Updates & Controversies in Perioperative Medicine

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Updates in Perioperative Medicine

1. Estimating mortality in surgical patients
2. Managing aspirin during surgery
3. Screening & treatment for postoperative myocardial injury
4. Anticoagulation for patients with postoperative atrial fibrillation
5. Opiate use & misuse after surgery
Predicting Surgical Mortality

Your 88-y.o. male patient has biliary colic without acute infection. Pertinent history includes: CAD, COPD, a remote stroke, IDDM & HTN. He needs help with some ADLs. His BMI is 22.

You ask a surgeon to consider a laparoscopic cholecystectomy.

The perioperative mortality for this patient is roughly…?

1. 1%
2. 5%
3. 10%
4. 15%
5. High…really high

Predicting Surgical Mortality

88-y.o. male patient has biliary colic without acute infection. Pertinent history includes: CAD, COPD, a remote stroke, IDDM & HTN. He needs help with some ADLs. His BMI is 22.

The surgeon recommends a percutaneous drain because mortality from lap chole is “high…really high.”

Are internists or surgeons better at predicting surgical mortality?

1. Internists (of course)
2. Surgeons
3. Equally good
4. Equally bad
Surgical Risk Calculator

Derived from American College of Surgeons’ National Surgical Quality Improvement Program (NSQIP)
-riskcalculator.facs.org/RiskCalculator/

- > 1.4 million patients in derivation & validation cohorts
- > 1500 unique CPT codes from nearly 400 hospitals
- Predicts 30-day risk of death, complications (cardiac, VTE, pneumonia, UTI, SSI, ARF), return to OR, readmission, and discharge to SNF or rehab
- Good-to-excellent predictive accuracy

Surgical Risk Calculator

Utility & Limitations:

- Most generally applicable (vs. population or procedure specific calculators)
- Estimates both absolute risk and relative risk compared to average patient undergoing same operation
- Useful in patients at higher risk from noncardiac disease
- Wide availability and “ease” of use
- Need to select specific procedure
- Accuracy for some types of surgery questioned

Predicting Risk: Medicine vs Surgery

Study design:
• Anonymous questionnaire given to internal medicine and general surgery residents
• Seven complex clinical cases in surgical patients (cholecystectomy, colectomy, DU repair, perforated viscus, small bowel resection, mastectomy, herniorrhaphy)
• Asked to predict mortality & complications
• Gold standard = ACS/NSQIP prediction tool


Predicting Risk: Medicine vs Surgery

• Both IM & Gen Surg residents overestimated risk
• Estimates were all over the place
• Internists more likely to use prediction models
• Surgeons more confident in their estimates
• Surgeons more comfortable not offering surgery and recommending palliative care
• Study demonstrates need to use validated tools

Managing Aspirin in Surgical Patients

You are asked to clear your patient with stable coronary disease and diabetes undergoing major head & neck surgery. She takes aspirin daily. The surgeon is “unexcited” about continuing it.

Do you advocate continuing the aspirin perioperatively?

1. No – it's not worth the argument
2. Only if the patient has a coronary stent
3. Yes – whether or not there is a stent

Trial of Perioperative Aspirin (POISE 2)

Before surgery:
- 10,100 patients with cardiac disease or risk factors undergoing major noncardiac surgery
- Included chronic user & new user cohorts
- Aspirin 200 mg or placebo started right before surgery

After surgery:
- Aspirin or placebo given daily x 30 days
- Study drug stopped if major or life-threatening bleed

Devereaux, PJ et al. NEJM 2014; 370:1494-03
POISE 2: Aspirin Results

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Placebo</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI</td>
<td>7.0%</td>
<td>7.1%</td>
<td>0.99 (NS)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>6.2%</td>
<td>6.3%</td>
<td>0.98 (NS)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>4.6%</td>
<td>3.8%</td>
<td>1.23 (p = 0.04)</td>
</tr>
</tbody>
</table>

- Similar outcomes in chronic ASA users and new users
- Less than 5% of patient in POISE 2 had stents

Devereaux, PJ et al. NEJM 2014; 370:1494-03

2014 ACC / AHA Guidelines

Aspirin (for patients without stent)

- Not unreasonable to continue ASA in elective surgery if benefits outweigh risks from bleeding (Class 2b)
- Initiation of ASA does not benefit patients undergoing elective noncardiac surgery (Class 3)

POISE 2 – Patients with PCI

Non-prespecified analysis of subgroup of the 470 patients with history of prior PCI:

