Perioperative Medicine in the Inpatient Setting

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Objectives

• What is the role of preoperative cardiac testing for inpatients?

• What are some pearls of perioperative medication management in the hospitalized patient?
  – Anti-rheumatic drugs (DMARDS/ Biologics)
  – Antiplatelet management in patients with stents
Disclosures

• Nothing to disclose
Case

- 78 year old female with R hip fracture
- Known CAD with a history of a NSTEMI 2 years ago, which was treated medically
- DSE 2 years ago revealed stress induced hypokinesis in the mid inferoseptal and mid inferior segments.
- Poor functional capacity from a prior stroke 10 yrs ago (some residual hemiparesis), but does ambulate with a walker in her home; denies chest pain episodes since NSTEMI
Case

• Meds: metoprolol, lisinopril, low dose aspirin, calcium and vitamin D
• BP 122/72  P 67
• Labs: normal CBC, lytes Creatinine 0.7
• ECG: normal sinus rhythm, non-specific ST-T wave abnormalities
You are asked to provide preoperative risk assessment prior to the planned bipolar hemiarthroplasty to repair the hip fracture. What do you recommend?

1. Delay surgery, recommend DSE
2. Delay surgery, recommend a nuclear stress test
3. Delay surgery, recommend a cardiac catheterization
4. Proceed with surgery
2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Vascular Medicine

Endorsed by the Society of Hospital Medicine
Estimated perioperative risk of MACE based on combined clinical/surgical risk

Low risk (< 1%)
Elevated risk (≥ 1%)
**Bottom Line**

- **RCRI or Gupta Score**
  - Estimated perioperative risk of major adverse cardiac event (MACE)

- **Low risk (< 1%)** → Surgery

- **Elevated risk (≥ 1%)**
  - **METS < 4 or unknown** → Stress Test If it will change management
  - **METS ≥ 4** → Surgery
Lee Revised Cardiac Risk Index (RCRI)

- High risk surgery (intraperitoneal, intrathoracic or suprainguinal vascular procedures) - 1 point
- History of ischemic heart disease - 1 point
- History of congestive heart failure - 1 point
- History of cerebrovascular disease - 1 point
- Diabetes on insulin - 1 point
- Renal insufficiency (Cr ≥ 2) - 1 point
## RCRI Score to Estimate Risk of MACE

*Cardiac Death, Nonfatal MI, Cardiac Arrest

<table>
<thead>
<tr>
<th>RCRI Score</th>
<th>Risk of Major Cardiac Outcomes*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.4% (0.1-0.8)</td>
</tr>
<tr>
<td>1</td>
<td>1% (0.5-1.4)</td>
</tr>
<tr>
<td>2</td>
<td>2.4% (1.3-3.5)</td>
</tr>
<tr>
<td>≥ 3</td>
<td>5.4% (2.8-7.9)</td>
</tr>
</tbody>
</table>

CMAJ 2005;173 (6):627-34
Important Limitations: RCRI

- Derived from fairly small subset of patients
- Overestimates risk in lower risk surgery
- Underestimates risk in vascular surgery
- Different versions
Gupta (NSQIP) Perioperative Risk Calculator:
5 factors contributed to risk of MI and cardiac arrest

- Age
- Creatinine
- ASA class
- Procedure Type
- Dependent Functional Status

Where to find:
http://www.surgicalriskcalculator.com (download for desktop)

Gupta et. al. Circulation, 2011;124:382-7
## ASA Class

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Normal, healthy patient</td>
</tr>
<tr>
<td>Class II</td>
<td>Patient with mild systemic disease—a mild to moderate systemic disorder related to the condition to be treated or to some other, unrelated process</td>
</tr>
<tr>
<td>Class III</td>
<td>Patient with severe systemic disease that limits activity but is not incapacitating</td>
</tr>
<tr>
<td>Class IV</td>
<td>Patient with incapacitating systemic disease that is life threatening</td>
</tr>
<tr>
<td>Class V</td>
<td>Moribund patient not expected to survive 24 hr without an operation</td>
</tr>
</tbody>
</table>
## Perioperative Myocardial Infarction or Cardiac Arrest Risk Calculator

