Update in Perioperative Medicine 2010

Steven L. Cohn, MD, FACP
Gerald W. Smetana, MD, FACP
Amir K. Jaffer, MD, FHM
Kurt Pfeifer, MD, FACP

SGIM
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Format

- Literature search 2009-2010
- Select potential articles of interest
- Group discussion
- Rate the articles
- Present those with the highest scores that have specific clinical interest or potential impact on clinical practice
Agenda

- Cardiac Risk
  - BB, statins, RCRI, BNP
- Q&A
- VTE Prophylaxis
  - Oral Xa inhibitors, mechanical compression
- Miscellaneous
  - Cancer surgery in the elderly, SSI, insulin in vasc surgery, tight glucose control
- Pulmonary Risk
  - Smoking cessation
- Q&A; evaluations
Update in Perioperative Medicine
Cardiac Risk

Steven L. Cohn, MD, FACP
Director – Medical Consultation Service
Kings County Hospital Center
Clinical Professor of Medicine
SUNY Downstate

Disclosures
Speakers Bureau – Sanofi–Aventis, Lilly/Daiichi Sankyo
Minor stock holdings – AZD, GSK, MRK, PFE
Perioperative Cardiac Risk

- Effect of chronic beta-blocker use on stroke after noncardiac surgery.
  - Am J Cardiol 2009; 104:429–433

- Impact of prophylactic beta-blocker therapy to prevent stroke after noncardiac surgery.
  - Am J Cardiol 2010; 105:43–47

- Bisoprolol and fluvastatin for the reduction of perioperative cardiac mortality and myocardial infarction in intermediate-risk patients undergoing noncardiovascular surgery. (DECREASE IV)
  - Ann Surg 2009; 249:921–926

- Fluvastatin and perioperative events in patients undergoing vascular surgery. (DECREASE III)

- ACC Focused Update on Perioperative Beta-Blockade.
  - J Am Coll Cardiol 2009; 54:2102–2128
Perioperative Cardiac Risk

- **Background – Beta-blockers**
  - Initial studies showed a benefit
    - Mangano (atenolol); Poldermans (bisoprolol)
    - Titrated to heart rate
  - Subsequent studies failed to show a benefit
    - MAVS, DIPOM, POBBLE (metoprolol)
    - Dose not titrated
  - Other studies stressed HRC (DECREASE II; Ferringa)
  - Admin database showed *role of RCRI* (Lindenauer)
  - POISE (high-dose metoprolol CR started hours before surgery) decreased non-fatal MI at expense of increased total mortality and non-fatal CVA
Perioperative Cardiac Risk

- Current clinical BB questions
  - Are BB beneficial or harmful?
    - Do they increase periop strokes?
  - When and how should they be used?
    - Indications/recommendations; HRC
  - Does the choice of BB matter?
    - Bisoprolol vs atenolol or metoprolol
Objective
- Assess the association between chronic BB use and periop stroke

Methods
  - 87 postop strokes; excluded 53 (intracranial/carotid)
  - 34 cases (0.02%) – confirmed postop CVA
  - 2 controls/case stratified by year, age, type of surgery
  - obtained info on possible risk factors
    - Meds and BB use, CHD, HTN, DM, CVA, AF, PAD
Results

- Median day for stroke – postop day 2
  - HTN, CVA, DM, ASA, statin more common in cases
  - BB use (29%) and % max dose (25%) similar

- Multivariate analysis
  - Prior CVA, DM were the most important risk factors
  - After adjustment, no diff in stroke with any meds
  - Limitations: case–control
    - Potential confounders
    - Hemodynamic data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>12.1</td>
<td>1.1–138</td>
</tr>
<tr>
<td>CVA</td>
<td>10.3</td>
<td>2.7–40</td>
</tr>
<tr>
<td>CHD</td>
<td>3.7</td>
<td>1.1–12</td>
</tr>
<tr>
<td>AF</td>
<td>5.2</td>
<td>1.1–24</td>
</tr>
<tr>
<td><strong>Beta-blocker</strong></td>
<td><strong>0.4</strong></td>
<td><strong>0.1–1.2</strong></td>
</tr>
<tr>
<td>Statin</td>
<td>1.4</td>
<td>0.3–5.6</td>
</tr>
<tr>
<td>ASA</td>
<td>1.6</td>
<td>0.6–4.4</td>
</tr>
</tbody>
</table>

Conclusion

- This case–control study showed no increased risk of postoperative stroke in pts taking chronic beta-blockers.

- Bottom Line: As per ACC guidelines, pts taking BB should continue them periop.
  - In these pts unexpected hypotension or bradycardia is less likely than in a beta-blocker naïve pt.
  - Authors urged other researchers to release data about clinical conditions and hemodynamic changes.

Impact of prophylactic beta-blocker therapy to prevent stroke after noncardiac surgery.

*Am J Cardiol* 2010; 105:43–47

- **Objective**
  - Assess the incidence, risk factors, and BB use associated with postop stroke in DECREASE trials

- **Methods**
  - Pooled analysis of 3,884 pts from DECREASE I,II,IV
  - Recorded potential risk factors for postop stroke
    - Age > 70, CAD, CHF, DM, CKD, prior CVA
    - Type and dose of BB
  - **Endpoint**: stroke or TIA within 30 days after surgery
Results

- Incidence of postop stroke: 0.46% (18/3884)
  - 12/18 (67%) stroke pts on BB
    - Avg dose 15% max
  - BB users: 0.5% (12/2366)
  - non-users: 0.4% (6/1518)
- Median day: postop day 2
  - All ischemic
- Risk factors
  - Hx of stroke (OR 3.79)
  - No assoc with bisoprolol

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adj OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>0.88</td>
<td>0.31–3.93</td>
</tr>
<tr>
<td>CVA</td>
<td>3.79</td>
<td>1.24–11.6</td>
</tr>
<tr>
<td>IHD</td>
<td>0.4</td>
<td>0.13–1.21</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>1.16</td>
<td>0.40–3.35</td>
</tr>
<tr>
<td>Statin</td>
<td>0.85</td>
<td>0.3–2.4</td>
</tr>
<tr>
<td>Antiplat</td>
<td>1.75</td>
<td>0.6–5.15</td>
</tr>
<tr>
<td>Anticoag</td>
<td>1.27</td>
<td>0.35–4.64</td>
</tr>
</tbody>
</table>

Conclusion

- Low-dose bisoprolol started ≥30 days before surgery is not associated with increased risk of postop stroke.
  - DECREASE: 0.5% OR 1.16 (0.4–3.4)
  - POISE: 1% OR 2.2 (1.3–3.8)

Objective
- Assess efficacy and safety of BB, statins, and their combination on incidence of periop MI and cardiac death in intermediate-risk surgical patients.

