Perioperative Potpourri

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Conflicts/Off label usage

- Non-Declaration Statement: I have no relevant relationships with ineligible companies to disclose within the past 24 months.
- No off-label medication usage will be discussed.

Learning Objectives

- Explain the common risks confronting perioperative patients
- Discuss the current evidence behind the management of perioperative patients
- Describe the role of common chronic conditions and their effect on perioperative risk

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Stents and Noncardiac Surgery

Postoperative Fever

OSA and Surgery

ASA and Noncardiac Surgery

Periop Glycemic Control

Perioperative Hypertension

Preoperative Functional Risk Assessment

Bradycardia

Bridging Anticoagulation

Stents and Noncardiac Surgery

Case: 62 yo man with a h/o MI 8 weeks ago for which he received a drug-eluting stent, now admitted and recovering from gallstone pancreatitis the previous couple of days. The gastroenterologist recommends a pre-discharge cholecystectomy b/c of the high risk for recurrence. Should you…

A. Stop his clopidogrel and continue aspirin through lap chole surgery
B. Stop clopidogrel and use a bridging IIb/IIIa inhibitor like eptifibitide
C. Put off surgery for another 1 months (3 months after stenting)
D. Put off surgery for another 4 months (6 months after stenting)

Facts about stents and in-stent thrombosis

- Risks after in-stent thrombosis
  - Lead to MI in approximately 60% of patients
  - Lead to death in as many at 40% of patients with MI
- Bare metal stents (BMS) ~1-2%
  - Most within first 48 hours
  - Almost all within 30 days of stent placement
- Drug-eluting stents (DES) ~1-2%
  - Most early as well
  - New generation stents closer to BMS than previous
  - Risk period extends further
- Risks for in-stent thrombosis
  - STOPPING $P2Y_{12}$ (clopidogrel, prasugrel), with an Odds Ratio of >30!
  - Stopping both ASA and $P2Y_{12}$

Guidelines:

- Elective noncards surgery should optimally be delayed 30 days after BMS and 6 months after DES placement
- If needing to discontinue $P2Y_{12}$, ASA should be continued if possible and $P2Y_{12}$ restarted as soon as possible
- Recommend a conversation among parties to discuss relative risks of no surgery, bleeding and thrombosis
- Elective noncards surgery after DES can be considered after 3 months if risk of further delay is greater than risk of in stent thrombosis
- Elective noncards surgery should not be performed w/i 30 days of BMS or 3 months of DES if $P2Y_{12}$ will need to be discontinued

Back to our case…

- Discussion needed b/w surgeon/cardiologist/patient/you
- Suggested Middle road: delay surgery for 4 more weeks (3 months after stenting)
- Stop clopidogrel 5 days preop (if prasugrel 7 dys, if tigrelor 3-5dys)
- Continue Aspirin through procedure
- Would complete surgery at a center with 24/7 interventional Cards
- As soon as possible restart clopidogrel with a 300mg loading dose

Stents and Noncardiac Surgery

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D. Put off surgery for another 4 months (6 months after stenting)

What if it were closer to stenting? Or what if surgery couldn't wait?

- No effective $P2Y_{12}$ reversal agents
- Minimal data re: using bridging IIb/IIIa inhibitors (eptifibitide, e.g.) or cangrelor (IV $P2Y_{12}$), Heparin ineffective as bridge
- No clear consensus recommendation

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Postoperative Fever

Case: you are called to see a 57 yo diabetic woman on POD#1 from a right total knee arthroplasty because she spiked a fever of 38.9 about 24 hours after her operation. Her wound has normal POD#1 look with mild right ankle swelling. She has a 1L oxygen requirement but no dyspnea, cough, sputum. No dysuria. What is your next step?

A. Order a chest radiograph to diagnose pneumonia
B. Do nothing unless her fever recurs/worsens
C. Check a UA, since she had a catheter briefly and postop UTIs are common
D. Doppler legs for DVT, as TKA patients are at high risk and acute DVT can cause fever

Postop Fever- Complication or Normal?

- Classic mnemonic: 4 W's, wind, water, wound, walking (wonder drugs)
- Causes can include:
  - Wind: pneumonia, pneumonitis, PE (*note the absence of atelectasis)*
  - Water: UTI
  - Wound: Surgical site infection
  - Walking: DVT/PE
- Others: drugs fever, Transfusion reactions, thyroid storm, gout/pseudogout, fat embolism, etc

The 5th W: *Wacky Cytokines*

- After Joint Replacement – elevations in IL-6, IL-1, TNFa present
- Level of elevation in joint predictive of systemic levels and fever

So how do you interpret fever in TJA patients?

