UPDATES FROM THE 2018 ANTIPLATELET GUIDELINES

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21st Annual Contemporary Therapeutic Issues in Cardiovascular Disease

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2018 CCS Antiplatelet Guidelines
https://www.ccs.ca/en/guidelines

- DAPT in PCI
- PCI + AF
- Switching
- Surgery
Bleeding

- The risk of bleeding with antiplatelet therapy is important but fatal or life-threatening bleeding is not common

- In order to minimize the risk of bleeding, consider the risk factors and try to minimize intensity of therapy when possible

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Need for OAC in addition to DAPT</td>
</tr>
<tr>
<td>2.</td>
<td>Advanced age (&gt; 75 years)</td>
</tr>
<tr>
<td>3.</td>
<td>Frailty</td>
</tr>
<tr>
<td>4.</td>
<td>Anemia with hemoglobin &lt; 110 g/dL</td>
</tr>
<tr>
<td>5.</td>
<td>Chronic renal failure (creatinine clearance &lt; 40 mL/min)</td>
</tr>
<tr>
<td>6.</td>
<td>Low Body Weight (&lt; 60 kg)</td>
</tr>
<tr>
<td>7.</td>
<td>Hospitalization for bleeding within last year</td>
</tr>
<tr>
<td>8.</td>
<td>Prior stroke/intracranical bleed</td>
</tr>
<tr>
<td>9.</td>
<td>Regular need for NSAIDS or prednisone</td>
</tr>
</tbody>
</table>
Goals of Antiplatelet Therapy Post PCI

- Contemporary DES has a low risk of thrombosis
  - Even 3-6 months of DAPT may be sufficient in some cases

- Examples:
  - Elective PCI
    - Shorter duration, less intense regimens are acceptable

- But in ACS and PCI....
  - To reduce the risk of stent thrombosis and recurrent plaque rupture, DAPT for at least 1 year but if not at high risk of bleeding for at least 3 years.
## High-risk clinical and angiographic features for thrombotic events

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<th>Angiographic</th>
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*Net benefit to diabetics in the absence of any of other high risk features is unclear*
PCI for STEMI or NSTEMI

DAPT for 1 year

ASA 81 mg OD +
Ticagrelor 90 mg BID or Prasugrel 10 mg OD
preferred over
Clopidogrel 75 mg OD

At 1 year, determine bleeding risk

Not at high risk of bleeding

Continue DAPT for up to 3 years

ASA 81 mg OD +
Ticagrelor 60 mg BID or
Clopidogrel 75 mg OD

High risk of bleeding

SAPT

ASA 81 mg OD
or
Clopidogrel 75 mg OD

2018 CCS Antiplatelet Guidelines
The PEGASUS Trial

CV death, MI or stroke
15% RRR
NNT 80
Take Home Message: DAPT for 6 months for most, 1 or 3 months for those at high risk of bleeding

2018 CCS Antiplatelet Guidelines
Triple Therapy in AF + PCI

- Bleeding rates are significantly increased with triple antithrombotic therapy

- Double therapy (ie. single antiplatelet + OAC) may provide less bleeding and similar efficacy compared to triple therapy

- Triple therapy should generally be avoided but not in those at high risk of thrombosis ie. ACS or high risk lesions

- Various combinations of DOAC + single antiplatelet therapy (SAPT) are being evaluated
Patients undergoing PCI with AF

Recommendation

23. We **recommend** that patients who have concomitant **atrial fibrillation** (AF) and **symptomatic coronary artery disease** (CAD) receive a regimen of antithrombotic therapy that is based on a balanced assessment of their risk of (1) ischemic stroke, (2) future coronary event(s) and (3) clinically significant bleeding associated with the use of antithrombotic agents (**Strong Recommendation, High Quality Evidence**).
### A Safety Major and Minor Bleeding Events