Methods
- Prospective, open-label, 2x2 factorial RCT (multicenter)
- 1066 pts with estimated risk of cardiac complications 1–6%
- Medications: started 34 days preop; cont’d 30 days postop
  - Bisoprolol (2.5 mg titrated to HR 50–70)
  - Fluvastatin XL (80 mg daily)
  - Both
  - Neither
- Endpoints: composite–cardiac death/MI within 30 days postop
  - Secondary: all cause mortality, arrh, CHF, revasc
  - Safety: bradycardia, hypotension, ALT>3x, CK>10x ULN, myopathy, rhabdo
Primary endpoint for each individual treatment group

**Results**

**Beta-blocker vs control**

- **Bisoprolol control**
  - Cardiac death or nonfatal myocardial infarction
  - Days after surgery
  - P-value 0.002

- **Bisoprolol**
  - Cardiac death or nonfatal myocardial infarction
  - Days after surgery

**Statin vs control**

- **Fluvastatin control**
  - Cardiac death or nonfatal myocardial infarction
  - Days after surgery
  - P-value 0.17

- **Fluvastatin**
  - Cardiac death or nonfatal myocardial infarction
  - Days after surgery

**Abn LFTs:** 8 (1.5%) vs 11 (2.1%) control

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Results

Primary endpoint by treatment group

Conclusions

- Bisoprolol treatment begun 1 month before surgery and titrated to heart rate significantly reduced the incidence of perioperative cardiac death and MI without increasing morbidity or noncardiac mortality.

- Fluvastatin showed a trend for improved outcome.

- Limitations:
  - Open label (lack of blinding)
  - Terminated early (enrollment problems)
  - Applicable only to intermediate risk patients
ACC Focused Update on Perioperative Beta–Blockade.

Class I

- BB *should be continued* perioperatively in pts *already receiving* them for treatment of conditions with ACC Class I guideline indications for them.
Class IIa

**BB titrated to HR and BP are:**
- *probably recommended* for pts undergoing vascular surgery with known CAD or ischemia on preop stress testing (B);
- *reasonable* for pts undergoing vascular surgery with >1 clinical risk factor (C);
- *reasonable* for pts undergoing intermediate risk surgery with CAD or >1 clinical risk factor (C)

Class IIb

**Usefulness of BB is uncertain** for pts undergoing:
- Intermediate-risk or vascular surgery with 1 clinical risk factor in the absence of CAD (C);
- Vascular surgery with no clinical risk factors (B)
Class III

- *Should not be given* to pts with absolute contraindications to BB (C);

- Routine administration of high-dose BB in the absence of dose titration *is not useful and may be harmful* to pts not currently taking BB who are undergoing noncardiac surgery (B)
Pts taking BB should continue them periop.

Bisoprolol, using the DECREASE protocol, appears to reduce cardiac events without increasing stroke or mortality.

Consider factors that affect outcome when prescribing prophylactic perioperative BB:

- Patient selection (high vs low–intermediate risk)
- Timing of initiation (hours before vs days–weeks)
- Type of BB (highly B1 selective, longer acting)
- Genetic/cultural differences (rs#2429511, Afr Amer)
- Heart rate control while minimizing side effects
Perioperative Cardiac Risk

- **Background – Statins**
  - Inadequate evidence showing a benefit
    - Retrospective studies and meta-analyses
    - Only 1 small RCT (100 pts)
      - Atorvastatin decreased a composite endpoint at 6 months
  - **Safety concerns**
    - Liver dysfunction, myopathy/rhabdo
  - **Conflicting recommendations:**
    - Manufacturers recommend withholding statins before major surgery
    - ACC guidelines recommend continuing statins periop
      - Concern about rebound
      - Start prophylactically?
Fluvastatin and perioperative events in patients undergoing vascular surgery. (DECREASE III)


- **Objective**
  - To assess whether perioperative statin therapy reduces the incidence of postoperative adverse cardiac events in pts undergoing elective vascular surgery.

- **Methods**
  - Double-blind placebo-controlled trial
  - Statin naïve pts scheduled for vascular surgery
    - aortic, lower limb, CEA
  - At least 51 points on a prespecified risk index
  - Randomized to extended-release fluvastatin 80mg or placebo
    - Also started on bisoprolol 2.5mg if not already on BB
  - Excluded pts on statin, emergency surgery, unstable CAD, extensive ischemia on stress test

- **Endpoints**:
  - Primary – myocardial ischemia
  - Secondary – composite– cardiac death/MI within 30 days postop
  - Safety – CK>10x, ALT>3x ULN; myopathy, rhabdo
## Results (DECREASE III)

Odd Ratios for primary & secondary outcomes (fluvastatin patients compared with placebo)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Fluvastatin (n=250)</th>
<th>Placebo (n=247)</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>Abs risk reduction (%)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myocardial ischemia</strong></td>
<td>27 (10.8%)</td>
<td>47 (19.0%)</td>
<td>0.55</td>
<td>0.34–0.88</td>
<td>-8.0</td>
<td>13</td>
</tr>
<tr>
<td><strong>Nonfatal MI</strong></td>
<td>8</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cardiovascular death</strong></td>
<td>4</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CV death or nonfatal MI</strong></td>
<td>12 (4.8%)</td>
<td>25 (10.1%)</td>
<td>0.47</td>
<td>0.24–0.94</td>
<td>-5.3</td>
<td>19</td>
</tr>
</tbody>
</table>

