Stopping Dual Antiplatelet Therapy (DAPT) Following Percutaneous Coronary Intervention (PCI) A Rational Approach

Paul Huang, MD
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Aspirin

• The foundation of antiplatelet treatment strategy
• Irreversible acetylation of the platelet COX-1 enzyme – inhibition of generation of TxA₂ and TxA₂-induced platelet aggregation

• Pharmacokinetics
  • Plasma half-life = 20 minutes
  • COX-1 inhibition for the lifespan of platelets ~ 10 days

• Current PCI guideline
  • 162-325 mg loading at time of PCI
  • Indefinite maintenance dose of 81 mg daily
P2Y$_{12}$ Inhibitors

- ADP binding to P2Y$_{12}$ receptors – sustained GP IIb/IIIa activation – platelet aggregation (via fibrinogen cross-linking) - thrombosis
- Clopidogrel (Plavix) & prasugrel (Effient) – active metabolites bind irreversibly to the ADP binding site of the P2Y$_{12}$ receptors on platelets
- Ticagrelor binds reversibly and independently from the ADP binding site
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

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


Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

Endorsed by Preventive Cardiovascular Nurses Association and Society for Vascular Surgery
DAPT Duration Post PCI (Drug-Eluting Stents)

• Stable ischemic heart disease (SIHD)
  • 6 months
  • 3 months for patients at high bleeding risk
  • 12 months for patients at high ischemic risk
  • ASA & clopidogrel

• Acute coronary syndrome (ACS – Unstable angina, NSTEMI & STEMI)
  • 12 months
  • 6 months for patients at high bleeding risk
  • 30 months (extension of 18-36 months) for patients at high ischemic risk/low bleeding risk
  (DAPT score ≥ 2)
    • Age, DM, Previous MI, HTN, PAD, smoking, CHF/EF < 30%, renal insufficiencuy
    • MI @ presentation, stent < 3 mm, SVG
    • ASA & ticagrelor; ASA & prasugrel (< 75 yo; weight > 60 kg, no h/o TIA or stroke); ASA &
clopidogrel

• Non-adherence – stent thrombosis, MI & death
### The DAPT Score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
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<tbody>
<tr>
<td><strong>Patient Characteristic</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>≥ 75</td>
<td>-2</td>
</tr>
<tr>
<td>65 - &lt;75</td>
<td>-1</td>
</tr>
<tr>
<td>&lt; 65</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Current Cigarette Smoker</td>
<td>1</td>
</tr>
<tr>
<td>Prior PCI or Prior MI</td>
<td>1</td>
</tr>
<tr>
<td>CHF or LVEF &lt; 30%</td>
<td>2</td>
</tr>
<tr>
<td><strong>Index Procedure Characteristic</strong></td>
<td></td>
</tr>
<tr>
<td>MI at Presentation</td>
<td>1</td>
</tr>
<tr>
<td>Vein Graft PCI</td>
<td>2</td>
</tr>
<tr>
<td>Stent Diameter &lt; 3mm</td>
<td>1</td>
</tr>
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</table>

**Distribution of DAPT Scores among all randomized subjects in the DAPT Study**

![Histogram showing distribution of DAPT scores](image)

*Yeh, Secemsky, Kereikses et al. JAMA. 2016.*
Treatment Effect by DAPT Score Quartile

- **Q1 = DAPT Score -2 to 0**
- **Q2 = DAPT Score 1**
- **Q3 = DAPT Score 2**
- **Q4 = DAPT Score > 2**

### Stent Thrombosis
- **Q1**: 0.07%
- **Q2**: 0.06%
- **Q3**: -1.34%
- **Q4**: -2.18%

### Myocardial Infarction
- **Q1**: -0.73%
- **Q2**: 0.59%
- **Q3**: -2.56%
- **Q4**: -3.48%

### GUSTO Moderate/Severe Bleeding
- **Q1**: 1.97%
- **Q2**: 1.17%
- **Q3**: 0.69%
- **Q4**: 0.03%
DAPT Score <2 (Low) - N=5731
DAPT Score $\geq 2$ (High) - N=5917

Myocardial Infarction or Stent Thrombosis

Cumulative incidence of ST/MI

- Continued Thienopyridine
- Placebo

- $2.7\%$ vs. $5.7\%$
- $P<0.001$

Death, MI or Stroke (MACCE)

Cumulative incidence of MACCE

- Continued Thienopyridine
- Placebo

- $4.9\%$ vs. $7.6\%$
- $P<0.001$

GUSTO Moderate/Severe Bleeding

Cumulative incidence of GUSTO Moderate/Severe Bleed

- Continued Thienopyridine
- Placebo

- $1.8\%$ vs. $1.4\%$
- $P=0.26$
Duration of DAPT

• The balance between ischemic and hemorrhagic risks with DAPT is nuanced.
• The risk of stent thrombosis extends beyond 3 years.
• 3rd generation drug-eluting stents (thinner struts, better polymer & better drug contributing to improved endothelialization & strut coverage) & improved implant techniques gradually abrogate the advantage of bare metal stents with regard to the shorter duration of DAPT.
• Shorter duration of DAPT (e.g., 1 month) may be possible for stable ischemic heart disease patients.
Noncardiac Surgery Following PCI with Stents