<table>
<thead>
<tr>
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<th>Aspirin</th>
<th>Placebo</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI</td>
<td>6.0%</td>
<td>11.5%</td>
<td>0.50 (p = 0.036)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>5.1%</td>
<td>11.0%</td>
<td>0.44 (p = 0.02)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>5.6%</td>
<td>4.2%</td>
<td>1.26 (p = 0.04)</td>
</tr>
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</table>


2016 ACC/AHA Guidelines for PCI

Delay elective surgery after elective PCI:
- Bare metal stent: 30 days
- Drug eluting stent: 6 months (optimal)
  3 months (if harm in delay)

Management of dual anti-platelet therapy:
- If P2Y₁₂ inhibitor must be stopped, then ASA should be continued if possible, and the P2Y₁₂ inhibitor resumed postoperatively as soon as possible

Screening for Myocardial Injury

Your patient with stable CAD and HFpEF had a colectomy last week. The hospitalist who comanaged him tells you:

“He had no cardiac symptoms, but I checked a postop troponin anyway because his cardiac risk was elevated. It peaked at 0.2 ng/mL. I didn’t do anything based on this result.”

How do you respond?

1. I’ll optimize his secondary risk reduction regimen
2. I’ll order a stress test or refer to cardiology for possible cath
3. I’ll likely start long-term anticoagulation
4. Why order the (!@#$%) troponin if didn’t change mgt?

Perioperative Myocardial Injury

Findings from POISE (beta-blocker) trial:

• 5% of these “elevated risk” patients had postop MI, defined as elevated biomarker + ECG changes
• Most MI occurred by POD #3 (74% within 48 hr)
• Postoperative MI predicted 5-fold mortality
• Majority of postoperative MI were asymptomatic
• Silent MI had similar mortality as symptomatic MI

### Postop Biomarkers Predicts Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Biomarker</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>POISE (2011)</td>
<td>Troponin or CK-MB</td>
<td>2.5x mortality with isolated biomarker elevation</td>
</tr>
<tr>
<td>VISION (2012)</td>
<td>Troponin-T</td>
<td>4x mortality with any Tn-T elevation</td>
</tr>
<tr>
<td>Meta-analysis of 14 earlier studies (2011)</td>
<td>Troponin</td>
<td>3x mortality with elevation</td>
</tr>
</tbody>
</table>


### Arguments Against Screening

**Insufficient Sensitivity:**
- Screening only identified 21% of patients who died in POISE

**Too late to do anything:**
- Nearly 2/3 of deaths in patients with MI occurred by POD 3  
- Many deaths in MI patients are not cardiac-related  
- Elevated troponin just identifies obviously crashing patients

**No known effective intervention:**
- Don’t order a test unless result will change management
MANAGE Trial

**Question:** Does the direct thrombin inhibitor dabigatran improve outcomes in patients with elevated postop troponin?

**Patients:** 1754 patients who evidence of myocardial injury after noncardiac surgery (MINS) = elevated postop troponin either with clinical, ECG or imaging evidence of new ischemia or no other explanation (e.g., PE, sepsis, atrial fib)

**Intervention:** Dabigatran 110 mg bid vs. placebo for up to 2 yrs

**Outcome:** CV mortality, nonfatal MI, stroke, peripheral arterial thrombosis, and symptomatic PE

Amputation and symptomatic proximal DVT added post hoc
### MANAGE Trial Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dabigatran</th>
<th>Placebo</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary cardiac or vascular outcome</td>
<td>11%</td>
<td>15%</td>
<td>25 (p = .012)</td>
</tr>
<tr>
<td>Mortality – CV</td>
<td>6%</td>
<td>7%</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality – All cause</td>
<td>11%</td>
<td>13%</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>4%</td>
<td>5%</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>3%</td>
<td>4%</td>
<td>NS</td>
</tr>
</tbody>
</table>

https://doi.org/10.1016/S0140-6736(18)30832-8

### Screening for Myocardial Injury

Limitations of MANAGE trial:
- Design problems (changing sample size & outcomes)
- Outcomes too broad and individually no significant effect
- Comparison group was placebo
- Just too weird -- very different from usual practice

So now what?

- **Screening for MINS?**: US guidelines ambivalent; Canadian guideline endorses it.
- **Statin & ASA**: Association between their use and lower mortality in patients with MINS or postop MI (retrospective study only)
Postoperative Atrial Fibrillation

70-y.o. woman with hypertension undergoes knee replacement. On POD #1, she develops new atrial fibrillation. She is started on metoprolol and converts spontaneously to sinus rhythm the next day. The comanaging hospitalist orders a TTE showing normal LV function with mild LAE. Her CHA$_2$DS$_2$VASc = 3. He defers decision about anticoagulation to you.