- Early post of fever (POD#0, 1) rarely infectious in nature (presuming a clean site of surgery)
- POD#3 and later much more likely to be caused by infection
- Recurrent fevers on multiple days more c/w infection
- Reasonable to explore non-infectious causes (review drug list, evaluate whether intraop transfusion given)
- Indiscreet testing can add as much as $2000 dollars to a hospital costs from blood cultures, imaging, lab testing

Back to our case…

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OSA and Surgery

Case: a 75 yo obese man admitted to the hospital is preoperative for a Whipple procedure. He has newly diagnosed OSA requiring CPAP with 10cm of water pressure and no day/night oxygen. The surgery team requests you to assess his pulmonary risk. What is the best answer?

A. OSA places pt at high risk for respiratory complications (>5%)
B. NSQIP pulm risk failure score would accurately describe a low risk
C. The patient's severity of OSA is the best marker for his periop risk
D. OSA does not increase risk whereas pulmonary htn would have

Sleep Apnea- the facts

- Highly prevalent disease among surgical patients (often undiagnosed)
- NSQIP and other risk tools generally do not account for Sleep Apnea
- OSA raises both postoperative pulmonary and cardiac risks
- Recommendation: Screen all patients
  - Tools: STOP-BANG (Snoring, tiredness, observed apnea, Press (HTN), BMI>35, age>50, neck>40cm, Gender-male) 3 or greater = increase risk of OSA
- Associated with other diseases: Pulmonary HTN

Risk Calculators- the facts

- Most currently used periop risk calculators utilize the NSQIP database
- Captures 135 variable following patients for 30-days post op
- 2021: 685 hospitals submitted 983,000 cases
- Obstuctive Sleep Apnea is information not collected
- Therefore: OSA not included in any large risk calculator

An approach- *entering a data free zone*

- Risk assess patient – severity of OSA, presence of pulmonary hypertension, intubation history, sedating medications, etc
- Be Practical- does patient have mask, do they wear it, any barriers to using CPAP in the hospital
- Monitoring- consider your postop monitoring plan, ICU/Stepdown?, Continuous pulse ox?
- Multimodal pain control, avoid additional sleepers, benzos, other psychotropic medications
- Early ambulation, out of bed positioning, monitor for fluid overload

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ASA and Noncardiac Surgery

Case: a 48 yo man with a history of NSTEMI 5 years ago who received a stent, completed 1 year of clopidogrel and is now on life-long aspirin in addition to other cardiac meds. He is undergoing a surgical removal of anterior neck mass with a predicted average bleeding risk. What should you do with his aspirin?

A. Stop the ASA 14 days prior to the operation
B. Stop the ASA 7 days prior to the operation
C. Stop the ASA 3 days prior to the operation
D. Continue the ASA through the perioperative period

POISE 2

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Aspirin in Patients Undergoing Noncardiac Surgery

N ENGL J MED 370;16 NEJM.ORG APRIL 17, 2014

- 10,000 Pts randomized to ASA or Placebo 3-7 days before surgery
- About ½ were already on ASA
- No difference in nonfatal MI or death
- Major bleeding in ASA 4.6% vs 3.8% in placebo

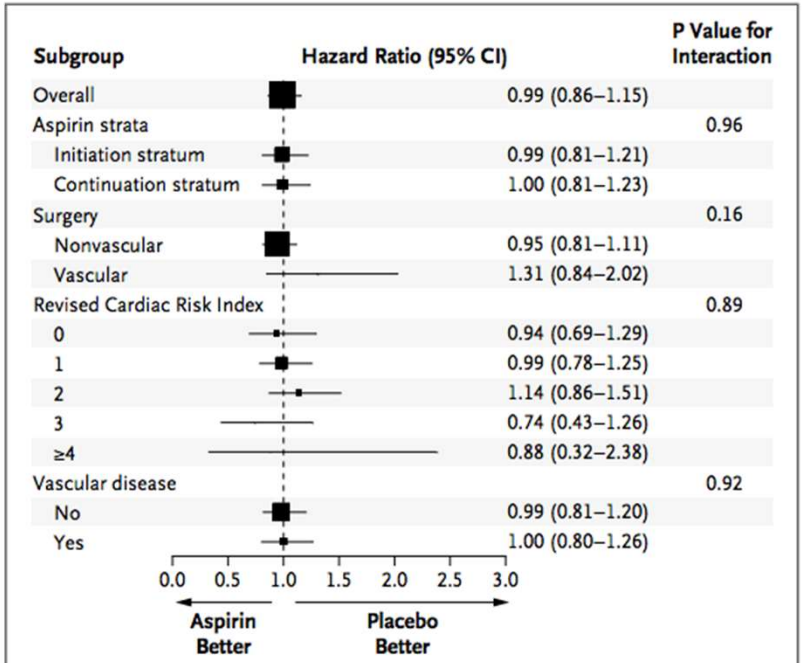


Figure 2. Subgroup Analyses of the Primary Outcome.

