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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Letter to the Editor

Letter to the editors in response to: Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic (Cure et al.)

Dear Editor,

We read with great interest the article by Cure et al. [1] in *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. The authors commented about the possible harmful effects of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in patients with diabetes mellitus during the COVID-19 pandemic. While we congratulate them for having tried to study this debated issue; we, herein, wish to advocate the possible "beneficial" roles of these drugs as well.

Since hypertension is one of the most significant risk factors for severe disease and mortality in COVID-19 and ACE2 is the entry receptor of 2 SARS-CoV-2 [1,2], the renin angiotensin system (RAS) has received much focus [1,2]. First, based on a few animal studies showing increased ACE2 expression due to RAS inhibitors, it is yet quite skeptical to discontinue RAS inhibitors, particularly in high-risk patients [2]. Further, a recent study has shown the protective effects of ACEIs/ARBs against mortality in COVID-19 [3]. ACEI/ARB users (almost 20% had diabetes mellitus) had lower risk of all-cause mortality [3].

Second, ACEIs/ARBs should actually be considered separately - as they inhibit different steps in the classical RAS pathway. ACEIs inhibit the step from angiotensin I to angiotensin II, whereas ARBs block angiotensin II type I (AT1) receptor. Indeed, both inhibit the deleterious effects of the classical pathway (i.e. angiotensin II/AT1 receptor interaction) such as peripheral vasoconstriction, skeletal muscle atrophy, fibrosis, and increased insulin resistance. However, ACEIs perform a multilevel block in both classical and non-classical pathways, which result in a strong augmentation of the non-classical pathway (i.e. angiotensin 1-7/Mas receptor axis). This activation also causes positive effects on the skeletal muscle anabolic processes. Lastly, ACEIs decrease the degradation of bradykinin, a potent vasodilator, and thus enhance the perfusion of different soft tissues including the muscle [4].

In this sense, another noteworthy example for the protective effects of ACEIs/ARBs would be the improvement of sarcopenia (age-related loss of muscle mass/function). Inhibition of the RAS activity exerts vasodilator, anti-hypertrophic, and anti-fibrotic effects on muscles [4]. It has been shown that ACEI users had higher lower extremity muscle mass than those using other antihypertensive drugs. For instance, in a three-year longitudinal study, ACEIs prevented the decline in knee extensor strength and gait speed [5]. Accordingly, we simply highlight that increased RAS activity causes both hypertension and sarcopenia; and ACEIs (and possibly ARBs) use can actually be preventive for both conditions during the Covid-19 pandemic.

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Declaration of competing interest

No conflict of interest.

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