Long-term DAPT after STEMI: What do the guidelines say?

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Agenda

• Background

• Case study

• What is the evidence (clinical trials) ?

• What do the ESC 2017 guidelines say ?
Background

- Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor inhibitor is standard therapy in patients with acute coronary syndrome (ACS) and in those undergoing drug-eluting stent (DES) implantation.

- There is emerging evidence that DAPT reduces the long-term risk of non-stent-related MI as well as stroke.

- DAPT has moved from a local (i.e. stent-related) to a systemic treatment strategy (i.e. capable of preventing thrombotic arterial vessel occlusion), conveying global patient protection.

- The potential benefit of DAPT beyond 1 year after a MI has not been established.

Case study

- 44 year old male
- Type 2 DM
- Dyslipidemia on atorvastatin 20 mg /d
- Obesity
- Smoker
- FH of CAD
- C/O : prolonged chest pain & sweating
ECG

- Troponin I = 20 ng/ml
- Hb = 14 gm/dl
- WBCs = 7000 units/mcL
- Creatinine clearance = 90 ml/min
• Inferior STEMI
• Transferred to the Cath Lab after giving:
  - ASA 300mg
  - Ticagrelor 180 mg
  - Heparin 5000 U IV

Coronary Angiography

• Normal LMT

• LAD & diagonals are normal

• Cx : normal & non dominant
1 Year post STEMI

• Most control of risk factors
• Kept on ticagrelor and aspirin for 12 months
• Compliant on medications without events (MI or bleeding)
• Asymptomatic
• Dual antiplatelet therapy considerations beyond 12 months?

Dual antiplatelet therapy considerations beyond 12 months?

Rationale

• In patients presenting with ACS, the cardiovascular risk remains substantially elevated beyond the first year, even if successful revascularization has been achieved

• Intensified antiplatelet therapy on top of aspirin has been shown to be an effective therapeutic strategy to prevent recurrent ischemic events but with associated bleeding risk
### Randomized controlled trials of extended dual antiplatelet therapy after stent placement

<table>
<thead>
<tr>
<th>Trial (No. of patients)</th>
<th>Design</th>
<th>Follow-up</th>
<th>Stent thrombosis (study vs control)</th>
<th>MACE (study vs control)</th>
<th>Bleeding events (study vs control)</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPT* (9,963)</td>
<td>DAPT vs aspirin alone beyond 12 months</td>
<td>18 months</td>
<td>0.4% vs 1.4%*</td>
<td>4.3% vs 5.9%*</td>
<td>2.5% vs 1.6%*</td>
<td>DAPT &gt; 1 year decreased risk of stent thrombosis and MACE</td>
</tr>
<tr>
<td>ARCTIC- Interruption* (1,258)</td>
<td>DAPT vs aspirin alone beyond 12 months</td>
<td>17 months</td>
<td>0% vs 1%</td>
<td>4% vs 4%</td>
<td>1% vs &lt; 0.5%</td>
<td>No benefit of DAPT beyond 12 months</td>
</tr>
<tr>
<td>DES-LATE* (5,045)</td>
<td>DAPT vs aspirin alone beyond 12 months</td>
<td>24 months</td>
<td>0.5% vs 0.3%</td>
<td>2.4 vs 2.6%</td>
<td>1.1% vs 1.4%</td>
<td>No benefit of DAPT for 24 more months at end of 1 year</td>
</tr>
<tr>
<td>Credo* (2,116)</td>
<td>DAPT vs aspirin and placebo up to 12 months</td>
<td>12 months</td>
<td>Not reported</td>
<td>8.5% vs 11.5%*</td>
<td>8.8% vs 6.7%*</td>
<td>Significant benefit of DAPT vs placebo at 1 year</td>
</tr>
<tr>
<td>OPTIMIZE* (3,118)</td>
<td>DAPT for 3 vs 12 months</td>
<td>12 months</td>
<td>0.3% vs 0.1%</td>
<td>2.6% vs 2.6%</td>
<td>0.2% vs 0.4%</td>
<td>Noninferiority of 3 vs 12 months of DAPT</td>
</tr>
<tr>
<td>RESET* (2,117)</td>
<td>DAPT for 3 vs 12 months</td>
<td>12 months</td>
<td>0.2% vs 0.3%</td>
<td>4.7% vs 4.7%</td>
<td>0.5% vs 1%</td>
<td>Noninferiority of 3 vs 12 months of DAPT</td>
</tr>
<tr>
<td>EXCELLENT* (1,493)</td>
<td>DAPT for 6 vs 12 months</td>
<td>12 months</td>
<td>0.9% vs 0.1%</td>
<td>8% vs 8.5%</td>
<td>0.3% vs 0.6%</td>
<td>Noninferiority of 6 vs 12 months of DAPT</td>
</tr>
<tr>
<td>PRODIGY* (1,970)</td>
<td>DAPT for 6 vs 12 months</td>
<td>12 months</td>
<td>3.9% vs 4.7%</td>
<td>10.1% vs 10%</td>
<td>1.6% vs 0.6%*</td>
<td>No significant benefit of 24 vs 6 months of DAPT with clopidogrel</td>
</tr>
<tr>
<td>SECURITY* (1,399)</td>
<td>DAPT for 6 vs 12 months</td>
<td>24 months</td>
<td>0.3% vs 0.4%</td>
<td>4.5% vs 3.7%</td>
<td>0.2% vs 0.3%</td>
<td>Noninferiority of 6 vs 12 months of DAPT</td>
</tr>
</tbody>
</table>