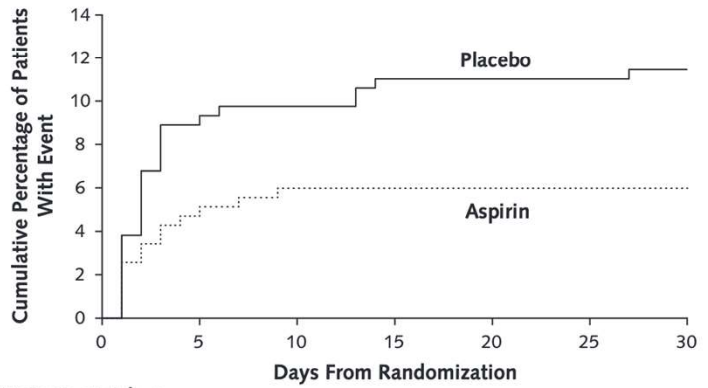
The primary composite outcome was death or nonfatal myocardial infarction at 30 days. The area of each square is proportional to the size of the corresponding subgroup. The Revised Cardiac Risk Index ranges from 0 to 6, with higher scores indicating greater risk.

POISE 2 – post-hoc analysis

Annals of Internal Medicine ORIGINAL RESEARCH

Aspirin in Patients With Previous Percutaneous Coronary Intervention Undergoing Noncardiac Surgery

Figure 2. Effect of aspirin on risk for composite of death and nonfatal myocardial infarction among patients with a history of percutaneous coronary intervention.



Patients at risk, *n*							
Placebo	236	215	212	209	209	209	208
Aspirin	234	223	221	221	221	221	221

P for interaction = 0.036.

- Of 10,000 Pts, 470 had prior PCI
- ASA arm compared with non-ASA arm, 6% reduction in MI w/ASA
- Similar bleeding risks

ASA and Noncardiac Surgery

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Preop Glycemic Control

Case: A 67 yo obese woman w/DM2, a1c of 9.5, is preop for a mastectomy for breast cancer. At home she takes 65 units of glargine each night. Recently her PCP added 5 units of lispro with each of 3 meals. What is the best approach to her insulin management on the night before surgery?

A. Give 24 units of glargine daily +SSI
B. Give 40 units of glargine daily +SSI
C. Give 65 units of glargine daily +SSI
D. Use an aggressive SSI and restart glargine on POD#2

ADA Guidelines

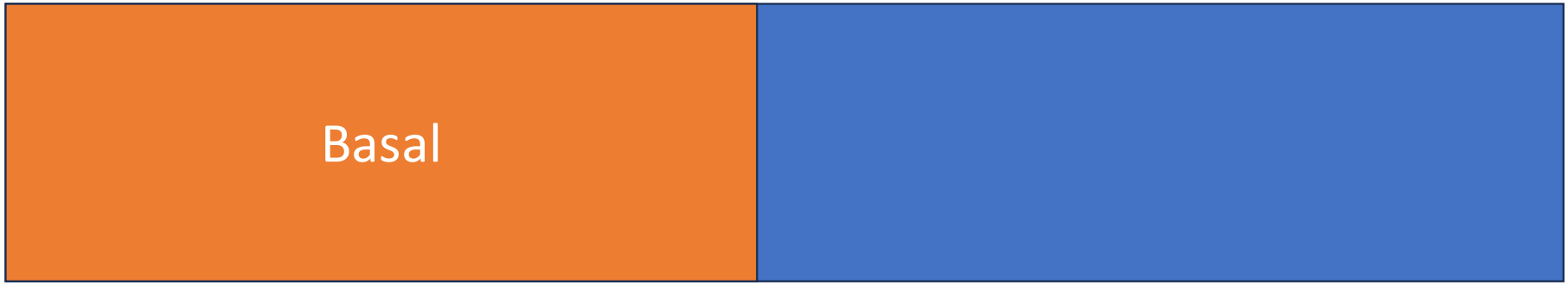
- No standardized approach accepted and well-tested
- Glycemic targets/recommendations:
  - Blood glucose goal: 100-180
  - But special effort avoiding hypoglycemia (even if needing to abandon targets)
  - Perioperative
    - Withhold any other oral hypoglycemic agents the morning of surgery or procedure
      (and SGLT2 inhibitors 3-4 days prior to surgery)
    - Give half of NPH dose
    - Give 75–80% doses of a long-acting analog or pump basal insulin