## Results (DECREASE III)

Effects on Lipids, Inflammatory Markers, & Safety Parameters

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Fluvastatin</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T Cholest</td>
<td>-20.0%</td>
<td>-3.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL</td>
<td>-24.1%</td>
<td>-3.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL</td>
<td>-1.2%</td>
<td>+1.3%</td>
<td>0.20</td>
</tr>
<tr>
<td>Triglyc</td>
<td>+1%</td>
<td>0%</td>
<td>0.58</td>
</tr>
<tr>
<td>CRP</td>
<td>-20.5%</td>
<td>+3.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-6</td>
<td>-32.7%</td>
<td>-4.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CPK&gt;10x</td>
<td>4.1%</td>
<td>3.0%</td>
<td>0.8</td>
</tr>
<tr>
<td>AST&gt;3x</td>
<td>3.1%</td>
<td>5.2%</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Conclusions

- Perioperative fluvastatin therapy begun 1 month before vascular surgery was associated with improved postoperative cardiac outcome and reduction in serum lipid levels and inflammatory markers.
  - This was on top on beta-blockers.
  - No increase in adverse events (stroke, total mortality, liver dysfunction, myopathy).

Pts taking statins should continue them periop as recommended by the current ACC guidelines

- despite warnings to the contrary from the manufacturers and earlier clinical advisory of the ACC/AHA/NHLBI.

Consider prophylactic statins.

- Extended-release fluvastatin (80 mg) started 30 days preop significantly reduced cardiac events in vascular surgery pts with a similar trend in intermediate-risk pts without increasing adverse events (liver dysfunction/myopathy).
Systematic Review: Prediction of Perioperative Cardiac Complications and Mortality by the Revised Cardiac Risk Index

BACKGROUND
Revised Cardiac Risk Index

• Originally published in 1999 & derived/validated in a single center from 1989-1994
• Derived from 2893 patients & validated in 1422
  – Age ≥50 years
  – Undergoing major elective noncardiac surgery
• Multivariable index for predicting perioperative cardiac complications
  – Coronary artery disease
  – Congestive heart failure
  – Cerebrovascular disease
  – DM requiring insulin
  – Renal insufficiency (creatinine >2 mg/dl)
  – High-risk noncardiac surgery
    • Intrathoracic
    • Intraperitoneal
    • Suprainguinal vascular

Revised Cardiac Risk Index

- Created 4 risk classes based on cardiac risk
- Superior prediction of risk (AUC 0.806) vs previous methods:
  - ASA
  - Cardiac Risk Index
  - Modified Cardiac Risk Index

<table>
<thead>
<tr>
<th>Risk Class</th>
<th># of RCRI factors</th>
<th>Cardiac Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0</td>
<td>0.4%</td>
</tr>
<tr>
<td>II</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>6.6%</td>
</tr>
<tr>
<td>IV</td>
<td>≥3</td>
<td>11.0%</td>
</tr>
</tbody>
</table>

Revised Cardiac Risk Index

Limitations

• Initial derivation & validation from single institution
• Subanalysis: lesser performance among vascular surgery patients (AUC 0.774)
• Subsequent studies noted aortic stenosis as a risk factor - not identified in the RCRI

METHODS

• Literature review through December 2008.
• Selected any cohort study that studied association of RCRI and major cardiac complications or all-cause mortality.
• 24 studies identified (most from 2006-2008)
  – 12 prospective
  – 10 focused on vascular surgery
• Total of nearly 800,000 patients
• Large degree of heterogeneity
  – Types of surgery
  – Outcomes – all-cause mortality vs. cardiac complications (varied definition of these)

## Results

### Perioperative Cardiac Complications

Differentiating between low and high risk pts

<table>
<thead>
<tr>
<th></th>
<th>Mixed noncardiac surgery</th>
<th>Vascular surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pooled AUC</strong></td>
<td>0.75 (CI, 0.72-0.79)</td>
<td>0.64 (CI, 0.61-0.68)</td>
</tr>
<tr>
<td><strong>Positive LR</strong></td>
<td>2.78</td>
<td>1.56 (CI, 1.42-1.73)</td>
</tr>
<tr>
<td><strong>Negative LR</strong></td>
<td>0.45</td>
<td>0.55 (CI, 0.40-0.76)</td>
</tr>
</tbody>
</table>
CONCLUSIONS

RCRI

• Moderate performance at discriminating between low and high risk patients for perioperative cardiac complications
• Lower performance in vascular surgery pts
• Also predicted all-cause mortality with lower performance (though not intended for this)

LIMITATIONS

• Included studies had large degree of variability in measured outcomes and definitions

• Only evaluated RCRI’s discriminatory capacity, not its ability to stratify risk

BOTTOM LINE

• RCRI remains the best available tool for predicting perioperative cardiac complications:
  – Easy to use
  – Predictive value (AUC) comparable to well-accepted models for prediction of other clinical risks
  – Now validated with multiple patient populations

• RCRI’s performance may be lower with vascular surgery patients but is still reasonable
Is a Preoperative Brain Natriuretic Peptide (BNP) or NT-ProBNP an Independent Predictor of Adverse outcomes in Non-cardiac Surgery?

Does BNP or NT-ProBNP Predict Outcomes in Non-cardiac Surgery

**Question:** In patients having non-cardiac surgery, is BNP or NT-ProBNP an independent predictor of adverse cardiovascular outcomes after non-cardiac surgery?

