Controversies in Perioperative Medicine

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• Cardiac Medications & Perioperative Risk
  – Beta-blockers, Statins & ACE-I / ARBs
• Coronary Stents
• Perioperative Anticoagulation
• Preoperative Smoking Cessation
Reducing Risk with Medical Management

You diagnose colon cancer in a 70-y.o. man admitted for anemia. Hemicolecotomy will be done in 2 wks.

Past Med Hx: MI 5 years ago, IDDM, HTN
Medications: ASA, Lisinopril, HCTZ
Examination: HR 75     BP 135/75
Normal cardiovascular exam
ECG:    NSR, LVH, old inferior Q waves

What should be done prior to surgery?

1. Start a β-blocker
2. Start a statin
3. Start both β-blocker & statin
4. No new medications needed
- 111 patients undergoing **vascular surgery**
- All had ischemic potential on dobutamine echo
- Randomized to beta-blocker started 2 weeks preop

**Cardiac Mortality & Nonfatal MI (%)**

**POISE: Treatment Protocol**

**Patients:** 8351 pts with s/f major noncardiac surgery
- CAD, CHF, CVA/TIA, CKD, DM, or high-risk surgery
- Not already taking \(\beta\)-blocker

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Dose Details</th>
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<tbody>
<tr>
<td>2-4 h</td>
<td>Metoprolol XL 100 mg*</td>
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<tr>
<td>0-6 h</td>
<td>Metoprolol XL 100 mg*</td>
</tr>
<tr>
<td>12 h</td>
<td>Metoprolol XL 200 mg*^</td>
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</table>

* Study drug held for SBP < 100 or HR < 50
^ Daily dose reduced to 100 mg if persistent bradycardia or hypotension

**Outcome:** 30-day cardiac mortality, nonfatal arrest or MI

**POISE: Results**

Metoprolol XL:
Reduced cardiac events (mostly nonfatal MI)
but
Increased risk of stroke & total mortality

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**Statins: DECREASE III**

**Patients:** 497 statin naive pts s/f major vascular surgery
- All patients also maintained or started on beta-blocker

**Treatment:** Fluvastatin XL 80 mg daily or placebo
- Median 37 days of treatment prior to surgery

**Outcomes:**
- Ischemia (ECG change or troponin elevation)
- Composite of cardiovascular death and nonfatal MI
- Safety outcome: CPK and ALT elevation

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Schouten et al. NEJM, 2009

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**DECREASE III: Results**

Fluvastatin XL:
- Reduced incidence of ischemia
- Reduced the composite outcome of cardiac death & nonfatal MI
- No difference in rates of LFT or CPK elevation

Schouten et al. *NEJM*, 2009

<table>
<thead>
<tr>
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<th>Placebo</th>
<th>Fluvastatin XL</th>
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<tbody>
<tr>
<td>Myocardial Ischemia</td>
<td>19.0%</td>
<td>10.9%</td>
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<tr>
<td>Cardiac Death or Nonfatal MI</td>
<td>10.1%</td>
<td>4.8%</td>
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**DECREASE-IV**

**Patients**: 1066 pts with estimated 1-6% risk of postoperative cardiac complications, undergoing elective non-CV surgery

**Treatment**: 1. Bisoprolol 2.5 mg daily started at randomization;
- dose titrated in hospital by 1.25 - 2.5 mg daily;
- maximum 10 mg daily;
- target heart rate = 50-70 with SBP >100
2. Fluvastatin XL 80 mg daily
3. Bisoprolol + Fluvastatin
4. Double placebo

- Drugs started median 34 days prior to surgery

**Outcome**: 30-day cardiovascular mortality or nonfatal MI

DECREASE-IV Results

Bisoprolol-treated patients had fewer complications
Trend towards benefit with statins
No safety issues

Lessons from POISE & DECREASE-IV

- β-blockers clearly do prevent postoperative MI
  - Aggressive β-blockade causes hypotension and bradycardia, leading to stroke & death
    - Initiating beta-blockade immediately prior to surgery may increase risk
    - Gradual postoperative dose titration may be safer than trying to achieve target HR before surgery
    - Avoid one-size fits all approach to dosage
    - Caution in patients with cerebrovascular disease
Perioperative β-blockers in 2009

**Indicated for patients:**
- Already using β-blocker to treat angina, HTN, arrhythmia
- With ischemic potential having vascular surgery

**Possible Indications:**
- Patients with ischemic potential having major nonvascular surgery (e.g., > 5 hours or > 500 cc blood loss)
- Multiple risk predictors* in vascular or other major surgery
  
