Updates in Acute Coronary Syndromes

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Disclosures

No Conflicts of Interest

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**TOPICS**

- Dual Antiplatelet Therapy (DAPT)
  - Choice and Dosing
  - Duration
  - Triple Therapy
  - Cessation for Surgery
  - Management in the Bleeding Patient

- ACS Performance Metrics in 2017

**Updates in Acute Coronary Syndromes**

- Major Society Guideline updates 2016-2017

- Clinical Trials Published 2016-2017

- Regulatory News and Events
Strength of Guideline Recommendations

**CLASS I (STRONG) Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative Effectiveness Phrases:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

**CLASS IIa (MODERATE) Benefit > Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative Effectiveness Phrases:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

**CLASS IIb (MILD) Benefit = Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

**CLASS III: No Benefit (MODERATE) Benefit > Risk**

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

**CLASS III: Harm (STRONG) Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

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**Acronyms**

- **ACS**: Acute Coronary Syndrome
- **BMS**: Bare Metal Stent
- **CAD**: Coronary Artery Disease
- **CABG**: Coronary Artery Bypass Graft Surgery
- **DAPT**: Dual Antiplatelet Therapy
- **DES**: Drug Eluting Stent
- **PCI**: Percutaneous Coronary Intervention
- **PPI**: Proton Pump Inhibitor
- **SIHD**: Stable Ischemic Heart Disease
- **TAVR**: Transcatheter Aortic Valve Replacement
TOPICS

- Dual Antiplatelet Therapy (DAPT)
  - Choice and Dosing
  - Duration
  - Triple Therapy
  - Cessation for Surgery
  - Management in the Bleeding Patient
- ACS Performance Metrics in 2017

ACC/AHA FOCUSED UPDATE

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS
A 65 yo male with DM, HTN, HL presents with acute onset substernal chest pain for three hours. Troponin is 1. EKG demonstrates sinus rhythm with lateral T wave inversions. He is now chest pain free and awaiting invasive angiography in the AM. Which antiplatelet regimen do you start?

A. Aspirin 81 daily alone
B. Aspirin 81 daily + Clopidogrel 75 daily
C. Aspirin 81 daily + Ticagrelor 90 mg BID
D. Aspirin 81 mg daily + Prasugrel 10 mg daily
E. Call your friendly cardiology consultant

### Antiplatelet Agents

<table>
<thead>
<tr>
<th>Indication</th>
<th>Aspirin</th>
<th>Clopidogrel (Plavix)</th>
<th>Prasugrel (Effient)</th>
<th>Ticagrelor (Brilinta)</th>
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<tr>
<td>ACS</td>
<td>ACS</td>
<td>ACS</td>
<td>Post PCI</td>
<td>ACS</td>
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<tr>
<td>Post PCI</td>
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<td>PVD</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dose Load</td>
<td>325 mg</td>
<td>300-600 mg</td>
<td>60 mg</td>
<td>180 mg</td>
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<tr>
<td>Maintenance</td>
<td>81 mg</td>
<td>75 mg DAILY</td>
<td>10 mg DAILY</td>
<td>90 mg BID</td>
</tr>
<tr>
<td>Class</td>
<td>NSAID</td>
<td>2nd gen thienopyridine (PRODRUG)</td>
<td>2nd gen thienopyridine (PRODRUG)</td>
<td>CTPT</td>
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<tr>
<td>Mechanism</td>
<td>IRREVERSIBLE COX 1</td>
<td>IRREVERSIBLE P2Y12</td>
<td>IRREVERSIBLE P2Y12</td>
<td>REVERSIBLE P2Y12</td>
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<tr>
<td>Peak Effect</td>
<td>1-3 hours</td>
<td>6 hours</td>
<td>4 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>CYP Metab</td>
<td>NA</td>
<td>2C19</td>
<td>3A4</td>
<td>3A4/5</td>
</tr>
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</table>
Aspirin Dosing in Patients with Coronary Artery Disease (CAD)

Aspirin Dosing in Patients Treated With DAPT

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.</td>
</tr>
</tbody>
</table>

- Higher doses of aspirin are associated with bleeding and no increased anti-ischemic benefit
- When used with ticagrelor (Brilinta), aspirin doses of >100 mg are contraindicated

Which P2Y12 Agent should I Recommend?

For Medically Managed ACS
Recommended over

For ACS with PCI
Recommended over

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**Other Pearls Regarding P2Y12 Inhibitors**

- **Ticagrelor**
  - can cause dyspnea and bradycardia

- **Prasugrel**
  - may be less effective in patients < 60 kg and > 75 years of age
  - should not be given until after invasive angiography (Class III)
  - do not give to patients with a history of TIA or stroke (Class III)

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**During angiography, the patient is found to have an 80% mid LAD lesion which is treated with a stent. How long should he remain on DAPT after stent placement for NSTEMI?**

A. 3 months  
B. 6 months  
C. 12 months  
D. More information needed  
E. As long as possible
Duration of Dual Antiplatelet Therapy (DAPT)

- Duration of DAPT depends on:
  - Underlying condition
  - Treatment provided

Stable Ischemic Heart Disease (SIHD)

Acute Coronary Syndromes (ACS)

Duration of Dual Antiplatelet Therapy (DAPT) in Patients with ACS

1 year

Stopping early at 6 months
Duration of Dual Antiplatelet Therapy (DAPT) in Patients with SIHD

Stable Ischemic Heart Disease (SIHD)

1 MONTH

PCI with Bare Metal Stent (BMS)

3 months

Stopping early at 3 months

PCI with Drug Eluting Stent (DES)

6 MONTHS

When should DAPT therapy be continued for LONGER Duration?

