Considering DAPT in Difficult Cases

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Cleveland, Ohio, USA
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
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<tbody>
<tr>
<td>Grant/Research Support</td>
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</tr>
<tr>
<td>Consulting Fees/Honoraria</td>
<td>Volcano-Philips</td>
</tr>
<tr>
<td>Major Stock Shareholder/Equity</td>
<td>Technology Solutions Group</td>
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<tr>
<td>Royalty Income</td>
<td>None</td>
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<tr>
<td>Ownership/Founder</td>
<td>Technology Solutions Group</td>
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<tr>
<td>Intellectual Property Rights</td>
<td>BioInfo Accelerator Fund</td>
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<tr>
<td>Other Financial Benefit</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>None</td>
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</tbody>
</table>
DAPT (Dual AntiPlatelet Therapy)

- Foundations for DAPT therapy
- Importance with drug eluting stents (DES)
- Difficult patient subsets
  - Those who also need antithrombin therapy, or oral anticoagulants (OAC)
  - Those who need surgery early after initiation
  - Those who develop serious bleeding
  - Those who develop stent thrombosis on DAPT
- Recommendations for general internists
Why DAPT?

- Original stents placed in early 1990’s without intravascular imaging and at low balloon pressure, usually for “bail out” indications
  - Required extensive anticoagulation to prevent thrombosis (coumadin, dextran, ASA, heparin, dipyridamole). 5-7 days in hospital
- In mid 90’s intravascular imaging showed marked stent under-expansion.
  - Columbo et al used higher pressure, better expansion and a new antiplatelet P2Y$_{12}$ inhibitor: ticlopidine.
  - No need for antithrombins or OAC: DAPT was born!
DAPT and DES

- In early 2000’s DES developed to combat restenosis
- Initial concern was on cost and proper allocation of these stents
- But then…….
  - Excessive rates of stent thrombosis led to work wide “crisis” regarding how long DAPT was needed
  - DAPT “education” efforts spread to all medical fields
Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy

Eugène P McFadden, Eugenio Stabile, Evelyn Regar, Edouard Cheneau, Andrew T L Ong, Timothy Kinnaird, William O Suddath, Neil J Weissman, Rebecca Torguson, Kenneth M Kent, August D Pichard, Lowell F Satler, Ron Waksman, Patrick W Serruys

Although the safety profiles of coronary stents eluting sirolimus or paclitaxel do not seem to differ from those of bare metal stents in the short-to-medium term, concern has arisen about the potential for late stent thromboses related to delayed endothelialisation of the stent struts. We report four cases of angiographically-confirmed stent thrombosis that occurred late after elective implantation of polymer-based paclitaxel-eluting (343 and 442 days) or sirolimus-eluting (335 and 375 days) stents, and resulted in myocardial infarction. All cases arose soon after antiplatelet therapy was interrupted. If confirmed in systematic long-term follow-up studies, our findings have potentially serious clinical implications.

Lancet 2004; 364:1519-21
A new issue with DES: Late thrombosis

Figure 5. Frequency distribution over time of ST in 152 of 8146 consecutive DES patients. Early ST cases are gray (91 patients); late ST cases (61 patients) are black. The line shows the cumulative number of events over time. Reproduced from Daemen et al, copyright © 2007, with permission from Elsevier.
Most Late ST patients NOT on DAPT

![Graph showing early and late stent thrombosis](image)

**Figure 7.** Antiplatelet treatment at the time of DES thrombosis in 152 patients. Proportion of patients with early (left column; 91 patients) and late (right column; 61 patients) ST, respectively, treated with dual, single, or no antiplatelet therapy. Data from Daemen et al.11

*Circulation. 2007;116:1952-1965*
Time Frame of Stent Thrombosis

1 month

Early ≤1 month

Acute ≤1 day

Subacute >1 day to 1 month

Late >1 month - 1 year

Very late >1 year

≤1 day to 1 month

Acute stent thrombosis

>1 day to 1 year

Subacute stent thrombosis

>1 month to 1 year

Late stent thrombosis

>1 year

Very late stent thrombosis

Further P2Y$_{12}$ development

- Clopidogrel: better than Ticlopidine with fewer side effects
- Ticagrelor: better than Clopidogrel
- Prasugrel: better than Clopidogrel
- Cangrelor: iv and ultrashort acting
ACC/AHA FOCUSED UPDATE

