Editorial

Hypertension and COVID-19

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The world is currently suffering from the outbreak of a pandemic caused by the severe acute respiratory syndrome coronavirus SARS-CoV-2 that causes the disease called COVID-19, first reported in Wuhan, Hubei Province, China on December 31, 2019.[1] As of March 29, 2020, there have been 732153 confirmed cases of COVID-19 reported worldwide, with 34686 deaths.[2] The clinical and epidemiological features of COVID-19 have been repeatedly published in the last few weeks. Interestingly, specific comorbidities associated with increased risk of infection and worse outcomes with development of increased severity of lung injury and mortality have been reported. The most common comorbidities in one report were hypertension (30%), diabetes (19%), and coronary heart disease (8%).[3] Another report showed that the most frequent comorbidities in patients with COVID-19 who developed the acute respiratory distress syndrome (ARDS) were hypertension (27%), diabetes (19%) and cardiovascular disease (6%).[4] The frequency with which COVID-19 patients are hypertensive is not entirely surprising nor does it necessarily imply a causal relationship between hypertension and COVID-19 or its severity, since hypertension is exceedingly frequent in the elderly, and older people appear to be at particular risk of being infected with SARS-CoV-2 virus and of experiencing severe forms and complications of COVID-19.

It is unclear whether uncontrolled blood pressure is a risk factor for acquiring COVID-19, or whether controlled blood pressure among patients with hypertension is or is not less of a risk factor. However, several organizations have already stressed the fact that blood pressure control remains an important consideration in order to reduce disease burden, even if it has no effect on susceptibility to the SARS-CoV-2 viral infection.[5] Nevertheless, the fact that hypertension, and

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other forms of cardiovascular disease also found frequently in COVID-19 patients, are often treated with angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB), and that SARS-CoV-2, the virus causing COVID-19, binds to ACE2 in the lung to enter cells,[6,7] has raised questions regarding the possibility that these agents could either be beneficial or actually nefarious in patients treated with them with respect to susceptibility to acquire COVID-19 or in relation to its outcome. It has been shown that ACE inhibitors and ARBs increase ACE2,[8,9] which could theoretically increase the binding of SARS-Cov-2 to the lung and its pathophysiological effects leading to greater lung injury. However, ACE2 has been actually shown to protect from lung injury in experimental studies.[10] ACE2 forms angiotensin 1-7 from angiotensin II, and thus reduces the inflammatory action of angiotensin II, and increases the potential for the anti-inflammatory effects of angiotensin 1-7. Thus, by reducing either formation of angiotensin II or increasing that of angiotensin 1-7 in the case of ACE inhibitors, or by blocking angiotensin AT_1 receptors in the case of ARBs,[11,12] these agents could actually contribute to reduce inflammation systemically and particularly in the lung, heart and kidney. Thus, ACE inhibitors and ARBs could diminish the potential for development of either ARDS, myocarditis or acute kidney injury, which can occur in COVID-19 patients. In fact, ARBs have been suggested as a treatment for COVID-19 and its complications.[13] Increased soluble ACE2 in the circulation could bind SARS-CoV-2, reducing its ability to injure the lungs and other ACE2 bearing organs.[14] Using recombinant ACE2 could be a therapeutic approach in COVID-19 to reducing viral load by binding circulating SARS-CoV-2 viral particles and reducing their potential attachment to tissue ACE2. None of these possibilities have however been demonstrated in patients yet.

In conclusion, there is as yet no evidence that hypertension is related to outcomes of COVID-19, or that ACE inhibitor or ARB use is harmful, or for that matter beneficial, during the

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COVID-19 pandemic. Use of these agents should be maintained for the control of blood pressure, and they should not be discontinued, at least on the basis of current evidence at this time.

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