Debate: Perioperative Cardiac Biomarkers

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Assistant Professor
University of Saskatchewan
Patients

Conflicts and Disclosures

Shannon:
• POISE-3 Investigator (non-industry funded)

Michael:
• POISE-3 Investigator (non-industry funded)

Our slides are copyright compliant.
All off-label indications for drug therapy are noted.
Join our poll!

Respond at PollEv.com/shannonruzyc900

Text SHANNONRUZYC900 to (780) 800-5606 once to join, then A or B
Objectives

Participants will be able to:

• Describe the utility of preoperative natriuretic peptide testing for cardiac risk assessment
• Identify the benefits and limitations of post-operative troponin surveillance
• Treat myocardial injury after noncardiac surgery
Postoperative Troponin Surveillance
Case
On GIM consult service, you are asked to see an 81-year-old woman with high blood pressure after OR for a hip fracture. Her blood pressure is 160/90. You address this issue.

Would you order daily post-operative troponin on this patient?
A) Yes
B) No
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
We recommend obtaining daily troponin measurement for 48-72 hours in patients with a baseline risk > 5% for cardiovascular death or non-fatal MI at 30 days after surgery.

Strong recommendation; Moderate quality evidence

Position

Post-operative troponin surveillance should be used to identify patients with increased mortality:

Troponin elevations identify patients at high-risk of death.
Many patients with elevated troponins are asymptomatic.
Multiple interventions change outcomes in patients with MINS.
Troponin elevations identify high-risk patients

30-day mortality rate is 1.9%

Troponin elevations identify high-risk patients

Mortality 3%
Troponin 20-65 ng/L

Mortality 9%
Troponin 65-1,000 ng/L

Troponin elevations identify high-risk patients

Mortality 30%
Troponin $\geq 1,000$ ng/L

Troponin elevations identify high-risk patients

Troponin elevations identify high-risk patients

Troponin elevations identify high-risk patients

One in ten patients with MINS dies within 30-days compared with 1.5% of patients without MINS.

The 1-year mortality rate for patients with MINS is 22.5% compared to 9.3% for patients without MINS.

Puelacher et al. (2018). Circulation, 137;1221-1232
Troponin elevations identify high risk patients

MINS affects 16-20% of patients after non-cardiac surgery.

Post-operative troponin surveillance should be used to identify patients with increased mortality:

Troponin elevations identify patients at high-risk of death.
Many patients with elevated troponins are asymptomatic.
Multiple interventions change outcomes in patients with MINS.
Many patients with troponin elevations are asymptomatic

739 with MINS

54% troponin elevation

46% MI

82% asymptomatic

83% asymptomatic

Puelacher et al. (2018). Circulation, 137;1221-1232
Position

Post-operative troponin surveillance should be used to identify patients with increased mortality:

Troponin elevations identify patients at high-risk of death.
Many patients with elevated troponins are asymptomatic.
Multiple interventions change outcomes in patients with MINS.
MINS leads to a change in cardiac management

<table>
<thead>
<tr>
<th></th>
<th>PMI (n=397)</th>
<th>No PMI (n=2,149)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiology consult</td>
<td>52%</td>
<td>3%</td>
</tr>
</tbody>
</table>

ASA and statin therapy reduces postoperative mortality

<table>
<thead>
<tr>
<th>Predictor</th>
<th>30-day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>aOR (95% CI)</td>
</tr>
<tr>
<td>Statin</td>
<td>0.54 (0.29-0.99)</td>
</tr>
<tr>
<td></td>
<td>0.26 (0.13-0.54)</td>
</tr>
</tbody>
</table>

Cardiovascular medication intensification improves outcomes

Cardiovascular optimization improves outcomes

Dabigatran reduces vascular events after MINS

Post-operative monitoring improves outcomes

Bundled Quality Intervention:

- Intensive vital sign monitoring
- Strict glycemic control
- Strict fluid monitoring
- Hypoxia avoidance
- Anemia avoidance
- Antiplatelet restarted early
- Universal VTE prophylaxis
- Pain management