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


JACC 2016;68:1082-1115
2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Marco Valgimigli* (Chairperson) (Switzerland), Héctor Bueno (Spain), Robert A. Byrne (Germany), Jean-Philippe Collet (France), Francesco Costa (Italy), Anders Jeppsson¹ (Sweden), Peter Jüni (Canada), Adnan Kastrati (Germany), Philippe Kolh (Belgium), Laura Mauri (USA), Gilles Montalescot (France), Franz-Josef Neumann (Germany), Mate Petricevic¹ (Croatia), Marco Roffi (Switzerland), Philippe Gabriel Steg (France), Stephan Windecker (Switzerland), and Jose Luis Zamorano (Spain)
Society Guidelines

2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy

Shamir R. Mehta, MD, MSc (co-chair), a Kevin R. Bainey, MD, b Warren J. Cantor, MD, c Marie Lordkipanidzé, BPharm, PhD, d Guillaume Marquis-Gravel, MD, d Simon D. Robinson, MBChB, MD, e Matthew Sibbald, MD, PhD, a Derek Y. So, MD, f Graham C. Wong, MD, MPH, g Joseph G. Abunassar, MD, f Margaret L. Ackman, PharmD, b Alan D. Bell, MD, h Raymond Cartier, MD, d James D. Douketis, MD, i Patrick R. Lawler, MD, MPH, j Michael S. McMurtry, MD, b Jacob A. Udell, MD, j Sean van Diepen, MD, b Subodh Verma, MD, k G.B. John Mancini, MD, g John A. Cairns, MD, g and Jean-François Tanguay, MD (co-chair); d and members of the Secondary Panel
General considerations

- Balancing thrombotic events with bleeding events
- Liberal use of risk estimating scores
- All aspirin doses are 81mg
- Choice of $\text{P2Y}_{12}$ depends on the balance
  - Clopidogrel less effect on platelets
  - Ticagrelor more effect on platelets
  - Prasugrel more effect, but risk in prior CVA
- Clinical syndrome class effect: Stable (SIHD) or acute coronary syndrome (STEMI, NSTEMI)
Risk Estimators

- Precise DAPT: “balanced score” for duration of DAPT only
- CHA₂DS₂-VASc: “thrombosis score” for afib
- HAS-BLED: “bleeding score” for OAC
**“Balanced” Risk Scores: DAPT duration**

<table>
<thead>
<tr>
<th>Time of use</th>
<th>At the time of coronary stenting</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPT duration strategies assessed</td>
<td>Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)</td>
</tr>
<tr>
<td>Score calculation&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>HB</td>
<td>≥12 11.5 11 10.5 ≤10</td>
</tr>
<tr>
<td>WBC</td>
<td>≤5 8 10 12 14 16 18 ≥20</td>
</tr>
<tr>
<td>Age</td>
<td>≤50 60 70 80 ≥90</td>
</tr>
<tr>
<td>CrCl</td>
<td>≥100 80 60 40 20 0</td>
</tr>
<tr>
<td>Prior Bleeding</td>
<td>No — Yes</td>
</tr>
<tr>
<td>Score Points</td>
<td>0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30</td>
</tr>
<tr>
<td>Score range</td>
<td>0 to 100 points</td>
</tr>
<tr>
<td>Decision making cut-off suggested</td>
<td>Score ≥25 → Short DAPT  Score &lt;25 → Standard/long DAPT</td>
</tr>
<tr>
<td>Calculator</td>
<td><a href="http://www.precisedaptscore.com">www.precisedaptscore.com</a></td>
</tr>
<tr>
<td>Score name</td>
<td>Online calculator</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------------------------------------</td>
</tr>
<tr>
<td>PRECISE-DAPT</td>
<td><a href="http://www.precisedaptscore.com/predapt/index.html">www.precisedaptscore.com/predapt/index.html</a></td>
</tr>
<tr>
<td>CALIBER</td>
<td><a href="http://https://farr-data-lab.shinyapps.io/caliber-prolonged_dapt_benefits_harms_risks">https://farr-data-lab.shinyapps.io/caliber-prolonged_dapt_benefits_harms_risks</a></td>
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<tr>
<td>DAPT</td>
<td><a href="http://tools.acc.org/DAPTriskapp/#1/content/calculator">http://tools.acc.org/DAPTriskapp/#1/content/calculator</a></td>
</tr>
</tbody>
</table>
Thrombosis risk score for afib: CHA$_2$DS$_2$-VASc

