Coronary Artery Stents: Implications for Anesthetic Management

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Why You Should Care:

- Percutaneous Coronary Interventions or PCI’s are now the primary treatment for ACS and unstable CAD
- 2 million PCI’s/year in the United States (vs. 500,000 CABG’s)
- 90% receive at least 1 coronary stent
- Oral antplatelet therapy is required for up to a year or perhaps longer
- 5% (100,000+) of patients with coronary stents will require surgery during that time
- Frequency of MACE events may not be related to the length of time between PCI and NCS
- This number will increase over time

Stent Thrombosis is Disastrous!

- Stopping antplatelet therapy (APT) can lead to thrombosis
- Thrombosis occurs in 30% of patients who stop APT
- 64% of those with thrombosis will have an MI
- Mortality between 20% - 45%
- Patients that undergo noncardiac surgery soon after stent placement are at ↑ risk of stent thrombosis
- Risk of thrombosis for DES > BMS
- About 60% of all stents placed are DES
- In retrospective studies, the mortality ranged from 2.5% - 21.4%

The management of patients with coronary artery stents during the perioperative period is one of the most important patient safety issues clinicians confront.

Perioperative stent thrombosis is a life-threatening complication for patients with either bare-metal or drug-eluting stents.

Noncardiac surgery appears to increase the risk of stent thrombosis, myocardial infarction, and death, particularly when patients undergo surgery early after stent implantation.
Clinician’s Responsibility

- Recognize that ideal management of the patient with a coronary stent is a complex issue.
- Not all patients or surgeries are at equal risk.
  - Related to type of stent, complexity of the intervention and duration of APT.
  - Patient’s co-morbidities and the risk of bleeding in the proposed surgery.
- Understand the ACC/AHA Guidelines so that we can appropriately:
  - Identify patients that are at increased risk and quantify that risk.
  - Confidently recommend that surgery be delayed, cancelled or performed at a tertiary care center.
  - Intelligently collaborate with the surgeon and cardiologist when surgery can’t be delayed.
- Customize dual APT to each patient’s individual situation thereby minimizing risk.

Evolution of PCI

“2 Steps Forward and 1 Step Back”

- Angioplasty (1977)
- Arthrectomy, laser angioplasty (1980’s)
- Bare metal stent (1993)
- Drug eluding stent (2003)
- Brachytherapy
- 2nd generation stents (2008)
- Titanium stents...
- Absorbable stent...
- Radioactive stent...

History

- First balloon coronary angioplasty in 1977
- Initial 30 patients:
  - 64% success rate
  - 14% required CABG
  - 6% MI
- As skill increased, success rate approached 90%

Balloon Dilation

- “Controlled” vascular damage causing:
  - Early damage:
    - Denuded endothelium, with accumulation of platelets and fibrin
    - Foulung, fracturing or disruption of existing plaque
    - Intimal dissection
    - Media tear
    - Aneurysmal dilatation
    - Elastic recoil of vessel
    - Inflammation
  - Late Damage:
    - Vascular scar formation
    - Scar contraction (negative remodeling)
    - Muscle hyper-proliferation
    - Lumen narrowing

Problem with Angioplasty

- 2 major limitations of angioplasty
  - Acute vessel closure:
    - Occurs in the first 24 hours
    - 4%-8% in early 1990’s
    - 20% patients requiring CABG
    - Overall mortality 4.9%
  - Restenosis:
    - 30% to 50%
    - Most often seen within 6 months
    - Defined as a ≥ 50% post-procedural narrowing
    - More prevalent with SVG and LAD lesions
    - Target lesion revascularization was needed in 20%-30%
Solution?

- Produce less vessel trauma
- Remove atherosclerotic plaque
- 1980's new devices
  - Laser angioplasty
  - Rotational atherectomy
- Trials demonstrated higher rates of:
  - Vessel closure 46% vs 35%
  - Peri-procedure MI
  - 1 yr mortality
- Rotablation (Percutaneous Transluminal Rotational Atherectomy or PTRA)

Problems with BMS

- Newly placed coronary stents are thrombogenic
- The risk is highest during the first month then levels off
- Acute (within 30 day) stent thrombosis
  - Thrombosis higher than with PTCA alone
- Restenosis:
  - 20% -30% (vs 40%-50% w/o stent)
  - Within 6 months
  - Mechanism is multifactorial and due to cascade of injury

Bare Metal Stents

- FDA approval for elective use in 1993
- Acts as a scaffold to prevent elastic recoil of vessel and decrease restenosis
- BENESTENT and STRESS studies: “significantly less acute vessel closure and restenosis”
  - Restenosis ↓ from 42%-32%
  - Target lesion revascularization ↓ from 30%-12%

