Steering Committee Disclosures

The Steering Committee reported the following relevant financial relationships that they or their spouse/partner have with commercial interests:

• Deepak L. Bhatt, MD, MPH, FACC, FAHA, FSCAI:
  Principal Investigator: Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, Sanofi Aventis, The Medicines Company

• Charles V. Pollack Jr., MA, MD, FACEP, FAAEM, FAHA:
  Honorarium: Merck, Forest

Non-faculty Disclosures

Non-faculty content contributors and/or reviewers reported the following relevant financial relationships that they or their spouse/partner have with commercial interests:

• Barry Watkins, PhD; Bradley Pine; Blair St. Amand; Jay Katz; Dana Simpler, MD: Nothing to Disclose
Educational Objectives

This program is designed to address the following IOM competencies: provide patient-centered care and employ evidence-based practice. At the conclusion of this activity, participants should be able to:

• Adopt ischemic risk assessment stratification strategies to choose the best course of action to manage patients with acute chest pain syndrome.
• Assess and stratify bleeding risk after antiplatelet treatment is initiated.
• Make treatment choices based on an understanding of the different mechanisms of action among antithrombotic agents and on pertinent clinical trial results.
• Analyze pharmacologic and clinical trial results of newer antithrombotic agents to determine how best to match treatment options with patients to achieve optimal clinical outcome.

Key Considerations for Clinical Management of ACS

• Need for differential diagnosis of the spectrum of ACS.
• Fundamental aspects of management of acute chest pain.
  – Elements for optimal early hospital care.
• The importance of risk stratification to guide practice decisions.
  – Options: initial conservative or invasive strategy.
  – If invasive strategy, rationale for early catheterization.
• The expanded field of existing antiplatelet treatment options.
  – Clopidogrel, prasugrel, ticagrelor.
• Emerging antiplatelet/anticoagulant therapies for ACS.
  – Strong contender: very low dose rivaroxaban.
• Standards of treatment for STEMI.
• The need to balance anti-ischemic effects versus bleeding risk.
• The growing importance of quality outcomes in ACS.

Chest Pain Case
Chest Pain Case

Initial Presentation

• 68-year-old female presents to the Emergency Department at 8:45 am
• Epigastric pain radiating to left shoulder for two hours; onset was with exertion but continued at rest
• Initial ECG shows widespread STT wave anomalies with T wave inversions (V2-V6)
• ECG shows marked ST-segment depression in the lateral precordial leads (V5, V6)
• CVD History: Suspected CAD with abnormal stress test, but declined catheterization one year ago; treated with beta-blockers and long-acting nitrates
• Additional Medical History: Significant only for hypertension

Chest Pain Case

Initial ECG

Choice of therapy depends at least in part on selection of management strategy for next 24h:

– Invasive or conservative?
– Patient’s creatinine clearance is 45 cc/min, her first troponin is negative, and she is not anemic
– Once decided, medical therapy that supports that approach should be initiated:
  - Anticoagulant?
    - Which one? What dose?
  - Oral antiplatelet (beyond aspirin)?
    - Which one? What dose?
  - GP IIb/IIIa antagonist?
    - Small or large molecule? What dose?
  - Beta blocker?
    - IV or PO?
Chest Pain Case

Initial Evaluation

• Two hours later, repeat troponin assay is positive, and patient’s diagnosis is changed from UA to NSTEMI

• Plan is to take her to cath lab as first case tomorrow morning if she remains stable and pain free

• What are your choices of anticoagulation, antiplatelet, and beta-blocker therapy?

• What therapy might you add (or change) in the cath lab?

Acute Coronary Syndromes

Clinical Spectrum and Presentation

• CHD is the leading cause of death in the US; 814,000 deaths in 2007

• 1,350,000 annual new or recurring ACS events annually

• 34% of those with a coronary event die within a year

• 14% of STEMI patients are rehospitalized within 30 days

• Direct and indirect cost of CHD is $287,000,000,000

• Hospital adherence to ACC/AHA ACS treatment guidelines is only 74%
Acute Coronary Syndromes:
From the Emergency Department to the Coronary Care Unit to the Office

Acute Coronary Syndromes

• Common Features of ACS
  – Similar pathophysiology
  – Similar presentation and early management rules
• Differentiating Features
  – Unstable Angina
    – Non-occlusive thrombus
    – No diagnostic ECG changes, but ischemic ST-T changes confer higher risk
    – Normal cardiac enzymes
  – NSTEMI
    – Occluding thrombus sufficient to cause myocardial damage
    – No diagnostic ECG changes, but ischemic ST-T changes: higher risk
    – Elevated cardiac enzymes
  – STEMI
    – Complete thrombus occlusion
    – ST elevation or new LBBB
    – Elevated cardiac enzymes
    – More severe symptoms