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA$_2$DS$_2$-VASc
(Note: maximum score is 9 since age may contribute 0, 1, or 2 points)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age $\geq$75</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/thrombo-embolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease$^a$</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (i.e. female sex)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum score</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

$^a$ Prior myocardial infarction, peripheral artery disease, aortic plaque.
### HAS-BLED score

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>H - Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A - Abnormal renal or liver function</td>
<td>1 or 2</td>
</tr>
<tr>
<td>(1 point each)</td>
<td></td>
</tr>
<tr>
<td>S - Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B - Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>L - Labile INRs</td>
<td>1</td>
</tr>
<tr>
<td>E - Elderly (&gt; 65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D - Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

**HAS-BLED score**

<table>
<thead>
<tr>
<th>HAS-BLED score</th>
<th>Bleeds per 100 patient-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.13</td>
</tr>
<tr>
<td>1</td>
<td>1.02</td>
</tr>
<tr>
<td>2</td>
<td>1.88</td>
</tr>
<tr>
<td>3</td>
<td>3.74</td>
</tr>
<tr>
<td>4</td>
<td>8.70</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Note: HAS-BLED has been validated for warfarin, but not for the new anticoagulants.
Smartphone calculator apps:

- Qx Calculate
- Precise DAPT
- SCAI AUC Tools

CHA₂DS₂-VASc
HAS-BLED
Balancing Ischemia vs. Bleeding

Table 1. High-risk clinical and angiographic features of stent-driven recurrent ischaemic events

<table>
<thead>
<tr>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>Before myocardial infarction or troponin-positive event</td>
</tr>
<tr>
<td>Diabetes mellitus treated with oral hypoglycaemic agent</td>
</tr>
<tr>
<td>Chronic kidney disease (i.e. creatinine clearance &lt;60 mL/min)</td>
</tr>
<tr>
<td>Previous stent thrombosis</td>
</tr>
<tr>
<td>Current smoker</td>
</tr>
<tr>
<td><strong>Angiographic</strong></td>
</tr>
<tr>
<td>Multiple stents (≥3 stents implanted, ≥ biodegradable vascular scaffold</td>
</tr>
<tr>
<td>Long lesion length (≥60 mm total stent length)</td>
</tr>
<tr>
<td>Complex lesions (bifurcation treated with 2 stents, stenting of chronic occlusion)</td>
</tr>
<tr>
<td>Left main or proximal LAD stenting</td>
</tr>
<tr>
<td>Multivessel PCI</td>
</tr>
<tr>
<td>LAD, left anterior descending artery; PCI, percutaneous coronary intervention.</td>
</tr>
</tbody>
</table>
Balancing Ischemia vs. Bleeding

Table 2. Factors associated with increased bleeding risk

<table>
<thead>
<tr>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for OAC in addition to DAPT</td>
</tr>
<tr>
<td>Advanced age (older than 75 years)</td>
</tr>
<tr>
<td>Frailty</td>
</tr>
<tr>
<td>Anemia with hemoglobin &lt; 110 g/L</td>
</tr>
<tr>
<td>Chronic renal failure (creatinine clearance &lt; 40 mL/min)</td>
</tr>
<tr>
<td>Low body weight (&lt;60 kg)</td>
</tr>
<tr>
<td>Hospitalization for bleeding within past year</td>
</tr>
<tr>
<td>Previous stroke/intracranial bleed</td>
</tr>
<tr>
<td>Regular need for NSAIDs or prednisone</td>
</tr>
</tbody>
</table>

DAPT, dual antiplatelet therapy; NSAIDs, nonsteroidal anti-inflammatory drugs; OAC, oral anticoagulation.
# Table 4
Clinical and Procedural Factors Associated With Increased Ischemic Risk (including Stent Thrombosis) or Increased Bleeding Risk (62-70)

