Primary PCI VS Thrombolysis in STEMI, Positional Statement

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Change in Approach to AMI

1990-2002

Acute MI
Lytic
Transfer for Cath with Lytic failure

2003-2011

Acute MI
“Facilitated” Lytic/LMWH
Transfer emergently all patients
**2007 focused update of the ACC/AHA STEMI guidelines**

![Diagram of STEMI treatment process]

**Goals**
- 5 min after symptom onset
- 1 min after dispatch
- 8 min within 8 min
- Prehospital fibrinolysis: EMS-to-injection within 30 min
- Total ischemic time: Within 120 min

*Golden Hour = First 60 minutes*

**Figure 1. Options for Transportation of STEMI Patients and Initial Reperfusion Treatment Goals**

Reperfusion or patients with STEMI can be accomplished by pharmacological fibrinolysis or catheter-based primary PCI approaches. The overarching goal is to keep total ischemic time within 120 minutes. Here are the options for transport and initial reperfusion treatment. Within this context, the following are points for the medical system (based on the needs of patient transport and the capabilities of the existing hospital):

- If EMS is capable of fibrinolysis and the patient qualifies for therapy, pre-hospital fibrinolysis should be started within 20 minutes of arrival of EMS to the scene.
- If EMS is not capable of administering pre-hospital fibrinolysis and the patient is transported to a non-PCI-capable hospital, the door-to-needle time should be within 30 minutes for patients for whom fibrinolysis is indicated.
- If EMS is capable of administering pre-hospital fibrinolysis, the patient is transported to a PCI-capable hospital, the EMS arrival to balloon time should be within 90 minutes.
- If PCI is to be performed at a non-PCI-capable hospital, it is appropriate to consider emergency pre-hospital transfer of the patient to a PCI-capable hospital for mechanical revascularization if:
  - Thrombosis in pump is not anticipated.
  - PCI can be initiated promptly within 90 minutes from initial arrival-time of the PCI-capable hospital.

**Reperfusion Therapy in STEMI**

- Improves survival by reestablishing blood flow within the occluded infarct-related artery
  - *Keeley NEJM 2007*

- Primary PCI is superior to fibrinolytic therapy when performed rapidly by expert teams
  - *Keeley Lancet 2003*

- Its effectiveness may be limited by delays in delivery
  - *Gugliano, Circ 2003*
Importance of Rapid Time to Treatment With Fibrinolysis in STEMI


PCI In-hospital Mortality vs Door to Balloon Time

Brodie BR, JACC 47, 2006
III. Timely Reperfusion

1. Time is Myocardium
2. Infarct Size is Outcome

- Symptom onset to hosp Arrival 2 hr
- Thrombolysis given, 2 ½ hr
- Lysis-induced reperfusion 3 ½ hr

- Extent of Myocardial Salvage
- Mortality Reduction

- Critical Time-dependent Period
- Time-Independent Period

Goal: Myocardial Salvage
Goal: Open Infarct-Related Artery


PCI is better than LYSIS!

Primary PCI vs Lysis for STEMI – Meta-analysis of 23 trials

Keeley, Lancet Jan 2003
Recent Influences of Practice
Salvage is Time Dependant

- Superiority of PPCI over fibrinolysis if Door-to-Balloon completed in a timely fashion
- Acknowledgement that Time Matters in PPCI
  - Recommendations for time to reperfusion updated

Mortality rates with primary PCI as a function of PCI-related time delay

Circle sizes = sample size of the individual study.

Solid line = weighted meta-regression.

For Every 10 min delay to PCI: 1% reduction in mortality difference towards lytics
*PPCI Better > Pre-Hospital Lysis > In-Hospital Lysis

The RIKS-HIA Registry
Consecutive pts admitted in 75 of 78 hospitals with CCUs in Sweden (N=26,206 STEMI)

Unadjusted Cumulative Mortality

- In-Hospital Thrombolysis
- Prehospital Thrombolysis
- Primary PCI

# at Risk
In-Hospital TL
Prehospital TL
Primary PCI
14260
2736
6030
12322
2691
5611
12100
2460
5807
11931
2442
5555

Days
Cumulative Mortality, %
0
5
10
15
20
15.9%
10.3%
7.6%

*Transfer for PCI is better than LYSIS! (In a timely manner)

Interhospital Transfer for PCI

- On-site Fibrinolysis
- Transfer for PCI

Mortality (%)