**Methods:** 5 search strategies to identify potentially eligible studies. Teams of 2 people independently determined eligibility and resolved disagreement thru consensus. Data abstraction and outcome adjudicators were blinded to BNP values. Included studies that measured BNP and NT-proBNP before NCS in patients ≥ 18;

- **Outcomes:** all-cause death, CV death, ACS, CABG, cardiac arrest, serious cardiac arrhythmia, HF, or rehospitalization for a cardiac cause) ≤ 30 days after surgery.
Flow Chart Showing Selection of Studies

Citations retrieved by search strategy (n=564)

Full text articles retrieved for detailed review (n=35)

Articles excluded after title and abstract screening (n=529)

Articles excluded after full text review (n=26)

Studies fulfilling eligibility criteria and included in systematic review (n=9)

### Characteristics of Studies Included

<table>
<thead>
<tr>
<th>Author, Year (Ref. #)</th>
<th>Study Period</th>
<th>Patient Population</th>
<th>Mean Age of Pts in Study (yrs)</th>
<th>Types of Surgery</th>
<th>Length of Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dernellis &amp; Panaretou, 2006</td>
<td>Not reported</td>
<td>Elective</td>
<td>70</td>
<td>Abdominal, genitourinary, orthopedic, head &amp; neck</td>
<td>3-17 days</td>
</tr>
<tr>
<td>Cuthbertson et al., 2007</td>
<td>Sept 2004 to Dec 2005</td>
<td>Elective</td>
<td>66</td>
<td>Major vascular, abdominal, genitourinary</td>
<td>72h</td>
</tr>
<tr>
<td>Cuthbertson et al., 2007</td>
<td>Jan 2006 to June 2006</td>
<td>Emergent</td>
<td>74</td>
<td>Abdominal, orthopedic</td>
<td>72h</td>
</tr>
<tr>
<td>Yun et al., 2008</td>
<td>Jan 2006 to Dec 2006</td>
<td>Elective</td>
<td>68</td>
<td>Thoracic, abdominal, genitourinary, orthopedic, head &amp; neck</td>
<td>30 days</td>
</tr>
<tr>
<td>Mahla et al., 2007</td>
<td>Oct 2002 to June 2003</td>
<td>Elective</td>
<td>70</td>
<td>Major vascular</td>
<td>30 days</td>
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<tr>
<td>Yen et al., 2005</td>
<td>Nov 2002 to Aug 2003</td>
<td>Elective</td>
<td>57</td>
<td>Thoracic, major vascular, abdominal</td>
<td>30 days</td>
</tr>
<tr>
<td>Gibson et al., 2007</td>
<td>Apr 2004 to Oct 2005</td>
<td>Elective</td>
<td>68</td>
<td>Thoracic, major vascular, abdominal</td>
<td>30 days</td>
</tr>
<tr>
<td>Feringa et al., 2006</td>
<td>Oct 2003 to Dec 2004</td>
<td>Elective</td>
<td>59</td>
<td>Major vascular</td>
<td>30 days</td>
</tr>
<tr>
<td>Cardinale et al., 2007</td>
<td>Oct 2004 to Dec 2005</td>
<td>Elective</td>
<td>62</td>
<td>Thoracic</td>
<td>8 days</td>
</tr>
</tbody>
</table>
## BNP Thresholds in the Studies

<table>
<thead>
<tr>
<th>Author, Year (Ref. #)</th>
<th>Marker</th>
<th>Assay Manufacturer</th>
<th>BNP Threshold (pg/ml)</th>
<th>Timing of BNP Measurement</th>
<th>Proportion of Pts with Elevated BNP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dernellis &amp; Panaretou, 2006</td>
<td>BNP</td>
<td>AxSYM system Axis Shield Diagnostics</td>
<td>189</td>
<td>Up to 3 days pre-operative</td>
<td>19.9</td>
</tr>
<tr>
<td>Cuthbertson et al., 2007</td>
<td>BNP</td>
<td>ADVIA Centaur Bayer</td>
<td>40</td>
<td>Within 24 h pre-operative</td>
<td>33.3</td>
</tr>
<tr>
<td>Cuthbertson et al., 2007</td>
<td>BNP</td>
<td>ADVIA Centaur Bayer</td>
<td>170</td>
<td>Immediately pre-operative</td>
<td>37.5</td>
</tr>
<tr>
<td>Yun et al., 2008</td>
<td>NT-proBNP</td>
<td>Elecsys 2010 Roche Diagnostics</td>
<td>201</td>
<td>Pre-operative</td>
<td>24.4</td>
</tr>
<tr>
<td>Mahla et al., 2007</td>
<td>NT-proBNP</td>
<td>Elecsys 2010 Roche Diagnostics</td>
<td>280</td>
<td>1 day pre-operative</td>
<td>38.1</td>
</tr>
<tr>
<td>Yen et al., 2005</td>
<td>NT-proBNP</td>
<td>Elecsys 2010 Roche Diagnostics</td>
<td>201</td>
<td>Immediately pre-operative</td>
<td>23.7</td>
</tr>
<tr>
<td>Gibson et al., 2007</td>
<td>BNP</td>
<td>Shinoria BNP Shinogi &amp; Co.</td>
<td>108.5</td>
<td>1 day pre-operative</td>
<td>23.7</td>
</tr>
<tr>
<td>Feringa et al., 2006</td>
<td>NT-proBNP</td>
<td>Elecsys 2010 Roche Diagnostics</td>
<td>533</td>
<td>21±11 days pre-operative</td>
<td>15.3</td>
</tr>
<tr>
<td>Cardinale et al., 2007</td>
<td>NT-proBNP</td>
<td>Elecsys 1010 Roche Diagnostics</td>
<td>Various</td>
<td>24 h pre-operative</td>
<td>17.8</td>
</tr>
</tbody>
</table>

Adjusted Odds Ratios for Preop BNP & NT-proBNP as Predictor of Postop CV Outcomes

15-38% of patients had an elevated BNP. 9.6% of patients had >1 perioperative CV event

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th># of pts</th>
<th># of events</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yun</td>
<td>2008</td>
<td>279</td>
<td>25</td>
<td>7.6 (2.2, 26.6)</td>
</tr>
<tr>
<td>Cuthbertson</td>
<td>2007</td>
<td>204</td>
<td>12</td>
<td>7.5 (1.9, 29.4)</td>
</tr>
<tr>
<td>Gibson</td>
<td>2007</td>
<td>190</td>
<td>26</td>
<td>104.0 (20.0, 540.0)</td>
</tr>
<tr>
<td>Mahla</td>
<td>2007</td>
<td>218</td>
<td>44</td>
<td>5.3 (1.04, 27.5)</td>
</tr>
<tr>
<td>Dernellis</td>
<td>2006</td>
<td>1590</td>
<td>96</td>
<td>34.5 (17.1, 68.6)</td>
</tr>
<tr>
<td>Feringa</td>
<td>2006</td>
<td>170</td>
<td>13</td>
<td>17.2 (2.8, 106.4)</td>
</tr>
<tr>
<td>Yeh</td>
<td>2006</td>
<td>190</td>
<td>15</td>
<td>76.3 (8.8, 661.8)</td>
</tr>
</tbody>
</table>

Random Effects, Heterogeneity p=0.03, I²=58%

Conclusion

- Patients with elevated preop BNP are at an increased risk for adverse cardiovascular outcomes within 30-days of non-cardiac surgery.