- 5-10% of patients undergo noncardiac surgery within one year following PCI.
- Discontinuation of DAPT may be necessary in anticipation of major surgery to decrease perioperative bleeding risk.
- Surgery is associated with prothrombotic and proinflammatory effects.
- Cessation of DAPT may lead to adverse cardiac events – stent thrombosis, MI & death.
- Observation studies – adverse cardiac events in patients undergoing major surgery within 6 weeks of PCI
- Increased risk extends as long as 12 months, regardless of BMS or DES.
- No proven benefit of bridging therapy with iv antipatelet therapy while holding DAPT.
PCI Patients Undergoing Elective Noncardiac Surgery
Revised Cardiac Risk Index (RCRI)
6 independent predictors of major cardiac complications

• High-risk type surgery (e.g., vascular surgery & any open intraperitoneal or intrathoracic procedures)
• History of ischemic heart disease
• History of heart failure
• History of cerebrovascular disease
• Insulin-dependent diabetes mellitus
• Preoperative serum creatinine > 2.0 mg/dL

Lee TH et al., Circulation 1999;100:1043
Perioperative Major Adverse Cardiac Events (Cardiac death, nonfatal MI & nonfatal cardiac arrest)

<table>
<thead>
<tr>
<th># Risk Factors</th>
<th>Rate of MACE (95% C.I.)</th>
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<tbody>
<tr>
<td>0</td>
<td>0.4% (0.1-0.8)</td>
</tr>
<tr>
<td>1</td>
<td>1.0% (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>

A cardiologist can only risk-stratify a patient’s risk of perioperative major adverse cardiac events but not “clear” a patient for surgery.

Devereaux PJ et al., CMAJ 2005;173:627
Non-Cardiac Surgery After PCI
Restropective & Observational Studies

• Factors most strongly associated with MACE – nonelective surgery (AOR 4.77), MI in the 6 months preceding surgery (AOR 2.63) & RCRI > 2 (AOR 2.13)\(^1\)

• MACE – 5.1% for BMS & 4.3% for DES; MACE between 6 weeks and 6 months following PCI lower for DES; no difference in MACE before 6 weeks & after 6 months\(^1\)

• Discontinuation of aspirin, clopidogrel or both – increased MACE with mean of 500 days post PCI\(^2\)

• Continuation of aspirin – significant lower risk of MACE (AOR 0.27)\(^2\)

• Excess bleeding with continuation of aspirin (up to 20%) and DAPT (up to 50%) – increased risk of RBC txn but not surgical mortality or morbidity\(^3,4\)

1. Hawn MT et al., JAMA 2013;310:1462
2. Rossini R et al., Thromb Haemost 2015;113:272
3. Chassot PG et al., Br J Anaesth 2007;99:316
No Randomized Trials Comparing Different Times for Surgery Following PCI and Different Antiplatelet Strategies Have Been Conducted
Discontinuation of DAPT

• 2016 ACC/AHA Guideline Focused Update on DAPT
  • Elective noncardiac surgery should be delayed 30 days after BMS implantation and optimally 6 months after DES implantation
  • P2Y$_{12}$ inhibitor may be stopped 3 months after DES PCI if the risk of delayed surgery > risk of stent thrombosis

• 2017 ESC focused update on DAPT
  • P2Y$_{12}$ inhibitor may be stopped 1 month after PCI (BMS & DES) if aspirin can be maintained throughout the perioperative period
A Rational Approach

• Non-emergent surgery deferred until recommended duration of DAPT
• For patients for whom surgery cannot wait – minimal 1-3 months of DAPT
• In many cases, DAPT may be continued perioperatively
  • Minor surgical and dental procedures
  • Exceptions = neurosurgery, posterior eye surgery or prostate surgery where risk of major bleeding > risk of stent thrombosis)
• Consider continuation of aspirin therapy while stopping P2Y₁₂ antagonist
• Consider platelet transfusion for emergent surgery
• Availability of interventional cardiology
Discontinuation of P2Y$_{12}$ Antagonists

- Clopidogrel & ticagrelor = 5 days
- Prasugrel = 7 days
- 300-600 mg of clopidogrel reloading as soon as possible following surgery
Conclusion

• DAPT is important following PCI to reduce the risk of MACE, including stent thrombosis.
• The duration of DAPT varies, depending on the risk of MACE and the risk of bleeding.
• Discontinuation of DAPT is associated with increased risk of MACE associated with noncardiac surgery.
• Antiplatelet strategy for PCI patients should be individualized.
• Continuation of aspirin therapy should be considered if P2Y\textsubscript{12} inhibition needs to be stopped perioperatively.