

## VIEWPOINT

# An Acute Respiratory Infection Runs Into the Most Common Noncommunicable Epidemic—COVID-19 and Cardiovascular Diseases

**Chengzhi Yang, MD, PhD**

Department of Cardiology and Macrovascular Disease, Beijing Tiantan Hospital, Capital Medical University, Beijing, China.

**Zening Jin, MD, PhD**

Department of Cardiology and Macrovascular Disease, Beijing Tiantan Hospital, Capital Medical University, Beijing, China.



Editorial

## Corresponding

**Authors:** Zening Jin, MD, PhD ([jin\\_zening@163.com](mailto:jin_zening@163.com)), and Chengzhi Yang, MD, PhD ([yangcz@hsc.pku.edu.cn](mailto:yangcz@hsc.pku.edu.cn)), Department of Cardiology and Macrovascular Disease, Beijing Tiantan Hospital, No. 119 South Fourth Ring West Rd, Beijing 100070, China.

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**The outbreak** of novel coronavirus disease 2019 (COVID-19), which emerged in Wuhan, China, in December 2019, has rapidly spread to more than 58 countries and areas.<sup>1</sup> As of March 1, 2020, about 79 968 cases in mainland China have been confirmed and 2873 deaths have occurred.<sup>1</sup> The Chinese government is mustering medical personnel around the country to treat patients in Hubei province and preventing further spread of COVID-19 in every region of the country.

At the same time, several studies concerning the epidemiological and clinical features of COVID-19 have been published in a timely manner, which has greatly helped health care workers and policy makers to understand COVID-19. Reading these reports, we noticed that many patients with COVID-19 had comorbid chronic cardiovascular diseases (CVDs), which collectively represent the most common noncommunicable epidemic in China currently. Among 44 672 individuals confirmed to have COVID-19 as of February 11, 2020, 2683 patients (12.8%) had hypertension and 873 (4.2%) had CVDs,<sup>2</sup> which were the most common coexisting conditions in patients hospitalized with COVID-19.<sup>3,4</sup> Furthermore, patients with comorbid CVDs were more likely to have severe illness associated with COVID-19 and had a much higher fatality rate: 10.5% for those with CVDs and 6.0% for hypertension, while the fatality rate was 0.9% in patients who reported no comorbid conditions.<sup>2</sup> This information indicated that individuals with underlying chronic CVDs were both more susceptible to COVID-19 and more prone to critical conditions and death. It is well known that acute pulmonary infection can potentially destabilize cardiac diseases, such as heart failure and coronary artery disease. Then deterioration of cardiac diseases would exacerbate COVID-19 management in turn.

However, inadequate attention has been paid to comorbid CVDs in patients with COVID-19. Hitherto, to our knowledge, academic reports regarding clinical features of COVID-19 did not classify cardiovascular disorders clearly. For instance, the number of patients with specific cardiovascular diseases, including ischemic heart disease, heart failure, cardiac arrhythmia, and other conditions, were not provided. In addition, hypertension was reported independently of CVDs, even though it is clearly a CVD. It is possible that these CVDs have varying associations with COVID-19 prognosis.

Dyspnea and fatigue, 2 cardinal symptoms of heart failure, are very common in patients with COVID-19, particularly in its severe stages.<sup>4,5</sup> Hence, the diagnosis of COVID-19 is made more difficult in patients with chronic heart failure. Also, both COVID-19 and heart failure give rise to hypoxemia, which is the basic pathophysiologi-

cal mechanism leading to death.<sup>5</sup> Additionally, the systemic inflammatory response in COVID-19 may trigger rupture or erosion of coronary plaques in patients with underlying coronary artery disease. Patients with active COVID-19 can hardly survive a myocardial infarction. Moreover, hypoxemia caused by COVID-19 may bring about atrial fibrillation, which is the most common arrhythmia among elderly individuals, and atrial fibrillation could be refractory before the pulmonary function is improved. The systemic inflammatory response would make the anticoagulation therapy for atrial fibrillation very complex.

Currently, there have been only scarce data with respect to cardiovascular complications of COVID-19. A recent study presented by Wang et al<sup>3</sup> showed that acute cardiac injury, defined as troponin I elevation or new abnormalities detected with electrocardiography and echocardiography, was found in 10 patients (7.2%) with COVID-19. In addition, arrhythmia was found in 23 patients (16.7%). However, they did not provide clear classification of arrhythmia and echocardiographic parameters. Notably, severe acute respiratory syndrome coronavirus (SARS-CoV), which caused a global epidemic in 2003, is recognized as a sister to severe acute respiratory syndrome coronavirus 2 that causes COVID-19 (SARS-CoV-2).<sup>6</sup> Therefore, it is possible that these 2 viruses have similar effects on the heart. Yu et al<sup>7</sup> reported that tachycardia was present in 71.9% of patients with SARS, and bradycardia occurred in 14.9% as a transient event. It is thus possible that tachycardia might be a common arrhythmia in patients with COVID-19.