### DAPT: Long-term DAPT in DES Patients, Months 12-30

**MI**

- HR: 0.47
  - (0.37-0.61)
  - \(P < 0.001\)

- 53% RRR
- 2.1% in Continued Thienopyridine (N = 5020)
- 4.1% in Placebo (N = 4941)

DAPT: GUSTO Bleeding, Severe or Moderate, Months 12-30

Bleeding Complications

- GUSTO Severe
  - Continued thienopyridine (n=4710)
  - Placebo (n=4649)

- GUSTO Moderate
  - Continued thienopyridine (n=4710)
  - Placebo (n=4649)


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DAPT: Mortality Outcomes

Months 12-30

- Death
- Cardiac death
- Vascular death
- Non-CV death

PEGASUS-TIMI 54: Trial Design

- Stable patients with history of MI 1-3 years prior + ≥1 additional atherothrombosis risk factor*
- Randomize double-blind
- Planned treatment with aspirin 75-150 mg and standard background care
- Minimum 1-year follow-up Event-driven trial
- Follow-up visits every 4 months for first year, then every 6 months

Primary efficacy endpoint: CV death, MI, or stroke
Primary safety endpoint: TIMI major bleeding

*Age ≥65 years, diabetes, second prior MI, multivessel CAD, or chronic non-end-stage renal dysfunction


PEGASUS – TIMI 54

N = 21,162
Median follow-up 33 months

- Ticagrelor 90 mg
  - HR 0.85 (95% CI 0.75 - 0.96)
  - P=0.008
- Ticagrelor 60 mg
  - HR 0.84 (95% CI 0.74 - 0.95)
  - P=0.004

Prolonged DAPT after myocardial infarction
- Benefit/risk ratio in DAPT -

Hazard ratios (credible intervals)  

MACCE  
Stent thrombosis definite/probable  
GUSTO bleeding moderate/severe  
All-cause death  

P_{int}  
0.03  
0.69  
0.21  
0.13  

Yeh RW et al., J Am Coll Cardiol 2015
Extended Dual Antiplatelet Therapy vs Aspirin Alone: Meta-analysis

Risk of individual CV and bleeding endpoints

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major adverse CV events</td>
<td>0.78 (0.67-0.90)</td>
</tr>
<tr>
<td>CV death</td>
<td>0.85 (0.74-0.98)</td>
</tr>
<tr>
<td>MI</td>
<td>0.70 (0.55-0.88)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.81 (0.68-0.97)</td>
</tr>
<tr>
<td>Stent Thrombosis (Definite/Probable)</td>
<td>0.50 (0.2-0.89)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>1.73 (1.19-2.50)</td>
</tr>
<tr>
<td>Non-CV death</td>
<td>1.03 (0.83-1.23)</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.92 (0.83-1.03)</td>
</tr>
</tbody>
</table>


Optimal Duration of DAPT?

<table>
<thead>
<tr>
<th>≤12 months DAPT</th>
<th>≥12 months DAPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-related factors</td>
<td></td>
</tr>
<tr>
<td>Patients with stable CAD</td>
<td>Patients with ACS</td>
</tr>
<tr>
<td>Patients with a history of bleeding</td>
<td>Patients with diabetes mellitus</td>
</tr>
<tr>
<td>Patients with high risk of bleeding</td>
<td>Patients with CHF</td>
</tr>
<tr>
<td>Anatomy-related factors</td>
<td></td>
</tr>
<tr>
<td>Short lesion Single-vessel disease</td>
<td>Long lesion</td>
</tr>
<tr>
<td>Bifurcation lesion</td>
<td>Small vessel</td>
</tr>
<tr>
<td>Complex anatomy</td>
<td>Left-main coronary artery</td>
</tr>
<tr>
<td>Stent-related factors</td>
<td></td>
</tr>
<tr>
<td>Second generation DES</td>
<td>First-generation DES</td>
</tr>
<tr>
<td>Long stent</td>
<td>Long stent</td>
</tr>
<tr>
<td>Multiple stents</td>
<td>Multiple stents</td>
</tr>
</tbody>
</table>

Eisen A, Bhatt DL. Nature Reviews Cardiology 2015.
What is new in the 2017 ESC focussed update on DAPT?

