Clinical Controversies in Perioperative Medicine

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Disclosures

- Perioperative beta-blockade & statin therapy are not FDA approved indications
- No discussion of unapproved medications
- No financial conflicts of interest
- I am not a witch

Update on Perioperative Medicine

- Cardiac Medications & Perioperative Risk
- DVT Prophylaxis: Arguing with the Surgeon
- Postoperative Transfusion Threshold
- Risk of Surgery in Cirrhotic Patients
Reducing Risk with Medical Management

Your 70-y.o. patient is diagnosed with colon cancer. Hemicolectomy is scheduled in 2 weeks.
Past Med Hx: IDDM, HTN
Medications: ASA, Lisinopril, HCTZ, Insulin
Examination: HR 75     BP 135/75
Normal cardiovascular exam
ECG: NSR with LVH; otherwise normal

What changes should be made to his medications prior to surgery?

70-y.o. man will undergo hemicolectomy in 2 wks. Past medical history noted for IDDM, HTN.

What should be done prior to surgery?
1. No new medications needed
2. Start a β-blocker
3. Start a statin
4. Start both β-blocker & statin

Revised Cardiac Risk Index

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Complications**</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.5%</td>
</tr>
<tr>
<td>1</td>
<td>1.3%</td>
</tr>
<tr>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>3 or more</td>
<td>9%</td>
</tr>
</tbody>
</table>

* Defined as intraperitoneal, intrathoracic, or suprainguinal vascular surgery
** Defined as MI, pulmonary edema, cardiac arrest, complete heart block

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 β-blocker

<table>
<thead>
<tr>
<th>Time</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd &amp; daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 h</td>
<td>Metoprolol XL 100 mg*</td>
<td>Metoprolol XL 100 mg*</td>
<td>Metoprolol XL 200 mg*^</td>
</tr>
</tbody>
</table>

^ Study dose 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)
- Increased risk of stroke & total mortality


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

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

2009 ACC / AHA Guideline for β-blockers

Definite indications (Class 1):
- Already using β-blocker to treat angina, HTN, arrhythmia

Probable indications (Class 2a):
- Vascular or intermediate-to-high risk surgery patients with coronary disease, or more than 1 risk predictor *

Uncertainty (Class 2b):
- Patients undergoing vascular or intermediate risk surgery without coronary disease & with only 1 risk predictor *

*Coronary disease, renal insufficiency, diabetes, CVA/TIA
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:
- Composite of cardiovascular death and nonfatal MI
- Safety outcome: CPK and ALT elevation

Schouten et al. NEJM, 2009

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

ACC/AHA Guidelines: Perioperative Statins

Definite indications (Class 1):
- Already taking statin prior to surgery

Probable indications (Class 2a):
- All vascular surgery patients, regardless of cholesterol

Possible indications (Class 2b):
- At least one risk predictor* in any intermediate risk surgery

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

ACC/AHA Guidelines, 2007
DVT Prophylaxis in Neurosurgery Patients

You are comanaging a patient undergoing craniotomy for tumor resection. The surgeon only uses compression device (CD) for DVT prophylaxis, rather than UFH or LMWH.

1. Agree with CD only
2. Argue for UFH
3. Beg for LMWH

DVT Prophylaxis in Neurosurgery Patients

Study: Meta-analysis of 18 RCTs & 12 cohort studies of patients undergoing craniotomy or spinal surgery.

Efficacy:
- 15% of patients developed DVT without prophylaxis
- CD better than placebo (RR = 0.4 [0.2-0.8])
- LMWH better than stockings (RR = 0.6 [0.4-0.9])
- No evidence of superiority of CD vs. UFH vs. LMWH

Safety:
- Slightly higher bleeding rates with anticoagulant use


DVT Prophylaxis in Neurosurgery Patients

Conclusions:
- Neurosurgical patients need DVT prophylaxis
- Compression device, UFH, LMWH are acceptable options (but elastic hose is not)
- Would not argue strongly for one modality over another
DVT Prophylaxis in Orthopedic Surgery Patients

You are comanaging a patient undergoing knee arthroplasty. Instead of using LMWH for DVT prophylaxis, the surgeon only wants to use aspirin. You wonder: "Is she crazy?"

1. She is ignorant of the data
2. She interprets the data differently
3. She is completely crazy

DVT Prophylaxis in Orthopedic Surgery Patients

American College of Chest Physicians (ACCP)
- Considers both symptomatic and asymptomatic endpoints
- Prefers other agents over aspirin, because they prevent more total VTE

American Academy of Orthopedic Surgery (AAOS)
- Only considers symptomatic endpoint (pulmonary embolism)
- Too few pulmonary emboli in most trials to prove aspirin is inferior to other agents


Trial of Aspirin in DVT Prophylaxis

13,356 patients undergoing hip fracture repair

Usual DVT prophylaxis plus ECASA 160 mg qd x 35 d

Usual DVT prophylaxis plus placebo

Monitored for in-hospital symptomatic DVT or PE and 35 day mortality

PEP Trial. Lancet, 2000
72 y.o. woman undergoes repair of a femoral neck fracture. She has diabetes and old pathologic Q-waves on her ECG. On post-op day #2, she only complains of hip pain.