6.7 6.7
14 7
12.1 8.4
10 6.8
8.5
6.5

Vermeer F. Heart 1999:82:426
Widimsky P. Eur Heart J 2000:21:823
Grines CL. JACC 2002:39:1713
Widimsky P. Eur Heart J 2003:24:94
Andersen HR. NEJM 2003:348:173
Assessing Reperfusion Options for Patients with STEMI

- **STEP 1:** Assess time from symptom onset, risk of STEMI, risk of thrombolysis, time for transport to PCI lab
- **STEP 2:** Determine whether fibrinolysis or invasive strategy is preferred

<table>
<thead>
<tr>
<th>Fibrinolysis preferred if:</th>
<th>Invasive strategy preferred if:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early presentation (&lt;3 hours)</td>
<td>Skilled PCI lab with surgical backup available</td>
</tr>
<tr>
<td>Invasive strategy not an option</td>
<td>High risk (i.e. cardiogenic shock)</td>
</tr>
<tr>
<td>Delay to invasive strategy, (heavy traffics)</td>
<td>Contraindications to fibrinolysis</td>
</tr>
<tr>
<td></td>
<td>Late presentation (&gt;3 hours)</td>
</tr>
<tr>
<td></td>
<td>Diagnosis of STEMI is in doubt</td>
</tr>
</tbody>
</table>

*If presentation is <3 hours from onset and no delay to an invasive strategy, there is no preference for either strategy*

JACC 44: 671, 200
PCI post thrombolysis in STEMI:

- **Prehospital TL + immediate transfer**
  - CAPTIM

- **Rescue PCI for failed TL**
  - RESCUE, REACT

- **Delayed PCI before discharge**
  - Open artery hypothesis »
    - OAT SWISSI II

- **<24h post lysis ESC PCI GL 05**

- **Immediate post-lysis « facilitated PCI »**

PCI post thrombolysis in STEMI:

- **Following successful thrombolytic therapy**, patients should undergo **early angiography** and **PCI of their IRA**
  - **Defined: more than 50% reduction in ST elevation in 60 to 90 min post TL Rx**
  - **Defined: less than 24 hours post TL Rx**
PCI post thrombolysis in STEMI: RATIONALE

1. Risk of **reocclusion** high
2. Early angiographic **risk stratification**
3. High likelihood of **residual complex stenosis** despite successful TL Rx

Rescue PCI is better than Lysis!!

**REACT**: 6 month Primary composite

![Graph showing the comparison of Repeat Thrombolysis, Rescue PCI, and Conservative Management for death, MI, CVA, or severe heart failure at 6 months. The primary composite endpoint was significantly lower in the rescue PCI group compared with either the repeat thrombolysis group or the conservative management group.](chart.png)

- The primary composite endpoint of death, MI, CVA or severe heart failure at 6 months was significantly lower in the rescue PCI group compared with either the repeat thrombolysis group or the conservative management group.

*Presented at AHA 20*
PCI is better than Facilitated PCI
Facilitation Enhances Pre – But not Post PCI TIMI-3 Flow: Meta-Analysis of 17 Trials Randomizing 4,504 Patients

Keeley and Grines, Lancet 2006;367:579

ASSENT- 4 PCI Trial: Mortality at 30 days

Analysis of mortality at 30 days (%) p = 0.04

*The primary endpoint of mortality was higher in the TNK + PCI treatment group compared with the PCI alone group (6.0% vs 3.8%, p=0.04) at 30 days

http://www.clinicaltrial.results.org/
### Primary, secondary and bleeding end points in FINESSE

<table>
<thead>
<tr>
<th>End points</th>
<th>Primary PCI (%)</th>
<th>Abciximab +PCI (%)</th>
<th>(abcixima/ reteplase) -facilitated PCI (%)</th>
<th>p, combined +PCI vs primary PCI</th>
<th>p, combin +PCI vs abciximab-facilitate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point*</td>
<td>10.7</td>
<td>10.5</td>
<td>9.8</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>4.5</td>
<td>5.5</td>
<td>5.2</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Complications of MI</td>
<td>8.9</td>
<td>7.5</td>
<td>7.4</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>4.5</td>
<td>5.5</td>
<td>5.2</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TIMI major bleeding</td>
<td>2.6</td>
<td>4.1</td>
<td>4.8</td>
<td>0.025</td>
<td>NS</td>
</tr>
<tr>
<td>TIMI minor bleeding</td>
<td>4.3</td>
<td>6.0</td>
<td>9.7</td>
<td>&lt;0.001</td>
<td>0.006</td>
</tr>
</tbody>
</table>

