

Risk of Covid-19 with renin-angiotensin-aldosterone system medications

There does not seem to be an association between receipt of drugs which act on the renin-angiotensin-aldosterone system (RAAS) and infection with coronavirus disease 2019 (Covid-19), according to the results of two studies reported in the *NEJM*.

Patients from Lombardy, Italy

The population-based study¹ included 6272 patients, >40 years of age, diagnosed with Covid-19 between 21 February 2020 and 11 March 2020 (cases) who were matched to 30 759 controls. The use of RAAS-acting medications was more frequent in cases than in controls, both for angiotensin-converting enzyme (ACE) inhibitors (23.9% vs 21.4%) and for angiotensin-receptor blockers (ARBs; 22.2% vs 19.2%). The use of other antihypertensives and other medications was also higher in cases compared with controls, especially loop diuretics and mineralocorticoid-receptor antagonists, and they tended to have worse clinical profiles.

However, there was no significant association between use of RAAS-acting medications and Covid-19 infection in multivariable analyses, either with ARBs (adjusted odds ratio [OR] 0.95; 95% CI 0.86, 1.05) or with ACE inhibitors (OR 0.96; 0.87, 1.07). In addition, there were no significant associations for patients with a severe/fatal disease course with either ARBs (OR 0.83; 0.63, 1.10) or ACE inhibitors (OR 0.91; 0.69, 1.21). No gender differences were detected.

"The present study does not provide evidence that the use of ACE inhibitors or ARBs is independently associated with the risk of Covid-19", note the authors.

Patients from New York

The observational study² included 12 594 patients in the New York University Langone Health electronic health record with Covid-19 test results between 1 March 2020 and 15 April 2020. There were 5894 positive tests (46.8%), and 1002 patients (17.0%) with severe illness, as indicated by ICU admission (n=726), mechanical ventilation (n=311) and death (n=447). Of the 4357 patients with a history of hypertension, 2573 patients (59.1%) had positive test results and 634 patients (24.6%) had severe illness, as indicated by ICU admission (n=422), mechanical ventilation (n=165) and death (n=343).

In the propensity score-matched cohorts with hypertension, there were no significant associations between the likelihood of a positive Covid-19 test and previous treatment with ACE inhibitors (median difference 0.1%; 95% CI -4.3%, 4.5%) or ARBs (1.6%; -2.6%, 5.8%) compared with untreated patients. In addition, there were no significant associations with other antihypertensive drug classes.

There was no substantially increased risk of serious illness compared with untreated patients ($\geq 10\%$) in those who had received ACE inhibitors (-3.3%; -8.2%, 1.7%) or ARBs (0.1%, -4.8%, 4.9%). There was a slightly higher risk in patients who had received calcium-channel blockers (4.4%; 0.5%, 8.2%), but no differences in recipients of other antihypertensive drug classes.

"Our findings may help to allay concerns on the part of patients and providers regarding the continued use of these agents in patients undergoing testing or receiving treatment for Covid-19", note the authors.

Accompanying editorial

In an accompanying editorial reported in the *NEJM*,³ John Jarcho (Boston University) and colleagues note that they "find it reassuring" that the study results "arrive at the consistent message that the continued use of ACE inhibitors and ARBs is unlikely to be harmful in patients with Covid-19". In addition, "the data from these studies support" the recommendation of professional scientific societies and experts that "patients should not discontinue ACE inhibitor or ARB therapy out of a concern that they are at increased risk for infection, severe illness, or death during the Covid-19 pandemic".

1. Mancia G, et al. Renin-Angiotensin-Aldosterone System Blockers and the Risk of Covid-19. *New England Journal of Medicine* : 1 May 2020. Available from: URL: <http://dx.doi.org/10.1056/NEJMoa2006923>.

2. Reynolds HR, et al. Renin-Angiotensin-Aldosterone System Inhibitors and Risk of Covid-19. *New England Journal of Medicine* : 1 May 2020. Available from: URL: <http://dx.doi.org/10.1056/NEJMoa2008975>.

3. Jarcho JA, et al. Inhibitors of the Renin-Angiotensin-Aldosterone System and Covid-19. *New England Journal of Medicine* : 1 May 2020. Available from: URL: <http://dx.doi.org/10.1056/NEJMe2012924>.