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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REPLY: ACE Inhibitors and Angiotensin II Receptor Blockers May Have Different Impact on Prognosis of COVID-19

In response to the letter from Dr. Wang and colleagues, we thank them for the opportunity to further discuss our paper regarding the impact of randomized administration of ramipril on coronavirus disease 2019 (COVID-19) risk. The main motivation to perform this interim analysis of the RASTAVI (Renin-angiotensin system blockade benefits in clinical outcomes and ventricular remodeling after transcatheter aortic valve implantation) trial was the concern that a simple retrospective analysis of this currently poorly known disease seemed to wipe out the well-known benefits of renin-angiotensin-aldosterone system (RAAS) inhibitors in various clinical settings (1). We believe that the clinical urge should not lead to "scientific sensationalism," and we join the plea for slow science. For the same reason, although we agree with our colleagues in the need for a separate analysis of angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), we have to disagree with the statement that "ARBs, but not ACE inhibitors, may have favorable effects on outcomes of COVID-19."

Experimental animal models and studies in humans showed an increase on ACE-2 expression with RAAS blockade, which theoretically favored severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) entry into the cells (2,3). However, other animal and human studies did not reproduce these results (4). The contradictory data might be explained by the differential regulation of the protease TMPRSS2, which is also needed for SARS-CoV-2 entry into the target cell, as well as dosage or timing of RAAS inhibitors or blockers used. A different effect on ACE-2 regulation was seen with various drugs of the same family. Taking these conflicting data together, it can be stated that effects of RAAS inhibitors on ACE-2 are complex, and with all likelihood, not uniform. Therefore, from our perspective, there is no evidence to stop RAAS inhibitors, neither to prevent COVID-19 nor to improve outcomes. This equally affects all RAAS inhibitors—no differences should be made in clinical practice yet. Long-term use of ramipril, according to our results, did not affect short-term prognosis in patients with high cardiovascular burden who experienced COVID-19. This first randomized study will be followed soon by the results of ongoing trials, including patients who have not received long-term RAAS blockers (Losartan for Patients With COVID-19 Requiring Hospitalization; NCT04312009; Do Angiotensin Receptor Blockers Mitigate Progression to Acute Respiratory Distress Syndrome With SARS-CoV-2 Infection; NCT04340557; Study of Open Label Losartan in COVID-19; NCT04335123).

Thorough respect for clinical evidence is mandatory while living in this confounding time.

***Ignacio J. Amat-Santos, MD, PhD**
Sandra Santos-Martinez, MD
Diego López-Otero, MD, PhD
Jose Raúl Delgado-Arana, MD
J. Alberto San Román, MD, PhD

*Cardiology Department
Hospital Clínico Universitario de Valladolid
Instituto de Ciencias del Corazón (ICICOR)
Ramon y Cajal 3
Valladolid, Valladolid 47005
Spain
E-mail: ijamat@gmail.com

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC* author instructions page.

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