Limitations

- Moderate heterogeneity
- Studies evaluated different outcomes
- Large differences in discriminatory threshold for BNP and NT-pro BNP may limit clinical application
Implications for IM Practice

- Only biochemical and noninvasive tool available to date to risk-stratify patients
- Could be used as a rapid and inexpensive method to enhance preoperative cardiovascular risk prediction. Results from the VISION study will help clarify the value in large adequately powered prospective study.
Disclosure of Financial Relationships for Amir Jaffer, MD

- Consultant
  - Sanofi-Aventis, Astra-Zeneca, Boehringer Ingelheim, Canyon Pharmaceuticals
- Research and Grant Support
  - Astra-Zeneca
- Board Member
  - SPAQI, Anticoagulation Forum
Rivaroxaban Vs Enoxapararin for Thromboprophylaxis after Total Knee Arthroplasty (TKA) [Record 4]

Turpie et al. Lancet 2009; 373:1673-80
**Rivaroxaban Vs Enoxaparin for Thromboprophylaxis after TKA**

**Question:** In patients having total knee arthroplasty, what is the efficacy and safety of thromboprophylaxis with rivaroxaban compared with enoxaparin?

**Methods:**
- Double blind RCT, multinational, 3148 patients age >18,
- Oral rivaroxaban 10 mg/day (6 to 8 h after surgery) or subcutaneous (SC) enoxaparin, 30 mg SC q12h (starting 12-24 h after surgery) for 10-14 days.
- Between days 11-15, patients had bilateral venography.
- Follow-up for safety outcomes was 96%; efficacy outcomes was 70% (modified intention-to-treat analysis)
Results: Rivaroxaban vs Enoxaparin after TKA

ARR = 3.2%, CI 0.71-5.67, p = 0.0118

Turpie et al. Lancet 2009; 373: 1673-80
Rivaroxaban Vs. Enoxaparin after TKA

Conclusion

• Once daily Rivaroxaban (Xarelto) was significantly more effective than Enoxaparin 30 mg SC twice daily. The two drugs had similar bleeding profiles.

Limitations

• Number of venograms that were inadequate was higher than expected.

• The exclusion of surgical site bleeding from the major bleeding definition may also be a limitation.
Implications for IM Practice

The drug is only approved in Canada and the EU - not yet FDA-approved, but once approved will provide an oral option with no monitoring alternative to established parenteral alternatives for VTE prophylaxis. However, ongoing surveillance for safety is warranted.
Apixaban Vs Enoxaparin for Thromboprophylaxis after Total Knee Arthroplasty (TKA) [ADVANCE-2]

Lassen et al. Lancet 2010; 375:807-15
Question: In patients having total knee arthroplasty, what is the efficacy and safety of thromboprophylaxis with Apixaban compared with Enoxaparin?

Methods:
- Double blind RCT, multinational, 3057 patients age >18,
- Oral apixapan 12-24h after surgery or enoxaparin 12-h preop, and both given for 10-14 d.
- Bilateral venography between 10-14 days post-op.
- Follow-up for safety outcomes was 97%. Follow-up for efficacy outcomes was 67% (modified intention-to-treat analysis).
Results: Apixapan vs. Enoxaparin after TKA

ARR = 9.3%; 95% CI, 5.8-12.7; P < 0.0001

Lassen et al. Lancet 2010;375: 807-15
Apixaban vs. Enoxaparin after TKA

Conclusion

• Twice daily Apixaban was significantly more effective than Enoxaparin 30 mg SC twice daily. The two drugs had similar bleeding profiles

Limitations

• ~78% of patients had an interpretable venogram
Implications for IM Practice

Apixaban is yet another oral Xa-inhibitor that has efficacy and safety for VTE prophylaxis in TKA but is not yet available for use in the US.
Mobile Compression Device Vs. LMWH for VTE Prevention after THA

CECT + SFT Vs Enoxaparin for Thromboprophylaxis after THA

**Question:** In patients having total hip arthroplasty, is thromboprophylaxis with Continuous Enhanced Circulation Therapy plus Synchronized Flow Technology safer than Enoxaparin without compromising efficacy?

**Methods:**
- RCT, multicenter, 414 patients age >18, scheduled for unilateral THA
- Rec’d either device or Enoxaparin 30 mg SC twice daily.
- Bilateral Compression Ultrasound 10-12 days post-op.
- Follow-up for safety outcomes was 95%; for efficacy outcomes was 70% (modified intention-to-treat analysis)
CECT + SFT Vs Enoxaparin for Thromboprophylaxis after THA

Major and Clinically Relevant bleeding
ARR=6%; P=0.0004

Conclusion

- Mobile Compression devices worn ~ 20hrs per day are safer than twice daily Enoxaparin.

Limitations

- Sample size was inadequate to show differences in the efficacy rates
- Lack of blinding
- Use of compression US instead of venogram to assess efficacy endpoint
Implications for IM Practice

Authors do not discuss cost or patient satisfaction; if they are comparable to pharmacologic options and larger studies confirm their efficacy, it would represent an advance in VTE prophylaxis.


Kurt Pfeifer, MD, FACP

Associate Professor of Medicine
Medical College of Wisconsin
Major Cancer Surgery in the Elderly: Results from the American College of Surgeons National Surgical Quality Improvement Program


Number of elderly patients requiring surgical resection of malignancies is expected to rise.

Current data on operative outcomes in elderly patients are conflicting:
  - Single center studies suggest mortality on par with younger adults.
  - Larger observational studies suggest increased complications.

