Myocardial Infarction In 2007

Dr. Yahya Kiwan
The term of myocardial infarction should be used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia.
Under these conditions any of the following criteria meets the Diagnosis of myocardial infarction.

1- Detection of rise and /or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile URL together with evidence of myocardial ischemia with at least one of the following:

1- Symptoms of ischemia.
2- ECG changes indicative of new ischemia (new ST-T changes or new LBBB).
3- Development of pathological Q wave in the ECG.
4- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities.
2- Sudden *unexpected* cardiac death involving cardiac arrest often with *symptoms* suggestive of myocardial ischemia, and accompanied by presumably new *ST elevation* or *new LBBB*, and/or evidence of *fresh thrombus* by coronary angiography and/or autopsy. *But* death occurring before blood samples could be obtained or at time *before* the appearance of cardiac biomarkers in the blood.
MI definition Cont...

3-For **PCI** in patients with **normal baseline troponin values**, elevation of biomarkers are above the 99th percentile **URL** are indicative of per procedural myocardial necrosis. By convection increase of biomarkers **greater than 3x 99th URL** p have been designated as defining **PCI related myocardial infarction**. A subtype related to documented **stent thrombosis** is recognized.
MI definition Cont…

4- For **CABG** in patients with normal baseline troponin values, elevation of biomarkers are above the 99th percentile URL are indicative of per procedural myocardial necrosis. By convection increase of **biomarkers** greater than 5x 99th URL plus either **Q waves** or **new graft or native coronary artery occlusion**, or **imaging evidence of new loss of viable myocardium** have been designated as defining **CABG –related myocardial infarction**.

5- **Pathological** findings of an acute myocardial infarction.
Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior myocardial infarction:

- Development of new pathological Q waves with or without symptoms.
- Imaging evidence of region loss of viable myocardium that is thinned and fails to contract in the absence of non ischemic cause.
- Pathological findings of healed or healing myocardial infarction.
Table 1  Clinical classification of different types of myocardial infarction

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Spontaneous myocardial infarction related to ischaemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2</td>
<td>Myocardial infarction secondary to ischaemia due to either increased oxygen demand or decreased supply, e.g. coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension, or hypotension</td>
</tr>
<tr>
<td>Type 3</td>
<td>Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischaemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood</td>
</tr>
<tr>
<td>Type 4a</td>
<td>Myocardial infarction associated with PCI</td>
</tr>
<tr>
<td>Type 4b</td>
<td>Myocardial infarction associated with stent thrombosis as documented by angiography or at autopsy</td>
</tr>
<tr>
<td>Type 5</td>
<td>Myocardial infarction associated with CABG</td>
</tr>
</tbody>
</table>
Any Evidence Of Pre Hospital Fibrinolysis (PHF)?

Acute Myocardial Infarction (AMI) is the prototype of a real emergency, and both efficacy and speed are necessary for effective management.

The most frequent complication of AMI is sudden death which still occur within the first hour after symptoms onset.

Thrombolytic therapy has been shown to reduce early and long term mortality about 20%.

Reducing the time to thrombolysis must therefore be the main objective of pre hospital treatment of AMI.
Data from a meta-analysis of 23 randomized controlled trials showing reduction in: 

Death, Recurrent MI & Strokes with primary PCI.
Primary PCI vs. Fibrinolysis for STEMI Meta-Analysis of 23 Trials (n = 7739)

Short-Term Clinical Events (4–6 weeks)

CVA = cerebral vascular accident (stroke), ICH = intracranial hemorrhage.
These data leave little room for doubt in experienced centers. **But what should we do in hospitals in which a cath lab is not available 24 hours of the day?** The important message of reperfusion therapy is that **time is muscle**, and **muscle is survival**...
Clinical Evidence

✦ **France**
  CAPTIM Study

✦ **North America Centre**
  Thrombolytic Regimen 3+ Trial

✦ **Sweden**
  (RIKS-HIA)
CAPTIM Study

French trial comparing pre hospital thrombolysis to primary angioplasty.

There is no difference between the two strategies in term of primary end points.

33% of patient had prehospital thrombolysis followed by fast angioplasty.
Prehospital Lysis vs. 1° PCI for STEMI: Impact of Time in CAPTIM

![Bar Chart]

<table>
<thead>
<tr>
<th></th>
<th>Prehospital Lysis (N=419)</th>
<th>Primary PCI (N=421)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2.2</td>
<td>5.7</td>
</tr>
<tr>
<td>Shock</td>
<td>0</td>
<td>3.6</td>
</tr>
<tr>
<td>Death</td>
<td>5.9</td>
<td>3.7</td>
</tr>
<tr>
<td>Shock</td>
<td>0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Time from sx to rand:
- < 2 h (n = 460)
- ≥ 2 h (n = 374)

NS = not significant, sx = symptoms.
Thrombolytic Regimen 3+ Trial

North America Centre.

Prospective observational comparative cohort of all patients with STEMI encountered during the assessment of the safety and efficacy of a new Thrombolytic Regimen 3+ enrollment period.

