Management of Acute Myocardial Infarction

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Vice Chairman, Department of Cardiovascular Medicine
Professor of Medicine
Spectrum of Acute Coronary Syndrome

ACC-AHA Guidelines

Class of Recommendation

- **I**: Intervention is useful and effective
- **IIa**: Evidence supportive; awaiting confirming data
- **IIb**: Evidence conflicts/opinions differ; neutral statement
- **III**: Intervention is not useful/effective and may be harmful
Management of Acute MI

- Initial evaluation
- Reperfusion therapy
- Adjunctive antithrombotic therapy
- Adjunctive medical therapy
- Complications
Management of Acute MI

- Initial evaluation
- Reperfusion therapy
- Adjunctive antithrombotic therapy
- Adjunctive medical therapy
- Complications
ACC-AHA STEMI Guidelines

Initial Management of Acute MI

Targeted history should be performed.

Targeted physical exam should be performed to assess extent and complications.

Neurologic examination should be performed to evaluate for prior or acute stroke prior to lysis.

12-lead ECG should be performed and shown to experienced physician within 10 min of arrival.

Antman EM. J Am Coll Cardiol 2008;51:210-47.
Initial Evaluation of Acute MI

Targeted History

- Prior coronary ischemia – stable or unstable
- Prior MI or coronary revascularization
- Description of chest discomfort, associated symptoms
- HTN, DM
- Possibility of aortic dissection
- Neurologic symptoms – TIA or CVA
- Risk factors for bleeding
Initial Evaluation of Acute MI

Targeted Physical Examination

- Airway, breathing, circulation
- Vital signs, general observation
- Systemic hypoperfusion
- JVD
- Pulmonary – CHF
- Cardiac – murmurs, gallops
- Pulses
- Signs of stroke
Acute MI - Risk Stratification

The GUSTO Pyramid - 30 Day Mortality Model

- Age (31%)
- Systolic Blood Pressure (24%)
- Killip Class (15%)
- Heart Rate (12%)
- MI Location (6%)
- Prior MI (3%)
- Diabetes (1%)
- Time-to-Rx (1%)
- Height (1.1%)
- Accel t-PA (0.8%)
- Prior CABG (0.8%)
- Smoker (0.8%)
- Weight (0.8%)
- HTN (0.6%)
- Age x Killip (1.3%)
- HX CV Disease (0.4%)

Lee et al. Circulation 1995;91:1659-1668
Management of Acute MI

- Initial evaluation
- Reperfusion therapy
- Adjunctive antithrombotic therapy
- Adjunctive medical therapy
- Complications
## Fibrinolytics: Placebo-Controlled Trials

### Meta-Analysis

<table>
<thead>
<tr>
<th>Agent</th>
<th>Trial</th>
<th>Deaths/Patients</th>
<th>Odds Ratio &amp; 95% CI</th>
<th>Odds Reduction &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptokinase</td>
<td>GISSI</td>
<td>495/4865</td>
<td>23% ± 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISAM</td>
<td>50/842</td>
<td>16% ± 18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISIS-2</td>
<td>471/5350</td>
<td>30% ± 5</td>
<td></td>
</tr>
<tr>
<td>Anistreplase</td>
<td>AIMS</td>
<td>32/502</td>
<td>50% ± 16</td>
<td></td>
</tr>
<tr>
<td>Alteplase</td>
<td>ASSET</td>
<td>182/2516</td>
<td>28% ± 9</td>
<td></td>
</tr>
<tr>
<td>Overall - Any Lytic</td>
<td>Pts &lt; 6 hrs</td>
<td>1230/14075</td>
<td>27% ± 3</td>
<td></td>
</tr>
</tbody>
</table>