Ausset et al. (2010). Anesthesiology, 113; 529-540.
Post-operative monitoring improves outcomes

Enhanced Perioperative Monitoring

Pre-implementation
- MINS: 8.9%
- MACE: 8.1%
- Mortality: 8.3%

Post-implementation
- MINS: 3.9%
- MACE: 1.9%
- Mortality: 4.4%

Ausset et al. (2010). Anesthesiology, 113; 529-540.
Cardiac optimization improves outcomes

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Design</th>
<th>Outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>Cohort</td>
<td>30d mortality</td>
<td>aOR 0.54</td>
</tr>
<tr>
<td>Intensification</td>
<td>Cohort</td>
<td>MACE</td>
<td>HR 0.36</td>
</tr>
<tr>
<td>Statins</td>
<td>Cohort</td>
<td>30d mortality</td>
<td>2.0%</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>RCT</td>
<td>Vascular</td>
<td>4.0%</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Pre/Post</td>
<td>1y mortality</td>
<td>3.9%</td>
</tr>
</tbody>
</table>
Post-operative troponin surveillance should be used to identify patients with increased mortality:

Troponin elevations identify patients at high-risk of death.
Many patients with elevated troponins are asymptomatic.
Multiple interventions change outcomes in patients with MINS.
Position: Troponin Surveillance

Post-operative troponin surveillance **should not** be routinely used in clinical practice:

- Lack of consensus definition of myocardial injury after non-cardiac surgery
- MINS is a non-specific marker of risk
- Limited evidence to guide the management of MINS
- Uncertain cost effectiveness of troponin surveillance
The measurement of natriuretic peptides and high-sensitivity troponin after surgery may be considered in high-risk patients to improve risk stratification.

Class IIb; Level of Evidence: B

The usefulness of postoperative screening with troponin levels in patients at high risk for perioperative MI ... is uncertain in the absence of established risks and benefits of a defined management strategy.

Class IIb; Level of Evidence: B

Fleisher et al. (2014). JACC, 64(22), e77-137.
MINS (4th Generation TnT)

Postoperative TnT $\geq 0.03$ ng/ml judged as resulting from myocardial ischemia

- 1000 patients screened
- 8.0% experience MINS
- 90.2% survive 30 days
- 9.8% die within 30 days
- 92.0% MINS-free
- 1.1% die within 30 days
MINIS (hs-TnT)

Postoperative hs-TnT $\geq 20$ ng/ml with either a change between postop values $\geq 5$ ng/ml or a value $\geq 65$ ng/ml

- 1000 patients screened
- 17.9% experience MINS
- 95.7% survive 30 days
- 4.3% die within 30 days
- 82.1% MINS-free
- 0.6% die within 30 days

Perioperative Myocardial Injury

Preliminary studies revealed that 51% of patients exhibited elevated hs-TnT levels of ≥14ng/L above their preoperative values. Additionally, the incidence of perioperative myocardial injury was reported to be 9.8% in patients with preoperative troponin elevation, compared to 1.6% in those without.

Task Force for Universal Definition of MI

• Myocardial injury: cardiac troponin above the 99th percentile upper limit of normal
• Baseline preoperative value needed to determine if whether acute or chronic

## Prognostic Implications of Myocardial Injury Criteria

<table>
<thead>
<tr>
<th></th>
<th>MINS (TnT)</th>
<th>MINS (hs-TnT)</th>
<th>PMI (5th Gen.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>8.0%</td>
<td>17.9%</td>
<td>16.0%</td>
</tr>
<tr>
<td>PPV (30-day mortality)</td>
<td>9.8%</td>
<td>4.1%</td>
<td>9.8%</td>
</tr>
<tr>
<td>NPV (30-day mortality)</td>
<td>98.9%</td>
<td>99.4%</td>
<td>98.3%</td>
</tr>
</tbody>
</table>
Clinical Implications of MINS Criteria