Mortality in Acute Coronary Syndromes
Death from Hospital Admission to 6 Months

Risk Stratification and Early Hospital Care

© 2012 PCME
Management of Acute Chest Pain Syndrome
Role of the Emergency Physician

• Stabilization
  – When required
• Differential Diagnosis of ACS
  – “Atypical is the new typical”
• Prompt STEMI Management
  – ~15% of our ACS population
• Risk Stratification of UA and NSTEMI
  – >50% of acute chest pain patients don’t have ACS
  – Of those who have ACS, fewer than 30% are at high ischemic risk

Acute Coronary Syndromes
Risk Stratification

Chest Pain Syndrome Suggestive of Ischemia
Immediate Assessment within 10 Minutes

<table>
<thead>
<tr>
<th>Initial Labs and Tests</th>
<th>Emergent Care</th>
<th>History &amp; Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 lead ECG</td>
<td>IV access</td>
<td>Establish diagnosis</td>
</tr>
<tr>
<td>Obtain initial</td>
<td>Cardiac monitoring</td>
<td>Read ECG</td>
</tr>
<tr>
<td>cardiac enzymes</td>
<td>Oxygen</td>
<td>Identify complications</td>
</tr>
<tr>
<td>Electrolytes, CBC</td>
<td>Aspirin</td>
<td>Assess for reperfusion</td>
</tr>
<tr>
<td>lipids, BUN/</td>
<td>Nitrates</td>
<td></td>
</tr>
<tr>
<td>creatinine, glucose, coags</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest x-ray</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
"Dynamic Risk Stratification" Tools

- History and physical
- Standard ECG and non-standard ECG leads
  - 15-lead ECGs should perhaps become "standard" in all but very-low-risk patients
- Biomarkers
  - CK-MB, troponin I and T, myoglobin
  - High-sensitivity troponin
- Non-invasive imaging
  - Echocardiogram
  - Stress testing
  - Technetium-99m-sestamibi
- Invasive imaging
  - Cardiac computed tomography angiography (CCTA)
- Predictive indices/schemes
  - Better as research tools than for real-time clinical decision-making

TIMI RISK SCORE for UA/NSTEMI

Risk Algorithms: TIMI, GRACE, PURSUIT; The Preponderance of Evidence Favors the TIMI Score

<table>
<thead>
<tr>
<th>Age ≥ 65</th>
<th>2 or 3 CAD risk factors</th>
<th>Known CAD (stenosis ≥ 50%)</th>
<th>ASA use in past 7 days</th>
<th>Recent (&lt; 24H) severe angina</th>
<th>↑ cardiac markers</th>
<th>ST deviation ≥ 0.5 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>HISTORICAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRESENTATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RISK SCORE = Total Points (0-7)

| 0/1 | 2 | 3 | 5 | 8 |
| 1/2 | 3 | 5 | 13 | 20 |
| 2/3 | 5 | 12 | 26 |
| 3/4 | 6/7 | 19 | 41 |

*Risk criteria: UA or NSTEMI defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or elevated cardiac marker)

Anterior ST Segment Depression

Classifications

- Troponin
  - Unstable angina
  - NSTEMI
  - TIMI flow grade 0/1 in culprit artery
- + Troponin
  - TIMI flow grade 2/3 in culprit artery
  - TIMI flow grade 0/1 in culprit artery

Anterior ST-segment depression

Gibson CM et al. 2008 AHA Scientific Sessions
Acute Coronary Syndromes: From the Emergency Department to the Coronary Care Unit to the Office

Troponin Levels Predict Risk of Mortality in UA/NSTEMI

Cardiac troponin I (ng/mL)

Mortality risk of death (% of patients)

0 to <0.4: 1.8 %

0.4 to <1.0: 1.7 %

1.0 to <2.0: 3.4 %

2.0 to <3.0: 3.7 %

3.0 to <5.0: 6.0 %

≥ 5.0: 7.5 %


Acute Coronary Syndromes

Early Hospital Care

Optimal Upstream Management of Ischemic Risk Assessment

- Basis for assessment
  - “Pain story”
  - Background CVD risk
  - ECG
  - Troponin elevation in pertinent time frame
  - Predictive risk score