<table>
<thead>
<tr>
<th>Trial</th>
<th>Dual Therapy</th>
<th>Triple Therapy</th>
<th>Odds Ratio (95% CI)</th>
<th>z-Score</th>
<th>Relative Weight</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOEST</td>
<td>54/279</td>
<td>126/284</td>
<td>0.30 (0.21-0.44)</td>
<td>-6.22</td>
<td>29.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PIONEER AF-PCI</td>
<td>109/696</td>
<td>167/697</td>
<td>0.59 (0.45-0.77)</td>
<td>-3.86</td>
<td>34.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RE-DUAL PCI</td>
<td>305/1744</td>
<td>196/764</td>
<td>0.61 (0.50-0.75)</td>
<td>-4.68</td>
<td>36.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>0.49 (0.34-0.72)</td>
<td>-3.70</td>
<td></td>
<td>&lt;0.001</td>
</tr>
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### B Efficacy: Major Adverse Cardiovascular Events

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<th>Relative Weight</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOEST</td>
<td>31/279</td>
<td>50/284</td>
<td>0.58 (0.36-0.95)</td>
<td>-2.18</td>
<td>25.5</td>
<td>0.03</td>
</tr>
<tr>
<td>PIONEER AF-PCI</td>
<td>41/694</td>
<td>36/695</td>
<td>1.15 (0.72-1.82)</td>
<td>0.59</td>
<td>27.0</td>
<td>0.55</td>
</tr>
<tr>
<td>RE-DUAL PCI</td>
<td>239/1744</td>
<td>131/764</td>
<td>0.77 (0.61-0.97)</td>
<td>-2.23</td>
<td>47.47</td>
<td>0.03</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>0.80 (0.58-1.09)</td>
<td>-1.40</td>
<td></td>
<td>0.16</td>
</tr>
</tbody>
</table>
PIONEER and REDUAL

- Significant reduction in bleeding with DOAC-containing regimens

- No apparent downside but some limitations...
  - Underpowered for stroke events
  - Very few patients at very high risk of stroke, complex subgroups excluded
  - Unknown how to apply to ticagrelor
  - Short follow-up

- In summary, there is a growing comfort with using reduced dose DOAC (i.e. rivaroxaban 15mg) + SAPT after PCI in most patients.
  - BUT patients with very high risk anatomy or ischemic burden (i.e. ACS) may still require triple therapy, with the duration being kept as short as possible.
In patients undergoing PCI for a non-ACS indication (e.g., stable ischemic heart disease):

Recommendations

3. We **recommend** 6 months (and up to 1 year) of DAPT with ASA and clopidogrel **(Strong Recommendation, Moderate Quality Evidence)**.

4. We **suggest** that in patients who have additional high-risk clinical or angiographic features for thrombotic cardiovascular events and who are at low risk of bleeding, it is reasonable to extend the duration of DAPT to greater than 1 year **(Weak Recommendation, Moderate Quality Evidence for up to 3 years of treatment)**.

5. We **suggest** that in patients who are at high risk of bleeding, the duration of DAPT be shortened to a minimum of 1 month (if a BMS was used) or 3 months (if a DES was used); **(Weak Recommendation, Low Quality Evidence)**.
AF and elective PCI without high-risk features

Age < 65 and CHADS₂ = 0

ASA + Clopidogrel
Duration: at least 1 month for BMS and at least 3 months for DES (and up to 12 months)

ASA +/- P₂Y₁₂ inhibitor³

Age ≥ 65 or CHADS₂ ≥ 1

OAC² + Clopidogrel
Duration: at least 1 month for BMS and at least 3 months for DES (and up to 12 months)

OAC⁴ +/- SAPT

2018 CCS Antiplatelet Guidelines
In patients with ACS (STEMI or NSTEMI or NSTEACS) who receive PCI:

Recommendations

1. We recommend dual antiplatelet therapy (DAPT) with ASA 81 mg daily plus either ticagrelor 90 mg twice daily or prasugrel 10 mg once daily over clopidogrel 75 mg once daily for 1 year (Strong Recommendation, High Quality Evidence).

2. We recommend that in patients who tolerate 1 year of DAPT without a major bleeding event and who are not at high risk of bleeding, DAPT should be extended beyond 1 year (Strong Recommendation, High Quality Evidence for up to 3 years of treatment). After 1 year, we recommend a DAPT regimen of ASA 81 mg daily plus either ticagrelor 60 mg twice daily or clopidogrel 75 mg once daily (Strong Recommendation, High Quality Evidence) or prasugrel 10 mg once daily (Weak Recommendation, Moderate Quality Evidence).

