Anti-Platelet Therapy: who needs it & what to prescribe?

Koen Deloose, MD
Anti-platelet therapies: targets

THIENOPYRIDINES
- **1st generation**: irreversible
  - Ticlopidine
  - Clopidogrel
  - Prasugrel
- **2nd generation**: reversible – competitive
  - Cangrelor
  - Ticagrelor
- **3rd generation**: reversible – competitive
  - Elinogrel

**PAR1 thrombine receptor ANTAGONIST**
- Voraxapar (Zontivity®) - Atopaxar

**GP IIB/IIIa INHIBITOR**
- ReoPro - Aggrastat

**CYCLO-OXYGENASE INHIBITOR**
- Aspirin

**PHOSPHO-DIËSTERASE INHIBITOR**
- Cilostazol - Dypridamole

Anti-platelet therapies: targets

CYCLO-OXYGENASE INHIBITOR
Aspirin

THIENOPYRIDINES
1st generation: irreversible
Ticlopidine
Clopidogrel

PHOSPHO-DIÉSTERASE INHIBITOR
Cilostazol – Dypridamole
Role of Anti-platelet therapies

- **Primary prevention**
- **Secondary prevention**
  - The cardiovascular patient
  - (Endo)vascular therapy
Role of Anti-platelet therapies

- **Primary prevention**

  **Physicians’ Health Study Research Group.** *NEJM 1989;321:129-35*

  22,071 men randomized to aspirin (325mg every other day) followed for an average of 5 years

<table>
<thead>
<tr>
<th>End point</th>
<th>Relative Risk (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal</td>
<td>0.34 (0.15-0.75)</td>
<td>0.007</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>0.59 (0.47-0.74)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Total</td>
<td>0.56 (0.45-0.70)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal</td>
<td>1.51 (0.54-4.28)</td>
<td>0.43</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>1.20 (0.91-1.59)</td>
<td>0.20</td>
</tr>
<tr>
<td>Total</td>
<td>1.22 (0.93-1.60)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Aspirin significantly reduces the MI-risk but not the stroke-risk in men
Role of Anti-platelet therapies

- **Primary prevention**


  39,876 women randomized to aspirin (100 mg every other day) or placebo for an average of 10 years

  Aspirin significantly reduces the risk of stroke but not this of MI in women
Role of Anti-platelet therapies

• **Primary prevention**

**Overall conclusion**: Aspirin is recommended for men & women whose 10-year risks for CVD is >10% over 10 years
Role of Anti-platelet therapies

- **Primary prevention**

  Optimal dose

<table>
<thead>
<tr>
<th>Aspirin Dose</th>
<th>No. of Trials</th>
<th>(%)</th>
<th>Odds Ratio for Vascular Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-1500 mg</td>
<td>34</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>160-325 mg</td>
<td>19</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>75-150 mg</td>
<td>12</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>&lt;75 mg</td>
<td>3</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Any aspirin</td>
<td>65</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

Antithrombotic Trialist Collaboration. *BMJ* 2002;324:71-86
Role of Anti-platelet therapies

• **Primary prevention**

No data to support the role of other anti-platelet agents in primary prevention

Antithrombotic Trialist Collaboration. *BMJ* 2002;324:71-86
Role of Anti-platelet therapies

- Secondary prevention in CV patients
  Effect of Aspirin on vascular events (MI, stroke, death)

Antithrombotic Trialist Collaboration. *BMJ* 2002;324:71-86

There is strong evidence to recommend Aspirin (75-162 mg daily) if known CHD/ASVD
Role of Anti-platelet therapies

- **Secondary prevention in CV patient @ risk**

Effect of Clopidogrel on vascular events

19,185 patients with ischemic CVA, MI, or PAD randomized to daily aspirin (325 mg) or clopidogrel (75 mg) for 2 years. 

