Acute Coronary Syndromes
Controversies and Conundrums

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Disclosures

• NHLBI (CTSN), NIDCR
• Medtronic, Apollo TMVR Trial
• Edwards Life Sciences, Early TAVR Trial
Outline

• Pathogenesis
• General principles
• STEMI
• NSTEMI
• Population health
Acute Coronary Syndromes

Plaque erosion

- Lipid poor
- Proteoglycan and glycosaminoglycan rich
- Non-fibrillar collagen breakdown
- Few inflammatory cells
- Endothelial cell apoptosis
- Secondary neutrophil involvement
- Female predominance
- High triglycerides

Plaque rupture

- Lipid rich
- Collagen poor, thin fibrous cap
- Interstitial collagen breakdown
- Abundant inflammation
- Smooth muscle cell apoptosis
- Macrophage predominance
- Male predominance
- High LDL

From: Requiem for the ‘vulnerable plaque’
Acute Coronary Syndromes

From IK Jang, Mass Gen Hosp
Acute Coronary Syndromes

From: Requiem for the ‘vulnerable plaque’
Universal Definition of MI

Thygesen K et al. Euro Heart J 2018; 00:1-33
General Principles of Care

• Risk stratification (Intensity ~ Risk)
• Reperfusion (STEMI)
• Revascularization (NSTEMI, STEMI)
• Anti-thrombotic therapy
• Beta-blockers, ACE-I/ARBs, others
• Secondary prevention
Reperfusion Therapy for Patients with STEMI

*Patients with cardiogenic shock or severe heart failure initially seen at a non-PCI-capable hospital should be transferred for cardiac catheterization and revascularization as soon as possible, irrespective of time delay from MI onset (Class I, LOE: B). †Angiography and revascularization should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.
Door-to-Balloon Times and 30-Day Unadjusted Mortality

Culprit Only or Multivessel PCI in STEMI

- Lesion in Non-infarct Related Artery (N-IRA)
- Occluded Infarct Related Artery (IRA)

Complete Revascularization:
Treat IRA and Treat N-IRA Stenoses

Lesion-Only Revascularization:
Treat IRA Only
Leave N-IRA Stenoses
STEMI with MVD

Multi-Vessel PCI

- At time of pPCI
- Planned, Staged
- Ischemia, + stress
## PCI Strategies in STEMI

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Culprit vessel-only primary PCI</th>
<th>Multivessel primary PCI</th>
<th>Staged PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial procedure</strong></td>
<td>Culprit vessel-only PCI</td>
<td>Culprit vessel PCI and non-culprit vessel PCI</td>
<td>Culprit vessel-only PCI</td>
</tr>
<tr>
<td>Days–weeks later</td>
<td>Non-culprit vessel PCI for spontaneous ischemia or intermediate/high risk findings on noninvasive testing</td>
<td>Decreased repeat revascularization</td>
<td>Non-culprit vessel PCI</td>
</tr>
</tbody>
</table>

### Pros
- Reduced contrast volume
  - Reduced risk of PCI complications
- Decreased hospital length of stay

### Cons
- Increased repeat revascularization risk
- Potential reduction in LV recovery
- Prolonged procedure time
  - Increased contrast volume
  - Increased periprocedural MI risk
  - Potentially unnecessary PCI of functionally insignificant stenosis
- Time to assess benefit vs. risk of non-culprit vessel PCI
  - Additional PCI access risk
  - Additional procedure costs

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>PCI of a noninfarct artery may be considered in <em>selected</em> patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned staged procedure.¹</td>
</tr>
</tbody>
</table>

¹. Modified recommendation from 2013 Guideline (changed class from III: Harm to IIb and expanded time frame in which multivessel PCI could be performed).

**Insufficient data to inform recommendation regarding optimal timing of staged PCI**
In cardiogenic shock, routine revascularization of non-IRA lesions is not recommended at the time of primary PCI.

