Update on Antiplatelet Therapy

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Objectives
- Explain the role of antiplatelet therapy in prevention of cardiovascular events
- Appreciate differences among antiplatelet alternatives
- Evaluate the role for dual versus triple antiplatelet therapy
- Analyze the current literature supporting various antiplatelet regimens

Epidemiology
- 780,000 will experience Acute Coronary Symptom (ACS)
  - 70% NSTEMI
- 690,000 will experience an ischemic stroke
Platelet Activation

Aspirin
- Dosing: 325 mg/81 mg daily
- Considerations in Prevention:
  - High dose (>160 mg) vs low dose
  - Avoid other NSAIDS
Platelet Activation

Clopidogrel (Plavix)
- Dosing: 300-600 mg/ 75mg daily
- Considerations:
  - Genetic variations: CYP2C19 “loss of function”
  - Drug interactions: PPI, antifungals

Ticagrelor (Brilinta)
- Dosing: 180mg/ 90mg BID
- Considerations:
  - Active bleeding, history of intracranial hemorrhage
  - Aspirin >100 mg
PLATO

18,624 ACS patients

Clopidogrel
300 mg LD
75 mg MD

Ticagrelor
180 mg LD
90 mg BID MD

Primary endpoint: Death from CV causes, nonfatal MI or stroke

PLATO Results


PLATO Results


PLATO Results

Prasugrel (Effient)

- Dosing: 60 mg/ 5-10 mg daily

- Considerations:
  - Active Bleed
  - History of cerebrovascular events
  - Age
  - Weight

TRITON-TIMI 38

13,608 ACS patients with scheduled PCI

Aspirin plus

- Clopidogrel 300mg LD
  - 75 mg MD
- Prasugrel 60mg LD
  - 10 mg MD

Primary endpoint: Death from CV causes, nonfatal MI or stroke

TRITON-TIMI 38 Results

<table>
<thead>
<tr>
<th>End Point</th>
<th>Prasugrel (n=4,605)</th>
<th>Clopidogrel (n=4,605)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from cardiovascular causes, nonfatal MI, or nonfatal stroke (primary end point)</td>
<td>667 (14.5)</td>
<td>771 (16.7)</td>
<td>0.95 (0.90-1.01)</td>
<td>0.10</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>477 (10.8)</td>
<td>503 (11.0)</td>
<td>0.98 (0.90-1.07)</td>
<td>0.60</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>105 (2.3)</td>
<td>118 (2.6)</td>
<td>0.95 (0.79-1.15)</td>
<td>0.61</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>652 (14.0)</td>
<td>797 (17.2)</td>
<td>0.83 (0.79-0.88)</td>
<td>&lt;0.001</td>
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<td>Death from any cause, nonfatal MI, or nonfatal stroke</td>
<td>602 (17.5)</td>
<td>822 (17.7)</td>
<td>0.88 (0.83-0.94)</td>
<td>&lt;0.001</td>
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<td>Urgent target vessel revascularization</td>
<td>314 (6.9)</td>
<td>331 (7.2)</td>
<td>0.94 (0.84-1.05)</td>
<td>0.18</td>
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<td>Death from cardiovascular causes, nonfatal MI, nonfatal stroke, or rehospitalization for MI, nonfatal stroke, or urgent revascularization</td>
<td>797 (17.2)</td>
<td>919 (19.6)</td>
<td>0.84 (0.75-0.93)</td>
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<td>Sudden death</td>
<td>68 (1.5)</td>
<td>142 (2.6)</td>
<td>0.68 (0.56-0.84)</td>
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### Oral P2Y12 receptor antagonist

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<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<td>Action</td>
<td>Irreversible</td>
<td>Reversible</td>
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<tr>
<td>Tmax</td>
<td>2 h</td>
<td>30 min</td>
<td>1.5 h</td>
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<tr>
<td>Onset of Action</td>
<td>No LD: 3-5 d 300mg LD &gt; 6 h 600mg LD 2-4 h</td>
<td>No LD: 3 d 60mg LD: 60 min</td>
<td>180mg LD 30-60min</td>
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<tr>
<td>Platelet Inhibition</td>
<td>35%</td>
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<td>T 1/2</td>
<td>6 h</td>
<td>7 h</td>
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### Cangrelor
- **IV P2Y12 receptor antagonist**
  - 100% bioavailability
- **Immediate, quickly reversible**
  - Onset: 2 min
  - $T_{1/2}$: 3-5 min
  - Platelet recovery: 60-90 min
CHAMPION-PHOENIX RESULTS

Primary Endpoint: All cause mortality, MI, ischemia-driven revascularization or stent thrombosis at 48 h


WHAT IS THE ROLE OF ANTIPLATELET THERAPY IN THE GUIDELINES?
NSTEMI Recommendations

Length of therapy

- No Stent vs.