Fibrinolysis for Acute MI

Electrocardiographic Criteria for Therapy
Pooled Analysis of Randomized Trials

<table>
<thead>
<tr>
<th>EKG</th>
<th>Odds Ratio &amp; 95% CI</th>
<th>Placebo</th>
<th>Lysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBB</td>
<td></td>
<td>23.6%</td>
<td>18.7%</td>
</tr>
<tr>
<td>ST↑ Anterior</td>
<td></td>
<td>16.9%</td>
<td>13.2%</td>
</tr>
<tr>
<td>ST↑ Inferior</td>
<td></td>
<td>8.4%</td>
<td>7.5%</td>
</tr>
<tr>
<td>ST↑ Other</td>
<td></td>
<td>13.4%</td>
<td>10.6%</td>
</tr>
<tr>
<td>ST↓</td>
<td></td>
<td>13.8%</td>
<td>15.2%</td>
</tr>
<tr>
<td>Other Abnorm</td>
<td></td>
<td>5.8%</td>
<td>5.2%</td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>2.3%</td>
<td>3.0%</td>
</tr>
</tbody>
</table>

Acute MI

Intracranial Hemorrhage Rates
Large-Scale Fibrinolytic Trials

Intracranial Hemorrhage (%)

- SK
- tPA
- rPA
- TNK
- nPA

GISSI-2: 0.30
ISIS-3: 0.30
GUSTO-1: 0.51
GUSTO-2: 0.37
GUSTO-3: 0.87
GUSTO-2: 0.91
ASSENT-2: 0.93
INTIME-2: 0.94

Cleveland Clinic AML
Fibrinolysis in Acute MI

Absolute Contraindications

- Any prior intracranial hemorrhage
- Intracranial neoplasm or vascular lesion (e.g. AVM)
- Ischemic stroke in prior 3 months
- Significant closed head or facial trauma in prior 3 months
- Active bleeding or diathesis (not menses)
- Suspected aortic dissection
Fibrinolysis in Acute MI

Relative Contraindications

- Uncontrolled HTN (BP > 180/110 mm) on presentation
- History of chronic, severe, uncontrolled HTN
- History prior CVA beyond 3 months, dementia, or intracranial pathology not covered in absolute contraindications
- Recent internal bleeding (within 2-4 wks)
- Traumatic or prolonged (>10 min) CPR
- Major surgery (within 3 weeks)
- Noncompressible vascular punctures
- Anticoagulant Rx with INR > 2-3
- Pregnancy
- Active peptic ulcer
### PCI vs Fibrinolysis for Acute MI

#### Pooled Analysis of 23 RCTs, 7739 Patients

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>N</th>
<th>Short-Term Outcome</th>
<th>Relative Risk &amp; 95% CI</th>
<th>PCI</th>
<th>Lysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptokinase</td>
<td>1837</td>
<td></td>
<td></td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>Fibrin-specific</td>
<td>5902</td>
<td></td>
<td></td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>re-MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptokinase</td>
<td>987</td>
<td></td>
<td></td>
<td>1%</td>
<td>10%</td>
</tr>
<tr>
<td>Fibrin-specific</td>
<td>5510</td>
<td></td>
<td></td>
<td>3%</td>
<td>6%</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptokinase</td>
<td>788</td>
<td></td>
<td></td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Fibrin-specific</td>
<td>5843</td>
<td></td>
<td></td>
<td>1%</td>
<td>2%</td>
</tr>
</tbody>
</table>

# On-Site Lysis vs Emergency Transfer for PCI

## Pooled Analysis of 5 RCTs - Death, MI, or Stroke

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Relative Risk &amp; 95% CI</th>
<th>PCI</th>
<th>Lysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maastricht</td>
<td>150</td>
<td></td>
<td>10.7%</td>
<td>18.7%</td>
</tr>
<tr>
<td>PRAGUE-1</td>
<td>200</td>
<td></td>
<td>7.9%</td>
<td>23.2%</td>
</tr>
<tr>
<td>Air-PAMI</td>
<td>137</td>
<td></td>
<td>8.5%</td>
<td>13.6%</td>
</tr>
<tr>
<td>DANAMI-2</td>
<td>1572</td>
<td></td>
<td>8.0%</td>
<td>13.7%</td>
</tr>
<tr>
<td>PRAGUE-2</td>
<td>850</td>
<td></td>
<td>8.4%</td>
<td>15.2%</td>
</tr>
<tr>
<td>Pooled</td>
<td>2909</td>
<td></td>
<td>8.3%</td>
<td>15.0%</td>
</tr>
</tbody>
</table>