Thiele H et al. NEJM 2017; 377: 2419-32
IABP SHOCK II Trial

Thiele H et al AHA/Circulation 2018;139:00
Current Challenges

- Patient awareness, delay
- Access
- Health system obstacles
- Medication adherence
- Rehabilitation services
NSTEMI
0-1 Hour “Rule-Out”

A

Suspected NSTEMI (n = 3123)

- 0h*< 5ng/L or 0h < 12ng/L and Δ0-1h < 3ng/L
- Others
- 0h ≥ 52ng/L or Δ0-1h ≥ 5ng/L

Rule-out
Young (n=1122)
Proportion: 956 (85%)
Sens.: 100% (94.9-100)
NPV: 100% (99.6-100)

Middle-age (n=935)
Proportion: 606 (65%)
Sens.: 99.3% (96-99.9)
NPV: 99.8% (99.1-100)

Old (n=1066)
Proportion: 317 (30%)
Sens.: 99.3% (97.5-99.8)
NPV: 99.4% (97.7-99.8)

Observe
Young (n=1122)
Proportion: 74 (7%)
Prevalence of NSTEMI: 15%

Middle-age (n=935)
Proportion: 188 (20%)
Prevalence of NSTEMI: 14%

Old (n=1066)
Proportion: 477 (45%)
Prevalence of NSTEMI: 14%

Rule-in
Young (n=1122)
Proportion: 92 (8%)
Spec.: 97% (95.8-97.9)
PPV: 66.3% (56.2-75.1)

Middle-age (n=935)
Proportion: 141 (15%)
Spec.: 96.1% (94.5-97.2)
PPV: 78% (70.5-84.1)

Old (n=1066)
Proportion: 272 (25%)
Spec.: 92.7% (90.7-94.3)
PPV: 79% (73.8-83.5)

<table>
<thead>
<tr>
<th>TIMI Score</th>
<th>GRACE Score</th>
<th>EDACS Score</th>
<th>HEART Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE ≥ 65</td>
<td>AGE</td>
<td>AGE ≥ 25 ≤ 65</td>
<td>AGE ≥ 25 ≤ 65</td>
</tr>
<tr>
<td>1 = ST changes ≥ 0.5 mm</td>
<td>1 = ST changes ≥ 0.5 mm</td>
<td>2 = Male</td>
<td>2 = Typical, 1 = Atypical</td>
</tr>
<tr>
<td>Coronal Disease 1 = Known stenosis</td>
<td>Systolic BP mmHg</td>
<td>Coronary Disease or ≥ 3 Risk Factors</td>
<td>2 = ST depression, 1 = T-wave inversion</td>
</tr>
<tr>
<td>Aspirin Use 1 = Within 7 days</td>
<td>Creatinine μmol/L</td>
<td>Typical Symptoms</td>
<td>Risk Factors 2 = 2 or more, 1 = 1</td>
</tr>
<tr>
<td>TROPTIN 1 = 99th centile</td>
<td>TROPTIN 1 = 99th centile</td>
<td>Atypical Symptoms</td>
<td>TROPTIN 2 = 3 x upper limit, 1 = 1</td>
</tr>
<tr>
<td>Risk Factors 1 = 3 or more</td>
<td>Heart Rate BPM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe Angina 1 = 2 in 24 hours</td>
<td>Cardiac Arrest Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Killip Class Category</td>
<td></td>
<td></td>
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**Low Risk Criteria**
- TIMI: 0 or 1
- GRACE: 108 or less
- EDACS: Less than 16
- HEART: 3 or less
Intensity and Timing of Therapy

Role of Risk Assessment

Invasive evaluation in Non-ST-Elevation Acute Coronary Syndromes

- **Very High-Risk**
  - Haemodynamic instability or cardiogenic shock
  - Recurrent/ongoing chest pain refractory to medical tx
  - Life-threatening arrhythmias or cardiac arrest
  - Mechanical complications of MI
  - Acute heart failure
  - Recurrent dynamic ST-T wave changes

- **High-Risk**
  - Established diagnosis of non-ST-elevation myocardial infarction based on cardiac troponins
  - Dynamic ST/T-changes (symptomatic or silent)
  - GRACE score >140

- **Intermediate Risk**
  - Diabetes mellitus or renal insufficiency
  - LVEF <40% or congestive heart failure
  - Early post-infarction angina or prior PCI/CABG
  - GRACE risk score >109 and <140 or recurrent symptoms/ischaemia on non-invasive testing.

