Management of Acute ST-Elevation MI (STEMI)

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Outline

- STEMI pathophysiology
- Treatment Options
  - Fibrinolytic
  - Primary PCI
  - Facilitated PCI
- 2004 ACC/AHA STEMI Guidelines

Spectrum of ACS (New Terminology)

Old term

Stable
Angina
Unstable
Angina
Non-
Q-wave MI
Q-wave MI

New term

Atherothrombosis
UA/NSTEMI
STEMI


Spectrum of Acute Coronary Syndromes

Acute Coronary Syndromes

Non-ST-segment Elevation ACS
ST-segment Elevation ACS (STEMI)

Unstable
Angina
NSTEMI

1.4 million discharges per year

50%
30%

American Heart Association: Heart Disease and Stroke Statistics—2004 Update

"Wavefront" Necrosis

CROSS SECTIONS OF LEFT VENTRICLE

Duration of Occlusion: 40 min. 3 h 24 h

= Necrosis
= Ischemic but viable
= Non-ischemic

Circulation 1977;56:786-94.

TIMI Risk Index = \[
\frac{HR \times (age/10)^2}{SBP}
\]

J Am Coll Cardiol 2004;44:783-9
Relative Speed and Magnitude of Patency

Fibrinolytic Nomenclature

Fibrinolytic Characteristics

Mechanism of Action of Fibrinolytic Therapy

Fibrinolytic Dosing

Fibrinogen Depletion and Bleeding
**Evolving Strategies in the Treatment of STEMI**

- 1990: SK vs. t-PA
- 1993: Accel. t-PA vs. SK
- 1997: GUSTO I
- 1999: GUSTO III
- 2001 & beyond: ASSENT 2

**GUSTO**

- GUSTO 5
- ASSENT 3

**Rationale For Combination Therapy**

**Fibrinolytic Plus GPIIb/IIIa Blocker**

- Potential for greater efficacy:
  - greater speed & extent of reperfusion
  - less microemboli downstream
  - less reocclusion & associated reinfarction
  - may improve procedural success in PCI
  - less death

- Potential for less bleeding:
  - reduced dose fibrinolytic

**ASSENT-2 Design**

- Equivalence trial
- STEMI ≤ 6 h
- n=16,500 pts
- ASA
- Heparin (aPTT 50-75s)
- 1:1 double-blind
- t-PA ≤ 100 mg/60 min
- TNK
- Combination Strategies
- Primary endpoint: All-cause mortality (30 days)

**ASSENT-2 Outcomes**

<table>
<thead>
<tr>
<th></th>
<th>TNK (n=8,461)</th>
<th>t-PA (n=8,488)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>6.18%</td>
<td>6.15%</td>
<td>NS</td>
</tr>
<tr>
<td>ICH</td>
<td>0.93%</td>
<td>0.94%</td>
<td>NS</td>
</tr>
<tr>
<td>Total bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>4.7%</td>
<td>5.9%</td>
<td>0.0002</td>
</tr>
<tr>
<td>Minor</td>
<td>21.8%</td>
<td>23.0%</td>
<td>0.055</td>
</tr>
<tr>
<td>Transfusions</td>
<td>4.3%</td>
<td>5.5%</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

**Evolving Strategies in the Treatment of STEMI**

- 1990: SK vs. t-PA
- 1993: Accel. t-PA vs. SK
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- 2001 & beyond: ASSENT 2

**Relative Speed and Magnitude of Patency**

- Lytic + 2b3a: 94% by 60 min.
- Lytic: 2 hour Door to Balloon

Adapted from Gibson CM. Am Intern Med. 1999;130:841-847.
GUSTO 5 – Study Design

16,588 patients with ST↑
Lytic eligible, < 6 h

- No Abciximab
- ASA
- 2 x 10 U bolus (30’)
  Reteplase
- 2 x 5 U bolus (30’)
  Reteplase

Standard Heparin:
5,000 U bolus followed by either
800 U/hr (pts < 80 kg) or
1,000 U/hr (pts ≥ 80 kg) infusion

Low-Dose Heparin:
60 U/kg bolus followed by a
7 U/kg/h infusion

1st endpoint: mortality at 30 days
2nd endpoint: clinical and safety events at 30 days

