Angiotensin II receptor blocker or angiotensin-converting enzyme inhibitor use and COVID-19-related outcomes among US Veterans


BACKGROUND

Angiotensin II receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) may positively or negatively impact outcomes in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

OBJECTIVE

Estimate the direction and magnitude of association between ARB and/or ACEI with all-cause mortality and hospitalization in outpatients and inpatients with SARS-CoV-2 and treated hypertension.

METHODS

• Retrospective cohort study in the Veterans Health Administration data.
• Two cohorts, separately derived and analyzed: 1) Outpatient: (+) SARS-CoV-2 test [index date] without hospitalization in prior 7 days 2) Inpatient: (+) SARS-CoV-2 test with subsequent hospitalization [admit date = index date]

Inclusion Criteria: Positive SARS-CoV-2 test between 1/19/2020 and 10/15/2020. 3) At least one antihypertensive medication fill in the 90-day pre-index period

Exposure groups assessed using 90-day pre-index period: 1) ARB/ACEI vs. non-ARB/ACEI [ref.]: further exclusion of those with compelling indications for ACEI/ARB (diabetes, chronic kidney disease, heart failure, coronary heart disease, or stroke) 2) ARB vs. ACEI [ref.]: exclusion of those taking both ARB and ACEI.

Primary Outcomes: All-cause hospitalization or mortality (outpatients) and all-cause mortality (inpatients)

Statistical Analysis:
• Matching-weighted Cox regression to estimate hazard ratios (HR)
• Censored at first outcome, 10/15/2020, or 30 days (inpatients)
• Multiple imputation with 10 imputed datasets to address missingness and bootstrapping with 2,000 iterations to estimate 95% confidence intervals (CI)

Secondary Analyses:
• Negative control outcomes (urinary tract infection, gastrointestinal bleed) to assess for unmeasured confounding
• Sensitivity analyses varying definition of medication exposure window

RESULTS

Table 1. Selected Veteran characteristics before weighting.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Outpatient</th>
<th>Inpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARB/ACEI vs. non-ARB/ACEI n = 4,969</td>
<td>ARB/ACEI vs. non-ARB/ACEI n = 485</td>
<td>ARB/ACEI vs. non-ARB/ACEI n = 3,178</td>
</tr>
<tr>
<td>Age, years</td>
<td>60.0</td>
<td>66.5</td>
</tr>
<tr>
<td>Male</td>
<td>88.4%</td>
<td>94.5%</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>37.2%</td>
<td>33.1%</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>31.8</td>
<td>32.3</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>131.7</td>
<td>132.1</td>
</tr>
<tr>
<td>eGFR, ml/min/1.73m²</td>
<td>86.2</td>
<td>73.3</td>
</tr>
<tr>
<td>Statin use</td>
<td>36.0</td>
<td>64.5</td>
</tr>
</tbody>
</table>

Table 1. Selected Veteran characteristics before weighting.

Secondary Analyses:
• There was no association between the exposures and negative control outcomes in outpatients or inpatients.
• Varying the medication exposure window did not materially change the results in outpatients or inpatients.

CONCLUSIONS

• We found no evidence of a harmful association of prevalent use of an ARB/ACEI- vs. non-ARB/ACEI-based antihypertensive medication regimen with adverse COVID-19-related outcomes.
• ARB or ACEI treatment among patients with hypertension and SARS-CoV-2 infection should be continued in the absence of an established indication to discontinue them.