<table>
<thead>
<tr>
<th>Age</th>
<th>Enter actual age in years</th>
<th>Estimated risk probability for perioperative MICA: 3.29%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA Class</td>
<td>Enter 1 - 5 for American Society of Anesthesiologists' Class</td>
<td></td>
</tr>
<tr>
<td>Creatinine (preoperative)</td>
<td>Enter 1 for &gt;=1.5 mg/dL, 0 for &lt;1.5 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Functional Status (preoperative)</td>
<td>Enter 2 for patients with totally dependent functional status, 1 for partially dependent, 0 for totally independent</td>
<td></td>
</tr>
<tr>
<td>Procedure:</td>
<td>Enter 1 for Anorectal, 2 for Aortic, 3 for Bariatric, 4 for Brain, 5 for Breast, 6 for Cardiac, 7 for ENT (except thyroid/parathyroid), 8 for Foregut/Hepatopancreatobiliary, 9 for Gallbladder, appendix, adrenal and spleen, 10 for Hernia (ventral, inguinal, femoral), 11 for Intestinal, 12 for Neck (Thyroid and Parathyroid), 13 for Obstetric/Gynecologic, 14 for Orthopedic and non-vascular Extremity, 15 for Other abdominal, 16 for Peripheral Vascular, 17 for Skin, 18 for Spine, 19 for non-esophageal Thoracic, 20 for Vein, 21 for Urology</td>
<td></td>
</tr>
</tbody>
</table>

ASA Classification:
1. A normal healthy patient.
2. A patient with mild systemic disease.
3. A patient with severe systemic disease.
4. A patient with severe systemic disease that is a constant threat to life.
5. A moribund patient who is not expected to survive without the operation.
Where Can I Find the Calculator?

- Qx Calculate
  - http://www.qxmd.com
  - Free app for phone
- http://www.surgicalriskcalculator.com
  - Free download for desktop
  - Request for password accepts anything
Important Limitations: GUPTA

- Likely underestimates risk because of how cardiac outcomes were defined in the dataset
  - ECG changes of acute MI
  - New elevation in troponin greater than 3 times normal in the setting of suspected myocardial ischemia

- Majority of postop cardiac outcomes are asymptomatic NSTEMIs

- Not externally validated beyond the original dataset
Bottom Line

RCRI or Gupta Score

- Low risk < 1%
- Elevated risk ≥ 1%
- METS < 4 or unknown
- METS ≥ 4
- Stress Test: If it will change management

- RCRI 2.4%
- Gupta 3.29%

Estimated perioperative risk of major adverse cardiac event (MACE)
Will Stress Testing Change Management?

• 78 years old with a hip fracture
• There is risk for delay of surgery
  – Increased risk of VTE, delirium
  – Increased risk of further debility
• Would I delay surgery for a coronary stent or angioplasty if the test were positive?
• What does the patient and family want?
Case

• 72 year old male scheduled for elective bilateral inguinal hernia surgery

• Past history significant for severe psoriasis for which he takes methotrexate 15 mg weekly. His last dose was 6 days ago
What do you recommend regarding his methotrexate perioperatively?

1. Take methotrexate without interruption during the perioperative period

2. Hold methotrexate for 1-2 weeks prior to surgery; resume after wound healing

3. Hold methotrexate 2 days prior to surgery; resume postoperatively before hospital discharge
DMARDs Perioperatively: Issues

- Increased wound and bone infection
- Decreased wound healing and increased wound dehiscence
- Concern for disease flare if stopped
- When to restart
- Very little high quality data to inform practice
Methotrexate

• Small observational studies have suggested MTX not associated with increased risk of postop complications
• Several experts recommend continuing MTX
• Issues to consider
  – Many studies had lower dose MTX than used now
  – Patients with renal insufficiency and diabetes at higher risk of toxicity (cytopenias)
  – Only ~8% of patients have disease flare when MTX held
  – No patients die of disease flare

Methotrexate

• Probably safe to continue in most situations
  – Multiple drug-drug interactions
  – Check CBC, liver enzymes, albumin, creatinine
  – Avoid volume depletion

• Consider holding is significant concern for perioperative infection or history of previous or severe septic complications
  – Hold 1-2 weeks preop
  – Resume 2 weeks postop or after complete wound healing
Non-Biologic DMARDs

• These are usually continued in the perioperative setting

• Caveats:
  – Studies suggest increased risk of infection
    • Penicillamine, Cyclosporine, Hydroxychloroquine
  – Some agents can cause leukopenia
    • Cyclophosphamide, Azathioprine, Sulfasalazine
  – Leflunomide often held (2 weeks)

• Check CBC, liver enzymes, creatinine

• Check for drug-drug interactions
Case

• 57 year old woman with rheumatoid arthritis scheduled to undergo multi-level lumbar spinal fusion
• Current medications include adalimumab (Humira) 40 mg every other week
• No other significant medical problems or past medical history
• Last dose of adalimumab was 13 days ago
What do you recommend regarding her adalimumab perioperatively?