Values and Preferences: These recommendations place greater emphasis on reduction of major cardiovascular events and stent thrombosis versus an increase in bleeding complications.
AF and PCI for ACS or high-risk\(^1\) elective PCI

- **Age < 65** and **CHADS\(_2\) = 0**
  - **ASA + P\(_2\)Y\(_{12}\) inhibitor\(^2\)**
    - (ticagrelor, prasugrel preferred over clopidogrel for ACS)
    - Duration after PCI: Up to 12 months
  - **ASA +/- P\(_2\)Y\(_{12}\) inhibitor\(^5\)**

- **Age ≥ 65** or **CHADS\(_2\) ≥ 1\(^*\)**
  - **Reduced OAC\(^3\) + ASA + clopidogrel**
    - ASA: stop 1 day post PCI or any time up to 6 months\(^4\)
    - Followed by: **clopidogrel + OAC**
    - Duration after PCI: Up to 12 months
  - **OAC\(^6\) +/- SAPT**

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\(^1\) high-risk defined by patient characteristics, lesion anatomy, or ongoing disease process potentially increasing the risk of adverse events during PCI.

\(^2\) P\(_2\)Y\(_{12}\) inhibitors: ticagrelor and prasugrel

\(^3\) Reduced OAC: dabigatran or rivaroxaban

\(^4\) Duration of reduced OAC: 1 day post PCI or any time up to 6 months

\(^5\) P\(_2\)Y\(_{12}\) inhibitor: ticagrelor or prasugrel

\(^6\) OAC: dabigatran, rivaroxaban, apixaban, or warfarin
**High-risk clinical and angiographic features for thrombotic events**

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## Peri-Operative Management

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<th>clopidogrel and ticagrelor</th>
<th>prasugrel</th>
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<tbody>
<tr>
<td>CABG after ACS</td>
<td>48-72 hours (ideal 5)</td>
<td>5 days (ideal 7)</td>
</tr>
<tr>
<td>Elective surgery (ie non cardiac)</td>
<td>5-7 days</td>
<td>7-10 days</td>
</tr>
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</table>

2018 CCS Antiplatelet Guidelines
Switching

- Switching is sometimes required
  - In most cases, especially ACS, a loading dose of the new agent should be given

<table>
<thead>
<tr>
<th>From:</th>
<th>To:</th>
</tr>
</thead>
<tbody>
<tr>
<td>clopidogrel</td>
<td>ticagrelor 180mg X 1 prasugrel 60mg X 1</td>
</tr>
<tr>
<td>ticagrelor</td>
<td>clopidogrel 600mg X 1 prasugrel 60mg X 1</td>
</tr>
<tr>
<td>prasugrel</td>
<td>ticagrelor (no load) clopidogrel (no load)</td>
</tr>
</tbody>
</table>
Switching Between Oral P2Y<sub>12</sub> Inhibitors

**A  Acute/Early phase**

- **Clopidogrel**
  - C 600 mg LD (24 hours after last P dose)<sup>*</sup>
  - P 80 mg LD (irrespective of timing and closing of C)
  - T 180 mg LD (irrespective of timing and closing of C)

- **Prasugrel**
  - C 600 mg LD (24 hours after last P dose)

- **Ticagrelor**
  - P 60 mg LD (24 hours after last T dose)

**B  Late/Very late phase**

- **Clopidogrel**
  - C 75 mg MD (24 hours after last P dose)
  - P 10 mg MD (24 hours after last C dose)
  - T 90 mg bid MD (24 hours after last C dose)

- **Prasugrel**
  - C 600 mg LD (24 hours after last P dose)

- **Ticagrelor**
  - P 60 mg LD (24 hours after last T dose)
Patient Education Video: Dual Antiplatelet Therapy

To learn about your antiplatelet medications and why they were prescribed visit: https://youtu.be/CEgSKTUvgk4

or www.ccpn.ca