  (*Coronary disease, renal insufficiency, diabetes)

Titrate dose up gradually (rarely start immediately preop)

Perioperative Statins in 2009

**Strong indications (class I):**
- Already taking statin prior to surgery

**Probable indications (class IIa):**
- All vascular surgery patients, regardless of cholesterol

**Possible indications (class IIb):**
- At least one risk predictor* in any intermediate risk surgery

*Coronary disease, renal insufficiency, diabetes, CVA/TIA

ACC/AHA Guidelines, 2007
Angiotensin Blockade & Intraoperative Hypotension

You diagnose colon cancer in a 70-y.o. man admitted for anemia. Hemicolecetomy will be done in 2 wks.

Past Med Hx: MI 5 years ago, IDDM, HTN
Medications: ASA, Lisinopril, HCTZ

What do you do with his ACE-inhibitor?
1. Give it on morning of surgery
2. Hold it on morning of surgery

Angiotensin Blockade & Intraoperative Hypotension

**Question**: Should ACE-inhibitors & ARBs be held prior to anesthesia?

**Methods**: Meta-analysis of 3 RCTs & 2 observational studies
- Total 434 patients
- Endpoint: intra-operative hypotension requiring pressor

**Results**:
- Pooled relative risk 1.5 (1.15,1.96) when ACE-I/ARB given
- Did not clearly correlate with more serious complications

**Conclusions**: Probably would hold ACE-I/ARB in most cases
Surgery After Coronary Stent Placement

A 70-y.o. man with newly diagnosed colon cancer received a paclitaxel-eluting stent 3 months ago. The manufacturer recommends dual therapy with ASA & clopidogrel for 6 months. However, the surgeon is willing to perform a hemicolecotony on aspirin, but not clopidogrel.

What do you recommend for this patient?

Patient with paclitaxel-eluting stent placed 3 months ago requires surgery for colon cancer. Surgeon will do the operation on aspirin, but not clopidogrel.

1. Stop clopidogrel & operate now
2. Delay surgery 3 months & stop clopidogrel
3. Delay surgery 3 months, and stop clopidogrel & ASA
4. Delay surgery until 1 year after PCI
Stopping Antiplatelet Drugs After Coronary Stenting

**Question**: How risky is temporary discontinuation of thienopyridine (clopidogrel) treatment in patients with stents?

**Methods**: Systematic review of reports of late stent thrombosis. Patients were categorized by how their antiplatelet drugs were managed prior to thrombosis event:

1. ASA & thienopyridine stopped simultaneously
2. Thienopyridine stopped first, then ASA stopped
3. Thienopyridine stopped, but ASA continued


**Medication management prior to stent thrombosis** | **Time (median) between stopping medication & thrombosis**
--- | ---
ASA & clopidogrel stopped simultaneously | 7 days after meds stopped
Clopidogrel stopped first, then ASA stopped | 7 days after ASA stopped
Clopidogrel stopped only (ASA continued) | 122 days after clopidogrel stopped

**Conclusions**: Short-term discontinuation of clopidogrel may be safe if aspirin continued

Effects of Delaying Surgery: BMS

Bare Metal Stents:
- High risk in first 30 days
- Significant drop in risk after first month
- Brief delay useful

Effects of Delaying Surgery: DES

Drug Eluting Stents:
- Risk remains steady for first 12 months
- Risk declines after 12 months
- Brief delay of surgery low yield
ACC/AHA Guidelines for PCI

- Avoid PCI unless patient has independent indications
- Avoid PCI if patient may have upcoming surgery that requires stopping dual antiplatelet therapy
- Delay elective surgery in patients with recent PCI
  - Balloon angioplasty: 2 - 4 weeks
  - Bare metal stent: 4 weeks
  - Drug eluting stent: 12 months
- If clopidogrel must be stopped, try to continue ASA
- No evidence for bridging with other agents

Managing Perioperative Anticoagulation

Two patients who take coumadin underwent THA. One has atrial fibrillation due to HTN. The other has a mechanical AVR. Neither has a history of stroke or any other comorbidity.

