Should ACE Inhibitors and ARBs be Discontinued in Patients with COVID-19?

A correspondence published in Lancet on March 11, 2020 hypothesized that patients who are receiving angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin II receptor blockers (ARBs) may be at increased risk of developing severe or fatal COVID-19 infections.¹ This hypothesis is based on initial studies from China describing patients with COVID-19 infections suggesting that cardiovascular disease, diabetes, hypertension, and cerebrovascular disease are common risk factors among patients who are hospitalized or have poor outcomes.²⁻⁴ Pathogenic human coronaviruses, such as severe acute respiratory syndrome coronavirus (SARS-CoV) and SARS-CoV-2, bind to epithelial cells in the lung, blood vessels, kidney, and intestines through ACE2.⁵ Data suggest that ACE2 is increased in patients with Type 1 or 2 diabetes or hypertension who are taking ACE inhibitors or ARBs.⁶⁻⁷ This upregulation of ACE2 could theoretically facilitate COVID-19 infection.¹ However, there is limited and sometimes conflicting information available to support this theory. On March 12, 2020, an abstract published online from the Chinese Medical Association Publishing House Ltd. proposed that ACE inhibitors and ARBs may reduce mortality and pulmonary inflammatory response in COVID-19 and could be used to control blood pressure in this patient population. This abstract cited evidence that ACE and angiotensin II are poor predictors of prognosis in patients with severe pneumonia and referenced animal studies that have indicated that renin-angiotensin system inhibitors could reduce symptoms in severe pneumonia and respiratory failure.8

Since these initial hypotheses, several researchers have sought to determine whether ACE inhibitors or ARBs are helpful or harmful in patients with COVID-19. The resulting published studies have indicated that stopping ACE inhibitors or ARBs in patients with COVID-19 either has no impact on disease severity⁹⁻¹⁵ or that continuing these agents may attenuate disease severity.¹⁶⁻¹⁹ The NIH COVID-19 guidelines and several other guideline panels have also issued statements to reinforce that patients currently prescribed ACE inhibitors or ARB treatment for other indications should continue these therapies as prescribed if infected with COVID-19.²⁰⁻²⁵ Prior to the COVD-19 pandemic, there was evidence that stopping these drugs in certain patient populations could lead to patient harms such as worsening of renal or cardiovascular disease.²⁶⁻²⁹ For these reasons, the Duke Antimicrobial Stewardship Outreach Network does not endorse discontinuation of ACE inhibitor or ARB therapies in patients with COVID-19 infections.

References:

- Lei F, et al. Lancet Respir Med 2020; published online Mar 11. DOI:10.1016/PII. Yang X, et al. Lancet Respir Med 2020; published online Feb 24. https://doi.org/10.1016/S2213- 2600(20)30079-5.
- 3.
- Guar W, et al. N Engl J Med 2020; published online Feb 28. DOI:10.1056/NEIMoa2002032. Zhang JJ, et al. Allergy 2020; published online Feb 19. DOI:10.1111/ all 14238. Guo, Y., et al. Military Med Res 7, 11 (2020). DOI:10.1186/s40779-020-00240-0.
- Van Y, et al. Ninkai Y, interest Y, interes
- 8. 10.3760/cma.j.issn.1001-0939.2020.0014. [Epub ahead of print].
- James PA, et al. JAMA 2014; 311:507. 19. Yang G, et. al. Hypertension. 2020. The European Society of Cardiology Council on Hypertension. Position Statement 20. European Society of Hypertension. ESH Statement on COVID-19 10. of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers. 13 Mar 2020. https://www.escardio.org/Councils/Council-or

-(CHT)/News/position-statement-of-th e-inhibitors-and-ang Accessed 16 March 2020.

11. HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19. Available at

- 505836 HESAAC CAHA-statement-addresses-cor Accessed 17 March 2020. ncerns-re-using-RAAS-antagonists-in-COVID-19.isp
- 12. de Abajo FJ, et al. Lancet. 2020;395(10238):1705. Epub 2020 May 14.
- Reynolds HR et. Al. N Engl J Med. 2020. Mancia G, et. al. N Engl J Med. 2020.
- 14. 15. Mackey K, et. al. Ann Intern Med. 2020
- Kuba K, et. al. Nat Med. 2005;11(8):875. Epub 2005 Jul 10.
- Sodhi CP, et. al. Am J Physiol Lung Cell Mol Physiol. 2018;314(1):L17. Epub 2017 Sep 21. 18. Zhang P, et. al. Circ Res. 2020;126(12):1671. Epub 2020 Apr 17.
- https://www.eshonline.org/spotlights/esh-statement-on-covid-19/ (Accessed on March 18, 2020).
- Statement from the American Heart Association, the Heart Failure Society of America and the American College of Cardiology. Patients taking ACE-i and ARBs 21. who contract COVID-19 should continue treatment, unless otherwise advised by 29. Halliday BP, et. al. Lancet. 2019;393(10166):61. Epub 2018 Nov 11. their physician. https://newsroom.heart.org/news/patients-taking-ace-i-and-

arbs-who-contract-covid-19-should-continue-treatment-unless-otherwise

Reviewed on 6/26/2020.

- advised-by-their-physician (Accessed on March 18, 2020).
- 22. International Society of Hypertension. A statement from the International Society of Hypertension on COVID-19. https://ish-world.com/news/a/A-statementthe-International-Society-of-Hypertension-on-COVID-19/ (Accessed on March 18, 2020).
- 23. Position Statement of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-
- hypertension-on-ace-inhibitors-and-ang (Accessed on March 18, 2020) 24. https://hypertension.ca/wp-content/uploads/2020/03/2020-30-15-Hypertension
- Canada-Statement-on-COVID-19-ACEi-ARB.pdf (Accessed on March 18, 2020). 25. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. NIH. Accessed 16
- June 2020 at: http://covid19treatmentguidelines.nih.gov/ 26. James PA, et al. JAMA 2014: 311:507
- 27. Qiao Y, et. al. JAMA Intern Med. 2020
 28. Pflugfelder PW, et. al. J Am Coll Cardiol. 1993;22(6):1557



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