus.

The primary pathology of COVID-19 is acute respiratory distress syndrome (ARDS), characterised by diffuse alveolar damage (e.g. including hyaline membranes). Pneumocytes with viral cytopathic effect are seen, implying direct virus damage rather than a purely hyper-inflammatory injury. Emerging evidence suggests that some patients may respond to COVID-19 with an exuberant "cytokine storm" reaction, with features of bacterial sepsis or haemophagocytic lymphohistiocytosis. Clinical markers of this cytokine storm include elevations of C-reactive protein, interleukin-6 and ferritin, which appear to track with disease severity and mortality.

Pathophysiologically, there are different stages of COVID-19: (i) an initial replicative phase, occurring over a period of several days characterised by an innate immune response and relatively mild symptoms due to direct viral cytopathic effect and innate immune responses; and (ii) an adaptive immunity stage characterised by falling viral titres and increased inflammatory cytokines, which lead to tissue damage, causing clinical deterioration. Disease progression may explain the clinical phenomenon where patients have mild symptoms for a few days, and then suddenly deteriorate when they enter the adaptive immunity stage.

Epidemiologically, disease spread in the population occurs in 3 phases: (i) stage 1 with only imported cases; (ii) stage 2 with limited community transmission; and (iii) stage 3 with widespread community transmission. Evidence-based public health interventions that reduce disease transmission include hand hygiene and social distancing.

COVID-19 AND CARDIOVASCULAR DISEASE

Although the clinical manifestations of COVID-19 are predominantly respiratory, some patients may have clinical evidence of cardiovascular injury.[2] Further, patients with cardiovascular disease (CVD) have an increased risk of severe presentations and increased mortality. Hence, understanding the damage caused by SARS-CoV-2 to the cardiovascular system is of importance.

SARS-CoV-2 and ACE2

ACE2 is a membrane-bound aminopeptidase important for the cardiovascular and immune systems.[3] ACE2 plays an important role in regulation of cardiovascular function, cardiovascular remodelling and genesis of hypertension and diabetes, and is highly expressed in the heart and lungs. ACE2 is the functional receptor for coronaviruses including SARS-CoV and SARS-CoV-2. Through binding the ACE2 receptor, SARS-CoV-2 mainly invades alveolar epithelial cells, resulting in respiratory symptoms, which are more severe in patients with CVD, likely due to increased secretion of ACE2 in these patients. Furthermore, ACE2 levels can be increased using renin–angiotensin–aldosterone system inhibitors. Given that ACE2 is a functional receptor for SARS-CoV-2, the safety and potential effects of antihypertension therapy with ACE inhibitors or angiotensin-receptor blockers in patients with COVID-19 have been considered and, to date, there has been no signal that use of ACE inhibitors, angiotensin receptor blockers and mineralocorticoid receptor antagonists are associated with adverse outcomes in COVID-19 patients.

SARS-CoV-2 and acute myocardial injury

Myocarditis and myocardial injury associated with the SARS-CoV-2 occurred in 5 of the first 41 patients diagnosed with COVID-19 in Wuhan, which mainly manifested as an increase in high-sensitivity cardiac troponin I levels.[4] Eighty percent of patients with myocardial injury were admitted to the intensive-care unit (ICU), which indicates the serious nature of the myocardial injury in patients with COVID-19. Blood pressure levels were significantly higher in patients treated in the ICU than in those not treated in the ICU.[4] In a different report, levels of biomarkers of myocardial injury were significantly higher in patients treated in the ICU than in those not treated in the ICU,[5] suggesting that patients with severe symptoms often have complications involving acute myocardial injury. Among the confirmed cases of SARS-CoV-2 infection reported by the National Health Commission of China, some of the patients first went to see a doctor because of cardiovascular symptoms. The patients presented with heart palpitations and chest tightness rather than with respiratory symptoms, such as fever and cough, but were later diagnosed with COVID-19. In patients with COVID-19, the incidence of cardiovascular symptoms is high, owing to the systemic inflammatory response and immune system disorders during disease progression. The mechanism of acute myocardial injury caused by SARS-CoV-2 infection might be related to ACE2-related signalling pathways, the cytokine storm triggered by an imbalanced response by type 1 and type 2 T helper cells, and respiratory dysfunction and hypoxaemia caused by COVID-19.

