Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

Commentary: What is the relationship between Covid-19 and cardiovascular disease?

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Compared to other sections of medicine, cardiology only has a marginal role in the fight against Covid-19. Nevertheless, cardiologists are potentially involved in this story in at least three ways:

1) **A number of cardiovascular diseases may increase mortality among affected patients**.

Covid-19 appears less pathogenic than previous viruses such as SARS-COV or MERS-COV. But, deaths in the Wuhan Province where the Covid-19 epidemic started were between 0.5% to 2.5% [1]. In Europe, where the virus has recently migrated, the rate may be higher from 4% to 6%. However, the death rate depends on the number of infected people which is, at present, still unknown. Hypertension or coronary heart disease is present in 38% and diabetes in 19% of COVID-19 patients [2]. A report on 136 Covid-19 patients shows that 26% of them required cardiovascular intensive care. They had a higher rate of death and a higher prevalence of diabetes and cardiovascular disease than those not requiring intensive care [3]. A recent report on 72.314 cases from the Chinese centre of the disease control shows a mean death rate of 2.3% which increases to 5% in patients with cardiovascular disease and to 7.3% in those with diabetes [4,5]. Although the vulnerability of the patients with heart diseases to Covid-19 is quite evident in these reports, the single study using multivariable regression analysis shows that only older age, higher Sequential Organ Failure Assessment Score and high values of d-dimer on admission are independent predictive values of mortality [2].

2) **Viral infection could be the cause or a contributory cause of a new heart disease**.

The National Health Commission of China reported that often the first contact of patients with doctors is with reported palpitations or chest pain rather than respiratory symptoms. Only later are they diagnosed as positive for Covid-19 [6]. Some Covid-19 patients have high sensitivity cardiac troponin 1 levels, suggesting myocardial injury [6]. 26% of patients hospitalised at Zhongnan University Hospital of Wuhan required cardiovascular intensive care. Of these, 16.7% developed arrhythmias and 7.2% and acute coronary syndrome [3].

It is unclear whether these cardiac conditions are provoked by Covid-19 or are just comorbidities or non-specific complications of infection. Studies during the flu epidemic in the USA and clinical practice show that inflammation due to flu may destabilise coronary plaque and cause myocardial infarction (MI) [6] This, in turn, is due to multiple mechanisms such as tachycardia, hypoxia, increased wall stress and inflammatory cytokines as well as thrombophilia [7]. Similar links with MI were shown for more recent epidemics of SARS and Covid-19 [8]. Only future studies will establish a possible relationship between Covid-19 and coronary artery disease. Only the awareness of such a link will encourage the cardiovascular community to search for it and to set appropriate studies to clarify this issue.

3) **Drugs for patients with cardiovascular disease could interfere with the pathophysiology of Covid-19**.

As was the case for the SARS-COV infection, the receptor for the new 2019 Covid-19 is human angiotensin-converting enzyme 2 (ACE2), a homologue of ACE1 [6]. The virus spike protein binds to ACE2 which allows the penetration of the virus into the epithelial cells of the lungs. ACE2 is found primarily in the lower respiratory tract, rather than in the upper airway [9]. This distribution can explain the few upper respiratory tract symptoms typical of flu and why Covid-19 is not just a common cold [9]. Contrary to ACE1 which converts angiotensin 1 to angiotensin 2 and is a therapeutic

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target for hypertension and heart failure, the biology of ACE2 and its therapeutic potential is unclear [6]. It is believed that ACE2 plays an antagonist part to the effects of ACE1, converting angiotensin 2 back to angiotensin 1. In view of the role of ACE2 in the penetration of 2019-nCov, drugs such as angiotensin 2 receptor blockers (ARBs) that increase angiotensin 2 plasma levels could activate ACE2 and an adverse Covid-19 pandemic [10]. ARBs are mainly prescribed for hypertension and it has been suggested that alternative drugs to ARBs should be used to treat hypertension during the Covid-19 pandemic [10]. The caveats here are a) there is no evidence of increased ACE2 expression with ARBs in the lung b) ACE2 expression is reduced in hypertension models c) hypertension and its treatment with ARBs did not affect previous coronavirus infections.

The same considerations apply to heart failure.

Although this hypothesis should be considered and further investigated, at present the discontinuation of ARBs in hypertensive and heart failure patients is not supported by any evidence.

Finally, although the cardiovascular side effects of the current drugs empirically used for the Covid-19 infection and now tested in experimental protocols (such as anti-viral–remdisivir or lopinavir+ritonavir– or anti-leukin 6 –tocilizumab– or other antinflammatory –chloroquine–) are rare and not serious, an active surveillance is mandatory.

In conclusion, besides the possible impact of Covid-19 on cardiology, the pandemic has created a perfect storm for the health organisations across the globe. Cardiologists must be aware of the organisational, emotional, and clinical consequences of this drama and should react accordingly.

Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

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