**Institutions**
- Complication rates
- Resource utilization

**Providers**
- Workload

**Patients**
- Benefits, risks, and costs of investigations and treatment
MINS is a Non-Specific Predictor of Risk

Botto et al. (2014). Anesthesiology, 120(3), 564-578
Etiology of Postoperative MI

Daewood et al. (1996)
- Autopsies of 42 patients with fatal postop MI
- 7% plaque rupture

Cohen and Aretz (1999)
- Autopsies of 26 patients with fatal postop MI
- 46% plaque rupture

Gualandro et al. (2012)
- 120 patients angiography after postop MI
- 45% patients had Ambrose II lesion
Etiologies of Elevated Troponin

<table>
<thead>
<tr>
<th>TYPE 1 ISCHEMIA</th>
<th>OTHER CAUSES (NON-ISCHEMIC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque rupture with thrombosis</td>
<td>Heart failure</td>
</tr>
<tr>
<td><strong>TYPE 2 ISCHEMIA (SUPPLY-DEMAND)</strong></td>
<td></td>
</tr>
<tr>
<td>Coronary artery spasm</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>Coronary artery embolism</td>
<td>Cardiomyopathy/infiltrative disease</td>
</tr>
<tr>
<td>Coronary artery dissection</td>
<td>Cardiac procedures</td>
</tr>
<tr>
<td>Sustained bradyarrhythmia</td>
<td>Cardiac contusion</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Stroke</td>
</tr>
<tr>
<td>Anemia</td>
<td>Pulmonary embolism/hypertension</td>
</tr>
<tr>
<td>Tachyarrhythmia</td>
<td>Critical illness</td>
</tr>
<tr>
<td>Severe hypertension</td>
<td>Strenuous exercise</td>
</tr>
</tbody>
</table>

ASA and Statins for Postoperative MI: Limitations

• 415 patients (5%) had postop MI

<table>
<thead>
<tr>
<th>Predictor</th>
<th>30-day mortality Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>0.54 (0.29-0.99)</td>
</tr>
<tr>
<td>Statin</td>
<td>0.26 (0.13-0.54)</td>
</tr>
</tbody>
</table>

Devereaux et al. (2011). 154(8), 523-528.
ASA and Statins for Postoperative MI: Limitations

- Observational design
- Effect size not consistent with ACS trials
  - MIRACL trial: atorvastatin vs. placebo in UA/NSTEMI
    - HR 0.84 (95% CI 0.70-1.00) for MACE
  - Generalizability to MINS uncertain

Devereaux et al. (2011). 154(8), 523-528.
Treatment Intensification: Limitations

Treatment Intensification: Limitations

- Single center, retrospective, case-control study
  - Incomplete balance of predictors between cases and controls
- Suboptimal pre-operative medical therapy
- Generalizability to non-vascular patients uncertain
MANAGE Trial: Limitations

• Under recruitment
  • 1754 patients randomized (target 3200)
• Drug discontinuation (dabigatran 46% vs. 43% placebo)
• Change in primary outcome
  • Vascular mortality, non-fatal MI, non-hemorrhagic stroke, peripheral arterial thrombosis, symptomatic PE
  • Amputation and symptomatic DVT added to enhance statistical power