Periop Insulin – Back to Basics

- When calculating insulin dosages, use total daily of insulin (TDDI)
- For example our patient:
  - 65 of glargine
  - 5 units of prandial insulin
  - TDDI= 80 units
- Rules of thumb:
  - Type 1 diabetics: usually about ½ TDDI (depending on diet) is needed for basal insulin needs
  - Type 2 diabetics: usually about ¼ to ½ of TDDI is needed for basal insulin needs

Basal insulin dosing

Type 1 Diabetes



Type 2 Diabetes

Insulin and avoiding hypoglycemia

- What is patient's risk
  - High A1c?
  - History of hypoglycemia? Symptomatic or Asymptomatic? Situation (hospitalization-related)?
- What is the surgery risk and plans?
  - Early day / Late day?
  - Long procedure?
  - Intraop plan for IV insulin/glucose
- Dose basal based on best guess of need with a decrease to prevent hypoglycemia: usually around 20% reduction, reduce more for higher risk

Back to our patient…

- TDDI is 80 units
- No history of hypoglycemia, high A1c
- Mid-morning procedure
- Recommend giving a 20% reduction of the basal insulin required by patient: 80 x (25-50%) = b/w 20-40 units
  so let's pick ~30 units and reduce this by about 20% = 24 units of glargine the night before
- *Key point: glargine dosing does not always reflect "basal" insulin needs. Misinterpretation can lead to hypoglycemia from overdosing.*

Preop Glycemic Control

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Other situations:

- DM2, diet controlled – sliding scale only (correction insulin)
- DM2, 1-2 oral hypoglycemics- Stop orals, sliding scale only (unless patient very poorly controlled in which glargine appropriate on a case-by-case basis), ***Stop SGLT2 inh 3-4 days prior to surgery***.
- DM1, basal/bolus- ask for morning surgery, consider D5 drip/IV insulin depending on length/complexity of case (usually anesthesia will guide). Typically follow TDDI rules (give about 80% of basal).
- DM1, pump managed. Recommend endocrine input.
  In general, reduce basal infusion, but care is highly variable.

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Postop hypertension

Case: 45 yo man with a history of hypertension, no on meds and no cardiovascular disease develops pressures of 205/105 on POD#1 from a fracture surgery. Pain is controlled, no significant bleeding, no chest pain/dyspnea or other complications. Best next step?

A. Transfer to ICU and start on IV nifedipine
B. Trial of small boluses of IV labetalol or IV hydralazine
C. Oral captopril or furosemide
D. Oral lisinopril or amlodipine
E. Observe

Periop Hypertension

- Preoperative hypertension
  - Severe hypertension – Older studies show SBPs > 211 and DBP >110 associated with worse outcomes
  - Other hypertension – no clear change in risk
- Med management Preop
  - Most meds can be continued
  - ACEi/ARB- if possible hold day of surgery – data mixed
  - Diuretics – goal is euvolemia, so based on clinical judgement, often held
  - Beta blockers – don't start anew, but also don't stop!
  - Clonidine – be aware of withdrawal potential if dose near 1mg/day

Acute Postoperative Hypertension (APH)

No clear definition:

- Related to surgery
- Develops within 20mins - 2 hrs after surgery
- Lasts a few hours at most with pressures >190/110

Who should we treat? What threshold?

- Some surgeries probably deserve aggressive BP control (140/90 goal)
  - Craniotomy patients
  - Nsgy patients
  - Ophth, complicated
  - Vascular
- Some patient's medical problems deserve tight BP goals
  - heart failure
  - ischemic heart disease
- Goals for other non-cardiac surgery patients unclear

Perioperative Hypertension

- Guidelines vary widely and in specificity how/when to treat
- Should we apply “hypertensive urgency” guidelines?
  - JNC 8- silent on the subject (2014)
  - ESC/ESH- should not be considered an emergency; intensify drug therapy
  - ISH- admit and treat with IV medications
- Preoperative patients BP>180/110 assoc with increase complications Should “treat” with delaying surgery or intensifying regimen
- Postoperative patients Answer not clear
- Search for cause: Pain, Urinary retention, Infection, agitation, hypercarbia, hypoxemia
- Consider Risks of Treatment vs Not… **But don’t just treat a number!**

So back to our patient…

A. Transfer to ICU and start on IV nifedipine
B. Trial of small boluses of IV labetalol or IV hydralazine
C. Oral captopril or furosemide
D. Oral lisinopril or amlodipine
E. Observe

You could argue for B, C, D or E depending on your bias and the clinical characteristics

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Functional risk assessment

Case: 68 year-old man w/stable CAD, CKD stage 3 is scheduled to undergo a R total knee surgery. Asymptomatic today except for knee pain. What is the most predictive functional risk assessment?