AMI and Primary PCI - ZWOLLE Group

1791 Patients: Total Ischemic Time and Mortality


RR = 1.075 [1.008-1.15, p = 0.041] for each 30 min delay

p <0.001
ACC-AHA STEMI Guidelines

PCI vs Fibrinolysis in Acute MI

Primary PCI if available within 90 min

Fibrinolysis within 30 min if pt presents to hospital without PCI capability, unless pt can be transferred to undergo PCI within 90 min of first medical contact

Antman EM. J Am Coll Cardiol 2008;51:210-47.
Rescue PCI

Meta-Analysis of Randomized Trials

PCI vs Conservative Therapy

Wijeysundera HC. JACC 2007;49:422.

<table>
<thead>
<tr>
<th>Mortality</th>
<th>PCI</th>
<th>Control</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belenkie et al.</td>
<td>1/16</td>
<td>4/12</td>
<td>0.19 (0.02-1.47)</td>
</tr>
<tr>
<td>RESCUE</td>
<td>4/78</td>
<td>7/73</td>
<td>0.53 (0.16-1.75)</td>
</tr>
<tr>
<td>TAMI</td>
<td>3/49</td>
<td>1/59</td>
<td>3.61 (0.39-33.64)</td>
</tr>
<tr>
<td>RESCUE II</td>
<td>1/14</td>
<td>0/15</td>
<td>3.20 (0.14-72.62)</td>
</tr>
<tr>
<td>MERLIN</td>
<td>15/153</td>
<td>17/154</td>
<td>0.89 (0.46-1.71)</td>
</tr>
<tr>
<td>REACT</td>
<td>9/144</td>
<td>18/141</td>
<td>0.49 (0.23-1.05)</td>
</tr>
<tr>
<td>Total</td>
<td>33/454</td>
<td>47/454</td>
<td><strong>0.69 (0.46-1.05)</strong></td>
</tr>
</tbody>
</table>

Absolute risk reduction 3% (95% CI 0%-7%)
NNT 33
Test for heterogeneity: χ² 6.1 df 5 (p 0.30) I² 18%

<table>
<thead>
<tr>
<th>Heart Failure</th>
<th>PCI</th>
<th>Control</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RESCUE</td>
<td>1/78</td>
<td>5/73</td>
<td>0.19 (0.02-1.56)</td>
</tr>
<tr>
<td>TAMI</td>
<td>9/49</td>
<td>14/59</td>
<td>0.77 (0.37-1.63)</td>
</tr>
<tr>
<td>MERLIN</td>
<td>37/153</td>
<td>46/154</td>
<td>0.81 (0.56-1.17)</td>
</tr>
<tr>
<td>REACT</td>
<td>7/144</td>
<td>11/141</td>
<td>0.62 (0.25-1.56)</td>
</tr>
<tr>
<td>Total</td>
<td>54/424</td>
<td>76/427</td>
<td><strong>0.73 (0.54-1.00)</strong></td>
</tr>
</tbody>
</table>

Absolute risk reduction 5% (95% CI 0%-9%)
NNT 20
Test for heterogeneity: χ² 2.0 df 3 (p 0.57) I² 0%

<table>
<thead>
<tr>
<th>Reinfarction</th>
<th>PCI</th>
<th>Control</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAMI</td>
<td>7/49</td>
<td>10/59</td>
<td>0.84 (0.35-2.05)</td>
</tr>
<tr>
<td>MERLIN</td>
<td>11/153</td>
<td>16/154</td>
<td>0.69 (0.33-1.44)</td>
</tr>
<tr>
<td>REACT</td>
<td>3/144</td>
<td>12/141</td>
<td>0.24 (0.07-0.85)</td>
</tr>
<tr>
<td>Total</td>
<td>21/346</td>
<td>38/354</td>
<td><strong>0.58 (0.35-0.97)</strong></td>
</tr>
</tbody>
</table>