Inaccurate risk assessment may lead to:
  - Avoidance of surgery in patients who would have benefited.
  - Performance of surgery in those who faced greater risk from surgery than from their cancer.

METHODS

• Utilized data collected in the American College of Surgeons National Surgical Quality Improvement Program (NSQUIP):
  – Prospectively gathered, multivariable database from 190 academic and private hospitals with 8781 patients over age 40 undergoing thoracic, abdominal or pelvic surgery

• Studied several outcomes:
  – 30-day mortality
  – Length-of-stay (LOS)
  – Major complications (i.e. deep surgical site infections, wound dehiscence, renal failure, respiratory failure, cardiac arrest, pneumonia, PE)
  – Minor complications (i.e. superficial surgical site infections, DVT, UTI)
  – Repeat operations

# RESULTS – Bivariant Analysis

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>40-54</th>
<th>55-65</th>
<th>66-74</th>
<th>≥75</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality</td>
<td>2.8%</td>
<td>1.1%</td>
<td>1.8%</td>
<td>3.5%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Major postop complication</td>
<td>26.7%</td>
<td>21.8%</td>
<td>24.9%</td>
<td>27.4%</td>
<td>30.7%</td>
</tr>
<tr>
<td>Prolonged LOS (≥75th percentile – 12 days)</td>
<td>26.9%</td>
<td>19.8%</td>
<td>24.3%</td>
<td>27.3%</td>
<td>33.7%</td>
</tr>
</tbody>
</table>

P values all <0.0001

## RESULTS – Multivariable Analysis

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio compared to 40-54 year-olds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>55-65</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>1.87</td>
</tr>
<tr>
<td>Major postop complication</td>
<td>-</td>
</tr>
<tr>
<td>Prolonged LOS (&gt;75th percentile – 12 days)</td>
<td>-</td>
</tr>
</tbody>
</table>

* Higher than any other variable

# Lower than most other variables, including high ASA class & receipt of transfusion

CONCLUSIONS

• Advanced age is an independent predictor of 30-day mortality, postoperative complications and extended LOS in surgical cancer patients.

• Age ≥75 most predictive variable for 30-day mortality but less predictive of postoperative complications
  – Suggests that mortality less related to immediate postoperative problems

• Though risk is increased in the elderly, it is not prohibitively high
LIMITATIONS

• NSQIP does not include information on hospital or surgeon volume – previously shown to be predictive of morbidity & mortality

• Not all postoperative complications are recorded in NSQIP, especially those specific to particular procedures
BOTTOM LINE

- Increased 30-day mortality and postoperative complications should be factored into the decision for or against surgery in elderly cancer patients.
- Basing surgical decisions purely on age is still ill-advised.
Timing of Antimicrobial Prophylaxis and the Risk of Surgical Site Infections: Results From the Trial to Reduce Antimicrobial Prophylaxis Errors

Prophylactic antibiotics reduce the risk of surgical site infections (SSIs)
Medicare & JCAHO utilize administration of antibiotics within 1 hour before incision as a publicly reported performance measure
Although many studies have clearly demonstrated the benefit of preoperative antibiotics in reducing SSIs, no studies have looked at the specific optimal timing of prophylactic antibiotics

METHODS

• Utilized data from Trial to Reduce Antimicrobial Prophylaxis Errors (TRAPE)
  – 44 hospitals in US (mostly teaching, most <250 beds)
  – Measured antimicrobial prophylaxis in cardiac surgery, hip & knee arthroplasty and hysterectomy
  – Used National Nosocomial Infections Surveillance (NNIS) system for SSIs

• 29 hospitals from TRAPE participated in this study – total of 4472 operations

RESULTS

• >90% used antibiotic consistent with Surgical Care Improvement Project (SCIP) guidelines
• 81% met SCIP parameters for antibiotic timing
• 113 SSIs
  – Cultures obtained for all but one & positive for all but 6
  – >60% were organisms likely resistant to first-generation cephalosporins (MRSA, MSSA, coagulase-negative Staph, Gram negatives)
• **Risk factors for SSI**
  – Teaching hospital (RR 1.74, P<0.04)
  – Prophylactic antibiotics given post-incision (RR 2.20, P<0.02)
  – Duration of surgery >4 hours (RR 2.75, P<0.001 for duration 4-7 hours)

RESULTS

Timing of Preoperative Antibiotics

• No statistically significant difference between administration 0-30 minutes vs 31-60 minutes before surgery

Intraoperative Redosing

• 24% cases >4 hours in duration but only 21% had intraoperative redosing when cephalosporin used

• No statistically significant difference in infection rate when redosing used, but trend toward decreased risk if appropriate preop dosing used

RESULTS

Duration of Prophylaxis

• Only 12.6% received no postoperative antibiotic prophylaxis
• >25% received Abx for up to 48 hours
• No statistically significant difference between patients who received extended durations of antibiotic prophylaxis
CONCLUSIONS

• Preoperative administration (within 1 hour of incision) reduces the risk of SSIs compared to postoperative administration.

• When SSIs occur in setting of appropriate prophylaxis, they are usually from organisms resistant to SCIP-recommended antibiotics.

• Redosing of cephalosporins (if used) in prolonged surgery may reduce SSIs.

• Extending prophylaxis beyond the preoperative/intraoperative period does not reduce SSIs.
LIMITATIONS

• Mostly academic hospitals – may not correlate with experiences of all
• Most infections diagnosed post-discharge, and surveillance protocols between hospitals not standardized
• Low infection rate reduces power of the study
BOTTOM LINE

• Adhere to SCIP guidelines – give prophylactic antibiotics within 1 hour before incision
• Redose short half-life antibiotics (i.e. cephalosporins) during prolonged surgery
• Discontinue routine prolonged antibiotic prophylaxis
Continuous Perioperative Insulin Infusion Decreased Major Cardiovascular Events In Patients Undergoing Vascular Surgery

BACKGROUND

- Hyperglycemia and DM are independent predictors of increased cardiovascular risk and perioperative morbidity & mortality
- Past studies have shown reduced mortality & sternal wound infections with aggressive glycemic control in perioperative patients
- Most focused on cardiac & surgical ICU patients & postoperative glycemic control