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dabigatran (n=877)</th>
<th>Placebo (n=877)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td>97 (11)</td>
<td>133 (15)</td>
<td>0.72 (0.55-0.93)</td>
</tr>
<tr>
<td>Vascular mortality</td>
<td>52 (6)</td>
<td>64 (7)</td>
<td>0.80 (0.56-1.16)</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>100 (11)</td>
<td>110 (13)</td>
<td>0.90 (0.69-1.18)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>35 (4)</td>
<td>43 (5)</td>
<td>0.80 (0.51-1.26)</td>
</tr>
<tr>
<td>Cardiac revascularization</td>
<td>32 (4)</td>
<td>21 (2)</td>
<td>1.53 (0.88-2.65)</td>
</tr>
<tr>
<td>Non-hemorrhagic stroke</td>
<td>2 (&lt;1)</td>
<td>10 (1)</td>
<td>0.20 (0.04-0.90)</td>
</tr>
<tr>
<td>Peripheral arterial thrombosis</td>
<td>0 (0)</td>
<td>4 (1)</td>
<td></td>
</tr>
<tr>
<td>Amputation</td>
<td>18 (2)</td>
<td>26 (3)</td>
<td>0.70 (0.38-1.27)</td>
</tr>
<tr>
<td>Symptomatic VTE</td>
<td>8 (1)</td>
<td>17 (2)</td>
<td>0.47 (0.20-1.08)</td>
</tr>
<tr>
<td>Rehospitalization for vascular reason</td>
<td>113 (13)</td>
<td>130 (15)</td>
<td>0.86 (0.67-1.11)</td>
</tr>
</tbody>
</table>

*vascular mortality, myocardial infarction, non-hemorrhagic stroke, peripheral arterial thrombosis, amputation, symptomatic VTE
<table>
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<th>Placebo(n=877)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary safety outcome</strong>*</td>
<td>29 (3)</td>
<td>31 (4)</td>
<td>0.92 (0.55-1.53)</td>
</tr>
<tr>
<td>Life-threatening bleed</td>
<td>9 (1)</td>
<td>8 (1)</td>
<td>1.11 (0.43-2.88)</td>
</tr>
<tr>
<td>Major bleed</td>
<td>21 (2)</td>
<td>25 (3)</td>
<td>0.83 (0.46-1.48)</td>
</tr>
<tr>
<td>Critical organ bleed</td>
<td>5 (1)</td>
<td>10 (1)</td>
<td>0.49 (0.17-1.43)</td>
</tr>
<tr>
<td>Intracranial bleed</td>
<td>4 (1)</td>
<td>3 (&lt;1)</td>
<td>1.32 (0.30-5.90)</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>2 (&lt;1)</td>
<td>2 (&lt;1)</td>
<td>0.98 (0.14-6.96)</td>
</tr>
<tr>
<td>Significant lower GI bleed</td>
<td>15 (2)</td>
<td>6 (1)</td>
<td>2.50 (0.97-6.44)</td>
</tr>
<tr>
<td>Non-significant lower GI bleed</td>
<td>33 (4)</td>
<td>7 (1)</td>
<td>4.77 (2.11-10.80)</td>
</tr>
<tr>
<td>Minor bleed</td>
<td>134 (15)</td>
<td>84 (10)</td>
<td>1.64 (1.25-2.15)</td>
</tr>
<tr>
<td>Fracture</td>
<td>39 (4)</td>
<td>28 (3)</td>
<td>1.38 (0.85-2.24)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>129 (15)</td>
<td>98 (11)</td>
<td>1.33 (1.02-1.73)</td>
</tr>
</tbody>
</table>

*life-threatening, major, and critical organ bleeding
Direct Costs

<table>
<thead>
<tr>
<th>Troponin Assay</th>
<th>Cost per test* (CDN dollars)</th>
<th>Total cost (3 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TnI</td>
<td>3.00</td>
<td>9.00</td>
</tr>
<tr>
<td>hs-TnI</td>
<td>3.00</td>
<td>9.00</td>
</tr>
<tr>
<td>TnT</td>
<td>6.75</td>
<td>20.25</td>
</tr>
<tr>
<td>hs-TnT</td>
<td>6.75</td>
<td>20.25</td>
</tr>
</tbody>
</table>