- Options
  - Antiplatelet therapy increasingly important as ischemic risk increases
  - UFH and enoxaparin established
  - Bivalirudin and fondaparinux: New options that are non-inferior
Treatment of Acute Coronary Syndrome

Initial Treatment of ACS

STEMI

Antithrombotic, anti-thrombin, or anticoagulant therapy

Thrombolytics

PCI or CABG

Conservative

Long-term medical management

NSTEMI

Antithrombotic, anti-thrombin, or anticoagulant therapy

PCI or CABG

Early invasive

Current Medical Management of Unstable Angina and NSTEMI

Acute Therapy

• Oxygen, Bed Rest
• ECG Monitoring
• Nitroglycerin
• Beta Blockers
• ACE Inhibitors
• Antiplatelet Therapy
• Anticoagulant Therapy

Maintenance Therapy

• Antiplatelet Therapy
• Beta Blockers
• Calcium Channel Blockers
• Lipid-lowering Agents
• ACE Inhibitors
• Oral Anticoagulant Therapy

Procedural Considerations:
Initial Conservative or Invasive Strategy –
Based on Risk Assessment
Conservative Therapy Option for UA/NSTEMI
Early Revascularization or PCI Not Planned

- **Antiplatelet therapy**
  - Aspirin
  - Clopidogrel
- **MONA + BAH (LMW or UFH)**
  - Morphine, Oxygen, Nitroglycerin, Aspirin + Beta Blocker, ACEI, Heparin
    (Morphine has only Class Ila recommendation due to increased mortality risk – CRUSADE)
- **Glycoprotein IIb/IIIa inhibitors**
  - Only in certain circumstances
  - Planning PCI, elevated troponin
- **Surveillance in hospital**
  - Serial ECGs
  - Serial cardiac markers

Invasive Therapy Option for UA/NSTEMI

- Coronary angiography and revascularization within 12 to 48 hours after presentation to ED
- For high-risk ACS
  - MONA + BAH (LMW or UFH)
  - Morphine, Oxygen, Nitroglycerin, Aspirin + Beta Blocker, ACEI, Heparin
    (Morphine has only Class Ila recommendation due to increased mortality risk – CRUSADE)
  - Antiplatelet therapy
    - Aspirin; thienopyridine (clopidogrel or prasugrel)
    - 20% reduction in death/MI/Stroke
    - PCI + BMS: at least 1 month, ideally 1 year
    - PCI + DES: at least 1 year
  - Glycoprotein IIb/IIIa inhibitor

ACCF/AHA Guidelines 2011 Focused Update
Early Invasive Strategies

High-risk patients with:
- Refractory ischemia
- Recurrent angina/ischemia
- Elevated cardiac biomarkers (T)
- New ST-segment depression
- New CHF or worsening MR
- High-risk on non-invasive testing
- LV dysfunction (EF <40%)
- Hemodynamic instability
- Sustained VT
- Diabetics with single vessel disease
- Mild to moderate kidney disease
- PCI within 6 months, prior CABG high-risk score
- Not in low-risk women
**TACTICS: Primary Endpoint**

*Death, MI, Rehospitalized for ACS at 6 Months*

![Graph showing TACTICS: Primary Endpoint](image)

- **Conservative:**
  - 19.4% patients

- **Invasive:**
  - 15.9% patients

**O.R. 0.79**

**95% CI (0.62, 0.97)**

**P=0.025**

---

**Updated Meta-analysis: Mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>Deaths, n</th>
<th>Invasive</th>
<th>Conservative</th>
<th>Follow-up Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRISC-II</td>
<td>45</td>
<td>67</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>TRICS</td>
<td>3</td>
<td>9</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>TIMI-18</td>
<td>37</td>
<td>40</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>VINO</td>
<td>2</td>
<td>9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>RITA-3</td>
<td>102</td>
<td>132</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>ISAR-COOL</td>
<td>15</td>
<td>15</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

**Overall RR (95% CI)**

- **0.75 (0.63-0.90)**

---

**Favors Early Invasive Therapy**

**Favors Conservative Therapy**

---

**Invasive Strategy**

*Rationale for Early Catheterization*
TIMACS
Rates of death, MI, or stroke within 6 months according to GRACE risk level and HR (95% CI), early versus delayed invasive strategy