- Bare Metal Stent (BMS) vs.

- Drug-Eluding Stent (DES) vs.
  - Sirolimus
  - Paclitaxel

Stroke: Secondary Prevention

- Initial therapy:
  - Aspirin 50-325 mg daily
  - Aspirin 25mg + dipyridamole 200mg BID
  - Clopidogrel 75mg daily

- Within 24 hours:
  - Aspirin + clopidogrel
HOW LONG SHOULD WE TREAT WITH DAPT?

DAPT Study

9,961 patients DES + DAPT x 12 mo.

Continue DAPT x 18 mo.
Placebo

Primary Endpoints: stent thrombosis and major adverse cardiovascular and cerebrovascular events from 12 to 30 mos.

DES: Drug Eluding Stent
DAPT: Dual Anti-Platelet Therapy

DAPT Results

Primary Endpoints: stent thrombosis and major adverse cardiovascular and cerebrovascular events from 12 to 30 mos.

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<tr>
<th>Outcome</th>
<th>Cardiac Thrombosis</th>
<th>Plaque</th>
<th>Hospital Adjs., Thrombosis, plaque (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>19 (0.4)</td>
<td>20 (1.0)</td>
<td>1.14 (1.00-1.30)</td>
<td>0.05</td>
</tr>
<tr>
<td>Cardiac</td>
<td>45 (0.9)</td>
<td>47 (0.9)</td>
<td>1.01 (0.88-1.16)</td>
<td>0.88</td>
</tr>
<tr>
<td>Vascular</td>
<td>7 (0.1)</td>
<td>13 (0.2)</td>
<td>0.58 (0.36-0.93)</td>
<td>0.04</td>
</tr>
<tr>
<td>Noncardiovascular</td>
<td>44 (0.9)</td>
<td>22 (0.5)</td>
<td>2.23 (1.32-3.73)</td>
<td>0.002</td>
</tr>
<tr>
<td>Inadvertent infection</td>
<td>50 (1.1)</td>
<td>198 (4.6)</td>
<td>0.47 (0.31-0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>37 (0.8)</td>
<td>45 (0.9)</td>
<td>0.80 (0.51-1.25)</td>
<td>0.33</td>
</tr>
<tr>
<td>Ischemic</td>
<td>57 (1.1)</td>
<td>71 (0.8)</td>
<td>0.08 (0.00-1.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>15 (0.3)</td>
<td>9 (0.2)</td>
<td>1.12 (0.54-2.31)</td>
<td>0.88</td>
</tr>
<tr>
<td>Type unspecified</td>
<td>0</td>
<td>3 (0.1)</td>
<td>—</td>
<td>0.32</td>
</tr>
</tbody>
</table>
WHAT IS THE ROLE OF TRIPLE THERAPY?

- DAPT + warfarin
- Considerations
  - Bleed vs. stroke
  - Acid suppressant therapy
  - INR
Conclusion

- Aspirin is the backbone of antiplatelet regimens in many cardiovascular disorders
- Treatment strategy and patient factors dictate length of DAPT therapy
- Decision to initiate triple therapy is a balance of risk vs. benefit

Question 1
T/ F Clopidogrel and Ticagrelor are irreversible P2Y12 receptor antagonist while Prasugrel is a reversible antagonist

Question 2
T/F Dual therapy with aspirin and clopidogrel is standard in patient with acute coronary syndromes (ACS) with or without ST-segment elevation and after stent procedures
Question 3

T/F Triple antiplatelet therapy has robust evidence to support standard incorporation into practice

References

- Kernan et al. Stroke Prevention in Patients With Stroke and TIA. Stroke.2014; 45: 2160-2236

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