*does not include phlebotomy costs

CADTH (2013)
## Downstream Cost

<table>
<thead>
<tr>
<th></th>
<th>PMI n = 397</th>
<th>No PMI n = 2149</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Postoperative cardiology consultation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac workup within 30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>31 (8%)</td>
<td>11 (1%)</td>
</tr>
<tr>
<td>Myocardial perfusion imaging</td>
<td>11 (3%)</td>
<td>6 (0%)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>88 (22%)</td>
<td>93 (4%)</td>
</tr>
<tr>
<td><strong>New cardiovascular medication at discharge</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any of the below</td>
<td>105 (29%)</td>
<td>263 (12%)</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>36 (10%)</td>
<td>48 (2%)</td>
</tr>
<tr>
<td>P2Y12 inhibitors</td>
<td>20 (5%)</td>
<td>20 (1%)</td>
</tr>
<tr>
<td>Statins</td>
<td>35 (10%)</td>
<td>34 (2%)</td>
</tr>
<tr>
<td>Betablockers</td>
<td>30 (8%)</td>
<td>57 (3%)</td>
</tr>
<tr>
<td>Renin-angiotensin-aldosteron-system inhibitors</td>
<td>32 (9%)</td>
<td>104 (5%)</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>17 (5%)</td>
<td>81 (4%)</td>
</tr>
</tbody>
</table>

## Downstream Costs

<table>
<thead>
<tr>
<th>Item</th>
<th>Fee (CDN dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>36.40</td>
</tr>
<tr>
<td>Specialist consultation</td>
<td>146.20</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>182.60</strong></td>
</tr>
<tr>
<td>Echocardiogram</td>
<td>232.60</td>
</tr>
<tr>
<td>Myocardial perfusion study</td>
<td>964.53</td>
</tr>
<tr>
<td>Cardiac angiogram</td>
<td>2048.00</td>
</tr>
<tr>
<td>Inpatient physician follow-up (per day)</td>
<td>40.00</td>
</tr>
<tr>
<td>Outpatient physician follow-up (per appointment)</td>
<td>69.00-146.20</td>
</tr>
<tr>
<td>Medications (ASA, statin) (per month)</td>
<td>7.33</td>
</tr>
</tbody>
</table>

Position: Troponin Surveillance

Post-operative troponin surveillance **should not** be routinely used in clinical practice:

- Lack of consensus definition of myocardial injury after non-cardiac surgery
- MINS is a non-specific marker of risk
- Limited evidence to guide the management of MINS
- Uncertain cost effectiveness of troponin surveillance
Postoperative Troponin Surveillance

Rebuttal
Preoperative Natriuretic Peptide Testing
Audience Survey

Case
In preadmission clinic, you are assessing an 80-year-old female prior to elective hip arthroplasty for arthritis. Her only past medical history is hypertension.

Would you order a preoperative BNP on this patient?
A) Yes
B) No
<table>
<thead>
<tr>
<th></th>
<th>Would you order a preoperative BNP on this patient?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
Do you have access to same-day NP testing at your centre?

When poll is active, respond at PollEv.com/shannonruzyc900

Text SHANNONRUZYC900 to (780) 800-5606 once to join

Yes

No
We recommend measuring NT-proBNP or BNP before noncardiac surgery to enhance perioperative cardiac risk estimation in patients who are 65 years of age or older, are 45-64 years of age with significant cardiovascular disease, or have an RCRI score ≥1.

Strong recommendation; Moderate quality evidence
Preoperative NP should be used to identify patients who could benefit from troponin surveillance:

Functional assessment cannot identify high-risk patients.

Stress testing can cause harm to low-risk patients.

NP testing adds to clinical risk prediction in identifying high-risk patients.
Functional Assessment cannot identify high-risk patients

Cohort study of 1,401 adults with ≥ 1 CVD risk factor

Compared subjective MET assessment by anesthesiology/IM to objective METs.

Correlated subjective and objective MET assessment with outcomes.