Absolute risk reduction 4% (95% CI 0%-9%)
NNT 25
Test for heterogeneity: χ² 2.7 df 2 (p 0.25) I² 27%
Early Revascularization in AMI and Shock

Mortality at 6 Months (%)

- Medical Therapy (n = 149)
- Revascularization (n = 151)

<table>
<thead>
<tr>
<th>Total</th>
<th>Age &lt;75 yr</th>
<th>Age &gt;75 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>63.1</td>
<td>65.0</td>
<td>56.3</td>
</tr>
<tr>
<td>50.3</td>
<td>44.9</td>
<td>79.2</td>
</tr>
</tbody>
</table>

- $p = 0.027$ for age-treatment interaction
- $p = 0.003$ for age-treatment interaction

Hochman JS et al. NEJM 1999;341:625.
ACC-AHA STEMI Guidelines

Rescue PCI for Acute MI

I  IIa  IIb  III

- Cardiogenic shock, age <75 yrs or severe CHF
- Hemodynamically compromising vent arrhythmias
- Cardiogenic shock, age ≥75 yrs
- Hemodynamic or electrical instability or persistent ischemic symptoms
- Failed lysis (<50% ST resolution) and moderate or large area at risk (anterior or large non-anterior)

Antman EM. J Am Coll Cardiol 2008;51:210-47.
**STEMI - Triage and Transfer for PCI**

### CAREESS in AMI Trial

<table>
<thead>
<tr>
<th>600 pts with STEMI &lt; 12 hrs</th>
<th>1059 pts with STEMI &lt; 12 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk – extensive ST changes, LBBB, Killip &gt; 2, prior MI, EF &lt;35%</strong></td>
<td><strong>High risk – extensive ST changes, Killip &gt; 2, HR &gt; 100 bpm</strong></td>
</tr>
</tbody>
</table>

**Reteplase (1/2 dose) + Abciximab**

- **Immediate transfer for PCI**
  - 85.6% PCI
  - Median 1.8 hrs

- **Transfer only for rescue PCI**
  - 30.3% PCI
  - Median 3 hrs

**Tenecteplase (full dose)**

- **Immediate transfer for PCI**
  - 84.9% PCI
  - Median 2.8 hrs

- **Transfer only for rescue PCI**
  - 67.4% PCI
  - Median 33 hrs

---

**DiMario et al. Lancet 2008;371:559.**

**Cantor et al. NEJM 2009;360:2705.**
CARESS in AMI Trial

Death, re-MI, Refractory Ischemia (%)

- Transfer: 4.4%
- Rescue: 2.3%
- Major Bleeding: Transfer 2.7%, Rescue 2.3%, p = 0.80

- p = 0.005

TRANSFER AMI Trial

Death, re-MI, Refractory Ischemia, CHF, Shock (%)

- Transfer: 11.0%
- Rescue: 7.4%
- Major Bleeding: Transfer 9.0%, Rescue 7.4%, p = 0.36

- p = 0.004


Cantor et al. NEJM 2009;360:2705.
Consider transfer of "non-high-risk" pts ASAP after lysis from hospitals without PCI facility to PCI-capable facility.

Transfer of "high risk" pts ASAP after lysis from hospitals without PCI facility to PCI-capable facility for "pharmacoinvasive" strategy.

