Management of Hypertension in the SARS-CoV2 Era: Current Knowledge and Future Perspectives

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Abstract
The new SARS-CoV2 pandemic has ignited research worldwide, regarding its parameters. Hypertension, a comorbidity with high prevalence among patients with COVID-19 infection, is being extensively studied in the setting of the pandemic. Furthermore, RAAS inhibitors, drugs widely used among hypertensive patients, are on the spotlight regarding their safety during the COVID-19 era. In this review, we present current knowledge regarding both these aspects, as well as the new guidelines for the treatment of hypertensive patients during the pandemic.

Keywords: Covid-19; Sars-CoV2; Hypertension; Comorbidities; RAAS Inhibitors

COVID-19 and Hypertension
The association between the new pandemic and HTN is being thoroughly studied. HTN is reported to be among the most common comorbidities of patients hospitalised with a severe case of SARS-CoV2 infection, according to scientific data originally published from China [2]. Furthermore, studies from China and Italy report high prevalence of hypertension among deceased patients with COVID-19 infection [3,4]. Data also propose a higher risk of hospital admission, intensive care unit admission and mortality, due to COVID-19, in patients receiving antihypertensive treatment, compared to those that receive none [5].

In a review, by European Society of Hypertension COVID-19 Task Force, it was highlighted that data supporting hypertension per se as...

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an independent risk factor for SARS-CoV2 infection are lacking [11]. In addition, the International Society of Hypertension on COVID-19 stated that patients over 60 years of age represent the majority in the COVID-infection cohorts; as hypertension prevalence is higher in these age groups, it tends to be overrepresented [12]. In June 2020, researchers found a two-fold increased risk of death from SARS-CoV2 infection for hypertensive patients [13]. It is, however, of great importance the finding that this risk affects mostly hypertensive patients that are not on any antihypertensive treatment. In the relevant meta-analysis published, researchers also found that RAAS-inhibitors use lowered the risk of death compared to the use of other drugs [13]. However, due to the small meta-analysis cohort number, authors suggested against the overinterpretation of this result.

**Hypertension Drugs**

Aforementioned scientific data regarding SARS-CoV2 infection, triggered speculation and extensive research around the safety of RAAS-inhibitors, during the pandemic. Angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), both widely prescribed RAAS-inhibitors highly recommended for the treatment of hypertension worldwide, were speculated to increase the risk of contracting and disease and predispose towards the severe manifestation of the infection. Largely, this theory was based on the mechanism of action of both drugs, which are thought to increase ACE2 levels in the lungs, thus making the respiratory tract more vulnerable to the virus [14]. The theory has not been supported by scientific data. In a study of 1139 patients, on RAAS inhibitors treatment, admitted to the hospital due to COVID-19 infection, ACEIs and ARBs use was not associated with a higher risk of hospital admission or severe complications, defined as clinical manifestations leading to intensive care unit admission or death. Interestingly, results were unbiased by age, sex and prior cardiovascular risk [5]. Furthermore, no differences regarding the main outcome were found when ACEIs and ARBs were compared [5]. In favour of those outcomes was data derived from similar studies as well. A higher prevalence of ACEIs and ARBs use among COVID-19 patients was noticed, possibly due to higher prevalence of cardiovascular disease. However, that study concluded that both categories do not correlate to the risk of COVID-19 disease [15]. Reynolds HR, et al. (2020) also concluded that the five categories of antihypertensive drugs (ACEIs, ARBs, beta-blockers, calcium-channel blockers, and thiazide diuretics) neither increase the risk of severe viral infection nor predispose to a positive COVID-19 test [16]. Interestingly enough, RAAS inhibitors have been found to lower the risk of adverse outcomes deriving from a COVID-19 infection, in diabetic patients, when compared to other hypertensive drugs [5]. On the other hand, while supporting the safety of ACEIs and ARBs in the setting of SARS-CoV2 infection, a recently published study proposed a possible benefit of ACEIs use over ARBs use regarding mortality; authors cautioned against overinterpretation though, due to potential unmeasured confounding [17]. However, studies have proposed a possible protective effect of RAAS inhibitors over other hypertensive drugs, regarding COVID-19 complications and mortality [18,19]. Conclusively, observational studies so far have concluded that there is no direct correlation between RAAS-inhibitors use and an increased COVID-19 risk or an increased risk of complications and mortality [5,15,16 and 20]. Larger, randomized studies could elucidate, confirm or discard, evidence that has derived so far.

**Current Guidelines**

Raised concern regarding management of hypertensive patients during the pandemic period has been the main concern of both patients and physicians. The Council on Hypertension of the European Society highlighted in a position statement March 2020, that there is no evidence from current data, that supports the seize, either as precaution or as treatment of the viral infection, of well tolerated ACEIs and ARBs use by stable hypertensive patients in the COVID-19 era and in the absence of not COVID-related indications [21]. In a review, published on April 2020, European Society of Hypertension COVID-19 Task Force reviewed available evidence and concluded that RAAS blockers do not have an adverse effect on the COVID-19 infection and highlighted that their discontinuation is not indicated in stable patients [11].

Similarly, the International Society of Hypertension underlined the lack of evidence supporting the seize of RAAS inhibitors in the COVID-19 era, highlighting that there are no data supporting that this class of medication increases the susceptibility to the virus or the risk of possible complications [12]. However, it is important that scientific data and studies derive constantly. As a result, guidelines, including contemporary and new evidence, may change in the attempt to reflect available data and in the service of providing the best possible advice to physicians regarding the management of patients.

**Conclusion**

During the unprecedented conditions of the ongoing pandemic, researchers are sprinting to elucidate its aspects. Due to its high prevalence and associated cardiovascular risk, hypertension has been on the spotlight of ongoing research. Evidence so far suggest that it does not increase the risk of contracting the virus nor of development of COVID-19 related complications; recent data suggest an increase in mortality risk for hypertensive patients, especially those not under hypertensive treatment. The theory proposing a risk deriving from RAAS-inhibitors use in the COVID-19 era has not been scientifically proven. Guidelines so far, advise against the discontinuation of this class of drugs as a precaution or treatment of SARS-CoV2 infection, as the cardiovascular benefit that RAAS inhibitors offer is of great importance. Further research is well expected.

**Abbreviations**

ACEI: Angiotensin Converting Enzyme Inhibitor  
ARB: Angiotensin Receptor Blocker  
HTN: Hypertension  
RAAS: Renin–Angiotensin–Aldosterone System

**References**

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