Primary Endpoint: 30 Day Mortality

- P=0.45 for superiority
- Non-Inferiority RR 0.95
  (95% CI, 0.84–1.08)

Standard Dose Reteplase (n=8260)
Abciximab + ↓ Dose Reteplase (n=8328)


GUSTO 5: 30-Day Mortality or 7-Day Non-Fatal Reinfarction

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>r-PA 10U + 10U</td>
<td>8.8% (n=8260)</td>
</tr>
<tr>
<td>r-PA 5U + 5U + abciximab</td>
<td>7.4% (n=8328)</td>
</tr>
</tbody>
</table>

P=0.0011

GUSTO 5: Intracranial Hemorrhage (ICH) By Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 75 yrs</td>
<td>0.5% (Standard Dose Reteplase)</td>
</tr>
<tr>
<td>&gt; 75 yrs</td>
<td>1.1% (Abciximab + ↓ Dose Reteplase)</td>
</tr>
</tbody>
</table>

P=0.27

*Significant treatment interaction for the age 75 dichotomy; P=0.033


Evolving Strategies in the Treatment of STEMI

<table>
<thead>
<tr>
<th>Year</th>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>SK vs. t-PA</td>
</tr>
<tr>
<td>1993</td>
<td>Accel. t-PA vs. SK</td>
</tr>
<tr>
<td>1997</td>
<td>t-PA vs. rPA</td>
</tr>
<tr>
<td>1999</td>
<td>rPA vs. TNK</td>
</tr>
<tr>
<td>2001 &amp; beyond</td>
<td>Combination Strategies</td>
</tr>
</tbody>
</table>

ASSENT-3 Trial Design

ST-Segment Elevation AMI (6095 patients)

150-325 mg Aspirin (daily)

Randomized

- Full-Dose TNK-IPA Plus Enoxaparin
- Full-Dose TNK-IPA Plus Abciximab
- Full-Dose TNK-IPA Plus Low-Dose Heparin
- Half-Dose TNK-IPA Plus Weight-Adjusted Heparin

Combination Therapy: Conclusions

- Results obtained with lytic-2b3a combination are consistent among trials (ASSENT 3 and GUSTO V)
- Modest reductions in reinfarction are obtained at the cost of a higher rate of major bleeding and transfusions, particularly in patients >75 years old
- ASSENT 3 results make a strong case for enoxaparin as an alternative to unfractionated heparin in conjunction with TNK

SJH Fibrinolytic Pathway

<table>
<thead>
<tr>
<th>CLINICAL ACTIVITY</th>
<th>DAY 1</th>
<th>DAY 2</th>
<th>DAY 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNK Protocol (ASA*) (150-200 mg嚼owed STAT, then 65-100 mg q6h)</td>
<td></td>
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</tr>
<tr>
<td>Enoxaparin/Heparin (enoxaparin protocol for most. If age&gt;75 and/or severe renal insufficiency, use heparin)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Metoprolol (5 mg IV q5 min, x3, then 50mg PO q6h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel (n* 324 mg chewed STAT, then 81-162 mg PO qd)</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

* if ASA allergic, then clopidogrel; if stented, clopidogrel added to aspirin

Meta-analysis: Primary PCI Superior to In-Hospital Fibrinolysis

<table>
<thead>
<tr>
<th>Death/Reinfarction/Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maastricht</td>
</tr>
<tr>
<td>8/101</td>
</tr>
<tr>
<td>23/59</td>
</tr>
<tr>
<td>14/75</td>
</tr>
<tr>
<td>0.58</td>
</tr>
</tbody>
</table>

P = 0.006


NORM-2: Primary PCI Door-to-Balloon time vs. Mortality

- N=27,000
- P < 0.000001
**DANAMI vs US AMI: Are We As Quick In The US?**

<table>
<thead>
<tr>
<th></th>
<th>Median Time (Min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DANAMI On Site 1° PCI</td>
<td>90 Min.</td>
</tr>
<tr>
<td>DANAMI Transfer 1° PCI</td>
<td>110 Min.</td>
</tr>
<tr>
<td>US AMI Transfer 1° PCI</td>
<td>198 Min.</td>
</tr>
</tbody>
</table>

**Door to Balloon Times Among Patients Transferred in NRMI 4**

- Door to Data: 50th: 8 Min., 25th: 4 Min., 75th: 16 Min.
- Cath Lab to Balloon: 50th: 39 Min., 25th: 29 Min, 75th: 53 Min.