Functional Assessment cannot identify high-risk patients

Subjective assessment had a sensitivity of 19.2% and a specificity of 94.7% for identifying patients with a true low exercise capacity.
Functional Assessment cannot identify high-risk patients

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30-day death/MI</strong></td>
<td></td>
</tr>
<tr>
<td>Poor function</td>
<td>1.33 (0.69-2.57)</td>
</tr>
<tr>
<td><strong>1-year death</strong></td>
<td></td>
</tr>
<tr>
<td>Poor function</td>
<td>1.59 (0.42-5.99)</td>
</tr>
</tbody>
</table>

Preoperative NP should be used to identify patients who could benefit from troponin surveillance:

- Functional assessment cannot identify high-risk patients.
- Stress testing can cause harm to low-risk patients.
- NP testing adds to clinical risk prediction in identifying high-risk patients.
Stress testing can cause harm in low-risk patients

Cohort study of 271,082 Canadians undergoing surgery.

Examined association of preoperative cardiac testing with postoperative mortality.

Stress testing can cause harm in low-risk patients

Stress testing can cause harm in low-risk patients

Stress testing can cause harm in low-risk patients

Preoperative stress testing did not improve survival
0.6% of the patients who had stress testing had PCI
0.5% of patients who had stress testing had CABG

Improved monitoring and cardiovascular risk management improved survival
Patients who had stress testing were more likely to:
Receive a statin
Receive beta-blockers
Be admitted to a monitored bed

Stress testing can cause harm in low-risk patients

NNT of 221
Patients with RCRI > 3: NNT 38

1 in 3
of the MIs & deaths at 30-days
occurred in patients with a normal stress test

Stress testing can cause harm in low-risk patients

Rates of inappropriate stress testing are very high

Review of 501 preoperative stress tests:
- 67% were “rarely appropriate”
- 74% were performed in patients with RCRI ≤ 1

Peterson et al. (2018). Am J Cardiol 122, 744-748.
Position

Preoperative NP should be used to identify patients who could benefit from troponin surveillance:

- Functional assessment cannot identify high-risk patients.
- Stress testing can cause harm to low-risk patients.
- NP testing adds to clinical risk prediction in identifying high-risk patients.
NP testing adds to clinical risk prediction in identifying high-risk patients

Karthikeyan et al. (2009). JACC 54(17), 1599-1606.
NP testing adds to clinical risk prediction in identifying high-risk patients

<table>
<thead>
<tr>
<th></th>
<th>BNP aOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day death/MINS</td>
<td>1.78 (1.21-2.62)</td>
</tr>
<tr>
<td>1-year death</td>
<td>2.91 (1.54-5.49)</td>
</tr>
</tbody>
</table>

NP testing adds to clinical risk prediction in identifying high-risk patients

Meta-analysis of 18 prospective cohort studies
2,179 patients undergoing elective, urgent and emergent noncardiac surgery
Retrospectively calculated a BNP threshold with the lowest p-value for 30-day death or non-fatal MI

NP testing adds to clinical risk prediction in identifying high-risk patients

<table>
<thead>
<tr>
<th></th>
<th>Risk of 30-day MI/death (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP &lt; 300 ng/L</td>
<td>4.9</td>
<td>3.9-6.1%</td>
</tr>
<tr>
<td>NT-proBNP &gt; 300 ng/L</td>
<td>21.8</td>
<td>19.0-24.8%</td>
</tr>
</tbody>
</table>

# Comparison of Methods of Preoperative Cardiac Risk Stratification

<table>
<thead>
<tr>
<th>Method</th>
<th>Evidence base</th>
<th>Risk of MI/death (%)</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional assessment</td>
<td>Prospective cohort</td>
<td>OR = 1.33 0.69-2.57 30-days</td>
<td>$0</td>
</tr>
<tr>
<td>Pharmacologic stress test</td>
<td>Retrospective cohort</td>
<td>HR = 0.92 0.86-0.99 1-year</td>
<td>$500</td>
</tr>
<tr>
<td>BNP measurement</td>
<td>Meta-analysis of prospective cohorts</td>
<td>OR = 3.40 2.57-4.47 30-days</td>
<td>$20</td>
</tr>
</tbody>
</table>

CADTH 2012
Position

Preoperative NP should be used to identify patients who could benefit from troponin surveillance:

- Functional assessment cannot identify high-risk patients.
- Stress testing can cause harm to low-risk patients.
- NP testing adds to clinical risk prediction in identifying high-risk patients.
We recommend obtaining daily troponin measurement for 48-72 hours in patients with a baseline risk > 5% for cardiovascular death or non-fatal MI at 30 days after surgery.

