Cardiology

ACEI/ARBs Linked With Survival In Hypertensive Chinese Coronavirus Patients

By Mitchel L. Zoler
From Circulation Research Internal Medicine News
May 2020, p 10.
MDedge.com

{micrograph}
Caption: This scanning electron microscope image shows SARS-CoV-2 (orange)—also known as 2019-nCoV, the virus that causes COVID-19.

Hospitalized COVlD-19 patients with hypertension and on treatment with an renin-angiotensin system-inhibiting drug had significantly better survival, compared with similar hypertensive patients not on these drugs, in observational, propensity score-matched analyses that drew from a pool of more than 3,430 patients hospitalized at any of nine Chinese hospitals during December 2019-February 2020.

"Among patients with hypertension hospitalized with COVID-19, inpatient treatment with ACEI [ACE inhibitor]/ARB [angiotensin receptor blocker] was associated with lower risk of all-cause mortality, compared with ACEI/ ARB nonusers, during 28 days of follow-up. While study interpretation needs to consider the potential for residual confounders, it is unlikely that inpatient ACEI/ ARB would be associated with an increased risk of mortality," wrote Peng Zhang, MD, a cardiology researcher at Renmin Hospital of Wuhan (China) University, and coauthors in *Circulations Research*, buttressing recent recommendations from several medical societies to maintain COVID-19 patients on these drugs.

"Our findings in this paper provide evidence supporting continuous use of ACEI/ ARB for patients with hypertension infected with SARS-COV-2," wrote the authors, backing up recent recommendations from cardiology societies that called for not stopping ACEI/ ARB prescriptions in patients at risk for contracting or who already have COVID-19 infection, including a statement from the American College of Cardiology, American Heart Association, and Heart Failure Society of America, and also guidance from the European Society of Cardiology.

The study included 1,128 patients with a history of hypertension, including 188 (17%) who received an ACEI/ARB drug during hospitalization. During 28 days of follow-up, 99 died (9%), including 7 deaths among the 188 patients (4%) on an ACEI/ ARB drug and 92 deaths among the 940 other hypertensive patients (10%).

The authors ran several analyses to try to adjust for the influence of possible confounders. A mixed-effect Cox model with four adjusted variables showed that treatment with an ACEI/ARB drug was tied to a statistically significant 58% lower death rate, compared with patients not receiving these drugs.

The researchers also ran several propensity score-adjusted analyses. One matched 174 of the patients who received an ACEI/ARB drug with 522 who did not, and comparing these two matched arms showed that ACEI/ARB use was linked with a statistically significant 63% cut in mortality, compared with patients not getting these drugs. A second propensity score-matched analysis first excluded the 383 patients who were hypertensive but received no anti-hypertensive medication during hospitalization. From the remaining 745 patients who received at least one anti-hypertensive medication, the authors identified 181 patients who received an ACEI/ARB and propensity score matched them with 181 hypertensive patients on a different medication class, finding that ACEI/ARB use linked with a statistically significant 71% lower rate of all—cause mortality.

Additional analyses also showed that patients with hypertension had a statistically significant, 41% increased rate of all-cause death, compared with patients without hypertension, and another propensity score—matched analysis showed that among hypertensive patients, treatment with an ACEI/ ARB drug was linked with a statistically significant 68% reduced rate of septic shock.

Although this report was received with caution and some skepticism, it was also acknowledged as a step forward in the creation of an evidence base addressing ACEI/ARB treatment during COVID-19 infection.

"These drugs are lifesaving and should not be discontinued" for patients with hypertension, heart failure, and other cardiovascular disease, commented Gian Paolo Rossi, MD, professor and chair of medicine and director of the high blood pressure unit

at the University of Padua (Italy). The analysis by Zhang and associates included the largest number of hospitalized COVID-19 patients with hypertension yet reported to assess the impact of treatment with ACEI/ ARB drugs, and adds important evidence in favor of continuing these drugs in patients who develop COVID-19 infection, Dr. Rossi said in an interview. He recently coauthored a review that argued against ACEI/ARB discontinuation in COVID-19 patients based on previously reported evidence (Elife. 2020 Apr 6. doi: 10.7554/ eLife.57278).

But other researchers take a wary view of the potential impact of ACEI/ARB agents. "If ACEl/ ARB therapy increases ACE2 and the virus down-regulates it, and because ACE2 is the viral entry port into cells, why would ACE2-mediated down-regulation of the renin-angiotensin-aldosterone system lead to amelioration of [COVID-19j disease?" asked Laurence W. Busse, MD, a critical care physician at Emory University, Atlanta. "A number of issues could potentially confound the results, including the definition of COVID-19 and imbalance of antiviral therapy," added Dr. Busse, who recently coauthored an editorial that posited using angiotensin II (Giapreza), an approved vasopressor drug, as an alternative renin-angiotensin system intervention for COVID-19 patients including both those in shock as well as potentially those not in shock (Crit Care. 2020 Apr 7. doi: 10.1186/s13054-020-0Z862-1). Despite these caveats, the new Chinese findings reported by Dr. Zhang and associates "are hypothesis generating and worth further exploration."

The authors of an editorial that accompanied the Zhang study in Circulation Research made similar points. "While the investigators used standard techniques to attempt to reduce bias in this observational study via propensity matching, it is not a randomized study and the residual confounding inherent to this approach renders the conclusions hypothesis generating at best," wrote Ravi V Shah, MD, and two coauthors in the editorial (Circ Res. 2020 Apr 17. doi: 10.1161/CIRCRESA~ HA. 120317174). They also agreed with the several society statements that have supported continued use of ACEI/ARB drugs in COVlD-19 patients. "Withdrawal of these medications in the context of those conditions in which they have proven benefit (e.g., heart failure with reduced left ventricular ejection fraction) may actually inflict more harm than good," they warned. "In the end we must rely on randomized clinical science," and while this level of evidence is currently lacking, "the study by Zhang and colleagues is a direct step toward that goal."

Dr. Zhang and coauthors had no commercial disclosures. Dr. Rossi and Dr. Busse had no disclosures. The authors of the *Circulation Research* editorial reported several disclosures.

mzoler@mdedge.com

Source: Zhang P, et al., Circ Res. 2020 Apr 17. doi: 10.1161/CIRCRESAHA.120.317134.