In addition, acute cardiac injury was found in 5 patients (14%) with COVID-19 in another study.<sup>4</sup> The cardiac injury may result from viral infection, hypoxemia, and deterioration of underlying cardiac diseases. Reports concerning myocarditis in humans by coronavirus are very rare. At present, to our knowledge, the sole pathological investigation<sup>8</sup> involved biopsy samples at autopsy of a patient who died of COVID-19, which showed a few mononuclear inflammatory infiltrates in the myocardial interstitium, without substantial damage in the heart tissue. This finding suggests that the SARS-CoV-2 virus might cause myocarditis. In a study of 46 patients with SARS, Li et al<sup>9</sup> found subclinical diastolic impairment, which may be reversible on clinical recovery, but there was no interstitial lymphocytic infiltrate or myocyte necrosis in the heart of a patient with the lowest left ventricular ejection fraction.<sup>9</sup> It was postulated that the temporary diastolic impairment detected by echocardiography might be attributable to systemic inflammatory storm resulting from an

overaggressive host immune response to viral infection, given that several studies suggested several cytokines, such as tumor necrosis factor and the interleukin-6 family, have clinically significant negative inotropic influence. Further detection by whole-genome sequencing, direct polymerase chain reaction, and culture with biopsy samples may help to identify whether SARS-CoV-2 is present in myocardium. Cardiac magnetic resonance imaging may be helpful to detect cardiac injury noninvasively.

Of note, several investigations have demonstrated that SARS-CoV-2 and SARS-CoV share the same host receptor, angiotensin-converting enzyme 2 (ACE2),<sup>6</sup> which may have many protective effects on CVDs.<sup>10</sup> A recent study revealed that affinity of SARS-CoV-2 binding to ACE2 was 10-fold to 20-fold higher than that of SARS-CoV,<sup>6</sup> which suggests SARS-CoV-2 could spread from human to human easily. Therefore, ACE2 may play 2 contrary roles in patients with COVID-19, especially those with comorbid CVDs. On the one hand, ACE2 may provide protection against hypertension, myocardial fibrosis, myocardial hypertrophy, arrhythmia, atherosclerosis, and sodium-water retention.<sup>10</sup> On the other hand, ACE2 acts as the gate for SARS-CoV-2 infection.<sup>6</sup> Previous studies have shown that angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) could upregulate the expression or prevent the loss of ACE2, which is one

of the mechanisms of ACEI/ARB activity.<sup>10</sup> At this point in our knowledge, it is conceivable that ACEI/ARB therapy might increase the risk of SARS-CoV-2 infection. However, experimental evidence indicates that the ARB losartan and recombinant human ACE2 can protect mice from severe acute lung injury induced by acid aspiration or sepsis. Considering that ACEI/ARB therapy is widely prescribed to patients with hypertension, heart failure, and ischemia heart disease, additional attention should be paid to patients with COVID-19 and close contacts who are using ACEI/ARB therapy.

To date, many patients with COVID-19 are still hospitalized in China and other countries, such as Italy and Iran. Therefore, continued observations of the cardiovascular complications of the disease are needed. In addition, further assessment is needed to identify risk factors for poor prognosis.

Emerging as an acute infectious disease, COVID-19 may become a chronic epidemic similar to influenza because of genetic recombination. Therefore, we should be ready for the reemergence of COVID-19 or other coronaviruses. Considering that CVDs represent the leading noncommunicable epidemic around the world and numerous patients with CVDs are using ACEI/ARB, clinical studies may be necessary to explore the potential associations of ACEI/ARB with susceptibility and prognosis of COVID-19.

#### ARTICLE INFORMATION

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#### REFERENCES

- World Health Organization. Coronavirus disease 2019 (COVID-19) situation report—41. Published March 1, 2020. Accessed February 29, 2020. [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200301-sitrep-41-covid-19.pdf?sfvrsn=6768306d\\_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200301-sitrep-41-covid-19.pdf?sfvrsn=6768306d_2)
- Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological

characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghua Liu Xing Bing Xue Za Zhi*. Article published in Chinese. 2020;41(2):145-151.

3. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. Published online February 7, 2020. doi:10.1001/jama.2020.1585

4. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5

5. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. doi:10.1016/S0140-6736(20)30211-7

6. Wrapp D, Wang N, Corbett KS, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion

conformation. *Science*. 2020;b2507. doi:10.1126/science.abb2507

7. Yu CM, Wong RS, Wu EB, et al. Cardiovascular complications of severe acute respiratory syndrome. *Postgrad Med J*. 2006;82(964):140-144. doi:10.1136/pgmj.2005.037515

8. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020;S2213-2600(20)30076-X. doi:10.1016/S2213-2600(20)30076-X

9. Li SS, Cheng CW, Fu CL, et al. Left ventricular performance in patients with severe acute respiratory syndrome. *Circulation*. 2003;108(15):1798-1803. doi:10.1161/01.CIR.0000094737.21775.32

10. Patel VB, Zhong JC, Grant MB, Oudit GY. Role of the ACE2/angiotensin 1-7 axis of the renin-angiotensin system in heart failure. *Circ Res*. 2016;118(8):1313-1326. doi:10.1161/CIRCRESAHA.116.307708