METHODS

• Single center, prospective, randomized, nonblinded, active-control study of 236 patients

• Inclusion criteria: age >18, expected to be hospitalized at least 48 hours & undergoing:
  – Peripheral vascular bypass
  – Abdominal aortic aneurysm surgery
  – Knee amputation (above- or below-knee)

• Exclusion criteria included “brittle diabetes (as previously diagnosed by an endocrinologist)”

METHODS

• All received half their usual dose of long-acting insulin on the morning of surgery

• Patients randomized to either continuous IV insulin infusion or intermittent sliding-scale insulin for 48 hours postoperatively
  – Both groups had therapy initiated at glucose of 150 mg/dl
  – Both groups received intravenous insulin
  – Continuous infusion patients’ target glucose was 100-150 mg/dl
  – Continuous infusion patients’ glucose measured hourly until confirmed stable in 100-150 range
  – Intermittent sliding scale patients’ glucose measured every 4 hours

RESULTS

• Slightly over half of patients in both groups had previously diagnosed DM
• Baseline characteristics of both groups not statistically different, except intermittent sliding-scale group was older (P=0.02)
• Perioperative statins & beta-blockers given to all patients, even if not on these previously
  – metoprolol given until one month postoperatively
  – no information provided on heart rates

RESULTS

• Composite end-point of MI & CHF significantly decreased in continuous infusion group (relative risk 0.29 [0.10-0.83], P=0.013)
  – Results similar for diabetics and nondiabetics but taken separately, insufficient numbers to demonstrate statistical significance

• No statistically significant decrease in infections, repeat surgery, length of stay, renal insufficiency or CHF alone

• Decreased glucose variability in continuous infusion group in first 24 hours

• Hypoglycemia rates also similar between both groups; no episodes of glucose <40 mg/dl

CONCLUSIONS

Moderately aggressive glycemic control (target glucose of 100-150 mg/dl) with continuous insulin infusion decreases the rate of major adverse cardiovascular events in patients with and without diabetes undergoing vascular surgery.

LIMITATIONS

• Small size – original target of patients not achieved
• Excluded “brittle diabetics” but no definition/criteria for this provided
• Utilized IV insulin in sliding-scale group
• Only significant effect was on combined incidence of MI & CHF

Avoidance of wide glucose variability and severe hypo- and hyperglycemia is most likely beneficial.

Continuous insulin infusion intra- and perioperatively may be an effective means of achieving favorable glycemic control and surgical outcomes in select patients.
Two Questions for Dr. Smetana

1. What is the impact of tight glycemic control on perioperative outcomes?
2. Does the duration of cigarette cessation before noncardiac surgery influence postoperative pulmonary complication rates?
Perioperative Glycemic Control: How Tight and How Low?
Mortality Rises with Average ICU Blood Sugar Results

In Hospital Mortality %

Mayo Clin Proc 2003;78:1471
Median Postop Blood Sugar Predicts Mortality in Diabetic and Non-Diabetic ICU Patients

N=7285

The graph shows the mortality rate (%) across different median glucose levels (mg/dL) for nondiabetic patients, diabetic patients, and the control group. The mortality rates increase with higher glucose levels, indicating a significant relationship between postoperative blood sugar levels and mortality in ICU patients.
Mean postoperative blood sugars predict mortality in diabetic and non-diabetic patients

Is high BS a marker for comorbidities or disease severity?

Or does the high BS itself increase morbidity?

Will aggressive control of BS actually reduce perioperative complications and mortality?
The First Salvo
NEJM 2001: Impact of Intensive Insulin Rx in Critically Ill Patients

- 1548 Surgical ICU patients
- 80% postoperative patients
- All mechanically Ventilated

1548 ICU Patients

Intensive Insulin Rx
- IV Insulin if BS > 110
- Goal BS 80-110

Conventional Insulin Rx
- IV Insulin if BS > 215
- Goal BS 180-200
Increased In-Hospital Survival for Patients Receiving Intensive Insulin Rx

Graph A: Survival in ICU (%)
- Intensive treatment
- Conventional treatment

Graph B: In-Hospital Survival (%)
- Intensive treatment
- Conventional treatment

Days after Admission:
- Graph A: 0 to 160
- Graph B: 0 to 250
Findings Not Replicated: No Mortality Benefit in Medical ICU Patients Increased Mortality if ICU stay < 3 days

Same Insulin Strategies as 2001 Study
More Concerns Raised: Tight Intraoperative BS Control Does not Reduce Risk in Cardiac Surgery

<table>
<thead>
<tr>
<th></th>
<th>Intensive Insulin Rx (%)</th>
<th>Conventional Rx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin Goals (mg/dl)</strong></td>
<td>80-100</td>
<td>&lt; 200</td>
</tr>
<tr>
<td><strong>30 Day Outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Stroke</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Sternal infection</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>New onset AF</td>
<td>29</td>
<td>32</td>
</tr>
</tbody>
</table>

*Ann Intern Med 2007;146:243*
NICE-SUGAR Study
Goal: To Resolve the Question

- 6104 ICU patients
- 63% postop
- 25% ED admits
- 93% ventilated

NEJM 2009;360:1283
Blood Sugars Conformed Well to Study Goals
# Intensive Control Confers Higher Mortality