A. Subjective assessment of activities that require at least 4 METS (walking up a hill, e.g.)
B. Cardiopulmonary Testing to assess METS
C. Duke Activity Status Index (DASI) standardized tool to assess METS

METS Study

- 1400 patients Measured:
  1) Subjective assessment
  2) DASI Score
  3) Cardiopulmonary testing
- Compared **Subjective Assessment** vs **DASI** to formal **CardioPulm Testing**
- Then compared all 3 in predicting Morbidity and Mortality
- Also compared BNP to CPE and evaluated outcomes

METS Study

- Subjective Assessment only identified 1/5 with <4 METS on formal testing
- DASI *slightly* better at predicting <4METS
- *DASI was better* at predicting clinical outcomes (MI or other complications) compared with either Subjective Assessment or Cardiopulmonary testing
- BNP also effective at identifying complications, but identified a different population than DASI or CPT

Risk Assessment – *the Skinny*

- Subjective assessments should not help determine risk
- DASI is probably the best tool we have currently – but far from perfect
- ACC/AHA guidelines rely heavily on METS assessment
- Canada/Europe uses BNP to differentiate high and low risk patients

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Bradycardia

A 50 yo man is s/p a large spine surgery. His postop regimen is: hydromorphone PCA (required 3mg/24h), cyclobenzaprine (Flexiril), tizanidine (Zanaflex), senna, docusate, lisinopril, terazosin. Prior to the OR he was on the BP, BPH and a different opioid. His pulse is now 40. BP 108/77. He is mildy lethargic but in pain when fully awake. You are asked to comment on the new bradycardia.

1. Secondary to his PCA
2. Secondary to cyclobenzaprine
3. Due to compression of his sympathetic nerve roots
4. Secondary to tizanidine

Fun Facts – Drug Side Effects

Tizanidine: alpha-2 blocker, most similar to clonidine
can cause hypotension, bradycardia,
liver test abnormalities

Linezolid: Watch its use in the setting of other serotonin
pathway medications

Cefepime: Can cause a severe neurotoxicity associated with
decreased level of consciousness, myoclonus,
an abnormal EEG

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Bridging Anticoagulation

Case: 75 yo man with a history of atrial fibrillation, stroke, HTN and compensated heart failure undergoing a right hip arthroplasty. His weight is normal, VSS, Cr 0.9 (GFR of 83). Meds include atorvastatin, lisinopril 10, metoprolol 25 q12h and warfarin with a goal of 2.0-3.0. Best management strategy for warfarin?

A. Stop warfarin 5 days before, bridge with heparin gtt
B. Stop warfarin 10 days before, bridge with LMWH
C. Stop warfarin 5 days before, no bridging
D. Stop warfarin 10 days before, no bridging

To Bridge or not to Bridge…

Bridge Trial

- Afib patients on warfarin
- Undergoing a variety of surgeries/procedures
- All patients had warfarin stopped 5 days preop
- Randomized to LMWH bridge or not (with a window for surgery)
- No difference in thrombosis
- Higher rates of bleeding in bridged arm

- Caveats: few high-risk patients (CHADS2 of 5-6)

What about DOACs? (who uses warfarin any more??)

- No need to bridge with any of these agents
- Use published tables to aid in timing of stoppage
- Usually based on renal function, type of drug, and bleeding risk
- When restarting anticoagulants, recommend restarting **24 hours after hemostasis is achieved**

Back to our patient…

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B. Stop warfarin 10 days before, bridge with LMWH
C. Stop warfarin 5 days before, no bridging
D. Stop warfarin 10 days before, no bridging

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Learning Objectives - Revisited

- Understand the common risks confronting perioperative patients
- Know the current evidence behind the management of perioperative patients
- Understand the role of common chronic conditions and their effect on perioperative risk

Take home points…

- Functional status best assessed by using DASI tool
- Develop a patient-specific based approach to managing insulin in the perioperative space

- I hope you enjoyed our “choose your own adventure talk”
- Feel free to reach out with questions/comments!

- Brian.Wolfe@cuanschutz.edu