Community STEMI system of care including transfer protocols.
Management of Acute MI

- Initial evaluation
- Reperfusion therapy
- Adjunctive antithrombotic therapy
- Adjunctive medical therapy
- Complications
Aspirin in Acute MI


Class I, LOE A:
Aspirin daily indefinitely after STEMI in all pts without true aspirin allergy. Initial dose – 165-325 mg. Maintenance dose – 75-162 mg.
Clopidogrel in STEMI

Cardiac Death, re-ML, Urgent Revascularization (%)

Placebo

Clopidogrel

Odds Ratio 0.80
(95% CI 0.65-0.97)
P=0.026

Death/MI/Occluded IRA (%)

Odds Ratio 0.64
(95% CI 0.53-0.76)
P<0.001

Sabatine MS et al. NEJM 2005; 352: 1179.
COMMIT Trial

Clopidogrel 75 mg qd vs. Placebo in Suspected AMI <24 Hrs
Primary PCI not planned, With or Without Lytic Reperfusion

D/re-MI/Stroke (%)

Placebo 10.1%
Clopidogrel 9.3%

9% relative risk reduction (2P=0.002)

Mortality (%)

Placebo 8.1%
Clopidogrel 7.5%

7% relative risk reduction (2P=0.03)

Days since randomization

TRITON – TIMI 38 Trial: Prasugrel vs Clopidogrel
13,608 Patients - ACS and PCI

### TRITON Trial

**STEMI Subgroup – 3534 Patients**

**2438 with Primary PCI, 1094 with Secondary PCI**

<table>
<thead>
<tr>
<th>Endpoint (% of patients)</th>
<th>Prasugrel (n = 1769)</th>
<th>Clopidogrel (n = 1765)</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 15 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary composite</td>
<td>6.5</td>
<td>9.5</td>
<td>0.68</td>
<td>0.002</td>
</tr>
<tr>
<td>CV death</td>
<td>1.4</td>
<td>2.4</td>
<td>0.61</td>
<td>0.047</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>4.9</td>
<td>7.0</td>
<td>0.70</td>
<td>0.011</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>0.4</td>
<td>0.9</td>
<td>0.43</td>
<td>0.06</td>
</tr>
<tr>
<td>Any death</td>
<td>1.6</td>
<td>2.6</td>
<td>0.62</td>
<td>0.45</td>
</tr>
<tr>
<td>Urgent TVR</td>
<td>1.3</td>
<td>1.9</td>
<td>0.66</td>
<td>0.13</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1.2</td>
<td>2.4</td>
<td>0.49</td>
<td>0.008</td>
</tr>
</tbody>
</table>

### ACC-AHA 2009 STEMI / PCI Update

#### Loading Doses of Thienopyridines in PCI

<table>
<thead>
<tr>
<th>I</th>
<th>IIa</th>
<th>IIb</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C</strong></td>
<td><strong>B</strong></td>
<td><strong>C</strong></td>
<td><strong>C</strong></td>
</tr>
</tbody>
</table>

- **Clopidogrel 300-600 mg as early as possible**
- **Prasugrel 60 mg as early as possible**
- **Prasugrel in pts with prior CVA or TIA**
- **For non-primary PCI with prior lysis:**
  - If after lysis and on clopidogrel, continue.
  - If after lysis without clopidogrel, load 300-600 mg clopidogrel

## Abciximab During Primary PCI for AMI

### Meta-Analysis of 3755 Patients in 6 RCT’s

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>p-value</th>
<th>Odds Ratio &amp; 95% CI</th>
<th>Abciximab Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stent (n = 2226)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0.12</td>
<td>3.8%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Re-MI</td>
<td>0.11</td>
<td>1.6%</td>
<td>2.6%</td>
</tr>
<tr>
<td>TVR</td>
<td>0.02</td>
<td>8.5%</td>
<td>11.6%</td>
</tr>
<tr>
<td>MACE</td>
<td>0.005</td>
<td>13.7%</td>
<td>19.1%</td>
</tr>
<tr>
<td><strong>Balloon (n = 1529)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0.13</td>
<td>3.0%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Re-MI</td>
<td>0.70</td>
<td>3.9%</td>
<td>3.6%</td>
</tr>
<tr>
<td>TVR</td>
<td>0.30</td>
<td>16.6%</td>
<td>18.6%</td>
</tr>
<tr>
<td>MACE</td>
<td>0.30</td>
<td>21.8%</td>
<td>23.9%</td>
</tr>
</tbody>
</table>

