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EDITORIAL NOTE

COVID-19 and cardiovascular comorbidities: An update

COVID-19 e comorbilidades cardiovasculares: uma atualização

On December 8, 2019, a case of pneumonia of unknown etiology was detected in Wuhan city, Hubei province, China.[1] On December 31, China reported a cluster of cases of pneumonia with unknown etiology to the World Health Organization (WHO), and seven days later, Chinese scientists identified the pathogen as a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The WHO declared the outbreak a pandemic on 11 March 2020, due to the increasing number of cases outside China.[2] The pandemic is spreading exponentially, with millions of people across the globe at risk of contracting coronavirus disease 2019 (COVID-19).

Since January 2020 various series of COVID-19 patients have been published from China,[3–6] Italy[7] and the US.[8] Most reports have focused on COVID-19 patients admitted to the hospital, in intensive care or in wards. The series, as expected, differ in terms of demographics, the definition of comorbidities such as chronic cardiovascular disease, and clinical outcomes. Nevertheless, some observations can be made regarding the interaction between cardiovascular comorbidities and COVID-19 infection.

Hypertension, diabetes, and cardiovascular disease were the most frequent comorbidities in infected patients requiring hospitalization, compared to other chronic diseases such as cancer, chronic kidney disease and even chronic obstructive pulmonary disease. In a meta-analysis that included six Chinese studies and 1527 COVID-19 patients, the overall prevalence of hypertension, cardiovascular and cerebrovascular disease, and diabetes were 17.1%, 16.4% and 9.7%, respectively.[9] More recent studies from Italy[7] and the US[8] which included older patients, the majority of whom were male, report higher proportions of hypertension (over 50%) and diabetes (25%) among COVID-19 patients, which is similar to the last coronavirus pandemic, Middle East respiratory syndrome (MERS), which mainly affected the Arabian Peninsula. A systematic analysis of 637 MERS cases showed that the prevalence of hypertension and diabetes was over 50% and cardiac diseases were present in 30% of cases.[10]

Consistently, the severity of the disease and case fatality rates have tended to be higher in COVID-19 patients with cardiovascular comorbidities. Another recent pooled analysis showed that hypertension and a history of cardiovascular disease conferred a 2.4 (95% confidence interval [CI] 1.5-3.8) and 3.4 (95% CI 1.9-6.2) times higher risk of severe COVID-19 disease, respectively.[11]

The exact mechanisms underlying the worse prognosis of hypertensive COVID-19 patients remain unknown. One current hypothesis is that the excessive activation of the renin-angiotensin system (RAS) typical of the hypertensive patient may contribute to the progression of COVID-19 lung injury by promoting an inflammatory response (cytokine storm), smooth muscle cell contraction and vasoconstriction.[12] Moreover, some authors speculate that the use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), commonly used to treat patients with cardiovascular disease, could explain their worse outcomes.[13] In animal studies, ACEIs/ARBs increase the expression of angiotensin-converting enzyme 2 (ACE2), the receptor which SARS-CoV-2 uses for viral entry and propagation in host cells.[14] On the other hand, the upregulation of ACE2 expression by ACEIs/ARBs may mitigate the deleterious ACE2 downregulation associated with COVID-19 infection, conferring pulmonary (and cardiac) protection.[15]

At the beginning of the pandemic, all published guidelines recommended continuing ACEIs/ARBs in patients with COVID-19.[14] In a recently published retrospective analysis of 1128 adult patients with hypertension diagnosed with COVID-19 from Hubei province, the use of ACEIs or ARBs was associated with a lower risk of both non-adjusted and adjusted all-cause mortality.[16] Two randomized phase II clinical trials in outpatient (ClinicalTrials.gov identifier: NCT04311177) and inpatient (ClinicalTrials.gov identifier: NCT04312009) settings are currently being planned to study the effect of losartan in the context of COVID-19 infection.[14]

At the end of March 2020, the Centers for Disease Control and Prevention (CDC) reported data on underlying health conditions in COVID 19 patients in the US.[17] Among 122 653 US COVID-19 cases, 7162 (5.8%) patients had data available on underlying health conditions and other potential risk factors for severe outcomes from respiratory infections, and similarly to other series, a higher proportion of patients with comorbidities were admitted to the hospital and to intensive care. On the other hand, the prevalence of common clinical conditions in the US is similar to that described in this CDC report. For example, in 2018 the prevalence of diabetes among US adults was 10.1%, similar to the COVID 19 patients (10.9%). Regarding all types of heart disease (excluding hypertension), the US prevalence in 2017 was 10.6%, comparable to that observed in the CDC data, and the findings are similar regarding chronic obstructive pulmonary disease and asthma.[17] Moreover, data from China are also in agreement: according to the Summary of the 2018 Report on Cardiovascular Diseases in China, the prevalence of hypertension and diabetes was 23.2% and 10.9%, respectively, which is in line with the above-mentioned pooled prevalence.[18]

In summary, a higher prevalence of hypertension, diabetes, and chronic heart disease compared to other chronic conditions has been reported among COVID-19 patients. The prevalence of these comorbidities may nevertheless be similar to that in the general population, and these patients may not be more susceptible to COVID-19 infection. Hypertension can function as a proxy for older age and cardiovascular and non-cardiovascular comorbidities, and hence for the association in these patients with more aggressive COVID-19 disease. There is no evidence to support the idea that ACEIs or ARBs could be harmful by increasing SARS-CoV-2 infectivity. It is as yet unknown whether the severity or level of control of underlying health conditions affects the risk for severe disease in COVID-19. Nonetheless, given the limited data and potential hazard to individual and public health, a precautionary approach should be followed by carefully protecting from infection and more closely monitoring patients with multiple comorbidities, in particular those with hypertension and cardiovascular disease.

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