Assessment:-
- Time-to-Treatment.
- ECG analysis.
- Peak Ck.
- Inhospital clinical events.
- Mortality.
Result

During 22 month study period.

1095 patients with STEMI were admitted to hospital.

46% (119/258) of eligible patients received PHF (<0r=6 hours of symptoms onset by ambulance).

Time-to-treatment was reduced with PHF versus Inhospital (1 hour 43 minutes vs (2 hours 38 minutes, p<.001)
Prehospital patient achieved more favorable outcome

- **Peak CK** (1413 vs 1549) ..... $P = .122$

- **Q wave** at discharge (56.3% vs 70.7%,) $P = .003$

- **Intracranial hemorrhage** (0% vs .8%) ... $p < 1.0$

- **In hospital mortality** for PHF versus IHP was 3.4% versus 4.8% ($p = .627$)
Conclusion

Feasibility and applicability of PHF was demonstrated with substantial reduction in treatment delay and favorable clinical outcomes.
Design:

A prospective observation cohort study of 26205 consecutive STEMI patients in the register of information and knowledge about Swedish Heart Intensive Care Admission (RIKS-HIA). Who received reperfusion therapy within 15 hours of symptoms onset.
Interventions

7084 patients.. Primary PCI.

3078 patients.. Prehospital thrombolysis (PHT).

16043 patients.. In hospital thrombolysis (IHT).

Main outcomes Measures:-

- Mortality
- Re infarction
- Readmission
## Result:

<table>
<thead>
<tr>
<th></th>
<th>Primary PCI</th>
<th>PHT</th>
<th>IHT</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td>4.9%</td>
<td>7.6%</td>
<td>11.4%</td>
</tr>
<tr>
<td>1 year</td>
<td>7.6%</td>
<td>10.3%</td>
<td>15.9%</td>
</tr>
</tbody>
</table>
Cont...

PHT predicted a lower mortality than IHT at 30 days and at 1 year.

Beyond 2 hours treatments delay, the observed mortality reduction with PHT tended to decrease while the benefit with primary PCI remain regardless of time delay.

Primary PCI was also associated with shorter hospital stay and less re infarction than either PHT or IHT.
Conclusion:

In unselected patients with **STEMI**, primary **PCI**, which compared favorably with IHT and **PHT**, was associated with reduced duration of hospital stay, readmission, reinfarction, and mortality.
Selection of Reperfusion Strategy

- Fibrinolysis Generally Preferred
  - Early presentation (<3 hours from symptom onset and delay to invasive strategy)
  - Invasive strategy not an option (catheterization lab not available, no vascular access, lack of skilled PCI lab)
  - Delay to invasive strategy DB—DN >1 hour; medical contact to balloon <90 minutes
- Invasive Strategy Generally Preferred
  - Skilled PCI lab available with surgical back-up (medical contact to balloon <90 minutes)
  - High risk from STEMI (cardiogenic shock, Killip class ≥3)
  - Contraindication to lysis (including increased bleeding/ICH risk)
  - Late presentation (>3 hours)
  - Diagnosis in doubt

ICH = intracranial hemorrhage.
What New Medication?

Targets for Therapy in STEMI
Clopidogrel...

- Clarity Study...
- Commit- 2 study.....
CLARITY
(addition of Clopidogrel to Aspirin and Fibrinolytic Therapy for Myocardial Infarction with ST-Segment Elevation)
NEJM March 2005
3491 patients, 18-75 y.o., who presented within 12 hours after the onset of an STEMI.

Randomly assigned them to receive Clopidogrel (300 mg loading dose followed by 75 mg daily dose) or a placebo.

Patient also received fibrinolytic therapy, Aspirin and when appropriate heparin and were scheduled to undergo angiography within 48-192 hours after the start of the study medication.
The rates of the primary end point were 21.7% in the placebo group and 15% in the clopidogrel group, representing an absolute reduction of 6.7% in the rates and a 36% reduction in the odds of the end point with clopidogrel therapy (95 CI, 24-47%; P <0.001).

By 30 days, clopidogrel therapy reduced the odds composite end point of death from cardiovascular causes, recurrent MI, or recurrent ischemia leading to the need for urgent revascularization by 20% (from 14.1-11.6%.P=o.03). The rates of major bleeding ad intra-cranial hemorrhage were similar in the two groups.
CLARITY-TIMI 28

Trial Design: CLARITY-TIMI 28 was a randomized, double-blind trial of clopidogrel (300 mg load, 75 mg/day; n=1752) or placebo (n=1739) in patients with ST elevation MI treated with an initial medical management strategy. Primary endpoint was an occluded infarct-related artery (TIMI Flow Grade 0/1) on angiography or death or MI by time of angiography.