FINESSE Trial

Primary Composite Endpoint

Death, CHF, Card Shock, Late VF - 90 Days (%)

- Primary PCI (n = 806) - 10.7%
- Abciximab Facil PCI (n = 818) - 10.5%
- Abcix + Retep Facil PCI (n = 828) - 9.8%

P-values:
- Primary PCI vs. Abciximab Facil PCI: p = 0.55
- Abciximab Facil PCI vs. Abcix + Retep Facil PCI: p = 0.86
- Primary PCI vs. Abcix + Retep Facil PCI: p = 0.68
GP IIb/IIIa Inhibitors in Acute MI

- **Abciximab at time of primary PCI**
- **Eptifibatide or tirofiban at time of primary PCI**
- **Facilitated PCI – use of GP IIb/IIIa antagonists as preparatory strategy before arrival in cath lab – usefulness is uncertain.**

## Heparin for Acute MI

### Death

<table>
<thead>
<tr>
<th>Group</th>
<th>Heparin-Allocated</th>
<th>Control-Allocated</th>
<th>Odds Ratio &amp; 95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>t-PA</td>
<td>17/476 (3.6%)</td>
<td>20/468 (4.3%)</td>
<td>0.43</td>
</tr>
<tr>
<td>SK/APSAC</td>
<td>28/402 (7.0%)</td>
<td>28/389 (7.2%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Aspirin</td>
<td>30/622 (4.8%)</td>
<td>29/609 (4.8%)</td>
<td>2.0</td>
</tr>
<tr>
<td>No Aspirin</td>
<td>15/256 (5.9%)</td>
<td>20/248 (8.1%)</td>
<td>2.5</td>
</tr>
</tbody>
</table>

### Any Bleeding

<table>
<thead>
<tr>
<th>Group</th>
<th>Heparin-Allocated</th>
<th>Control-Allocated</th>
<th>Odds Ratio &amp; 95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>t-PA</td>
<td>114/476 (23.9%)</td>
<td>83/468 (17.7%)</td>
<td>0.43</td>
</tr>
<tr>
<td>SK/APSAC</td>
<td>85/402 (21.1%)</td>
<td>56/389 (14.4%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Aspirin</td>
<td>141/622 (22.7%)</td>
<td>97/609 (15.9%)</td>
<td>2.0</td>
</tr>
<tr>
<td>No Aspirin</td>
<td>58/256 (22.7%)</td>
<td>42/248 (16.9%)</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Mahaffey et al. AJC 77:551-6, 1996
Enoxaparin vs UFH for Fibrinolysis with STEMI
20,506 Patients, STEMI < 6 hrs, Lytic Eligible

Antman et al. NEJM 2006;354:1477.
OASIS-6

Fondaparinux vs Heparin or Placebo in STEMI
Efficacy by Stratum

OASIS-6 Investigators. JAMA 2006;295.
Fondaparinux vs Heparin in STEMI
Primary PCI Subgroup (N = 3768 pts)

<table>
<thead>
<tr>
<th></th>
<th>UFH (n=1898)</th>
<th>Fondaparinux (n=1890)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural heparin</td>
<td>100%</td>
<td>20.8%</td>
<td>-</td>
</tr>
<tr>
<td>Death or re-MI</td>
<td>93</td>
<td>114</td>
<td>N.S.</td>
</tr>
<tr>
<td>Severe bleeding</td>
<td>9</td>
<td>16</td>
<td>N.S.</td>
</tr>
<tr>
<td>Guide catheter thrombus</td>
<td>0</td>
<td>22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary complication</td>
<td>225</td>
<td>270</td>
<td>0.04</td>
</tr>
</tbody>
</table>

OASIS-6 Investigators. JAMA 2006;295.
Anticoagulant Therapy in Acute MI

**Anticoagulant Options**

- **Class I**
  - UF Heparin: 60 u/kg (max 4000 U), 12 U/kg-hr (max 1000 U/hr) x 48 hrs. Adjust aPTT to target 1.5-2.0 x control (50-70 sec).
  - Enoxaparin (if Cr <2.5 in men, <2.0 in women) for up to 8 days. Dose adjusted by age (< or ≥ 75 yrs) and renal function (CrCl < 30 mL/min).
  - Fondaparinux (if Cr <3.0) for up to 8 days. Initial 2.5 mg IV, then 2.5 mg SQ daily.
  - If pt undergoing PCI received fondaparinux, give additional anticoagulant with anti-IIa activity IV.