<table>
<thead>
<tr>
<th>Increased Ischemic Risk/Risk of Stent Thrombosis (may favor longer-duration DAPT)</th>
<th>Increased Bleeding Risk (may favor shorter-duration DAPT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased ischemic risk</td>
<td>History of prior bleeding</td>
</tr>
<tr>
<td>Advanced age</td>
<td>Oral anticoagulant therapy</td>
</tr>
<tr>
<td>ACS presentation</td>
<td>Female sex</td>
</tr>
<tr>
<td>Multiple prior MIs</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Extensive CAD</td>
<td>Low body weight</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>CKD</td>
</tr>
<tr>
<td>CKD</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td><strong>Increased risk of stent thrombosis</strong></td>
<td>Anemia</td>
</tr>
<tr>
<td>ACS presentation</td>
<td>Chronic steroid or NSAID therapy</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction &lt;40%</td>
<td></td>
</tr>
<tr>
<td>First-generation drug-eluting stent</td>
<td></td>
</tr>
<tr>
<td>Stent undersizing</td>
<td></td>
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<tr>
<td>Stent underdeployment</td>
<td></td>
</tr>
<tr>
<td>Small stent diameter</td>
<td></td>
</tr>
<tr>
<td>Greater stent length</td>
<td></td>
</tr>
<tr>
<td>Bifurcation stents</td>
<td></td>
</tr>
<tr>
<td>In-stent restenosis</td>
<td></td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; MI, myocardial infarction; and NSAID, nonsteroidal anti-inflammatory drug.
Medical treatment: NO stent

12 months DAPT
Unless high bleeding risk (HBR)
Simple Stent Case: STEMI

February 5, 2017 @ 18:22

January 2, 2017

Total Occlusion of LAD

Interventional wire & balloon established flow

DES to the LAD
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\(^1\)

Continue DAPT for up to 3 years
ASA 81 mg OD +
Ticagrelor 60 mg BID or
Clopidogrel 75 mg OD\(^2\)

High risk of bleeding\(^1\)

SAPT
ASA 81 mg OD
or
Clopidogrel 75 mg OD

\(^1\) Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranial bleed, regular need for NSAIDS or prednisone

\(^2\) Instead of ticagrelor or clopidogrel, prasugrel 5-10 mg daily is also an option (weak recommendation)
Elective PCI: some nuances

IVUS will not pass lesion

Reference diameter: 2.9mm
Pre-dilate with 3.0 noncompliant balloon, then re-check IVUS: dissections seen
After 3.5mm post-dilation @ 26 atm

6.2 mm$^2$
Elective PCI

Not at high risk of bleeding\(^1\)

- **DAPT** for 6 months
  - ASA + clopidogrel

High-risk clinical or angiographic features for thrombotic cardiovascular events\(^2\), and not at high risk of bleeding?\(^1\)

- **YES**
  - Extend **DAPT** up to 3 years
    - ASA 81 mg daily
    - Clopidogrel 75 mg daily

- **NO**
  - **SAPT**
    - ASA 81 mg daily
    - Clopidogrel 75 mg daily

High risk of bleeding\(^1\)

- **DAPT** for 1 month if BMS, or 3 months if DES

- **SAPT**
  - ASA 81 mg daily
  - Clopidogrel 75 mg daily

\(^1\) See guidelines for specific criteria.

\(^2\) Clinical features include: advanced age, prior ST elevation MI, prior CABG, prior stroke, prior TIA, peripheral arterial disease, abdominal aortic aneurysm, CAD in the setting of prior percutaneous coronary intervention, or chronic kidney disease. Angiographic features include: total occlusion, thrombus, severe proximal disease, heavily calcified lesion, or large-vessel disease.
Percutaneous Coronary Intervention

Treatment indication

- Stable Coronary Artery Disease
- Acute Coronary Syndrome

Device used

- DES/BMS or DCB

High Bleeding Risk

Time

- 1 mo.
- 3 mo.
- 6 mo.
- 12 mo.
- 30 mo.

- 6 mo. DAPT
- 3 mo. DAPT
- 1 mo. DAPT
- 12 mo. DAPT
- Continue DAPT

A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor

©ESC 2017

Eur Heart J 2018;39:213-254
Acute anterior STEMI

In ED:
ASA 325
Ticagrelor 180 mg

In Lab:
Bivalirudin
After DES to LAD and also of non-culprit D1
Four hours later: recurrent pain and shock
After Impella and re-opening
Persistent shock

Upgrade to Impella 5L
Move to transplant center
Spent 10 days on Impella
What if my patient has stent thrombosis?