Risk of Ischemia

Increased risk of stent thrombosis
- ACS presentation
- Diabetes mellitus
- Left ventricular ejection fraction <40%
- First-generation drug-eluting stent
- Stent under-sizing
- Stent under-deployment
- Small stent diameter
- Greater stent length
- Bifurcation stents
- In-stent restenosis

Risk of Bleeding

Increased Bleeding Risk (may favor shorter-duration DAPT)
- History of prior bleeding
- Oral anticoagulant therapy
- Female sex
- Advanced age
- Low body weight
- CKD
- Diabetes mellitus
- Anemia
- Chronic steroid or NSAID therapy
The DAPT Score can guide risk / benefit of longer therapy

Score ≥ 2
Favorable benefit/risk
For prolonged DAPT

Score <2 NOT
Favorable benefit/risk
For prolonged DAPT

Our patient has a score of 1. 12 months of DAPT should be adequate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
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<tbody>
<tr>
<td>Age ≥75 y</td>
<td>-2</td>
</tr>
<tr>
<td>Age 65 to &lt;75 y</td>
<td>-1</td>
</tr>
<tr>
<td>Age &lt;65 y</td>
<td>0</td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>MI at presentation</td>
<td>1</td>
</tr>
<tr>
<td>Prior PCI or prior MI</td>
<td>1</td>
</tr>
<tr>
<td>Stent diameter &lt;3 mm</td>
<td>1</td>
</tr>
<tr>
<td>Paclitaxel-eluting stent</td>
<td>1</td>
</tr>
<tr>
<td>CHF or LVEF &lt;30%</td>
<td>2</td>
</tr>
<tr>
<td>Saphenous vein graft PCI</td>
<td>2</td>
</tr>
</tbody>
</table>

10/20/2017

You are writing the discharge medication list and receive a page from Pharmacy

“Ticagrelor is not covered by this patient’s insurance and he won’t be able to receive the medication at home unless he pays out of pocket”

What do you do?
Switching Between Oral P2Y12 Inhibitors

Acute Settings (ACS)

ESC Class IIb recommendation

Stable Settings (SIHD)
The patient returns to the Emergency Room 7 days later with shortness of breath. An EKG reveals that he is now in Atrial Fibrillation. Troponin is normal. CHADS2Vasc score is 4. What regimen do you place him on?

A. Aspirin + Ticagrelor (No change)
B. Aspirin + Ticagrelor + Coumadin
C. Aspirin + Clopidogrel + Coumadin
D. Clopidogrel + Coumadin
E. Clopidogrel + Rivaroxaban
F. That’s a hard choice!

What’s the update on triple therapy?

**American Guidelines**

**TABLE 6** Summary and Synthesis of Guideline, Expert Consensus Documents, and Comprehensive Review Article Recommendations on the Management of Patients Treated With Triple Therapy (54, 68, 91–93)

- Assess ischemic and bleeding risks using validated risk predictors (e.g., CHA2DS2-VASc, HAS-BLED)
- Keep triple therapy duration as short as possible; dual therapy only (oral anticoagulant and clopidogrel) may be considered in select patients
- Consider a target INR of 2.0–2.5 when warfarin is used
- Clopidogrel is the P2Y12 inhibitor of choice
- Use low-dose (<100 mg daily) aspirin

PPIs should be used in patients with a history of gastrointestinal bleeding and are reasonable to use in patients with increased risk of gastrointestinal bleeding.

CHA2DS2-VASc indicates congestive heart failure, hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism (doubled), vascular disease, age 65–74 years, sex category, HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, stable INR, elderly, drugs/alcohol

For patients who require triple therapy:
- **Use Coumadin** (keep INR at low end of range)
- **Use Clopidogrel** *(NOT Prasugrel/Ticagrelor)*
- **Use low dose aspirin**
- **Consider PPI**
What's the update on triple therapy?  
European Guidelines

- **Major differences**
  - NOACs can be used (IIa indication)
  - Consider lower dose rivaroxaban (15 mg daily)

Timeline for Triple Therapy

Patients with an indication for oral anticoagulation undergoing PCI

- Concerns about ischemic risk
  - Time from treatment initiation:
    - 1 mo.
    - 3 mo.
    - 6 mo.
    - 12 mo.
    - Beyond 12 mo.

- Concerns about bleeding risk

- Dual Therapy up to 12 mos.
  - Class IIa A

- OAC alone
  - Class IIa B

- Triple Therapy up to 6 mos.
  - Class IIa B

- 1 mo. Triple Therapy

- OR

- 1 mo. Triple Therapy

- Class IIa

- Aspirin

- Clopidogrel

- Oral anticoagulation
72 yo man underwent PCI with a drug eluting stent to the LAD 2 months ago. He now has severe knee osteoarthritis and is asking you when he can have surgery. How long after his stent should he wait?