1. Heparin bridge for AVR only
2. Heparin bridge for AF only
3. Heparin bridge for both
4. Heparin bridge for neither
Thromboembolic Risks with Non-rheumatic Atrial Fibrillation

CHADS-2 Score:
1 point for CHF, HTN, Age > 75, DM
2 points for Stroke/TIA
Score 0 - 2: < 5% annual stroke risk
Score 3 - 4: 5-10%
Score 5 - 6: > 10%

Albers et al.  Chest, 2001

Thromboembolic Risks with Mechanical Valves

Effect of Mechanical Valve Location & Design on Thromboembolic Risk

Valve Location:
- Aortic: RR = 1.0
- Mitral: RR = 1.8

Valve Design:
- Caged Ball: RR = 1.0
- Tilting Disk: RR = 0.7
- Bi-leaflet: RR = 0.6

Perioperative Anticoagulation:
2008 ACCP Guidelines

<table>
<thead>
<tr>
<th>Atrial Fibrillation</th>
<th>Mechanical Valve</th>
<th>Recommend</th>
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<tbody>
<tr>
<td>CHADS2 = 5-6, recent CVA, or rheumatic AF</td>
<td>Any MVR; older (caged-ball or tilting disc) AVR; recent CVA</td>
<td>Full dose heparin bridge</td>
</tr>
<tr>
<td>CHADS2 = 3-4</td>
<td>Bileaflet AVR plus one additional stroke risk factor</td>
<td>Full or low dose heparin</td>
</tr>
<tr>
<td>CHADS2 = 0-2</td>
<td>Bileaflet AVR without AF or other stroke risk factor</td>
<td>Low dose or no heparin</td>
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*Full dose = therapeutic dose of heparin IV or LMWH SC
Low dose = DVT prophylaxis dose of heparin SC or LMWH SC*
**Bridging Anticoagulation: Where’s the Evidence?**

- RCTs finally in progress; expect results in 2013!
- Current evidence comes from large cohort studies:

<table>
<thead>
<tr>
<th>Bridging Cohort</th>
<th>Non-Bridging Cohort</th>
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<tbody>
<tr>
<td>• 1262 patients</td>
<td>• 1293 interruptions</td>
</tr>
<tr>
<td>• 52% Atrial Fibrillation</td>
<td>• 54% Atrial Fibrillation</td>
</tr>
<tr>
<td>• 17% DVT or PE</td>
<td>• 14% DVT or PE</td>
</tr>
<tr>
<td>• 15% Mechanical Valve</td>
<td>• 13% Mechanical Valve</td>
</tr>
<tr>
<td>• 100% received bridge</td>
<td>• 9% received bridge</td>
</tr>
<tr>
<td>30-day TE risk = 0.4% (0.1,0.9)</td>
<td>30-day TE risk = 0.7% (0.3,1.4)</td>
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<tr>
<td>Major Bleeding = 1.2%</td>
<td>Major Bleeding = 0.6%</td>
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Garcia et al. *Arch Intern Med*, 2008

**Preoperative Smoking Cessation**

A middle-aged man will undergo repair of a ventral hernia in 1 month. He currently smokes one pack of cigarettes per day. How do you counsel him?

1. Quit smoking now to prevent postoperative complications.
2. It’s always good to quit, but it’s too late to affect your risk of complications.
3. Don’t stop smoking! You will actually increase your surgical risk by quitting!
Effect of Smoking Cessation

Time since quitting

- Never quit
- Less than 2 weeks
- 2 - 4 weeks
- 4 - 8 weeks
- 8 or more weeks
- Nonsmokers

Warner, Anesthesiology 1984

Preoperative Smoking Cessation Counseling

RCTs of Preoperative Smoking Cessation Counseling:
1. 120 patients undergoing arthroplasty in 6-8 weeks
2. 117 patients undergoing various operations in 4 weeks
3. 60 patients undergoing colorectal resection in 2-3 weeks

**Intervention:** Smoking cessation counseling at weekly meetings (or by telephone) & offer free nicotine replacement products

**Outcomes:** Postop complications, especially wound related (e.g., dehiscence, infection, hematoma)
Smoking Cessation 6-8 Weeks Before TKA or THA

- Quit or Reduced Smoking: 7% Control, 83% Intervention
- Wound Complication: 5% Control, 31% Intervention
- Any Complication: 18% Control, 52% Intervention

Moller et al. Lancet, 2002

Smoking Cessation 4 Weeks Before Surgery

- Wound Complication: 26% Control, 13% Intervention
- Any Complication: 41% Control, 21% Intervention

Take Home Points

- Start $\beta$-blocker cautiously & only in high risk patients
- Consider statins for vascular & other high risk cases
- Avoid surgery after recent stent placement, but if necessary, try to continue aspirin perioperatively
- Individualize thrombotic risk assessment when managing perioperative anticoagulation
- Smoking cessation for $\geq 4$ weeks may be beneficial