- Consider timing
- Acute: inadequate P2Y$_{12}$ level; mechanical stent issue
  - Solution: use “crush and chew” strategy; use IVUS guidance; use coverage with IIbIIIa inhibitor
- Subacute: ineffective P2Y$_{12}$; mechanical stent issue
  - Solution: upgrade to ticagrelor or prasugrel; use IVUS guidance
- Late: unclear
  - Recommendation: upgrade to ticagrelor or prasugrel; use IVUS guidance
IVUS Predictors of DES Thrombosis (within 30 days)

*Residual edge stenosis = edge lumen CSA <4.0mm² & plaque burden >70%.

*(Fujii et al. J Am Coll Cardiol 2005;45:995-8)*
Mal apposition resulting in SAT
ADAPT-DES (3361 pts treated with IVUS-guidance vs 5221 pts treated with angiographic guidance)

**Definite/Probable ST**

HR: 0.47 [95% CI: 0.28, 0.80]  
P = 0.004

<table>
<thead>
<tr>
<th>Time in Months</th>
<th>IVUS Used</th>
<th>IVUS Not Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3361</td>
<td>5221</td>
</tr>
<tr>
<td>6</td>
<td>3260</td>
<td>5019</td>
</tr>
<tr>
<td>12</td>
<td>3182</td>
<td>4886</td>
</tr>
<tr>
<td>18</td>
<td>3065</td>
<td>4713</td>
</tr>
<tr>
<td>24</td>
<td>1791</td>
<td>2279</td>
</tr>
</tbody>
</table>

# Target Lesion Stent Thrombosis at 2 Years

<table>
<thead>
<tr>
<th></th>
<th>IVUS Use n = 3361</th>
<th>No IVUS n = 5221</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite ST</td>
<td>0.46% (15)</td>
<td>0.85% (43)</td>
<td>0.036</td>
</tr>
<tr>
<td>Definite/probable ST</td>
<td>0.55% (18)</td>
<td>1.16% (59)</td>
<td>0.004</td>
</tr>
<tr>
<td>- Acute &lt;1day</td>
<td>0.00% (0)</td>
<td>0.04% (2)</td>
<td>0.26</td>
</tr>
<tr>
<td>- Subacute (1-30 days)</td>
<td>0.24% (8)</td>
<td>0.52% (27)</td>
<td>0.047</td>
</tr>
<tr>
<td>- Late (&gt;30 days to 1 yr)</td>
<td>0.24% (8)</td>
<td>0.40% (20)</td>
<td>0.24</td>
</tr>
<tr>
<td>- Very late (1 yr to 2 yrs)</td>
<td>0.06% (2)</td>
<td>0.21% (10)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Impact of IVUS Guidance of Unprotected LM Propensity Matched 1010 pts in 4 Registries

- Distal LM lesion ~60%, 2 stent technique ~13%
- IVUS guidance was an independent predictor of MACE

De la Torre Hernandez et al. JACC Cardiovasc Interv 2014;7:244-54
Post stent thrombosis: ESC suggests

- The number of recurrent events is significantly decreased by treatment with ticagrelor or prasugrel as compared to clopidogrel. Hence, the use of clopidogrel after stent thrombosis cannot be regarded as an effective treatment option.

- Considering the long-term risk of recurrence after first stent thrombosis, it may be reasonable to make every effort to maintain DAPT for a very long-term period in this highly selected high-risk patient population, if tolerated.
Routine Stenting

Stent size selection:
**Reference** lumen diameter
(package size)

Result optimization:
**Stent** lumen
cross sectional area
> 80% of reference
(Bernoulli)
Ultimate trial: IVUS vs Angio Guidance of DES

1795 all-comers with de novo lesions were screened for this study

347 patients were excluded
261 refused to participate
86 met exclusion criteria

1448 all-comers with de novo lesions were eligible for randomization

1:1 Randomization

IVUS-guided group (N=724)

Angiography-guided group (N=724)

No patient crossover to angiography guidance

8 crossover to IVUS guidance
3 CTO lesions
2 left main lesions
1 ruptured plaque
1 diffuse lesion
1 calcified lesion

Clinical follow-up at 12 months (N=722)
Angiographic follow-up at 13 months (N=478)

Clinical follow-up at 12 months (N=722)
Angiographic follow-up at 13 months (N=446)

JACC Intervent 2018; September: epub
Ultimate: all comor population

Diameter: 67% B2/C, diameter 3 mm, length 50 mm, Post dilate to 19 atm
Of the 6 stent thrombosis cases, only 1 was IVUS guided: Patient received 5 stents, 150mm, thrombosed @ 16 d