Strong recommendation; Moderate quality evidence

Position: Preoperative Natriuretic Peptide Testing

Preoperative natriuretic peptide (NP) testing should not be routinely used in clinical practice:

- Clinical risk indices provide adequate risk stratification
- Incremental improvement in risk prediction with NP modest
- Impact on clinical outcomes uncertain
- Practical barriers preclude routine use in clinical practice
The measurement of natriuretic peptides and high-sensitivity troponin after surgery may be considered in high-risk patients to improve risk stratification.

Class IIb; Level of Evidence: B

American College of Cardiology/American Heart Association

| No Recommendation |

Fleisher et al. (2014). JACC, 64(22), e77-137.
Revised Cardiac Risk Index

- High-risk surgery
- Ischemic heart disease
- Congestive heart failure
- Cerebrovascular disease
- Insulin therapy for DM
- Creatinine >177 umol/L

<table>
<thead>
<tr>
<th>Total RCRI points</th>
<th>30 day risk of MI, cardiac arrest, or death</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3.9 (2.8-5.4)</td>
</tr>
<tr>
<td>1</td>
<td>6.0 (4.9-7.4)</td>
</tr>
<tr>
<td>2</td>
<td>10.1 (8.1-12.6)</td>
</tr>
<tr>
<td>≥3</td>
<td>15.0 (11.1-20.0)</td>
</tr>
</tbody>
</table>

Revised Cardiac Risk Index

- Validated in 24 studies (792,740 patients)
  - 12 studies prospective design
  - Multiple surgical populations: vascular, orthopedic, general, thoracic, urologic, and urgent/emergency surgery

Revised Cardiac Risk Index: Cardiac Events and All-cause Mortality

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>AUC (95% CI)</th>
<th>$\hat{r}^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed noncardiac surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee et al, 1999 (7)</td>
<td>0.78 (0.73–0.82)</td>
<td></td>
</tr>
<tr>
<td>Kumar et al, 2001 (34)</td>
<td>0.73 (0.67–0.79)</td>
<td></td>
</tr>
<tr>
<td>Cuthbertson et al, 2007 (29)</td>
<td>0.54 (0.37–0.71)</td>
<td></td>
</tr>
<tr>
<td>van Klei et al, 2007 (43)</td>
<td>0.78 (0.72–0.84)</td>
<td></td>
</tr>
<tr>
<td>Fisher et al, 2008 (31)</td>
<td>0.74 (0.69–0.79)</td>
<td></td>
</tr>
<tr>
<td>Ausset et al, 2008 (26)</td>
<td>0.59 (0.43–0.76)</td>
<td></td>
</tr>
<tr>
<td>Yun et al, 2008 (46)</td>
<td>0.80 (0.71–0.89)</td>
<td></td>
</tr>
<tr>
<td>Maia and Abelha, 2008 (37)</td>
<td>0.86 (0.75–0.98)</td>
<td></td>
</tr>
<tr>
<td>Moran et al, 2008 (38)</td>
<td>0.76 (0.69–0.83)</td>
<td></td>
</tr>
<tr>
<td>Leibowitz et al, 2008 (36)</td>
<td>0.68 (0.51–0.85)</td>
<td></td>
</tr>
<tr>
<td>Pooled estimate</td>
<td>0.75 (0.72–0.79)</td>
<td>48%</td>
</tr>
</tbody>
</table>

Preoperative Natriuretic Peptides

• Systematic review and meta-analysis
• Inclusion criteria:
  • Preoperative NP measurement
  • Major cardiovascular events within 30 days of surgery
• 9 studies (3281 patients)
  • 2 studies at risk of ascertainment bias
  • Difference in timing of NP testing
  • Study-specific NP cut-points