More improvements → Thrombosis

- Use of intravascular ultrasound and high balloon pressures to optimize placement
- Replacement of anticoagulation with dual-antiplatelet therapy
  - Thienopyridines
    - Inhibit ADP/P2Y12 pathway
    - Initially Ticlopidine (Ticlid®)
    - New Clopidogrel (Plavix®), 75 mg for 4-6 weeks
  - ASA
    - Inhibits arachidonate-thromboxane A2 (TxA2)
    - 75-325 mg for life
- Standard of care
  - By 1999, 84% of PCI’s involved stents

Despite Advancements, Restenosis remains…the “Achilles Heel”

- Overall 20%-25% restenosis 1st 6 months
  - Pesos at 3 months
  - Plateaus between 3-6 months
  - Can persist beyond 1 yr
- Rates approach 80% in “high risk”
  - Diabetes
  - Renal Insufficiency
  - Complex lesions
- Catastrophic event
  - 35% ACS requiring re-intervention
  - Mortality 9.3%
  - Mortality 0.7%

Drug-eluting Stents
**First generation DES**

**Stainless steel**

- **CYPHER** Eludes sirolimus
- **TAXUS** Eludes paclitaxel

**BMS vs. DES**

- BMS is coated with a polymer containing antiproliferative and immunosuppressive material that delays endothelialization
- Effectively prevents neointimal hyperplasia and restenosis
- DES ↓ risk of restenosis to 5%-20%

**Advent of DES**

- Initial FDA approval 2003 and 2004
- Expedited and enthusiastic review
- FDA required manufacturers to follow patients for 5 years and conduct registry studies
- Recommended DAPT for 3-6 months and ASA for life
- Superiority of the DES is accepted by the cardiology community
- By 2005 nearly 80% PCI included a DES
- Then the case reports and new randomized study results started rolling in....

**Meta-analysis**

- **2006- BASKET-LATE**
  - 746 patients randomized to receive BMS or DES kept on DAPT for 6 months (no events) then plavix stopped....

**Meta-analysis Ignores a Firestorm**

- **2006- BASKET-LATE**
  - Mortality 19%
  - Composite death or MI 88%
  - DES Late stent thrombosis events (death/MI)
    - 2-3x’s greater than BMS
    - 4x’s greater mortality
  - Complications continued for > 1 year
  - The original studies that led to FDA approval were reanalyzed including a 4 yr follow up and showed a 3 fold greater composite risk of death or MI in the DES cohort
  - More trials (EVASTENT) and registries⇒ controversy and confusion
Dec 2006, the FDA Convenes

- When DES are used for their “approved purposes” (40% of implanted stents) the risk of thrombosis does not outweigh the advantages over BMS
- Off-label use (60% of implanted stents) is associated with higher rates of stent thrombosis, MI and Death
- There is sufficient data to recommend a prolonged course of DAPT but the ideal duration is yet unknown

Clopidogrel and Long Term Outcome

- 4666 patients
  - 3165 with BMS
  - 1501 with DES
- 6 month vs. 12 month Clopidogrel
- Long term Clopidogrel significantly improves prognosis with DES
  - Significantly lower death and death or MI compared with patients with DES not receiving the medication
  - Continued clopidogrel therapy conveys an important prognostic benefit for patients with DES not seen with BMS

AHA/ACC/SCAI/ACS/ADA Science Advisory

- Premature discontinuation non surgical patients
  - Catastrophic stent thrombosis
  - Occurs between 8%-30% of patients
  - Pooled analysis 6 trials
  - Incidence of MI or death 64.4%
  - “doubling the rates of MI and death”
- Prevention of Premature Discontinuation of Dual Antiplatelet Therapy in Patients with Coronary Artery Stents
  - 12 months of dual therapy
  - Education
  - Collaboration

So...the problem of restenosis improving but... acute thrombosis is a big problem!

Acute Thrombosis

- DES don’t endothelialize so they are prone to clots
- Coronary blood flow ceases
- Two-thirds of patients will have MI
  - Mortality rate of 20% to 45%
  - Occurs in at least 1% of DES
  - Assuming 4 million DES
  - 40,000 stents thrombosis/year
  - 26,000 MI’s/year
  - 13,000 deaths/year

Drug-eluting Stents (DES)

- Numerous publications on perioperative M&M suggest that acute stent thrombosis, MI and death may be more prevalent than previously thought
- Especially when there is incomplete endothelialization
- There are no clinical tests to determine if there is adequate endothelialization
- Periop stent thrombosis can occur as late as 4 yrs after insertion
- Median time was 242 days, range (39-927)
When will I see this? (never, I hope)

- Early stent thrombosis
  - Occurs in the first 30 days after PCI
  - Usually due to technical aspects of the PCI
  - Incidence is 1% for both BMS and DES
- Late stent thrombosis
  - 30 day to 1 year
  - Incidence: BMS 0.19%, DES 0.5%-3.1%
- Very late stent thrombosis
  - > 1 year

Withdrawal of APT

- Independent predictor for mortality in patients with ACS and CAD
- Abrupt cessation of ASA causes rebound hypercoagulability
- Collet et al. found a 2 fold ↑ in MI and death in patients that recently withdrew APT
- Recent withdrawals compromise 5% of patients with ACS
- ASA withdrawal was also a predictor for bleeding!