Total Door to Balloon Time: 198 minutes (25th: 137; 75th: 281)

% of Patients with Door to Balloon Time < 90 Min.: 4.8%

Sample Size: 1,292; Time Period: October 2000 – September 2001

Gibson CM, 2002
NRMI 4 Transfer-In Annual Data Report 2002

**STEMI Treatment Options May Expand**

- **Fibrinolytic**
  - preferred if PCI cannot be performed within 90min
  - door-to-drug time <30 min
  - do not administer to asymptomatic patients whose initial symptoms began >24 hrs earlier

- **Primary PCI**
  - preferred in general (esp. if cardiogenic shock or other high-risk, >3hr since symptom onset, or lytic contraindicated)
  - door-to-balloon time <90 min
  - do not perform in asymptomatic patients >12 hrs after onset of STEMI if they are hemodynamically and electrically stable

- **Fibrinolytic (full dose)**
- **Fibrinolytic (half dose) + GPIIb/IIIa**
- **GPIIb/IIIa alone**

**2004 ACC/AHA Guidelines**

- **Fibrinolysis**
  - preferred if PCI cannot be performed within 90min
  - door-to-drug time <30 min
  - do not administer to asymptomatic patients whose initial symptoms began >24 hrs earlier

- **Primary PCI**
  - preferred in general (esp. if cardiogenic shock or other high-risk, >3hr since symptom onset, or lytic contraindicated)
  - door-to-balloon time <90 min
  - do not perform in asymptomatic patients >12 hrs after onset of STEMI if they are hemodynamically and electrically stable

  Choice of treatment based on predetermined, institution-specific, written protocol

**Large Ongoing Facilitated PCI Trials**

- **ASSENT 4**
  - N=4000
  - 1. TNK + PCI
  - 2. PCI alone

- **FINESSE**
  - N=3000
  - 1. Abciximab + rPA + PCI
  - 2. Abciximab + PCI
  - 3. PCI alone

**2004 ACC/AHA Guidelines**

- Combination Pharmacological Reperfusion
  - Abciximab + half-dose rPA or TNK

- May be considered for prevention of reinfarction in selected patients
  - age < 75 yrs
  - anterior location of MI
  - no risk factors for bleeding

- Do not give to patients aged >75 yrs due to increased risk of ICH
### 2004 ACC/AHA Guidelines

**Heparin with lytics**
- Bolus: 60 U/kg (max 4000 U)
- Infusion: 12 U/kg/hr (max 1000 U/hr)

**Enoxaparin with lytics**
- Acceptable alternative to heparin
- Patient must be <75yo
- Not for patients with severe renal dysfunction (CrCl<30)
- Dose: 30mg IV bolus, then 1 mg/kg SQ q12h until discharge

**Insulin infusion to normalize blood glucose is recommended during acute phase**
- ASA 162-325mg (chewed) initially, then 75-162mg daily (alternative: clopidogrel or warfarin w/ INR 2.5-3.5)
- Clopidogrel 75mg daily x 1-12mos if stent placed
- Warfarin if Afib, LV thrombus or severe LV dysfunction
- Beta blocker IV/PO
- ACE inhibitor orally within 24h (ARB if intolerant to ACEI)
- ACE-I + ARB if systolic heart failure
- Aldosterone blocker if EF<0.4 and symptomatic HF or DM
- Statin therapy on discharge (goal LDL substantially <100mg/dl)

### 2004 ACC/AHA Guidelines

**Meds to avoid**
- Avoid nitrates if phosphodiesterase inhibitor used for erectile dysfunction within 24hrs (48hrs for Cialis)
- Avoid routine IV magnesium in the absence of electrolyte deficits or torsade de pointes
- Avoid ibuprofen (blocks the antiplatelet effects of aspirin)
- Avoid diltiazem and verapamil if LV dysfunction
- Nifedipine immediate-release is contraindicated in all STEMI
- Avoid thiazolidinediones if NYHA Class III-IV HF
- Do not give hormone therapy de novo for secondary prevention
- Do not give antioxidant vitamins (E or C) for secondary prevention

### 2004 ACC/AHA Guidelines

**Adjuvant Meds**
- Insulin infusion to normalize blood glucose is recommended during acute phase
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