Perioperative Medicine: Beta-blockers

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Benefits of beta-blockers in non-cardiac surgery

- **↓ HR → ↑ diastolic time → ↑ LV perfusion**
- **Anti-arrhythmic**
- **Stabilize coronary plaques → ↓ risk of plaque rupture**
- **Modulating inflammatory response?**
The perioperative beta-blocker controversy

• In the 1990s, two RCTs (n=312) suggested that perioperative beta-blockers reduced perioperative MI and CV mortality\(^1,2\)
  • Studies were criticized for methodological flaws
  • Mangano study did not follow intention to treat principles\(^1\)
  • DECREASE I trial stopped early due to “large” benefit\(^2\)


• Retrospective cohort study at hospitals across U.S.
• Assessed the use of perioperative beta-blockers and association with in-hospital mortality in routine clinical practice
Beta-blockers and in-hospital mortality

POISE Trial (2008)

• **Patients:** 8351 patients at risk for perioperative cardiac events in 190 hospitals in 23 countries

• **Intervention:** Metoprolol 100 mg 2-4 hours pre-op, then metoprolol XL 200mg/day post-operatively

• **Primary outcome:** Composite of CV death, non-fatal MI, non-fatal cardiac arrest within 30 days

POISE Trial Results

<table>
<thead>
<tr>
<th></th>
<th>β blocker</th>
<th>Control</th>
<th>Relative risk (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total mortality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-POISE</td>
<td>33/1080</td>
<td>36/1070</td>
<td>0.89 (0.49–1.64)</td>
</tr>
<tr>
<td>POISE</td>
<td>129/4174</td>
<td>97/4177</td>
<td>1.33 (0.95–1.87)</td>
</tr>
<tr>
<td>Total</td>
<td>162/5254</td>
<td>133/5247</td>
<td>1.21 (0.90–1.63)</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>0.10</td>
<td></td>
<td>0.37%</td>
</tr>
<tr>
<td><strong>Non-fatal myocardial infarction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-POISE</td>
<td>25/958</td>
<td>42/919</td>
<td>0.58 (0.32–1.06)</td>
</tr>
<tr>
<td>POISE</td>
<td>152/4174</td>
<td>215/4177</td>
<td>0.71 (0.54–0.92)</td>
</tr>
<tr>
<td>Total</td>
<td>177/5132</td>
<td>257/5096</td>
<td>0.69 (0.54–0.87)</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>&lt;0.0001</td>
<td></td>
<td>31%</td>
</tr>
<tr>
<td><strong>Non-fatal stroke</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-POISE</td>
<td>12/972</td>
<td>3/967</td>
<td>2.98 (0.74–12.0)</td>
</tr>
<tr>
<td>POISE</td>
<td>27/4174</td>
<td>14/4177</td>
<td>1.93 (0.83–4.50)</td>
</tr>
<tr>
<td>Total</td>
<td>39/5146</td>
<td>17/5144</td>
<td>2.19 (1.06–4.50)</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>0.005</td>
<td></td>
<td>0%</td>
</tr>
</tbody>
</table>

POISE Trial Results

Compared to placebo, perioperative beta-blocker was associated with:

• ↓↓ in primary endpoint (HR 0.84; 95%CI 0.70-0.99)
• ↓↓ in MI (HR 0.73; 95%CI 0.60-0.89).
• ↑↑ in stroke (HR 2.17; 95%CI 1.26-3.74)
• ↑↑ in periop mortality (HR 1.33; 95%CI 1.03-1.74)

DECREASE IV trial (2009)

• DECREASE IV trial demonstrated a benefit of perioperative bisoprolol in reduction of cardiac death and non-fatal MI

• However, Dr. Polderman’s research and results in the DECREASE trials have been questioned due to scientific misconduct

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines
ACC/AHA: beta-blockers and mortality

ACC/AHA systematic review (2014)

• “In summary, this systematic review found that perioperative beta blockade started within 1 day or less before noncardiac surgery helps prevent nonfatal MI but at the cost of increased risks of stroke, death, hypotension, and bradycardia.”

ACC/AHA systematic review (2014)

• With the exclusion of the DECREASE trials:

• “There are insufficient robust data on the efficacy and safety of perioperative beta-blocker regimens that use agents aside from metoprolol or initiate treatment 2 to 45 days prior to surgery”
ACC/AHA perioperative guidelines (2014)

• Beta blockers should be continued in patients undergoing surgery who have been on beta blockers chronically (Class I, LOE B)
ACC/AHA perioperative guidelines (2014)

• In patients with intermediate- or high-risk myocardial ischemia noted in preoperative risk stratification tests, it may be reasonable to begin perioperative beta blockers (Class IIb, LOE C)

• In patients with RCRI ≥ 3, it may be reasonable to begin beta blockers before surgery (Class IIb, LOE B)

ACC/AHA perioperative guidelines (2014)

• In patients in whom beta-blocker therapy is initiated, it may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably more than 1 day before surgery (Class IIb, LOE B)
Beta-blockers and acute anemia

Nadir hemoglobin (g/L)

Probability of MACE

No beta-blockers

Beta-blocker group

MACE = Major Adverse Cardiovascular Event

Antihypertensive therapy with beta-blockers associated with ↑ risk of perioperative MACE and all-cause mortality in patients with uncomplicated HTN.

Jørgensen ME, et al. JAMA Intern Med. 2015;175(12)
Recommendations for perioperative beta-blockers

• Do not initiate on the day of surgery
• Continue chronic therapy if tolerated (even if for HTN)
• Do not initiate for uncomplicated HTN
• Consider pre-operative initiation if
  • Long-term indication (CAD, CHF, arrhythmia)
  • RCRI score > 3?
  • Able to start ≥ 1 week before surgery to ensure tolerance
• May be continued postoperatively if clinically safe (SBP>100, HR>55, no acute anemia)
References