SARS-CoV-2 and chronic cardiac injury

Given that SARS-CoV-2 has a similar structure to SARS-CoV, this novel virus might also cause chronic damage to the cardiovascular system, and attention should be given to cardiovascular protection during treatment for COVID-19. A 12-year follow-up survey of 25 patients who recovered from SARS-CoV infection found that 68% had hyperlipidaemia, 44% had cardiovascular system abnormalities and 60% had glucose metabolism disorders.[6] COVID-19 is also associated with a hypercoagulable state and increased risk of deep vein thrombosis and pulmonary embolism.

SARS-CoV-2 and pre-existing cardiovascular disease

Elderly people with comorbidities are more likely to be infected with SARS-CoV-2, especially those with hypertension, coronary heart disease or diabetes. Furthermore, patients with CVD are more likely to develop severe symptoms if infected with SARS-CoV-2. Therefore, patients with CVD account for a large proportion of deaths from COVID-19. For patients with severe symptoms of COVID-19, 58% had hypertension, 25% had heart disease and 44% had arrhythmia.[6] Thirty-five percent of patients with SARS-CoV-2 infection had a history of hypertension and 17% had a history of coronary heart disease. Patients with acute coronary syndrome (ACS) who are infected with SARS-CoV-2 often have a poor prognosis. In patients with ACS, cardiac functional reserve can be reduced owing to myocardial ischaemia or necrosis. Drug-related heart damage during COVID-19 treatment is a concern. In particular, the use of antiviral drugs should be monitored. Many antiviral drugs can cause cardiac insufficiency, arrhythmia or other cardiovascular disorders; therefore, during treatment of COVID-19, especially with the use of antivirals, the risk of cardiac toxicity must be closely monitored.[7]

COVID-19 AND CARDIOVASCULAR HEALTHCARE WORKERS

Worldwide, as millions of people stay at home to minimise transmission of SARS-CoV-2, healthcare workers prepare to do the exact opposite. As the pandemic accelerates, access to personal protective equipment (PPE) for health workers is a key concern. Medical staff are prioritised in many countries, but PPE shortages have been described in the most affected facilities. Some medical staff are waiting for equipment while already seeing patients who may be infected or are supplied with equipment that might not meet requirements. Alongside concerns for their personal safety, healthcare workers are anxious about passing the infection to their families. Healthcare workers who care for elderly parents or young children will be drastically affected by school closures, social distancing policies, and disruption in the availability of food and other essentials.

Sonographers, nurses, technicians, radiographers and physicians have a duty to care for patients and are at the frontlines in the battle against disease. We are at high risk, particularly when we participate in the care of patients who are suspected or confirmed to have highly contagious diseases. While dedication to patient care is at the heart of our profession, we also have a duty to care for ourselves and our loved ones and to protect all our patients by preventing the spread of disease. This means reducing our own risk while practicing judicious use of PPE. Cardiology staff who undertake procedures that increase the risk of transmission, including echocardiography, cardiac catheterisation and cardiopulmonary resuscitation (including endotracheal intubation) need to take precautions to protect themselves from the risk of COVID-19. Echocardiographic services should not be ordered if they are unlikely to provide clinical benefit. Repeat echocardiograms should not be performed unless there has been a clear change in clinical status. The portability of echocardiography affords a clear advantage in imaging patients without having to move them and risk virus transmission in the clinic or hospital. In addition, staff should be vaccinated against influenza, as the flu season has been particularly devastating in the northern hemisphere this year.

Healthcare systems globally could be operating at more than maximum capacity for many months. Healthcare workers, unlike ventilators or wards, cannot be urgently manufactured or run at 100% capacity or occupancy for long periods. It is vital that governments see workers not simply as pawns to be deployed, but as human individuals. In the global response, the safety of healthcare workers must be ensured. Adequate provision of PPE is just the first step; other practical measures must be considered, including cancelling non-essential services to prioritise resources; provision of food, rest, and family support; and psychological support. Presently, healthcare workers are every country's most valuable resource.

CONCLUSION

SARS-CoV-2 is a new virus that infects host cells through ACE2 to cause COVID-19, while also causing damage to the myocardium. Patients with underlying CVD and SARS-CoV-2 infection have an adverse prognosis. Therefore, attention should be given to cardiovascular protection during treatment for COVID-19. Cardiovascular staff are at a particularly increased risk and need to take important precautionary measures to reduce infection.

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HELPFUL RESOURCES

https://sacoronavirus.co.za
http://www.nicd.ac.za
https://www.who.int/emergencies/diseases/novel-coronavirus-2019

Conflict of interest: none declared.

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