**Exam:**
- BP 140/80
- HR 75
- Heart, Lung, Abdomen exams normal
- Labs: Hemoglobin = 8.5 g/dL (Hct = 26%)

When should she receive a blood transfusion?

1. Transfuse to keep Hgb > 10
2. Keep Hgb > 9
3. Keep Hgb > 8
4. Only if she has symptoms
5. Give her a copy of the *Watchtower*, and hope that makes the question moot
Blood Transfusion & Mortality After Hip Fracture Repair

Retrospective cohort study of 8787 hip fracture patients

FOCUS* Trial
(*Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair)

Patients: 2016 patients undergoing hip fracture repair. All patients had either diagnosis of or risk factors for cardiovascular disease.
- Mean age = 82
- HTN (82%); CAD (40%); DM (25%); CVA (24%); CHF (17%)

Treatment: Randomized to 2 transfusion strategies:
1. Hemoglobin < 10 g/dL
2. Symptoms of anemia (also permitted for hgb < 8)

FOCUS Trial Results

<table>
<thead>
<tr>
<th>Hgb level prior to transfusion</th>
<th>Hgb level prior to transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC Units Transfused</td>
<td>Total Units Transfused</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td></td>
</tr>
<tr>
<td>10 g/dL Trigger</td>
<td>2 (1,2)</td>
</tr>
<tr>
<td>Symptomatic Trigger (or 8 g/dL)</td>
<td>0 (0,1)</td>
</tr>
</tbody>
</table>

FOCUS Trial Results

<table>
<thead>
<tr>
<th></th>
<th>In-hospital mortality</th>
<th>In-hospital mortality, MI, or UA</th>
<th>60-day mortality</th>
<th>60-day mortality + disability</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 g/dL Trigger</td>
<td>2.0%</td>
<td>4.3%</td>
<td>7.6%</td>
<td>35%</td>
</tr>
<tr>
<td>Symptom Triggered</td>
<td>1.4%</td>
<td>5.2%</td>
<td>6.5%</td>
<td>35%</td>
</tr>
</tbody>
</table>

Conclusion: No increased mortality or morbidity with a restrictive transfusion protocol.


Surgical Risk in Cirrhotic Patients

A 65-y.o. man with cirrhosis from HCV desires a hip arthroplasty. He feels well and has no current signs of ascites or encephalopathy on examination.

Labs: Creatinine = 1.6  
Total Bilirubin = 1.9  
Albumin = 3.5  
INR = 1.6

How would you advise this patient about his perioperative mortality risk?

65-y.o. man with cirrhosis from HCV desires a hip arthroplasty. He's asymptomatic and has no signs of encephalopathy or ascites.

1. Patients with cirrhosis are not candidates for elective surgery
2. Your mild cirrhosis (Childs-Pugh class A) makes you an acceptable surgical candidate
3. Perioperative risk is acceptable, but long-term mortality risk makes surgery unappealing
Surgical Risk in Cirrhotic Patients

Question: How does his cirrhosis affect mortality risk?

Background:
- Risk traditionally assessed by Childs-Pugh classification
  (http://www.mdcalc.com/child-pugh-score-for-cirrhosis-mortality)
- Mortality after GI surgery:
  - Class A = 10%
  - Class B = 30%
  - Class C = 70%
- Limitations: single time point, less known about non-GI surgery; sensitive to minor laboratory result differences

MELD Score as Risk Predictor

MELD Score (Model for Endstage Liver Disease):
- Main use in organ allocation
- Variables: INR, bilirubin, creatinine
- Retrospective multivariate analysis of 772 cirrhotic patients undergoing GI, orthopedic, and CV surgery
  - Independent predictors of mortality: Age & MELD Score
  - Predicts mortality @ 1 wk, 1 mo, 3 mo, 1 yr, 5 yr
  - mayoclinic.org/meld/mayomodel9.html

65 y.o. man with stable HCV-related cirrhosis. He has no current signs of encephalopathy or ascites.

Labs: Creatinine = 1.6
      Total Bilirubin = 1.9
      Albumin = 3.5
      INR = 1.6

Childs-Pugh Class A
MELD Score = 19

Mortality Prediction:
- Childs-Pugh: 10% in-hospital mortality
- MELD Score: 6.5% 1 week mortality
  24% 1 month mortality
  36% 3 month mortality
  50% 1 year mortality
### Take Home Points

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<tbody>
<tr>
<td>1.</td>
<td>Start β-blocker cautiously &amp; only in higher risk pts</td>
</tr>
<tr>
<td>2.</td>
<td>Start statins in vascular (? and other higher risk) surgery patients</td>
</tr>
<tr>
<td>3.</td>
<td>Recognize the evidence for more aggressive DVT prophylaxis is often limited or open to interpretation</td>
</tr>
<tr>
<td>4.</td>
<td>Transfuse less aggressively in asymptomatic patients</td>
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<tr>
<td>5.</td>
<td>Use MELD score to assess surgical risk in cirrhosis</td>
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