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ACKNOWLEDGMENTS

Conflict of Interest: The author has no conflicts of interest to disclose.

Author Contributions: The author is solely responsible for the content.

Sponsor's Role: There are no sponsors.

Comment on: COVID-19 and Older Adults: What We Know

To the Editor: The conclusion by Shahid and colleagues may be misleading.[1] They suggest that older patients taking inhibitors of the renin-angiotensin-aldosterone system (RAAS) could be at greater risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection as well as of a worse outcome of COVID-19.

Results of available studies have not supported the hypothesis that patients treated with RAAS inhibitors, either angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), are more susceptible to COVID-19.[2-4] Furthermore, the outcome of COVID-19 is not worse in patients treated with either ACE inhibitors or ARBs compared with patients not taking RAAS inhibitors in terms of organ dysfunction, admission to the intensive care unit, need for mechanical ventilation, and death.[2-4] Rather, the use of these drugs is associated with a lower probability of severe illness in patients with high-risk underlying conditions, such as diabetes mellitus, type II.[2] It is important to emphasize these points because COVID-19 patients have a background cardiovascular risk due to the high prevalence of coexisting conditions, such as hypertension, diabetes mellitus, type II, coronary heart disease, heart failure, and chronic kidney disease, for which ACE inhibitors and ARBs are a cornerstone of therapy, according to guidelines.[5] Advancing age and the presence of comorbidities stand as independent adverse prognostic factors in COVID-19 patients rather than the exposure to RAAS inhibitors.[2-5]

Concern about the harmful effects of RAAS inhibitors in the setting of SARS-CoV-2 infection and COVID-19 has been raised by results, although conflicting, of experimental studies showing that RAAS inhibitors have the potential to upregulate the expression of ACE2.[6] ACE2 is the major binding receptor for SARS-CoV-2 and is broadly expressed in human tissues, including in the lung alveolar epithelial cells and the respiratory tract (i.e., the main targets for SARS-CoV-2).[7,8] This has been viewed to indirectly support the hypothesis that subjects taking RAAS inhibitors could be more susceptible to SARS-CoV-2 infection. However, on the other hand, ACE2 is a counterregulatory enzyme that inactivates and degrades angiotensin II to angiotensin-1 (1-7), therefore attenuating the vasoconstriction, sodium retention, and pro-oxidant, proinflammatory, profibrotic, prothrombotic, and arrhythmogenic effects driven by angiotensin II.[9] Furthermore, ACE2 is internalized and downregulated after SARS-CoV-2 infection, which could lead to unopposed angiotensin II effects and more severe inflammation and lung injury in COVID-19 patients.[10] Not surprisingly, some experimental studies have highlighted a protective role of ACE2 in models of lung injury and the acute respiratory distress syndrome.[6] In conclusion, under both a clinical and mechanistic point of view, there is no evidence in favor of an adverse effect of RAAS inhibitors, either ACE inhibitors or ARBs, in COVID-19 patients.

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ACKNOWLEDGMENTS

Conflict of Interest: The author has no conflicts of interest.

Author Contributions: The author reviewed the data and wrote the article.

Sponsor's Role: There was no role for any sponsor.

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Caring for Caregivers During COVID-19

To the Editor: Older adults are often dependent on informal caregivers who provide home-based assistance with personal care and household tasks, and with complex medical and

DOI: 10.1111/jgs.16739

DOI: 10.1111/jgs.16726