1. Take adalimumab without interruption during the operative period
2. Hold next dose, and resume per regular schedule postoperatively
3. Hold for 3 weeks preop and resume 2 weeks postop or after wound healing complete
4. Hold for 12 weeks preop and resume 2 weeks postop or after wound healing complete
Biologic Immunomodulators

• TNF alpha inhibitors
  – Infliximab (Remicade)
  – Etanercept (Enbrel)
  – Adalimumab (Humira)
  – Golimumab (Simponi)
  – Certolizumab (Cimzia)

• Non-TNF alpha inhibitors
  – Interleukin antagonists [Anakinra (Kineret), Tocilizumab (Actemra)]
  – T-cell co-stimulation blocker [Abatacept (Orencia)]
  – B-cell depleting agents [Rituximab (Remicade)]
  – Janus kinases (JAK) inhibitors [tofacitinib (Xeljanz)]
No Definitive Evidence or Guideline

- British Society for Rheumatology Standards: hold 3-5 half lives (2005)
- American College of Rheumatology: hold TNF-a inhibitors for $\geq 1$ week (2008)
- Canadian Rheumatology Association: hold for 2 half lives (2012)
Rule of Thumb for Managing Biologics Perioperatively

- Balance risk of disease flare vs infection and wound healing
- Hold for 1-2 half lives prior to surgery
- For most, resume after 2 weeks or after COMPLETE wound healing and NO evidence of ongoing infection

Goodman SM. Optimizing Perioperative Outcomes for Older Patients with RA Undergoing Arthroplasty. Drugs Aging 2015. 32:361-9
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Instructions</th>
</tr>
</thead>
</table>
| Abatacept (Orencia)       | • Hold for 2 weeks preop for SC dosing  
                          | • Hold for 4 weeks preop for IV dosing |
| Adalimumab (Humira)       | • Hold 3 weeks preop                       |
| Anakinra (Kineret)        | • Hold for 2 days preop  
                          | • Check CBC                           |
| Certolizumab (Cimzia)     | • Hold for 6 weeks preop                    |
| Etanercept (Enbrel)       | • Hold 2 weeks preop  
                          | • Check CBC                           |
| Golimumab (Simponi)       | • Hold for 6 weeks preop                    
                          | • Check CBC                           |
| Hydroxychloroquine        | • Continue perioperatively  
                          | • Check CBC                           
                          | • Multiple drug-drug interactions      |
| (Plaquenil)               |              |
| Infliximab (Remicade)     | • Hold 6 weeks preop  
                          | • Check CBC                           |
| Purine analogues          | • Continue preoperatively  
                          | • Check CBC, liver enzymes            
<pre><code>                      | • Monitor renal function              |
</code></pre>
<p>| (6-mercaptopurine/Azathioprine) |              |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Preoperative Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leflunomide (Arava)</td>
<td>- Hold 2 weeks preop&lt;br&gt;- Check CBC, liver enzymes, creatinine&lt;br&gt;- If infection occurs, use cholestyramine purge to clear drug</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>- Continue for most surgical procedures&lt;br&gt;- Hold 1-2 weeks preop if significant risk for infection&lt;br&gt;- Check CBC, liver enzymes, albumin, creatinine&lt;br&gt;- Multiple drug-drug interactions</td>
</tr>
<tr>
<td>Rituximab* (Rituxan)</td>
<td>- Continue preoperatively&lt;br&gt;- Check CBC, creatinine</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>- Continue preoperatively&lt;br&gt;- Check CBC, liver enzymes, creatinine</td>
</tr>
<tr>
<td>Tocilzumab (Actemra)</td>
<td>- Hold for 3 weeks preop for SC dosing&lt;br&gt;- Hold for 4 weeks preop for IV dosing&lt;br&gt;- Check CBC, liver enzymes</td>
</tr>
<tr>
<td>Tofacitinib (Xeljanz)</td>
<td>- Hold for 3 days preop&lt;br&gt;- Check CBC, liver enzymes</td>
</tr>
</tbody>
</table>

*some references recommend holding for 4 weeks preop and waiting 4 weeks before resuming
Some Help is on the Way....

Case

• 68 year old woman with obesity, DM2, CKD stage 3 with NSTEMI 4 weeks ago; DES placed in the proximal LAD and started on ASA and clopidogrel
• Developed uterine bleeding and diagnosed with FIGO grade 2 uterine adenocarcinoma
• Her cardiologist stopped her ASA and clopidogrel 5 days ago in the setting of moderate bleeding
• No transfusions were necessary
• You are consulted by gynecology for a preoperative evaluation prior to planned robotic hysterectomy/BSO with sentinel LN biopsy
Case

- BP 162/69, P 78, regular, BMI 42, Asymptomatic
- CBC normal, A1C 7.2%, creatinine 1.3
- ECG: Rate 73, NSR, Nonspecific ST and T wave abnormality
- Exam unremarkable
In addition to having a discussion with the surgeon about alternative treatment options, what do you recommend?

1. Proceed with surgery. Resume ASA and clopidogrel postoperatively
2. Restart ASA and clopidogrel now and proceed with surgery
3. Restart ASA and clopidogrel now and postpone surgery for at least 5 more months
4. Restart ASA and clopidogrel now and postpone surgical procedure for 11 more months
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

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