**FINESSE**

- Best trial available
- Slow enrollment, therefore underpowered
- 40% spoke hospitals with D-B 155 min
- Increase bleeding (are all regimens =?)
- Signals in Ant MI, High Risk, < 3 hrs
Immediate PCI is better than LYSIS +/- Delayed PCI!
### In the Current Era, Immediate PCI After Thrombolysis is Safe

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Randomized</th>
<th>PCI Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRACIA-I</td>
<td>500</td>
<td>Cath within 24 hrs vs conservative</td>
<td>TIMI-3 in 97% ↓ revasc ($p=.001$) ↓ death/MI ($p=.07$) ↓ rehoop ($p=.005$)</td>
</tr>
<tr>
<td>(Lancet 2004;364:1045)</td>
<td>12 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIAM-III</td>
<td>163</td>
<td>Stent within 6 hrs vs delayed (2 wks)</td>
<td>TIMI-3 in 97.6% ↑ EF ($p=.018$) ↓ Ischemia</td>
</tr>
<tr>
<td>(JACC 2003;42:634)</td>
<td>6 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAPITAL AMI</td>
<td>170</td>
<td>Immed. PCI (3 hrs) vs conservative care</td>
<td>↓ re-MI 5.8 vs 14.6% ↓ Ischemia 8.1 vs 20.7% ↓ MACE 11.6 vs 24.4%</td>
</tr>
<tr>
<td>(JACC 2005;46:417-24)</td>
<td>High risk</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SIAM 3

**Event Free Survival**

*(Death, Re-infarction, Intervention, Ischemia)*

![Graph showing event free survival](image-url)
Pharmacoinvasive (Facilitated) PCI is better than Lytic + Rescue PCI
CARESS: Treatment summary

ASA 300-500 mg iv
2 x 5 U bolus (30') Replase
UFH (40 U/kg (max 3000); 7 U/kg/h)
Abciximab 0.25 mg/kg bolus
0.125 μg/kg/min x 12 h

FACILITATED PCI
40 U/kg Heparin Bolus (max. 3,000 U) + 7 U/Kg/h during transfer
PCI ACT adjusted to 200-250° and heparin stopped after procedure

MEDICAL TREATMENT/ RESCUE
40 U/kg Heparin Bolus (max. 3,000 U) + 7 U/Kg/h for 24 hours
In case of Rescue PCI ACT adjusted to 200-250° and heparin stopped after procedure

Clopidogrel Started in the Cath Lab and Maintained for 1-12 months only after Stenting up to Nov 2005 (514 Pts, 82%)

Primary Outcome at 30 days

Death, re-ML, refractory ischaemia

<table>
<thead>
<tr>
<th>FACILITATED PCI</th>
<th>Med. Treatment/Rescue</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n= 294</td>
<td>n= 298</td>
<td></td>
</tr>
<tr>
<td>Death, re-ML, refract isch (adjudicated)</td>
<td>12 (4.1)</td>
<td>33 (11.1)</td>
</tr>
<tr>
<td>Death, re-ML, refract isch (unadjudicated)</td>
<td>15 (5.1)</td>
<td>42 (14.1)</td>
</tr>
</tbody>
</table>
Comments on CARESS

- Again use of potent antiplatelet agent (abciximab), platelets inactivated at time of PCI, (In ASSENT IV < 10% use!!)
- Bleeding reassuring as pts > 75yo excluded
- Median time from TL Rx to PCI 212 min

Post-Lysis PCI studies

\[ N = 1436 \]
**‘High Risk’ ST Elevation MI within 12 hours of symptom onset**

- TNK + ASA + Heparin / Enoxaparin + Clopidogrel

**“Pharmacoinvasive Strategy”**
- Urgent Transfer to PCI Centre

**“Standard Treatment”**
- Assess chest pain, ST resolution at 60-90 minutes after randomization

**PCI Centre**
- Cath / PCI within 6 hrs regardless of reperfusion status
- Cath and Rescue PCI ± GP IIb/IIIa Inhibitor
- Elective Cath ± PCI > 24 hrs later

**Repatriation of stable patients within 24 hrs of PCI**

* ST segment resolution < 50% & persistent chest pain, or hemodynamic instability

Randomization stratified by age (≤75 vs. > 75) and by enrolling site

**Primary Endpoint: 30-Day Death, re-MI, CHF, Severe Recurrent Ischemia, Shock**

**Preliminary**

- % of Patients
- Days from Randomization
- n=496
- n=508

**OR=0.537 (0.368, 0.783); p=0.0013**
Summary

- "Pharmacoinvasive Strategy" of routine early PCI within 6 hrs after thrombolysis is associated with a 6% absolute (46% relative) reduction in the composite of death, re-MI, recurrent ischemia, HF and shock