Karthikeyan et al. (2009). JACC 54(17), 1599-1606.
Preoperative NP and 30-day Cardiac Complications

Karthikeyan et al. (2009). JACC 54(17), 1599-1606.
The Prognostic Value of Pre-Operative and Post-Operative B-Type Natriuretic Peptides in Patients Undergoing Noncardiac Surgery

- Systematic review and individual patient meta-analysis
- Inclusion criteria:
  - Patients undergoing non-cardiac surgery
  - Pre- and post-operative BNP/NT-proBNP levels
  - Major cardiovascular events within 30 days of surgery
- 18 studies (n=2179)
  - Inconsistent outcome definitions

The Prognostic Value of Pre-Operative and Post-Operative B-Type Natriuretic Peptides in Patients Undergoing Noncardiac Surgery

- NT-proBNP threshold 300ng/L and BNP threshold 92ng/L
- AUC 0.70 (95% CI 0.66-0.74)

### Variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>aOR Death/MI (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated preoperative NP</td>
<td>3.4 (2.6-4.5)</td>
</tr>
<tr>
<td>RCRI ≥3</td>
<td>2.7 (1.8-4.0)</td>
</tr>
<tr>
<td>Urgent/Emergent Surgery</td>
<td>1.6 (0.8-3.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Classification Using</th>
<th>Risk Classification Using Baseline and Pre-Operative NP</th>
<th>Patients With Primary Outcome*</th>
<th>Patients Without Primary Outcome*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;5%</td>
<td>5%-10%</td>
<td>&gt;10%-15%</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>12</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>5%-10%</td>
<td>29</td>
<td>7</td>
<td>32</td>
</tr>
<tr>
<td>&gt;10%-15%</td>
<td>2</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>&gt;15%</td>
<td>0</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

Net correctly reclassified 16.2%

Evaluation of Novel Risk Markers

1. Proof of concept studies
2. Prospective validation
3. Incremental value
4. Clinical utility (marker influences therapy)
5. Clinical outcomes
6. Cost-effectiveness

Preoperative Natriuretic Peptides: Practical Barriers

1. Access to NP testing
2. Responsibility for NP ordering
3. Optimal time for NP testing
4. Follow-up of NP results
5. Interpretation of NP testing in context of clinical risk indices
6. Interpretation in chronic kidney disease
Preoperative BNP Measurement

Rebuttal
Case
On GIM consult service, you are asked to see an 81-year-old woman with high blood pressure after OR for a hip fracture. Her blood pressure is 160/90. You address this issue.

Would you order daily post-operative troponin on this patient?
A) Yes
B) No
Would you order daily post-operative troponin on this patient?

Yes

No
Case
In preadmission clinic, you are assessing an 80-year-old female prior to elective hip arthroplasty for arthritis. Her only past medical history is hypertension.

Would you order a preoperative BNP on this patient?
A) Yes
B) No
Would you order a preoperative BNP on this patient?

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
Thank you!

Shannon.Ruzycki@ahs.ca    Michael.Prystajecky@usask.ca
@ShannonRuzycki
## DASI & BNP correlate with outcomes

<table>
<thead>
<tr>
<th></th>
<th>BNP aOR</th>
<th>DASI aOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30-day death/MI</strong></td>
<td>1.88 (0.89-3.96)</td>
<td>0.91 (0.83-0.99)</td>
</tr>
<tr>
<td><strong>30-day death/MINS</strong></td>
<td>1.78 (1.21-2.62)</td>
<td>0.96 (0.92-0.99)</td>
</tr>
<tr>
<td><strong>1-year death</strong></td>
<td>2.91 (1.54-5.49)</td>
<td>0.94 (0.87-1.02)</td>
</tr>
</tbody>
</table>

Wijeysundera 2018
Inpatient Surgical Discharges

CIHI (2018)