**Clopidogrel provides a slightly greater MI, stroke, CVD risk reduction in the all CV patients, but especially in the PAD patients**

Role of Anti-platelet therapies

• **Secondary prevention in CV patient @ risk**

Effect of Aspirin + Clopidogrel on vascular events:

**CHARISMA trial:** 15,603 patients with multiple CV risk factors or known CVD randomized to aspirin (75-162 mg) or aspirin (75-162 mg) & clopidogrel (75 mg) for a mean of 30 months

Bhatt DL et al. *NEJM* 2006;354:1706-17

**Routine DAP offers no long term benefit**
Role of Anti-platelet therapies

• Secondary prevention in CV patient at risk

Effect of Aspirin + Clopidogrel on vascular events: CHARISMA trial:

<table>
<thead>
<tr>
<th>Population</th>
<th>RR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualifying CAD, CVD or PAD</td>
<td>0.99</td>
<td>0.04</td>
</tr>
<tr>
<td>Multiple Risk Factors</td>
<td>0.99</td>
<td>0.20</td>
</tr>
<tr>
<td>Overall</td>
<td>0.99</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Longer term DAP offers benefit to those with severe CV disease

Bhatt DL et al. NEJM 2006;354:1706-17
Role of Anti-platelet therapies

• **Secondary prevention post (endo) vascular R/**

In contrast to the coronary field, there is **no evidence** for the optimal anti-platelet therapy and duration after peripheral interventions.

Decision is based on **“good clinical practice”**, mainly derived from the coronaries or device studies.
Role of Anti-platelet therapies

- **Secondary prevention post (endo) vascular R/**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet therapy with aspirin is recommended in all patients with angioplasty for LEAD to reduce the risk of systemic vascular events.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Dual antiplatelet therapy with aspirin and a thienopyridine for at least one month is recommended after infrainguinal bare-metal-stent implantation.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

European Society of Cardiology guidelines 2011
Role of Anti-platelet therapies

- Secondary prevention post (endo) vascular R/

MIRROR: 1yr results RCT post endo R/ for PAD

80 patients, 1:1 randomization DAPT vs ASA mono

6 months: significant in favor of DAPT for TLR
12 months: no significant difference in TLR anymore

Strobl F et al; JEV T 2013;20:699–706
For patients undergoing peripheral artery percutaneous transluminal angioplasty with stenting, we suggest single rather than dual antiplatelet therapy.
Role of Anti-platelet therapies

• **Secondary prevention post (endo) vascular R/**

  Dual antiplatelet therapy can be considered current state of the art after infrainguinal stent implantation

  because it is …

  * supported by a multitude of data from the coronary field
  * applied in nearly all major endovascular centers and ongoing stenting trials and
  * propagated by key opinion leaders all over the world
Role of Anti-platelet therapies

- Secondary prevention post (endo) vascular R/

**POBA / PTA-DCB / BMS**

**DAPT 1 month, thereafter ASA lifelong**
Role of Anti-platelet therapies

- Secondary prevention post (endo) vascular R/

*DAPT > 2 month, thereafter ASA lifelong*

Zilver PTX trial: Dake M et al; JEVT 2011; 18:613–623
Role of Anti-platelet therapies

• Secondary prevention post (endo) vascular R/

DES BTK

3 randomized studies:

Achilles (Cypher - Sirolimus): DAPT 6 months
Destiny (Xcience V - Everolimus): DAPT 12 months
Yukon (Sirolimus): DAPT 6 months

DAPT ≥ 6 month, thereafter ASA lifelong
Role of Anti-platelet therapies

- Secondary prevention post (endo) vascular R/

Covered stents PAD

**DAPT > 6 month, thereafter ASA lifelong**

Zeller et al; JEVT 2014;21:765–774
Conclusion

• Only Aspirin is proven to play an important role in primary prevention of CVD, especially in higher risk patients.

• There is a level Ia evidence to recommend Aspirin as a secondary prevention in known CV-patients.

• Longer term DAPT offers only benefit in secondary prevention in severe CV disease.

• There is weaker evidence to recommend DAPT post (endo)vascular intervention as secondary prevention.
Conclusion

- Based on world-wide (KOL) experiences and coronary/peripheral device trials, DAPT is recommended for 1 (POBA; DCB; BMS) up to 6-12 months (DES; Covered stents).