Withdrawal of Anti-platelet Therapy

- Premature complete cessation of DAPT
- Only long-term DAPT and aspirin continued
- Rarely unless patients receive DAPT

Surgery Compounds the Problem

- Premature discontinuation of DAPT
- Withdrawal of antiplatelet therapy

References:
Risk Factors for Stent Thrombosis

**Clinical Risk Factors**
- Acute coronary syndrome
- Platelet activity (surgery, malignancy, diabetes)
- LV dysfunction
- Renal failure
- Diabetes
- Prior brachytherapy
- Resistance to APT
- Inappropriate d/c of APT

**Angiographic Risk Factors**
- Left main stents
- Stents at bifurcations or across branches
- Multiple stents
- Long and/or overlapping stents
- Small vessels
- Plaque disruption into non-stented segment
- Penetration of stent into a necrotic core


Risk Score for LST

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<tr>
<th>Risk Factor for LST</th>
<th>Points</th>
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<td>Poor risk</td>
<td>2</td>
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<tr>
<td>Moderate risk</td>
<td>1</td>
</tr>
<tr>
<td>Low risk</td>
<td>0</td>
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Proposed treatment for patients requiring PCI who subsequently need surgery

Adapted from Fleisher L A et al. Circulation 2007;116:e418-e500

### Preoperative Evaluation

**TABLE 5**

**Preoperative evaluation of patients with stents: A checklist**
- Determine type of stents (bare metal or drug-eluting)?
- Timing of stent implantation?
- Determine the time since stent was implanted?
- Determine location of each stent in the coronary circulation?
- Determine the mechanical complications?
- Are there any medical complications (e.g., hypertension)?
- Are there any complications of the previous PCI?
- Check for any other complications?
- Determine if the patient has any other risk factors (e.g., diabetes, renal insufficiency)?
- Additional risk factors for stent thrombosis

*What is the recommended duration of dual antiplatelet therapy for the specific patient at risk?*
- Consult with patient's cardiothoracics on current antiplatelet management and discuss optimal management strategy.
Upon agreement between cardiology and surgery, eptifibatide infusion will be restarted according to the above paradigm if clopidogrel cannot be reinitiated.
Convert to heparin?

- Heparin has no effect on platelets
- Vicenzi et al. found an association between periop heparin rx and cardiac M&M in pts with stents
- Heparin infusion causes ↑ in thrombin and platelet activity that outlasts the protective anticoagulant effect
- Webster et al. found ↑ platelet aggregation despite rx with ASA
- Combining heparin with ASA and glycoprotein (GP) IIb/IIIa platelet inhibitors (ReoPro, Integrisil, Aggrastat) seems to negate the effect (Theroux et al)

Opponents to Bridging

- Does not offer complete protection
- Must be continued into the post op period as this is the greatest risk period
- Exposes patient to risks of prolonged hospitalization
- Expensive
- Logistically difficult
- Unproven

Preop Management of DAPT

Managing Stent Thrombosis

- Usually presents as STEMI or sudden malignant dysrhythmia
- Must be treated with PCI
- Thrombolytic (IV or intracoronary) therapy is significantly less effective
- Cardiogenic shock is common

Summary Recommendations

- Discontinuing DAPT in newly placed stents is associated with increased risk of life-threatening stent thrombosis
- “Best Practice” management requires collaboration between surgery, cardiology and anesthesiology
- High risk patients should be referred to a tertiary care center where 24 hour invasive cardiology services are available
- Delay surgery if possible till the recommended course of DAPT is complete
- 6 weeks after MFS
- 1 year after DES
- Possibly longer in high risk patients
- If not possible, ASA should be continued (last dose within 2 hours of surgery) and aspirin stopped 3 days prior to surgery. Restart the pills. ASA using a 600mg loading dose
- If it is determined that no anticoagulation is possible, clearly document the reasoning. Stop the APT for 7 days and proceed to OR
- In high risk situations, the GP-IIb-IIIa inhibitors or direct thrombin inhibitors may be used as bridging
Thank you for your attention!

An angioplasty a day keeps the cardiologist healthy!

Your Attention Was Appreciated

Thank You!

North Dakota Association of Nurse Anesthetists