**Antman EM. J Am Coll Cardiol 2008;51:210-47.**
**Bivalirudin vs GP IIb/IIIa in AMI**

**Ischemic and Bleeding Endpoints**

- **MACE - % of Pts**
  - Heparin + GP IIb/IIIa (n = 1802) 5.5%
  - Bivalirudin (n = 1800) 5.5%
  - HR [95%CI] = 1.00 [0.75, 1.32]
  - \(P=0.98\)

- **Major Bleeding - % of Pts**
  - Heparin + GP IIb/IIIa (n = 1802) 8.4%
  - Bivalirudin (n = 1800) 5.0%
  - HR [95%CI] = 0.59 [0.45, 0.76]
  - \(P<0.0001\)
ACC-AHA 2009 STEMI / PCI Update

Bivalirudin in Primary PCI for STEMI

For patients proceeding to primary PCI who have been treated with aspirin and thienopyridine, either:

- Bivalirudin (with or without prior UFH treatment)
- For prior treatment with UFH, additional boluses of UFH to maintain therapeutic ACT, taking into account whether GP IIb/IIIa inhibitors used.

Management of Acute MI

- Initial evaluation
- Reperfusion therapy
- Adjunctive antithrombotic therapy
- Adjunctive medical therapy
- Complications
CAPRICORN Trial

Carvedilol After MI with LV Dysfunction

Endpoints to Mean 1.3 Yr Follow-Up (%)

- **Placebo (n = 984)**
  - Death: 15.3%
  - Re-MI: 5.8%
  - Death or Re-MI: 19.5%
  - p = 0.002

- **Carvedilol (n = 975)**
  - Death: 11.9%
  - Re-MI: 3.5%
  - Death or Re-MI: 14.3%
  - p = 0.031

# COMMIT Trial

## Metoprolol in Acute MI

### 45,852 Patients - Metoprolol 15 mg IV, 200 mg daily vs Placebo

###Endpoints (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Metoprolol</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-MI</td>
<td>2.0</td>
<td>2.5</td>
<td>0.001</td>
</tr>
<tr>
<td>VF</td>
<td>2.5</td>
<td>3.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Shock</td>
<td>5.0</td>
<td>3.9</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

###Mortality (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Metoprolol</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-MI</td>
<td>1.7</td>
<td>2.2</td>
<td>0.001</td>
</tr>
<tr>
<td>VF</td>
<td>2.2</td>
<td>2.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Shock</td>
<td>3.9</td>
<td>4.0</td>
<td>0.0002</td>
</tr>
<tr>
<td>Other</td>
<td>3.9</td>
<td>4.0</td>
<td></td>
</tr>
</tbody>
</table>

ACC-AHA STEMI Guidelines

Beta Blockers in Acute MI

- Oral beta blocker in first 24 hrs in patients without early contraindications*

- Patients with early contraindications* in first 24 hrs should be re-evaluated for 2° prevention

- IV beta blocker at presentation in patients with hypertension without early contraindications*

- IV beta blocker in patients with early contraindications*

Antman EM. J Am Coll Cardiol 2008;51:210-47.
Beta Blockers in Acute MI

Early Contraindications

- **Signs of heart failure**
- **Evidence of low output state**
- **Increased risk for cardiogenic shock**
  - Age > 70 yrs
  - SBP < 120 mm Hg
  - Pulse > 120 bpm or < 60 bpm
  - Increased time from onset symptoms
- **Other relative contraindications**
  - PR interval > 0.24 sec
  - 2º or 3º AV block
  - Active asthma or reactive airway disease
# ACE Inhibitors in Acute MI