- is not associated with any increase in transfusions, severe bleeding despite high use of GP IIb/IIIa in PCI

- Benefit seen despite high cath/PCI rates in Standard Treatment group (including ~40% rescue PCI)

NORDISTEMI

Facilitated PCI for long-distance transfers

266 patients with acute STEMI < 6 hours
Expected time delay to PCI > 90 min

ASA 300 mg, TNK, Clopidogrel 300 mg
Enoxaparin 30 mg IV + 1 mg/kg SC

Immediate transfer for PCI (mean 130 min) vs
Ischemia-driven transfer for rescue PCI (mean 5.5 days)

86% radial access

JACC doi:10.1016/j.jacc.2009.08.007
Thrombolysis catching up with PCI in STEMI, especially in lower-risk patients

- Observational prospective database (July 2007 to December 2009) of patients with STEMI admitted to 73 Belgian hospitals: 25 hospitals had PCI facilities and 48 hospitals did not.
- Outcome was in-hospital mortality, and patients were stratified into low, intermediate, and high risk according to TIMI score.
- Arch Intern Med 2011; 171: 544-9
Thrombolysis catching up with PCI in STEMI, especially in lower-risk patients

• There were 5,295 eligible patients in the registry, 4,574 (86.4%) were treated with primary PCI and 721 (13.6%) received thrombolysis. Of those receiving thrombolysis, 603 (83.6%) underwent subsequent invasive evaluation. TIMI risk scores were low in 1,934, intermediate in 2,382, and high in 979.

Arch Intern Med 2011; 171: 544-9

Thrombolysis catching up with PCI in STEMI, especially in lower-risk patients

• In-hospital mortality was similar in the two groups, 5.9% (PCI) vs. 6.6%, and after adjustment for baseline risk profile the difference was significant only in the high-risk group.
The authors conclude that in current practice

- **thrombolysis is normally followed by invasive intervention**, immediate PCI only has an advantage for in-hospital mortality in patients at high risk.

- **Early thrombolysis followed by later invasive evaluation** seems to be superior to delayed PCI when door to balloon time is over 60 minutes.

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In summary: European GL

- STEMI within 12 hours after onset of symptoms
  - Patient presenting in a hospital with PCI
  - Patient presenting in a hospital without PCI
    - ≥ 3 - 12 hours
    - < 3 hours
  - Immediate transfer

- Thrombolysis
  - Failed
  - Successful
    - PCI ≤ 24 hours available
    - PCI ≥ 24 hours not available
  - Pre-discharge ischaemia

- Primary PCI
- Rescue PCI
- Post thrombolysis PCI
- Ischaemia-guided PCI
(From 2007 STEMI Update, Section 5)

• 1. Facilitated PCI using regimens other than full-dose fibrinolytic therapy might be considered as a reperfusion strategy when all of the following are present:
  a. Patients are at high risk,
  b. PCI is not immediately available within 90 minutes,
  c. Bleeding risk is low (younger age, absence of poorly controlled hypertension, normal body weight).
(Level of Evidence: C)

2009 Joint STEMI/PCI Focused Update

• Class IIa
  1. It is reasonable for high-risk* patients who receive fibrinolytic therapy as primary reperfusion therapy at a non–PCI-capable facility to be transferred as ASAP to a PCI-capable facility where PCI can be performed either when needed or as a pharmaco-invasive strategy.

  Consideration should be given to initiating a preparatory antithrombotic (anticoagulant plus antiplatelet) regimen before and during patient transfer to the catheterization laboratory (14,15).

(Level of Evidence: B)
Latest European and US STEMI Guidelines Compared and Contrasted

- Both Discourage Facilitated Reperfusion
- Both Endorse Newer Anticoagulants
- Both note it would be "reasonable" to perform early angiography for risk stratification in patients not undergoing primary PCI, but the ESC goes a step further by supporting routine angiography (with PCI if indicated) 3 to 24 hours after successful fibrinolysis based on several recent studies, including the GRACIA trials.

What conclusions can we make!

- PCI centers should do PCI (in a timely manner <90 min)
- Short Distance Transfer Pts should have PCI (in a timely manner <120?)
- Pharmcoinvasive PCI is an excellent choice for Pts with expected delay!!
- The ideal regimen and timing of PCI remain unclear!
See you in EGYPT COMBATMI
Heart Attack 2012/
6th Acute Cardiac Care Course

Cairo, April 11-12, 2012