E

Hazard ratio: 0.466 (95% CI: 0.211, 1.030)
Log-Rank: p = 0.053

Clinically-driven TLR or definite ST (%)

Number at risk
Angiography 724 714 707 695 686
IVUS 724 720 716 710 703

Time Since Randomization (months)
PCI without IVUS:

INSANITY
is doing the
same thing
over and over
again expecting
different results

© 2000, Inspire21.com  Art use free to subscribers  UNKNOWN
What if my patient also needs antithrombin therapy, or oral anticoagulants (OAC)

- Most common is atrial fibrillation
- Also applies to recent VTE, heart valves
- Key is to assess both bleeding and thrombosis risk and then craft a strategy that will allow discontinuing “triple therapy” at the earliest possible safe interval.
- Consider new “low dose” OAC combinations
- Risk estimating scores must be utilized.
### Table 6: Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short life expectancy</td>
</tr>
<tr>
<td>Ongoing malignancy</td>
</tr>
<tr>
<td>Poor expected adherence</td>
</tr>
<tr>
<td>Poor mental status</td>
</tr>
<tr>
<td>End stage renal failure</td>
</tr>
<tr>
<td>Advanced age</td>
</tr>
<tr>
<td>Prior major bleeding/prior haemorrhagic stroke</td>
</tr>
<tr>
<td>Chronic alcohol abuse</td>
</tr>
<tr>
<td>Anaemia</td>
</tr>
<tr>
<td>Clinically significant bleeding on dual antithrombotic therapy</td>
</tr>
</tbody>
</table>
### Table 4 Strategies to avoid bleeding complications in patients treated with oral anticoagulant

- Assess ischaemic and bleeding risks using validated risk predictors (e.g. \( \text{CHA}_2\text{DS}_2\text{-VASc} \), \( \text{ABC} \), \( \text{HAS-BLED} \)) with a focus on modifiable risk factors.

- Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.

- Consider the use of NOACs instead of VKA.

- Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.

- Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.\(^a\)

- Clopidogrel is the \( \text{P2Y}_{12} \) inhibitor of choice.

- Use low-dose (≤ 100 mg daily) aspirin.

- Routine use of PPIs.

<table>
<thead>
<tr>
<th><strong>Table 4. Dual pathway and triple therapy regimens evaluated in clinical trials</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dual pathway</strong></td>
</tr>
<tr>
<td>1. Rivaroxaban 15 mg OD with clopidogrel 75 mg OD$^{99}$</td>
</tr>
<tr>
<td>2. Dabigatran 110* or 150 mg BID with clopidogrel 75 mg OD$^{101}$</td>
</tr>
<tr>
<td>3. Warfarin with clopidogrel 75 mg OD$^{97}$</td>
</tr>
<tr>
<td><strong>Triple therapy</strong></td>
</tr>
<tr>
<td>1. Rivaroxaban 2.5 mg BID with ASA 81 mg OD and clopidogrel 75 mg OD$^{99}$</td>
</tr>
<tr>
<td>2. Warfarin (INR, 2.0-2.5) with ASA 81 mg OD and clopidogrel 75 mg OD$^{98}$</td>
</tr>
</tbody>
</table>

ASA, acetylsalicylic acid; BID, twice daily; INR, international normalized ratio; OD, every day.
AF and elective PCI without high-risk features

Age < 65 and CHADS$_2$ = 0

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

ASA +/- P$_2$Y$_{12}$ inhibitor

Age ≥ 65 or CHADS$_2$ ≥ 1

OAC$^2$ + Clopidogrel
Duration: at least 1 month for BMS and at least 3 months for DES (and up to 12 months)

OAC$^4$ +/- SAPT
AF and PCI for ACS or high-risk\textsuperscript{1} elective PCI

\begin{itemize}
  \item Age $< 65$ \textbf{and} \text{CHADS}_{2} = 0
    \begin{itemize}
      \item ASA + \text{P}_{2}\text{Y}_{12} \text{ inhibitor}\textsuperscript{2}
        \begin{itemize}
          \item (ticagrelor, prasugrel preferred over clopidogrel for ACS)
          \item Duration after PCI: Up to 12 months
        \end{itemize}
    \end{itemize}
  \item Age $\geq 65$ \textbf{or} \text{CHADS}_{2} $\geq 1$\textsuperscript{*}
    \begin{itemize}
      \item \textbf{Reduced OAC}\textsuperscript{3} + ASA + clopidogrel
        \begin{itemize}
          \item ASA: stop 1 day post PCI or any time up to 6 months\textsuperscript{4}
          \item Followed by: \textbf{clopidogrel + OAC}
          \item Duration after PCI: Up to 12 months
        \end{itemize}
    \end{itemize}
  \item ASA +/− \text{P}_{2}\text{Y}_{12} \text{ inhibitor}\textsuperscript{5}
  \item OAC\textsuperscript{6} +/− \text{SAPT}
\end{itemize}