A. 1 month  
B. 3 months  
C. 6 months  
D. 12 months  
E. He should be managed medically indefinitely

**Perioperative Management and Timing of Non Cardiac Surgery**

Wait 30 days after PCI with BMS

Wait at least 3 months and preferably 6 months after PCI with DES

Wait 30 days after PCI with DES
Perioperative Management and Timing of Non Cardiac Surgery

During perioperative period:
- Continue aspirin if possible
- Restart P2Y12 as soon as possible

Perioperative Management and Timing of Non Cardiac Surgery

How long before surgery should DAPT be stopped?
- CONTINUE ASPIRIN if possible!
What to do when the patient bleeds on DAPT?

**Bleeding during treatment with dual antiplatelet therapy ± OAC**

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

**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 hemoptysis

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

- **Stop DAPT, continue with SAPT (P2Y12) preferred**
- **If bleeding persists, stop all meds**
- **Once bleeding ceased, re-evaluate need for DAPT**
- **If restarted use less potent agent for minimal duration**
Key Points Regarding DAPT (1/3)

- Dose of Aspirin for all patients is **81 mg daily**
- Duration of DAPT:
  - ACS Patients: **1 YEAR for ALL** (with/without stent)
  - SIHD (Stable Ischemic Heart Disease) Patients:
    - Drug Eluting Stent (DES): **6 MONTHS**
    - Bare Metal Stent (BMS): **1 MONTH**
- Stopping Early:
  - DAPT could be stopped **3 months** after DES (drug eluting stent) for high bleeding risk patients
- Longer Therapy:
  - Risk benefit between bleeding and ischemia
  - DAPT score can be helpful

Key Points Regarding DAPT (2/3)

- Choice of Agents:
  - Medical Management of ACS: **Ticagrelor** > Plavix
  - PCI in ACS: **Ticagrelor or Prasugrel** > Plavix
  - **Do NOT USE Prasugrel** if history of **stroke or TIA**
- Triple Therapy:
  - Short Duration
  - Use clopidogrel/coumadin
  - Target INR 2-2.5
  - Use PPI (Proton Pump Inhibitor)
Key Points Regarding DAPT (3/3)

- Timing of Non-Cardiac Surgery:
  - Ideally > 1 month after BMS, 6 months after DES
  - Continue Aspirin if possible
  - Hold:
    - Ticagrelor 3 days prior to surgery
    - Clopidogrel 5 days prior to surgery
    - Prasugrel 7 days prior to surgery

- Stopping for Bleeding
  - Consider severity of bleeding
  - Continue DAPT, SAPT when possible if indicated

Topics

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  - Choice and Dosing
  - Duration
  - Triple Therapy
  - Cessation for Surgery
  - Management in the Bleeding Patient

- ACS Performance Metrics in 2017
2017 AHA/ACC Clinical Performance and Quality Measures for Adults With ST-Elevation and Non-ST-Elevation Myocardial Infarction

**Arrival**
- Aspirin
- Troponin within 6 hours

**Hospitalization**
- Evaluation of LVEF
- ACEi or ARB
- Non invasive stress test (if no cath)

**Discharge**
- Aspirin
- P2Y12 Inhibitor
- Beta Blocker
- Statin (High intensity)
- Cardiac Rehab
2017 ACS Quality Measures

- Metrics that may be useful for local quality improvement but are not yet appropriate for public reporting or pay for performance programs.
- New measures are initially evaluated for potential inclusion as performance measures.

- Avoid Using NSAIDS for pain control!
- Don’t prescribe prasugrel for patients with a history of Stroke/TIA
- Use Aspirin 81 mg daily with Ticagrelor

What Have We Learned?

Dual Antiplatelet Therapy
- Choice of Antiplatelet Agents
- Duration of DAPT after ACS and PCI
- An Approach to Anticoagulation and DAPT
- Timing of Non Cardiac Surgery after PCI
- Management of DAPT for patients with bleeding

Performance Measures for ACS in 2017
- Medications on discharge (Aspirin, P2Y12, Beta Blocker, ACEi)
- Assessment of LV function
- Referral to Cardiac Rehab
Thank You!

Questions / Final syllabus:

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415-476-6541
References

Guidelines


- Marco Valgimigli* (Chairperson) (Switzerland), Hector Bueno (Spain), Robert A. Byrne (Germany), Jean-Philippe Collet (France), Francesco Costi (Italy), Anders Jeppsson1 (Sweden), Peter Juni (Canada), Adrian Kastrati (Germany), Philippe Koh (Belgium), Laura Mauri (USA), Gilles Montalescot (France), Franz-Josef Neumann (Germany), ate Petricevic1 (Croatia), Marco Roffi (Switzerland), Philippe Gabriel Steg (France), Stephan Windecker (Switzerland), and Jose Luis Zamorano (Spain). 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. European Heart Journal (2017) 0, 1–48. doi:10.1093/eurheartj/ehx419.