<table>
<thead>
<tr>
<th></th>
<th>Early (%)</th>
<th>Delayed (%)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low/Intermediate</td>
<td>7.6</td>
<td>6.7</td>
<td>1.12 (0.88–1.56)</td>
<td>0.48</td>
</tr>
<tr>
<td>High</td>
<td>13.9</td>
<td>21.0</td>
<td>0.65 (0.48–0.89)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*Low/Intermediate risk=GRACE score <140
High risk=GRACE score ≥140


CRUSADE Registry
Mortality Rates by Early Catheterization

<table>
<thead>
<tr>
<th>Modified PURSUIT Risk Category</th>
<th>Early Catheterization</th>
<th>No Early Catheterization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (n=4520)</td>
<td>0.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Moderate (n=4462)</td>
<td>1.1</td>
<td>2.5</td>
</tr>
<tr>
<td>High (n=9108)</td>
<td>3.9</td>
<td>8.6</td>
</tr>
</tbody>
</table>


Antithrombotic Therapy in ACS
Evolving Antiplatelet Therapies
CURE Study
Primary End Point: MI/Stroke/CV Death

Placebo + Aspirin (n=6303)
Clopogrel + Aspirin (n=6259)

20% Relative Risk Reduction


CREDO
Long-Term (1 Year) Benefits of Clopogrel in PCI Patients

MI, stroke, or death – ITT population

Placebo* Clopogrel*

11.5% 8.5%
P=0.02

* Plus ASA and other standard therapies


Primary Endpoint (MI/Stroke/CV Death) in Patients with Previous MI, IS, or PAD*
CHARISMA: "CAPRIE-like Cohort"

Placebo + ASA
Clopogrel + ASA

0 10 8 6 4 2 0

Primary Outcome Event Rate (%)

0 6 12 18 24 30

8.8% 7.3%

RRI: 17.1% (95% CI: 4.4%, 28.1%)
P<0.01

* Post hoc analysis

**TRITON – TIMI 38**

**CV Death, MI, Stroke**

- Clopidogrel
- Prasugrel

**PLATO: Kaplan-Meier Estimate of Time to First Primary Efficacy Event (Composite of CV Death, MI or Stroke)**

- Clopidogrel
- Ticagrelor

**Glycoprotein IIb/IIIa Inhibitors**

- Only indicated in highest risk UA/NSTEMI patients (dynamic changes on ECG, elevated biomarkers, electrical instability) and/or in whom early PCI is planned
- Abciximab is a choice if early angiography and PCI are planned
- Eptifibatide or tirofiban might be indicated when no PCI planned
- Initiate in conjunction with your cardiologist
- Discontinue anticoagulant therapy after PCI
- Use of glycoprotein IIb/IIIa inhibitors is on the decline
Antithrombotic Therapy in ACS

Emerging Therapies

Key Investigational Antithrombotic Drugs

- Factor Xa inhibitors
  - Rivaroxaban
  - Apixaban
- PAR-1 thrombin inhibitors
  - Vorapaxar
  - Atopaxar

RIVAROXABAN: ATLAS ACS 2 TIMI 51
Primary Efficacy Endpoint: CV Death / MI / Stroke

Placebo

Rivaroxaban
(bid dosage 2.5 mg bid and 5 mg bid)

Acute Coronary Syndromes:
From the Emergency Department to the Coronary Care Unit to the Office

**RIVAROXABAN: ATLAS ACS 2 TIMI 51**
Efficacy Endpoints: Very Low Dose 2.5 mg BID
Patients Treated with Aspirin + Thienopyridine

- **CV Death / MI / Stroke**
  - Estimated Cumulative Incidence (%)
  - Placebo: 4.2%
  - Rivaroxaban 2.5 mg BID: 10.4%
- **Continues: CV Death / MI / Stroke**
  - mITT
  - HR 0.84, p=0.04
  - HR 0.66, p<0.001
- **ITT**
  - HR 0.84, p=0.04
  - HR 0.66, p<0.001
- **NNT**
  - 71
  - 59


**RIVAROXABAN: ATLAS ACS 2 TIMI 51**
Treatment Emergent Fatal Bleeds and ICH

- **ICH: Intracranial hemorrhage**
  - Placebo: 0.2%
  - 2.5 mg Rivaroxaban: 0.4%
  - 5.0 mg Rivaroxaban: 0.4%


**Apixaban: APPRAISE-2 Trial**
Primary Outcome: CV Death, MI, Ischemic Stroke

- **Apixaban** 279 (7.5%)
- **Placebo** 293 (7.9%)
- HR 0.95; 95% CI 0.80-1.11; p=0.509