\textsuperscript{*}If CHADS\textsubscript{2} = 1 and Age$< 65$ another option for initial treatment (especially if high-risk for ischemic events) is DAPT alone using ASA+ticagrelor or ASA+prasugrel, similar to the recommendation for the CHADS\textsubscript{2}=0 patient.
Triple therapy: key takeaways

- Always calculate risk scores
- P2Y12 is always Clopidogrel
- ASA is always 81mg
- PPI should be used
- If ischemia risk > bleeding risk use triple therapy for 3-6 months
- If bleeding risk > ischemia risk use one month triple therapy
- De-escalate by removing ASA
What if my patient bleeds?

- Specific details matter:
  - Clinical indication for stent: stable or ACS
  - Type of stent: DES or BMS
  - How severe is bleeding
  - What are the risk scores

- Let’s process two examples
Bleeding during treatment with dual antiplatelet therapy ± OAC

**TRIVIAL BLEEDING**
Any bleeding not requiring medical intervention or further evaluation
- e.g. skin bruising or ecchimosis, self-resolving epistaxis, minimal conjunctival bleeding

- Continue DAPT

**MILD BLEEDING**
Any bleeding that requires medical attention without requiring hospitalization
- e.g. not self resolving epistaxis, moderate conjunctival bleeding, genitourinary or upper/lower gastrointestinal bleeding without significant blood loss, mild haemoptysis

- Continue DAPT
- Consider shortening DAPT duration or switching to less potent P2Y₁₂ inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

**MODERATE BLEEDING**
Any bleeding associated with a significant blood loss (>3 g/dL HB) and/or requiring hospitalization, which is haemodynamically stable and not rapidly evolving
- e.g. genitourinary, respiratory or upper/lower gastrointestinal bleeding with significant blood loss or requiring transfusion

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y₁₂ inhibitor especially in case of upper GI bleeding
- Reinitiate DAPT as soon as deemed safe
- Consider shortening DAPT duration or switching to less potent P2Y₁₂ inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

Eur Heart J 2018;39:213-254
**Bleeding during treatment with dual antiplatelet therapy ± OAC**

- **SEVERE BLEEDING**
  - Any bleeding requiring hospitalisation, associated with a severe blood loss (>5 g/dL HB) which is haemodynamically stable and not rapidly evolving
  - e.g. severe genitourinary, respiratory or upper/lower gastrointestinal bleeding

- **LIFE-THREATENING BLEEDING**
  - Any severe active bleeding putting patient’s life immediately at risk
  - e.g. massive overt genitourinary, respiratory or upper/lower gastrointestinal bleeding, active intracranial, spinal or intraocular haemorrhage, or any bleeding causing haemodynamic instability

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y$_{12}$ inhibitor especially in case of upper GI bleeding
- If bleeding persists despite treatment or treatment is not possible, consider stopping all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y$_{12}$ inhibitor especially in case of upper GI bleeding
- If DAPT is re-started, consider shortening DAPT duration or switching to less potent P2Y$_{12}$ inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

- Immediately discontinue all antithrombotic medications
- Once bleeding has ceased, re-evaluate the need for DAPT or SAPT, preferably with the P2Y$_{12}$ inhibitor especially in case of upper GI bleeding
Case Example 1

- 50 yo man presents with anterior STEMI
- Acute PCI performed with DES to proximal LAD with TIMI II-III flow post; no IVUS
- EF 30% acutely
- Smoker, DM, HBg 13.5, WBC 8.5, Creat 0.8 (GFR =90)
- NSR, no prior bleed or TIA/CVA
- Discharged on Ticagerlor and ASA
- No PPI prescribed
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<td>First-generation drug-eluting stent</td>
</tr>
<tr>
<td>Stent undersizing</td>
</tr>
<tr>
<td>Stent underdeployment</td>
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ACS indicates acute coronary syndrome; CAD, coronary artery disease; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; MI, myocardial infarction; and NSAID, nonsteroidal anti-inflammatory drug.
Case example 1

