Does Perioperative Use of Renin-Angiotensin System Inhibitors Improve Patient Outcomes in Cardiac Surgery?

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Introduction
- 2012 ACCF/AHA Guidelines for CABG: Uncertain about the safety of the preoperative administration of ACE inhibitors or ARBs in patients on chronic therapy and the safety of initiating ACE inhibitors or ARBs before hospital discharge
- 2014 ESC Guidelines: ACE inhibitors might be stopped 1 to 2 days before CABG to avoid the potential deleterious consequences of perioperative hypotension

Methods
- Examine the association between perioperative renin-angiotensin system inhibitors (RASi) and outcomes in patients undergoing CABG and/or valve surgery
- Postoperative renal failure, readmission, ICU length of stay, and major adverse cardiovascular events (MACE)
- Design: Multicenter, retrospective cohort study
- Consecutive patients undergoing CABG and/or valve surgery at three tertiary medical centers 2001-2015
- Definitions:
  - Preoperative RASi (PreRASi): RASi within 48 hours prior to surgery
  - Postoperative RASi (PostRASi): prescribed RASi on discharge from hospital
- Analysis:
  - Anticipated that baseline characteristics would differ significantly between patients with or without perioperative or postoperative RASi
  - Logistic regression was used to develop propensity scores reflecting the probability that a patient would receive preoperative RASi to adjust for between-group differences

Results
- In both the PreRASi and PostRASi cohorts, patients taking RASi tended to be older, have more comorbidities, and take more prescription medications; after propensity score matching, all variables were well balanced between those taking and not taking RASi in both the Pre- and PostRASi cohorts
- Preoperative RASi was associated with reduced mortality at 1, 3, 5, and 6 years postoperatively compared to no preoperative RASi after propensity score matching (5.4% vs 7.6%, p = 0.01) (Table 1)
- Postoperative RASi was associated with reduced mortality at 2, 3, 4, 5, and 6 years postoperatively compared to no postoperative RASi (Figure 2)

Discussion
- Previous clinical studies on perioperative RASi are conflicting and vasoplegia has been implicated in studies that failed to demonstrate a survival benefit
- Blockade of the renin-angiotensin system by RASi provides a hypothetical benefit via reversal of LV remodeling, attenuation of aortic valve thickening, and prevention of thrombosis and plaque rupture
- Careful titration of low-dose RASi to avoid hypotension in patients undergoing cardiac surgery may unmask the outcome benefits provided by perioperative RASi therapy

Conclusion
- The results of this study suggest that perioperative use of RASi has a significant benefit for the postoperative and long-term survival among patients undergoing cardiac surgery
- Further investigations including RCTs and pragmatic studies are still needed to assess the safety and effectiveness of RASi in patients undergoing cardiac surgery

References

Figure 1.

Table 1.

<table>
<thead>
<tr>
<th>Outcome a (%)</th>
<th>Unadjusted</th>
<th>RAS (n = 3056)</th>
<th>Non-RAS (n = 4979)</th>
<th>OR 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>427 (14.1)</td>
<td>829 (16.8)</td>
<td>0.74 (0.67-0.82)</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Postoperative</td>
<td>29 (0.9)</td>
<td>60 (1.2)</td>
<td>0.74 (0.5-0.98)</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Heart block</td>
<td>51 (1.7)</td>
<td>91 (1.8)</td>
<td>0.74 (0.5-0.98)</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>88 (2.9)</td>
<td>133 (2.7)</td>
<td>1.00 (0.7-1.40)</td>
<td>0.31</td>
<td>0.69</td>
</tr>
<tr>
<td>Perioperative</td>
<td>60 (2.0)</td>
<td>112 (2.2)</td>
<td>1.00 (0.7-1.40)</td>
<td>0.31</td>
<td>0.69</td>
</tr>
<tr>
<td>PA</td>
<td>19 (0.6)</td>
<td>31 (0.7)</td>
<td>0.60 (0.4-0.9)</td>
<td>0.66</td>
<td>0.03</td>
</tr>
<tr>
<td>CVA</td>
<td>2.0 (0.5)</td>
<td>3.2 (0.6)</td>
<td>0.60 (0.4-0.9)</td>
<td>0.66</td>
<td>0.03</td>
</tr>
<tr>
<td>Renal failure</td>
<td>187 (6.4)</td>
<td>202 (4.1)</td>
<td>1.00 (0.7-1.40)</td>
<td>0.31</td>
<td>0.69</td>
</tr>
<tr>
<td>Total in-hospital</td>
<td>132.4 ± 138.7</td>
<td>124.7 ± 138.6</td>
<td>1.00 (0.7-1.40)</td>
<td>0.31</td>
<td>0.69</td>
</tr>
<tr>
<td>Readmission</td>
<td>91.5 (31.1)</td>
<td>124 (31.4)</td>
<td>1.00 (0.7-1.40)</td>
<td>0.31</td>
<td>0.69</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>3.0 (1.0)</td>
<td>3.2 (0.7)</td>
<td>0.60 (0.4-0.9)</td>
<td>0.66</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Values are means ± SE. OR number or %; p-values are obtained via analysis using Pearson chi-square test or Wilcoxon rank-sum test (censored and) and/or IPW or PSO (adjusted). MACE major adverse cardiovascular events, MI myocardial infarction, TIA transient ischemic attack.