Apixaban: APPRAISE-2 Trial

TIMI Major Bleeding

Apixaban: 48 (1.3%)
Placebo: 18 (0.5%)
HR 2.59; 95% CI 1.50–4.46; p<0.001


TRACER: Vorapaxar in ACS Patients

Primary Endpoint – CV Death, MI, Stroke, Hospitalisation for Ischemia, Urgent Revascularisation

No. at risk
Placebo 6471 5846 5408 5121 3794 2291 795
Vorapaxar 6473 5897 5570 5199 3881 2318 832
HR (95% CI): 0.92 (0.85, 1.01)
P-value= 0.072


Secondary Endpoint – CV Death, MI, Stroke

No. at risk
Placebo 6471 5895 5575 5263 3922 2383 830
Vorapaxar 6473 5949 5684 5356 4023 2427 868
HR (95% CI): 0.89 (0.81, 0.98)
P-value= 0.018

Acute Coronary Syndromes:
From the Emergency Department to the Coronary Care Unit to the Office

**TRACER: Bleeding Outcomes**

**GUSTO Moderate/Severe**

<table>
<thead>
<tr>
<th>Group</th>
<th>2-year KM Rate</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>5.2%</td>
<td>3.39 (1.78, 6.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>7.2%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Intracerebral Hemorrhage**

<table>
<thead>
<tr>
<th>Group</th>
<th>2-year KM Rate</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0.24%</td>
<td>1.35 (1.16, 1.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>1.07%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


---

**ATOPAXAR in ACS Patients: LANCELOT-ACS**

**Incidence of CV Death, MI, or Stroke**

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence Rate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>4.4%</td>
<td></td>
</tr>
<tr>
<td>Active combined atopaxar 50mg QD</td>
<td>3.7%</td>
<td>0.19</td>
</tr>
<tr>
<td>Active combined atopaxar 100mg QD</td>
<td>4.1%</td>
<td>0.10</td>
</tr>
<tr>
<td>Active combined atopaxar 200mg QD</td>
<td>3.4%</td>
<td>0.05</td>
</tr>
</tbody>
</table>


---

**ATOPAXAR in ACS Patients: LANCELOT-ACS**

**Incidence of Any TIMI Bleeding**

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence Rate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>8.3%</td>
<td></td>
</tr>
<tr>
<td>Active combined atopaxar 50mg QD</td>
<td>8.3%</td>
<td>0.63</td>
</tr>
<tr>
<td>Active combined atopaxar 100mg QD</td>
<td>6.7%</td>
<td>0.30</td>
</tr>
<tr>
<td>Active combined atopaxar 200mg QD</td>
<td>8.0%</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Acute Coronary Syndromes:
From the Emergency Department to the Coronary Care Unit to the Office

**Acute Coronary Syndromes**

*Treatment of STEMI*

**Time to Treatment Is Critical in STEMI**

0.4 million discharges per year for STEMI in US

- **GOALS**
  - Time to reperfusion is a critical determinant of the extent of myocardial damage and clinical outcomes in patients with STEMI
  - Key factors in STEMI care are rapid, accurate diagnosis and keeping the encounter time to reperfusion as short as possible

*Effect of Door-to-Balloon Time on Mortality in Patients with STEMI*

- In-hospital mortality and door-to-balloon times; \( P \) for trend <0.001

Reproduced with permission from McNamara RL et al. *J Am Coll Cardiol.* 2006;47:2180-2186.
**Acute Coronary Syndromes:**  
*From the Emergency Department to the Coronary Care Unit to the Office*

**Door to Balloon (DTB)**  
*An Alliance for Quality Campaign*

**STRATEGIES ASSOCIATED WITH A SIGNIFICANT REDUCTION IN DTB TIME**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Mean reduction in door-to-balloon time, min*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Having emergency medicine physicians activate the cath lab</td>
<td>8.2</td>
</tr>
<tr>
<td>Having a single call to a central page operator activate the cath lab</td>
<td>13.8</td>
</tr>
<tr>
<td>Having the ED activate the cath lab while patient is still en route</td>
<td>15.4</td>
</tr>
<tr>
<td>Expecting staff to arrive at the cath lab within 20 minutes after page</td>
<td>19.3</td>
</tr>
<tr>
<td>Having an attending cardiologist always on site</td>
<td>14.6</td>
</tr>
<tr>
<td>Having staff in the ED and cath lab use and receive real-time feedback</td>
<td>8.6</td>
</tr>
</tbody>
</table>