- **Calculate Risk scores:**
- **Precise DAPT:** 6. “low risk” 1 yr bleed: 0.45%
- **Stent thrombosis risk factors:** prox LAD, smoker, DM, low EF, no IVUS guidance
Case example 1

- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
- Presents 30 days post PCI with same bleeding as above
- Presents 11 months post PCI with same bleeding as above.
Bleeding during treatment with dual antiplatelet therapy ± OAC

SEVERE BLEEDING
Any bleeding requiring hospitalisation, associated with a severe blood loss (>5 g/dL HB) which is haemodynamically stable and not rapidly evolving

- Consider stopping DAPT and continue with SAPT, preferably with the P2Y<sub>12</sub> inhibitor especially in case of upper GI bleeding
- If bleeding persists despite treatment or treatment is not possible, consider stopping all antithrombotic medications
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- If DAPT is re-started, consider shortening DAPT duration or switching to less potent P2Y<sub>12</sub> inhibitor (i.e. from ticagrelor/prasugrel to clopidogrel), especially if recurrent bleeding occurs

LIFE-THREATENING BLEEDING
Any severe active bleeding putting patient’s life immediately at risk

- Immediately discontinue all antithrombotic medications
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e.g. massive overt genitourinary, respiratory or upper/lower gastrointestinal bleeding, active intracranial, spinal or intraocular haemorrhage, or any bleeding causing haemodynamic instability

e.g. severe genitourinary, respiratory or upper/lower gastrointestinal bleeding
Case example 1

- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
  - Stop ASA, de-escalate to clopidogrel; try to make it 6 months. If IVUS guided: 3 months
- Presents 30 days post PCI with same bleeding as above
  - Stop ASA, continue ticagrelor, unless more bleeding, then de-escalate to clopidogrel; try to make it 6 months.
- Presents 11 months post PCI with same bleeding as above.
  - Stop both, if stabilizes, consider restart clopidogrel
Case example 2

- 85 yo woman with chronic stable angina
- Elective PCI with DES to OM2.
- Discharged on ASA and Clopidogrel
- Prior Hx of TIA, remote history of black stools and anemia, easy bruising in the past
- Non smoker, no DM, Hbg 10.2, WBC 5.3, GFR 45
Case example 2

- Calculate Risk scores:
- Precise DAPT: 70. “high risk” 1 yr bleed: > 4%
- Stent thrombosis risk factors: CKD
### TABLE 4
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<td>Oral anticoagulant therapy</td>
</tr>
<tr>
<td>ACS presentation</td>
<td>Female sex</td>
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<td>Multiple prior MIs</td>
<td>Advanced age</td>
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<td>Low body weight</td>
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Case example 2

- Presents 90 days post PCI with LGI bleed and hemoglobin down to 6.5. Transfused 3 u PRBC. Hemodynamically stable
  - Stop ASA, stop clopidogrel;
- Presents 30 days post PCI with same bleeding as above
  - Stop ASA, stop clopidogrel; alternative try for 3 mo
- Presents 11 months post PCI with same bleeding as above.
  - Stop both. Should have had clopidogrel stopped prior
What if my patient needs surgery?

- Individualize
  - Type of surgery. Surgeons will ALWAYS want EVERYBODY off ALL anticoagulant/platelet drugs
  - Urgency, ability to wait
  - Type of DAPT used
Interruption schedules for surgery

Minimal delay for P2Y₁₂ interruption

Days after surgery
What if my patient needs to switch drugs

- **Common reasons:**
  - Cost of ticagrelor
  - Breathlessness with ticagrelor
  - Rash with clopidogrel
  - Change in insurance/finances
General considerations

- Balancing thrombotic events with bleeding events
- Liberal use of risk estimating scores
- All aspirin doses are 81mg
- Choice of P2Y$_{12}$ depends on the balance
  - Clopidogrel less effect on platelets
  - Ticagrelor more effect on platelets
  - Prasugrel more effect, but risk in prior CVA
- Clinical syndrome class effect: Stable (SIHD) or acute coronary syndrome (STEMI, NSTEMI)