- **Immediate Invasive** (<2 hours)
  - IC

- **Early Invasive** (<24 hours)
  - IA

- **Invasive** (<72 hours)
  - IA

2018 ESC Revascularization Guidelines Euro Heart J 2018; 00:1-96
MVD in NSTEMI: SMILE Trial

Multi-Vessel PCI in NSTEMI

CENTRAL ILLUSTRATION  Complete Versus Culprit-Only Lesion Intervention in Patients With Acute Coronary Syndrome and Multivessel Disease: Survival Curves

Cumulative Incidence of All-Cause Mortality (%)

Years Since Procedure

Likelihood Ratio Test \( p = 0.0001 \)

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>Complete Revascularization</th>
<th>Culprit Vessel Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9,990</td>
<td>9,990</td>
</tr>
<tr>
<td>1</td>
<td>9,848</td>
<td>9,953</td>
</tr>
<tr>
<td>2</td>
<td>7,890</td>
<td>8,252</td>
</tr>
<tr>
<td>3</td>
<td>5,231</td>
<td>6,584</td>
</tr>
<tr>
<td>4</td>
<td>3,687</td>
<td>4,316</td>
</tr>
<tr>
<td>5</td>
<td>1,941</td>
<td>2,019</td>
</tr>
</tbody>
</table>

Extended Duration DAPT

Triple Therapy

Ischemia

Bleeding
Treatment Algorithm for Duration of P2Y\textsubscript{12} Inhibitor Therapy in Patient With Recent ACS (NSTE-ACS or STEMI)

1. **Recent ACS (NSTE-ACS or STEMI)**
   - CABG
     - **Class I:** After CABG, resume P2Y\textsubscript{12} inhibitor to complete 1 y of DAPT (clopidogrel, prasugrel, ticagrelor)
   - Medical Therapy
     - **Class I:** At least 12 mo (clopidogrel, ticagrelor)
   - Lytic (STEMI)
     - **Class I:** At least 14 d and up to 12 mo (clopidogrel)
   - PCI (BMS or DES)
     - **Class I:** At least 12 mo (clopidogrel, prasugrel, ticagrelor)
     - **High bleeding risk* or significant overt bleeding**
       - **Class IIb:** Discontinuation after 6 mo may be reasonable
   - **No high risk of bleeding and no significant overt bleeding on DAPT**
   - **Class IIIb:** >12 mo may be reasonable
Case

75 year old woman with NSTEMI

- RCA PCI 2015: 9 months DAPT
- PAF 2016: Apixaban monotherapy
- ICH 2016 (off A/C): Cerebellar AVM
- Gamma knife surgery 2017
- No antithrombotics x 16 months
- Presently in sinus rhythm
Case

75 year old widow with NSTEMI

• How to proceed?
  • ASA?
  • P2Y$_{12}$?
  • Cangrelor?
  • Heparin?
  • Bivalirudin?
  • PCI or CABG?
  • Post-procedure management
Patients with an indication for oral anticoagulation undergoing PCI

**Concerns about ischaemic risk** prevailing

**Concerns about bleeding risk** prevailing

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**Time from treatment initiation**

- **1 mo.**
- **3 mo.**
- **6 mo.**
- **12 mo.**
- **Beyond 12 mo.**

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- **ACO** 1 mo. Triple Therapy
  - Class IIa B

- **ACO** 1 mo. Triple Therapy
  - Class IIa B

- **CO** OR **AO**
  - Dual Therapy up to 12 mo.
  - Class IIa A

- **CO**
  - Dual Therapy up to 12 mo.
  - Class IIa A

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**OAC alone**
- Class IIa B

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**A** = Aspirin
**C** = Clopidogrel
**O** = Oral anticoagulation
PIONEER AF-PCI: Rivaroxaban

Group 1: R 15 mg daily + P2Y12
Group 2: R 2.5 mg bid + DAPT
Group 3: VKA + DAPT

Hazard ratio for group 1 vs. group 3, 0.59 (95% CI, 0.47–0.76) P<0.001
Hazard ratio for group 2 vs. group 3, 0.63 (95% CI, 0.50–0.80) P<0.001

Gibson CM et al. NEJM 2017
Mortality Following NSTEMI

Berg DD et al. Euro Heart J 2018; 39:3810-20
Szummer K et al. Euro Heart J 2018;39:3766-76
The Cycle of Improvement

Antman EM Euro Heart J 2018; 39:3777-9