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REFERENCES

1. Giannoni A, Gentile F, Sciarone P, et al. Upright Cheyne-Stokes respiration in patients with heart failure. *J Am Coll Cardiol* 2020;75:2934-46.
2. Giannoni A, Gentile F, Navari A, et al. Contribution of the lung to the genesis of Cheyne-Stokes Respiration in heart failure: plant gain beyond chemoreflex gain and circulation time. *J Am Heart Assoc* 2019;8:e012419.
3. Francis DP, Willson K, Davies LC, Coats AJ, Piepoli M. Quantitative general theory for periodic breathing in chronic heart failure and its clinical implications. *Circulation* 2000;102:2214-21.
4. Somers VK, Mark AL, Abboud FM. Interaction of baroreceptor and chemoreceptor reflex control of sympathetic nerve activity in normal humans. *J Clin Invest* 1991;87:1953-7.

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



Amat-Santos et al. (1) conducted a randomized open-label study, in which they demonstrated that ramipril did not affect mortality outcomes in patients with coronavirus disease-2019 (COVID-19) (users: 4.0% vs. nonusers: 3.8%). We appreciate the open discussion on the use of renin-angiotensin-aldosterone system inhibitors in the context of COVID-19.

However, recent evidence indicated that using angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) was associated with better survival (3.7% [7 of 188 patients] vs. 9.8% [92 of 940 patients]) (2). Another meta-analysis of 9 studies also arrived at a similar conclusion (odds ratio: 0.57; 95% confidence interval [CI]: 0.38 to 0.84) (3). There are opposing hypotheses on the effects of ACE inhibitors and ARBs on COVID-19. Zhou et al. (4) found that in-hospital use of ARBs was associated with lower mortality (adjusted hazard ratio: 0.31; 95% CI: 0.18 to 0.53), whereas ACE inhibitors had no

impact on mortality outcomes. Thus, the differing therapeutic effects exerted by ACE inhibitors and ARBs could account for the conflicting findings. It has been shown that the effects of losartan, an ARB, would be favorable to prevent severe acute respiratory syndrome-coronavirus-induced acute lung injury in severe acute respiratory syndrome-coronavirus-S protein-treated mice (5).

In conclusion, ARBs and ACE inhibitors should be studied separately in adequately powered randomized trials, and the risks and benefits of ACE inhibitors and ARBs must be reconsidered separately. ARBs, but not ACE inhibitors, may have favorable effects on outcomes in COVID-19.

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REFERENCES

1. Amat-Santos IJ, Santos-Martinez S, López-Otero D, et al. Ramipril in high risk patients with COVID-19. *J Am Coll Cardiol* 2020;76:268-76.
2. Zhang P, Zhu L, Cai J, et al. Association of inpatient use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. *Circ Res* 2020;126:1671-81.
3. Guo X, Zhu Y, Hong Y. Decreased mortality of COVID-19 with renin-angiotensin-aldosterone system inhibitors therapy in patients with hypertension: a meta-analysis. *Hypertension* 2020;76:e13-4.
4. Zhou F, Liu YM, Xie J, et al. Comparative impacts of ACE (angiotensin converting enzyme) inhibitors versus angiotensin II receptor blockers on the risk of COVID-19 mortality. *Hypertension* 2020;76:e15-7.
5. Kuba K, Imai Y, Rao S, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. *Nat Med* 2005;11:875-9.