Relationship between high-sensitivity Troponin T measurements and 30-day mortality after noncardiac surgery

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Background

- >5 Million Americans ≥45 yrs undergo in-patient noncardiac surgery annually and 1.3% die in-hospital
  - cardiac complications are leading cause
- Myocardial injury after noncardiac surgery (MINS) is
  - defined as myocardial injury caused by ischemia that occurs during or within 30 days after surgery and is independently associated with mortality
- Diagnostic criteria for MINS, based on non-high sensitivity Troponin T assay, have been identified
- FDA recently approved usage of high-sensitivity Troponin T (hsTnT) assay, and globally many hospitals are using high-sensitivity troponin assays
- Little is known about relationship between perioperative hsTnT measurements and 30-day mortality and MINS
VISION design and methods

• Prospective, international, cohort study
• Eligibility criteria
  – ≥45 yrs underwent in-patient noncardiac surgery
• Representative sample
• Participating countries (23 centres in 13 countries)
  – North and South America, Europe, Asia, Africa, Australia
• Patients had hsTnT measurements 6-12 hours after surgery and daily for 3 days
  – 40.4% had preoperative hsTnT measurement
Analytic approach

• Iterative process (Cox proportional hazards models) exploring potential hsTnT thresholds to determine if there were hsTnT thresholds that independently altered patients’ risk of 30-day mortality and had aHR ≥3.0 and risk of 30-day mortality ≥3.0%

• To determine diagnostic criteria for MINS
  – Cox proportional hazards model to ascertain if postoperative hsTnT elevations required an ischemic feature (e.g., ischemic symptom, ECG finding) to impact 30-day mortality
Results

• Among 21,842 participants
  – mean age 63 years
  – 49% were female
• most common types of surgery
  – major orthopedic (16%)
  – major general (20%)
  – low-risk (35%)
• 21,050 (96.4%) completed 30-day follow-up
• 266 patients (1.2%; 95% CI, 1.1-1.4) died within 30 days of surgery
### Peak postoperative hsTnT thresholds associated with 30-day mortality

<table>
<thead>
<tr>
<th>hsTnT thresholds</th>
<th># of patients (%)</th>
<th># of deaths (%)</th>
<th>aHR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 ng/L</td>
<td>5318 (24.4)</td>
<td>6 (0.1)</td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td>5 to &lt;14 ng/L</td>
<td>8750 (40.1)</td>
<td>40 (0.5)</td>
<td>3.73 (1.58-8.82)</td>
<td>0.003</td>
</tr>
<tr>
<td>14 to &lt;20 ng/L</td>
<td>2530 (11.6)</td>
<td>29 (1.1)</td>
<td>9.11 (3.76-22.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20 to &lt;65 ng/L</td>
<td>4049 (18.6)</td>
<td>123 (3.0)</td>
<td>23.63 (10.32-54.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>65 to &lt;1000 ng/L</td>
<td>1118 (5.1)</td>
<td>102 (9.1)</td>
<td>70.34 (30.60-161.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥1000 ng/L</td>
<td>54 (0.2)</td>
<td>16 (29.6)</td>
<td>227.01 (87.35-589.92)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- No interaction b/w postop hsTnT threshold ≥20 ng/L and eGFR or sex (interaction p=0.83 and 0.20)
• Absolute hsTnT change ≥5 ng/L increased patients’ risk of 30-day mortality
  – aHR, 4.69; 95% CI, 3.52-6.25

• Among 4385 patients with elevated postop hsTnT
  – (i.e., 20 to <65 ng/L with change ≥5 ng/L or hsTnT ≥65 ng/L)
  – 481 (11.0%) had non-ischemic (e.g., sepsis) non-MINS hsTnT elevation
  – 13.8% of patients with elevated perioperative hsTnT had their peak value before surgery

• Elevated postoperative hsTnT without ischemic feature predicted 30-day mortality (aHR, 3.20; 95%, 2.37-4.32)
  – Identifying diagnostic criteria for MINS as
    • elevated postop hsTnT judged as resulting from myocardial ischemia (i.e., no evidence of a non-ischemic etiology), without requirement of ischemic feature
## Postop variables associated with 30-day mortality after surgery

<table>
<thead>
<tr>
<th></th>
<th>Incidence (%)</th>
<th>Adjusted HR (95% CI)</th>
<th>Attributable Fraction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINS</td>
<td>3904 (17.9)</td>
<td>3.69 (2.80-4.85)</td>
<td>24.2 (10.6-44.1)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>3101 (14.2)</td>
<td>2.77 (2.11-3.62)</td>
<td>14.4 (4.3-29.9)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>886 (4.1)</td>
<td>4.96 (3.54-6.96)</td>
<td>9.4 (2.2-21.1)</td>
</tr>
<tr>
<td>New AF</td>
<td>273 (1.2)</td>
<td>1.85 (1.19-2.87)</td>
<td>1.9 (1.2-2.9)</td>
</tr>
<tr>
<td>Stroke</td>
<td>69 (0.3)</td>
<td>5.19 (2.75-9.78)</td>
<td>1.5 (0.3-3.1)</td>
</tr>
</tbody>
</table>
MINS

- 94.1% of MINS occurred by day 2 after surgery
- 3633 patients (93.1%) who had MINS did not experience an ischemic symptom
  - probably would have gone undetected without hsTnT monitoring
- Among 3904 patients who had MINS,
  - 846 (21.7%; 95% CI, 20.4-23.0) fulfilled universal definition of MI
    - elevated hsTnT with ≥1 ischemic feature
- CV complications increased among MINS patients
  - composite of nonfatal cardiac arrest, CHF, coronary revascularization, and mortality
    - odds ratio, 8.47; 95% CI, 6.94-10.34
Conclusions

- Elevated postoperative hsTnT measurements were strongly associated with 30-day mortality
  - results consistent regardless of eGFR and sex
- Given relevance of absolute change in hsTnT measurements in diagnosing MINS and 13.8% of patients had their peak value before surgery suggests
  - physicians should consider obtaining preoperative hsTnT measurement in patients who they plan to measure hsTnT after surgery
- MINS may explain 24% of perioperative deaths
- 93% of MINS would probably go undetected without troponin monitoring