## Pooled Analysis of Randomized Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Agent</th>
<th>N</th>
<th>Mortality Odds Ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During MI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISIS-4</td>
<td>Captopril</td>
<td>58,050</td>
<td></td>
</tr>
<tr>
<td>GISSI-3</td>
<td>Lisinopril</td>
<td>19,394</td>
<td></td>
</tr>
<tr>
<td>CONSEN II</td>
<td>Enalaprilat</td>
<td>6,090</td>
<td></td>
</tr>
<tr>
<td><strong>Post MI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAVE</td>
<td>Captopril</td>
<td>2,231</td>
<td></td>
</tr>
<tr>
<td>AIRE</td>
<td>Ramipril</td>
<td>2,006</td>
<td></td>
</tr>
<tr>
<td>TRACE</td>
<td>Trandolapril</td>
<td>1,749</td>
<td></td>
</tr>
</tbody>
</table>

Hennekens et al. NEJM 1996;335:1660.
RAAS Blockade in Acute MI

Therapy Beyond ACE-Inhibitors

Aldosterone Blockade

- RALES trial – spironolactone in Class III-IV CHF produced 24% relative risk reduction in mortality over 24 months
- EPHESUS trial – eplerenone post MI in pts with EF<40% and CHF or diabetes significantly reduced mortality and cardiac hospitalization

Angiotensin Receptor Blockers (ARBs)

- OPTIMAAL trial – mortality trended better with captopril than losartan after MI
- VALIANT – no difference in mortality between captopril, valsartan, or combination
RAAS Blockade in Acute MI

I  IIa  IIb  III

**A**

- Oral ACE-I in first 24 hr with anterior MI, EF<40% or CHF (unless SBP<100 mm or 30 mm below baseline)
- Oral ACE-I in first 24 hr in pts without anterior MI, EF<40% or CHF.
- ARB in pts intolerant of ACE-I with EF<40% or CHF
- IV ACE-I in first 24 hrs due to risk of hypotension.
- Long-term aldosterone blockade if EF<40% and CHF or DM, if adequate renal function and [K+] <5.0

**B**

**C**

---

Antman EM. 2004 STEMI Practice Guidelines
Calcium Blockers in Acute MI

Verapamil or diltiazem if beta blockers ineffective or contraindicated for ongoing ischemia or rapid atrial fibrillation or flutter (in pts without CHF, LV dysfunction or AV block)

Verapamil or diltiazem in pts with LV dysfunction or CHF

Nifedipine – immediate release form

Antman EM. 2004 STEMI Practice Guidelines
Management of Acute MI

- Initial evaluation
- Reperfusion therapy
- Adjunctive antithrombotic therapy
- Adjunctive medical therapy
- Complications
Complications of Acute MI

- Extension / Ischemia
- Arrhythmia
- Expansion / Aneurysm
- Acute MI
- Mechanical
- Heart Failure
- RV Infarct
- Pericarditis
- Mural Thrombus
Management of Acute MI

Indications for Invasive Hemodynamic Monitoring
Right Heart Catheterization (Swan-Ganz Catheter)

- Severe or progressive CHF that does not respond rapidly to therapy
- Suspected mechanical complication (VSD, free wall rupture, or papillary muscle rupture)
- Cardiogenic shock
- Progressive hypotension
- Hypotension unresponsive to fluid Rx
- Need for inotropic or vasopressor agents
- Persistent signs of hypoperfusion without CHF
Intra-Aortic Balloon Pump in Acute MI

Indications for IABP

- Unresponsive hypotension
- Cardiogenic shock not quickly reversed
- Low output state
- Recurrent ischemia with hemodynamic instability, poor LV function, large areas of myocardium at risk
- Refractory polymorphic VT
- Refractory pulmonary congestion

Useful as a bridge to revascularization and for support during recovery of extensive “stunned myocardium”
Acute MI - CHF and Shock

Hemodynamic Subsets