Association of Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Use and Covid-19 Infection Among Patients with Hypertension

Jaejin An, Rong Wei, Hui Zhou, Tiffany Q. Luong, Ran Liu, Michael K. Gould, Matthew T. Mefford, Teresa N. Harrison, Beth Creekmur, Ming-Sum Lee, John J. Sim, Jeffrey W. Brettler, John P. Martin, Angeline L. Ong-Su, Kristi Reynolds

AHA Scientific Sessions, November 13-17, 2020
Disclosures

This work was supported by the American Heart Association (AHA) grant #810957. Prior to AHA funding, part of this work was supported by the Regional Research Committee of Kaiser Permanente Southern California, grant #KP-RRC-20200402.

• JA reports grants from Novartis, Vital Strategies, and Merck & Co. outside the submitted work.
• RW and TQL report grants from Novartis and Vital Strategies outside the submitted work.
• KR reports grants from Novartis, Vital Strategies, Merck & Co., and Amgen outside the submitted work.
• HZ, MKG, MTM, TNH, BC, ML, JJS, JWB, JPM, and ALO have no financial disclosures.
Background

• The Covid-19 pandemic has generated concerns that use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) may be associated with increased risk of Covid-19 infection or disease severity.
  ▪ ACEIs or ARBs may upregulate angiotensin-converting enzyme 2 (ACE2) receptors and increase SARS-CoV-2 infectivity.\(^1\)
  ▪ ACEIs or ARBs may be protective against Covid-19 by upregulating ACE2 and mitigating the inflammatory response in the lungs of infected patients.\(^2\)

• Epidemiologic studies have emerged to address this question, and these reports showed no increased risk of severity of Covid-19 associated with ACEI or ARB exposure.\(^3\)-\(^8\)
  ▪ Limited information is available on the susceptibility of Covid-19.
Objective

Determine the risk of Covid-19 infection among patients with hypertension taking ACEIs or ARBs, compared with other frequently used antihypertensive medications* within a large, diverse hypertension population at Kaiser Permanente Southern California.

*Calcium channel blockers (CCB), beta-blockers (BB), thiazide or thiazide-like diuretics (TD)
Methods

Retrospective Study Cohort

- Patients with hypertension as of March 1, 2020 (index date) from Kaiser Permanente Southern California
- Had a test for Covid-19 between March 1 – May 6, 2020

Variables of Interest

- **Exposure:**
  1) Any ACEIs
  2) Any ARBs
  3) CCB/BB/TD (reference group)
  4) Other antihypertensives
  5) No antihypertensives

- **Outcome:**
  Positive reverse transcription polymerase chain reaction (RT-PCR) test for Covid-19

Statistical Analysis

- Propensity score matching based on patient demographics, neighborhood income and education, insurance, body mass index, smoking, blood pressure, baseline comorbidities, and medication use.
## Results

Among 824,650 patients with hypertension, 16,898 (2.0%) were tested for Covid-19.

Table 1. Patient demographic and clinical characteristics by antihypertensive drug exposure

<table>
<thead>
<tr>
<th></th>
<th>ACEI 4,878 (29%)</th>
<th>ARB 3,473 (21%)</th>
<th>CCB or BB or TD 4,177 (25%)</th>
<th>Other Antihypertensives 377 (2%)</th>
<th>No Antihypertensives 3,993 (24%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean</td>
<td>64</td>
<td>66</td>
<td>65</td>
<td>71</td>
<td>61</td>
</tr>
<tr>
<td>Male, %</td>
<td>53</td>
<td>40</td>
<td>39</td>
<td>58</td>
<td>45</td>
</tr>
<tr>
<td>Race/Ethnicity, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>11</td>
<td>20</td>
<td>14</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Black</td>
<td>12</td>
<td>14</td>
<td>18</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Hispanic</td>
<td>36</td>
<td>31</td>
<td>27</td>
<td>28</td>
<td>39</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>White</td>
<td>39</td>
<td>33</td>
<td>39</td>
<td>48</td>
<td>33</td>
</tr>
<tr>
<td>Blood Pressure, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;140/90 mm Hg</td>
<td>82</td>
<td>80</td>
<td>82</td>
<td>87</td>
<td>72</td>
</tr>
<tr>
<td>&lt;130/80 mm Hg</td>
<td>44</td>
<td>40</td>
<td>43</td>
<td>53</td>
<td>36</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>46</td>
<td>49</td>
<td>29</td>
<td>39</td>
<td>28</td>
</tr>
<tr>
<td>Heart failure, %</td>
<td>7</td>
<td>8</td>
<td>10</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>Chronic kidney disease, %</td>
<td>10</td>
<td>14</td>
<td>14</td>
<td>18</td>
<td>6</td>
</tr>
</tbody>
</table>
## Results