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Intensive Control (N=3010)</th>
<th>Conventional Control (N=3012)</th>
<th>Odds Ratio for Death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of deaths/no. with data available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>272/1111</td>
<td>222/1121</td>
<td>1.31 (1.07–1.61)</td>
</tr>
<tr>
<td>No</td>
<td>557/1898</td>
<td>529/1891</td>
<td>1.07 (0.93–1.23)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>195/615</td>
<td>165/596</td>
<td>1.21 (0.95–1.55)</td>
</tr>
<tr>
<td>No</td>
<td>634/2394</td>
<td>586/2416</td>
<td>1.12 (0.99–1.28)</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>202/673</td>
<td>172/626</td>
<td>1.13 (0.89–1.44)</td>
</tr>
<tr>
<td>No</td>
<td>627/2335</td>
<td>579/2386</td>
<td>1.15 (1.01–1.31)</td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>41/421</td>
<td>57/465</td>
<td>0.77 (0.50–1.18)</td>
</tr>
<tr>
<td>No</td>
<td>788/2587</td>
<td>694/2547</td>
<td>1.17 (1.04–1.32)</td>
</tr>
<tr>
<td>APACHE II score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥25</td>
<td>386/927</td>
<td>363/944</td>
<td>1.14 (0.95–1.37)</td>
</tr>
<tr>
<td>&lt;25</td>
<td>442/2080</td>
<td>387/2066</td>
<td>1.17 (1.01–1.36)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>134/392</td>
<td>140/378</td>
<td>0.88 (0.66–1.19)</td>
</tr>
<tr>
<td>No</td>
<td>695/2616</td>
<td>611/2634</td>
<td>1.20 (1.06–1.36)</td>
</tr>
<tr>
<td>All deaths at day 90</td>
<td>829/3010</td>
<td>751/3012</td>
<td>1.14 (1.02–1.28)</td>
</tr>
</tbody>
</table>
If High BS Predicts Mortality, Why Would Tight BS Control Increase Mortality?

- NICE-SUGAR – Severe hypoglycemia rates
  - Intensive control – 6.8%
  - Conventional Rx – 0.5%
- Increases in catechols, cortisol, and inflammatory cytokines due to hypoglycemia
- Potential for organ ischemia, CNS insults
- Increase deaths due primarily to excess CV mortality
AACE/ADA 2009 Consensus Statement on Inpatient Glycemic Control in ICU’s

- Start insulin at threshold no higher than 180 mg/dl
- Maintain glucose in 140-180 mg/dl range
- IV insulin infusions preferred
- Targets < 110 or > 180 mg/dl not recommended
<table>
<thead>
<tr>
<th>Blood Pressure Range</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;180</td>
<td>Not Recommended</td>
</tr>
<tr>
<td>140-180</td>
<td>Recommended</td>
</tr>
<tr>
<td>110-140</td>
<td>Acceptable</td>
</tr>
<tr>
<td>&lt;110</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
Does the duration of cigarette cessation before surgery matter?
Do Recent Quitters Have Higher PPC Rates?

- Many patients note increased cough and sputum in first 1-2 months after cigarette cessation.
- Plausible mechanism that recent quitters may be at risk for increased PPCs.
- How can we ignore the *teachable moment* before major surgery?
The Origins of the Controversy: Mayo Clinic 1989

200 Patients Undergoing CABG

PPC Rates

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Smokers</td>
<td>30%</td>
</tr>
<tr>
<td>Quit &lt; 8 Weeks</td>
<td>60%</td>
</tr>
<tr>
<td>Quit &gt; 8 Weeks</td>
<td>20%</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>0%</td>
</tr>
</tbody>
</table>
Similar Findings After Lung Resection: The Osaka Study

288 Patients: Recent Smoker = < 4 weeks

Current Smoker
Recent Smoker
Ex-Smoker
Never Smoker

PPC Rate

Chest 2001;120:705
Major PPCs After Pneumonectomy: Timing of Cessation Only Predictor in MV Analysis

- Retrospective study
- N=261
- Pneumonectomy
- Major PPC = pneumonia or ARDS

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette cessation &lt; 1 month</td>
<td>2.70</td>
<td>0.02</td>
</tr>
<tr>
<td>Age &gt; 60</td>
<td>1.14</td>
<td>0.76</td>
</tr>
<tr>
<td>Preop adjuvant Rx</td>
<td>0.92</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Ann Thorac Surg 2002;73:420
Could Confounders Bias These Observational Studies? Let’s Turn to the RCT’s
RCT’s of Smoking Cessation: Only Two Small Studies of Low Risk Surgery: Inadequate Power for PPCs

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Rx</th>
<th>#PPC</th>
<th>#PPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moller et al 2002</td>
<td>120</td>
<td>6-8 wks NRT</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lindstrom et al 2008</td>
<td>117</td>
<td>4 wks NRT</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Recent Pneumonectomy Trials: No Evidence of Paradoxical Increase for Recent Quitters

<table>
<thead>
<tr>
<th>Study</th>
<th>Smokers %</th>
<th>Recent Quitters %</th>
<th>Principal Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrera et al 2005</td>
<td>23</td>
<td>23</td>
<td>No Increase</td>
</tr>
<tr>
<td>Groth et al 2008</td>
<td>44</td>
<td>19</td>
<td>No increase</td>
</tr>
<tr>
<td>Mason et al 2009</td>
<td>7</td>
<td>6</td>
<td>No increase</td>
</tr>
</tbody>
</table>

Time for a Systematic Review

- Systematic review
- Included RCTs only
- Any type of surgery
- Preoperative smoking intervention
- Preoperative counseling and/or pharmacotherapy (NRT or bupropion)
- Complications ranged from wound infections to major adverse events
- 11 eligible studies (n=1194)
Preop Smoking Interventions Reduce Complications but Driven by One Study

![Risk ratio chart showing intervention vs standard care with values: 0.34 (0.19, 0.64), 0.94 (0.51, 1.73), 0.82 (0.06, 11.33), 0.86 (0.24, 3.03), 0.71 (0.21, 2.41), 0.51 (0.27, 0.97), 0.56 (0.41, 0.78).]
Caveats

- Only high intensity interventions reduced complications
- Positive trials included NRT and lasted at least 4 weeks
- Complications were heterogeneous and did not specifically address PPC
- Trials did not address if brief duration cessation increased PPC rates
Five Steps (5 A’s) for Smoking Cessation

1. **Ask** (Identify patients who smoke)
2. **Advise** patients to quit
3. **Assess** patient’s willingness to quit
4. **Assist** patients in efforts to quit (pharmacotherapy and counseling)
5. **Arrange** close follow up

*JAMA 1996;275:1270*
What to Advise?

- Brief duration cigarette cessation most likely will not increase your risk of pneumonia
- Let’s use this teachable moment to work on quitting
- Counseling plus NRT most likely to help
- Varenicline unstudied but may be more effective based on studies in non-surgical settings