*P<0.05 for all  

**2009 ACC/AHA STEMI/PCI Guidelines Focused Update**  
Pathway: Triage and Transfer for PCI in STEMI

**PCI vs Fibrinolysis**  
*Systematic Overview*
Acute Coronary Syndromes: From the Emergency Department to the Coronary Care Unit to the Office

Medical Therapy for STEMI Managed by Primary PCI

ASA
Anticoagulant
USN (Bival)
UFH (Bival)

Thienopyridine
Clopidogrel 600
Prasugrel 60

GP IIb/IIIa
Eptifibatide
Abciximab

Beta Blocker
IV q4h
Oral within 24h

Statin

Acute Coronary Syndromes

Anti-ischemic Effects Versus Bleeding Risk

Recent ACS Trials
Forging a New Paradigm for Upstream Management

ISCHEMIA: The traditional concern of the emergency physician
BLEEDING: Newer, important concern for the cardiologist
A novel issue for the emergency physician
Possible Relationship Between Bleeding and Mortality

![Diagram showing possible relationship between bleeding and mortality]

CURE: Life-Threatening Bleeding

<table>
<thead>
<tr>
<th></th>
<th>Placebo + ASA*</th>
<th>Clopidogrel + ASA*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 6303 (%)</td>
<td>n = 6259 (%)</td>
</tr>
<tr>
<td>Life-threatening Bleeding</td>
<td>1.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Fatal</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Causing 5 g/dL drop hemoglobin</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Hypotension requiring inotropic therapy</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Surgery required</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Causing hemorrhagic stroke</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Transfusion of ≥ 4 blood units</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Transfusion of ≥ 2 blood units</td>
<td>2.2</td>
<td>2.8</td>
</tr>
</tbody>
</table>

* In combination with standard therapy


TRITON TIMI 38

Bleeding Events – Safety Cohort (n=13,457)

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI Major Bleeds</td>
<td>0.0 (0%)</td>
<td>0.0 (0%)</td>
</tr>
<tr>
<td>Life-Threatening</td>
<td>0.0 (0%)</td>
<td>0.0 (0%)</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>0.2 (0.2%)</td>
<td>0.2 (0.2%)</td>
</tr>
<tr>
<td>Fatal</td>
<td>0.3 (0.3%)</td>
<td>0.3 (0.3%)</td>
</tr>
<tr>
<td>ICH</td>
<td>0.0 (0%)</td>
<td>0.0 (0%)</td>
</tr>
</tbody>
</table>

* In combination with standard therapy

Quality Outcomes in ACS

Mean 30-day Hospital Readmission Rates Following PCI: By Hospital Decile of Readmission

Acute Coronary Syndromes: From the Emergency Department to the Coronary Care Unit to the Office

**Hospitals**
Quality of Care for Heart Attack

<table>
<thead>
<tr>
<th>Percent of patients who received recommended care</th>
<th>Heart attack 30-day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% (best)</td>
<td>18</td>
</tr>
<tr>
<td>95% (good)</td>
<td>17</td>
</tr>
<tr>
<td>90% (average)</td>
<td>16</td>
</tr>
<tr>
<td>80% (at-risk)</td>
<td>15</td>
</tr>
<tr>
<td>75% (worst)</td>
<td>14</td>
</tr>
</tbody>
</table>

Data: IPRO analysis of data from CMS Hospital Compare.
Source: Commonwealth Fund National Scorecard on US Health System Performance, 2011.

**OPTIMAL MANAGEMENT OF ACS PATIENTS**
Reducing Risk of Hospital Readmissions

- Selection of antiplatelet medications should be made based on the following patient-specific considerations
  - Risk of major adverse ischemic events
  - Risk of bleeding complications
  - Likelihood of poor adherence to prescribed medications

**CONCLUSIONS**
Key Considerations for Clinical Management of ACS

- Need for differential diagnosis of the spectrum of ACS
- Fundamental aspects of management of acute chest pain
  - Elements for optimal early hospital care
  - The importance of risk stratification to guide practice decisions
    - Options: initial conservative or invasive strategy
    - If invasive strategy, rationale for early catheterization
  - The expanded field of existing antiplatelet treatment options
    - Clopidogrel, prasugrel, ticagrelor
- Emerging antiplatelet/anticoagulant therapies for ACS
  - Strong contender: very low dose rivaroxaban
- Standards of treatment for STEMI
- The need to balance anti-ischemic effects versus bleeding risk
- The growing importance of quality outcomes in ACS