Table 2. Incidence of Covid-19 Infection per 1000 Patients by Antihypertensive Drug Exposure

<table>
<thead>
<tr>
<th></th>
<th>ACEI</th>
<th>ARB</th>
<th>CCB or BB or TD</th>
<th>Other Anti-hypertensives</th>
<th>No Anti-hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covid-19 Infection per 1000 tested patients</td>
<td>107.6</td>
<td>102.8</td>
<td>81.9</td>
<td>58.4</td>
<td>137.2</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(98.8-117.2)</td>
<td>(92.7-114.0)</td>
<td>(73.6-91.0)</td>
<td>(38.4-88.6)</td>
<td>(126.2-149.2)</td>
</tr>
</tbody>
</table>

ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BB = beta-blockers; CCB = calcium channel blockers; TD = thiazide diuretics
Figure 1. Odds Ratio (95% CI) of Covid-19 Infection Associated with Antihypertensive Drug Exposure Stratified by Sex, Age, and Race/ethnicity After Propensity Score Matching

(A) ACEI vs. CCB/BB/TD
(B) ARB vs. CCB/DD/TD
(C) No antihypertensives vs. CCB/BB/TD

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Male</th>
<th>Female</th>
<th>18-39</th>
<th>40-64</th>
<th>65-84</th>
<th>85+</th>
<th>Asian</th>
<th>Black</th>
<th>Hispanic</th>
<th>White</th>
<th>CKD</th>
<th>No</th>
<th>Yes</th>
<th>Heart Failure</th>
<th>No</th>
<th>Yes</th>
<th>Diabetes</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACEI vs. CCB/BB/TD</strong></td>
<td><strong>1.06 (0.90-1.25)</strong></td>
<td><strong>0.91 (0.71-1.16)</strong></td>
<td><strong>1.20 (0.96-1.51)</strong></td>
<td><strong>1.16 (0.93-1.44)</strong></td>
<td><strong>1.07 (0.81-1.41)</strong></td>
<td><strong>0.30 (0.12-0.77)</strong></td>
<td><strong>1.19 (0.30-4.73)</strong></td>
<td><strong>1.01 (0.80-1.29)</strong></td>
<td><strong>1.28 (0.95-1.73)</strong></td>
<td><strong>1.02 (0.48-2.18)</strong></td>
<td><strong>0.95 (0.66-1.37)</strong></td>
<td><strong>1.28 (0.79-2.08)</strong></td>
<td><strong>1.09 (0.81-1.42)</strong></td>
<td><strong>1.34 (0.91-1.98)</strong></td>
<td><strong>1.15 (0.95-1.40)</strong></td>
<td><strong>0.76 (0.42-1.37)</strong></td>
<td><strong>1.06 (0.89-1.26)</strong></td>
<td><strong>1.12 (0.93-1.35)</strong></td>
<td><strong>1.07 (0.43-2.68)</strong></td>
<td><strong>2.79 (0.94-8.23)</strong></td>
</tr>
</tbody>
</table>
Summary of Findings/Discussion

• In our racially and ethnically diverse cohort, neither ACEI nor ARB use was associated with increased likelihood of Covid-19 infection.

• The decreased odds of Covid-19 infection among adults ≥85 years using ACEIs warrants further investigation.

• This study showed an increased likelihood of Covid-19 infection for those without antihypertensive medications compared to those with CCB/BB/TD.

• These results reinforce that patients with hypertension should continue their ACEIs or ARBs as recommended by scientific communities.

• Study has limitations from unmeasured confounding and changes in testing criteria for Covid-19.
References