New recommendations 2017:
- The documentation of undesirable bleeding events on DAPT should prompt reconsideration of type and duration of DAPT regimen.
- The decision for DAPT duration should be dynamic and reassessed during the course of the initially selected DAPT regimen.
- Discontinuation of P2Y12 inhibitors therapy after 6 months when starting ACS patients with PRECISE DAPT ≥ 25.
- 6-month DAPT regimen in patients with STEMI treated with drug-eluting balloons.
- Early administration of aspirin / clopidogrel in non-ACS with invasive approach.
- Ticagrelor 90 mg is preferred over other P2Y12 inhibitors for DAPT continuation ≥12 months in post-MI.

New/revised concepts:
- Metallic stent and DAPT duration
- Switch between P2Y12 inhibitors
- Risk score to guide DAPT duration
  - PRECISE DAPT score
  - DAPT score
- Specific profiling:
  - Definition of complex PCI
  - Unfavorable profile for OAC and DAPT
  - Gender consideration and special populations
- DAPT duration without stenting:
  - Medical management
  - CABG or cardiac surgery
- Anticoagulation and DAPT
  - Acute and chronic setting
  - Crossing regimen

Table 3: Risk scores validated for dual antiplatelet therapy duration decision-making

<table>
<thead>
<tr>
<th>Time of use</th>
<th>PRECISE-DAPT score</th>
<th>DAPT score</th>
</tr>
</thead>
<tbody>
<tr>
<td>At the time of coronary stenting</td>
<td>Short DAPT (3-6 months) vs Standard/long DAPT (12-24 months)</td>
<td>Standard DAPT (12 months) vs Long DAPT (30 months)</td>
</tr>
<tr>
<td>DAPT duration strategies assessed</td>
<td>Score calculation</td>
<td>Score calculation</td>
</tr>
<tr>
<td></td>
<td>Hb</td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>WBC</td>
<td>≥75</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>Cigarette smoking</td>
</tr>
<tr>
<td></td>
<td>CCI</td>
<td>Prior PCI or prior MI</td>
</tr>
<tr>
<td></td>
<td>Prior Bleeding</td>
<td>CHF or LVEF &lt;30%</td>
</tr>
<tr>
<td>Score range</td>
<td>0 to 100 points</td>
<td>-2 to 10 points</td>
</tr>
<tr>
<td>Decision making cut-off suggested</td>
<td>Score ≥25 = Short DAPT</td>
<td>Score ≥2 = Long DAPT</td>
</tr>
<tr>
<td></td>
<td>Score &lt;25 = Standard DAPT</td>
<td>Score &lt;2 = Standard DAPT</td>
</tr>
<tr>
<td>Calculator</td>
<td><a href="http://www.precisedaptscore.com">www.precisedaptscore.com</a></td>
<td><a href="http://www.daptsstudy.org">www.daptsstudy.org</a></td>
</tr>
</tbody>
</table>
Stent implanted (type): DES
Stent implanted (brand):
Total number of stent implanted: 1
Intended DAPT duration: 24
Antiplatelet agents implemented: ASA+Ticagrelor
Did score calculation change your treatment duration strategy? Yes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin value</td>
<td>14.0 g/dL</td>
</tr>
<tr>
<td>Age</td>
<td>58 years</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>7000 cells/μL</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>100 mEq/L</td>
</tr>
<tr>
<td>Prior bleeding</td>
<td>No</td>
</tr>
</tbody>
</table>

PRECISE DAPT Score

Risk Category

RESULT
Cluster of risk
Very low
Score Calculated
5
12 months risk of TIMI major or minor bleeding
0.4%
12 months risk of TIMI Major bleeding
0.3%
Long-term DAPT after STEMI: What do the guidelines say?
Treatment Algorithm for Duration of P2Y$_{12}$ Inhibitor Therapy in Patient With Recent ACS (NSTE-ACS or STEMI)

ACC/AHA guidelines, 2016

Prolonged DAPT after ACS

- Death
- MI
- Major Bleeding
- Minor Bleeding

Ischemic Complications

Composite Adverse Event Endpoints

Hemorrhage
Take Home Message

• Dual antiplatelet therapy indicated for at least 1 year after ACS

• Likely benefit > 1 year in patients w/ prior MI – CHARISMA subgroup

• PEGASUS showed a significant reduction in CV death/MI/stroke but at the cost of excess bleeding

• Important to individualize therapy based on ischemic/bleeding risk

THANK YOU