Would you recommend chronic anticoagulation?
1. No
2. Yes
3. Are you the same hospitalist who called about my patient with an elevated troponin?

Hospitalist Mentality

My problem

Not my problem

Also not my problem

Apologies to Demetri Martin
Stroke Risk with Postop AF

Does postop AF (POAF) have similar risk for stroke as "regular" non-valvular AF (NVAF)?

California database: 12,874 patients with new POAF

<table>
<thead>
<tr>
<th></th>
<th>POAF</th>
<th>No POAF</th>
<th>Adjusted HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-yr Stroke Risk</td>
<td>1.47%</td>
<td>0.36%</td>
<td>2.0 [1.7-2.3]</td>
</tr>
</tbody>
</table>

- 1.47% risk is similar to NVAF with CHA$_2$DS$_2$VASc between 1-2
- Median CHA$_2$DS$_2$VASc in this study = 3. Expected stroke risk in NVAF would be 3.2% (twice higher)


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Stroke Risk with Postop AF

Danish registry: 3830 patients with new onset POAF

- Adjusted HR for thromboembolism = 1.9 compared to surgical patients who did not develop POAF
- Matched by CHA$_2$DS$_2$VASc score to patients with new onset NVAF:

<table>
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<th>NVAF</th>
<th>Adjusted HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolism (TE) Risk (events per 1000 person-yrs)</td>
<td>32</td>
<td>30</td>
<td>0.95 (NS)</td>
</tr>
<tr>
<td>Hazard ratio for TE if anticoagulant prescribed</td>
<td>0.52</td>
<td>0.56</td>
<td>NS</td>
</tr>
</tbody>
</table>

J Am Coll Cardiol 2018;72:2027–36
Stroke Risk Conclusions

Long-term stroke risk from POAF underappreciated:
  • Patients with POAF have 2-fold (adjusted) risk of stroke compared to surgical patients who do not develop AF
  • Stroke risk for POAF may be similar to patients with usual, non-surgical NVAF
  • Anticoagulation may have similar benefit in POAF

What to do?
  • Take POAF seriously; not unreasonable to offer AC, especially if higher CHA\textsubscript{2}DS\textsubscript{2}VASc score
  • Limited by retrospective data, lack of consensus & guidelines

Opiate Use after Surgery

Background:
  • Growing concern about overuse of opiates, especially for chronic, non-cancer pain
  • Less concern about opiate use for acute pain
  • Little attention to opiate use to treat postoperative pain
  • ~100 million operations per year (inpatient & ambulatory) means a large risk pool
New Chronic Postop Opiate Use

Question: What is the risk of new persistent opiate use after surgery?

Study design:
- 36,177 surgical patients having one of 13 common operations (80% minor surgery, no ortho/spine cases)
- Only studied opiate naïve patients (no opiate rx for 12 months prior to perioperative period)
- Determine incidence and risk factors for persistent opiate use more than 90 days after surgery

Published online April 12, 2017

Chronic Opiate Use after Surgery

Findings:
- Overall 6% incidence of new persistent opiate use
  - Similar for major & minor surgery
- Risk factors for developing chronic use:
  - Alcohol, tobacco, drug use
  - Higher baseline comorbidity
  - Anxiety & mood disorder
  - Other pain (back, neck, arthritis)

Published online April 12, 2017
Opiate Misuse after Surgery

Question: How does the duration of postoperative opiate prescription relate to opiate misuse?

Study design:

- Over 500,000 opiate-naïve patients who were prescribed opiates after surgery (administrative database)
- Looked at association between opiate refills and subsequent diagnosis of opiate use disorder

Findings:

- In follow-up period, 0.6% of patient received a new opiate misuse disorder diagnosis
- Single refill associated with 40% increase in the risk of a new misuse disorder diagnosis
- Duration of prescription (rather than dose) was most predictive of opiate misuse

BMJ 2018;360:j5790
Take Home Points

1. We’re bad at predicting surgical risk – so use a prediction tool (NSQIP) to discuss risk with patients and surgeons
2. Benefit of continuing aspirin perioperatively appears limited to patients with stents
3. Silent myocardial injury predicts mortality – unfortunately effective management remains uncertain
4. Take postoperative atrial fibrillation seriously and consider offering anticoagulation
5. Think twice before refilling an opiate prescription for postoperative pain

Thank You

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