Primary Endpoint

| OR 0.64 | p<0.001 |

CV death, MI or Re-ischemia → Urgent revasc by 30 days

| p=0.03 |

Results

- Median time to angiography 94 hours
- Primary endpoint ↓ in clopidogrel group (Figure), driven by reduction in infarct-artery occlusion (11.7% vs 18.4%, OR 0.59, p<0.001)
- TIMI myocardial perfusion grade 3 ↑ in clopidogrel group (55.8% vs 51.2%, OR 1.21, p=0.008)
- CV death, MI or re-ischemia leading to urgent revascularization by 30 days ↓ in clopidogrel group (Figure)
- No difference in TIMI major bleed through day after angiography (1.3% for clopidogrel vs 1.1% for placebo, p=0.64)

Conclusions

- Among patients with ST elevation MI treated with an early medical management strategy, use of clopidogrel was associated with a reduction in infarct-artery occlusion, without increase in major bleed

www.cardiosource.com

COMMIT/CCS-2: Clopidogrel and Metoprolol in Myocardial Infarction Trial\textsuperscript{1,2}
# Components of Primary Endpoint

<table>
<thead>
<tr>
<th>Events</th>
<th>Clopidogrel (n=22,958)</th>
<th>Placebo (n=22,891)</th>
<th>Odds ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1,728 (7.5%)</td>
<td>1,846 (8.1%)</td>
<td>Clopi better</td>
</tr>
<tr>
<td>Non-fatal Re-MI</td>
<td>273 (1.2%)</td>
<td>330 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Non-fatal stroke</td>
<td>126 (0.5%)</td>
<td>142 (0.6%)</td>
<td>Placebo better</td>
</tr>
<tr>
<td>ALL COMBINED</td>
<td>2,125 (9.3%)</td>
<td>2,311 (10.1%)</td>
<td>9% SE 3 reduction</td>
</tr>
</tbody>
</table>

(p = 0.002)
**COMMIT: Clopidogrel Decreased Re-Infarction**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Clopidogrel (n=22,958)</th>
<th>Placebo (n=22,891)</th>
<th>Odds ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal MI</td>
<td>209 (0.9%)</td>
<td>223 (1.0%)</td>
<td>Clopi better</td>
</tr>
<tr>
<td>Non-Fatal MI</td>
<td>273 (1.2%)</td>
<td>330 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>ALL COMBINED</td>
<td>482 (2.1%)</td>
<td>553 (2.4%)</td>
<td>Placebo better</td>
</tr>
</tbody>
</table>

13% SE 6 Reduction, p=0.02
Effects of Clopidogrel on Death, Re-MI, or Stroke by Time Delay and Fibrinolytic Use\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Baseline Features</th>
<th>Clopidogrel (n=22,958)</th>
<th>Placebo (n=22,891)</th>
<th>Odds ratio &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Delay (hrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6</td>
<td>776 (9.3%)</td>
<td>904 (10.9%)</td>
<td>Clopi better</td>
</tr>
<tr>
<td>7-12</td>
<td>672 (9.7%)</td>
<td>735 (10.7%)</td>
<td>Placebo better</td>
</tr>
<tr>
<td>13-24</td>
<td>666 (8.8%)</td>
<td>666 (8.7%)</td>
<td></td>
</tr>
<tr>
<td>Lytic Given</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1,005 (8.8%)</td>
<td>1,123 (9.9%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,120 (9.7%)</td>
<td>1,188 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>ALL PATIENTS</td>
<td>2,125 (9.3%)</td>
<td>2,311 (10.1%)</td>
<td></td>
</tr>
</tbody>
</table>
**COMMIT: Conclusions**

- **Adding clopidogrel (75 mg daily) to aspirin** was **beneficial** for a wide range of acute STEMI patients, including older patients and those without a fibrinolytic.

- **Clopidogrel reduced the risk of in-hospital death** by 7% (p=0.03)

- **Clopidogrel reduced the risk of death, non-fatal MI or non-fatal stroke** by 9% (p=0.002)
COMMIT: Conclusions$^{1,2}$

- **No** significant increase in the **risk** of **major** (fatal or transfused) **bleeding**
- **For every million MI treated in hospital for about 2-3 weeks**, clopidogrel could **save 5,000 lives** and **prevent another 4,000 major vascular events**
## ST-Elevation MI: Clopidogrel Trials¹-³

<table>
<thead>
<tr>
<th>COMMIT / CCS-2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>46,000 patients</td>
<td>3,500 patients</td>
</tr>
<tr>
<td>Mortality, D / MI / CVA</td>
<td>Infarct artery patency</td>
</tr>
<tr>
<td>AMI &lt; 24 hrs</td>
<td>AMI &lt; 12 hrs</td>
</tr>
<tr>
<td>Age up to 100</td>
<td>Age ≤ 75</td>
</tr>
<tr>
<td>~ 50% lytic</td>
<td>100% fibrinolytic</td>
</tr>
<tr>
<td>No loading dose</td>
<td>Loading dose</td>
</tr>
<tr>
<td>China</td>
<td>Europe / N. America</td>
</tr>
<tr>
<td>Non-invasive strategy</td>
<td>Invasive strategy</td>
</tr>
</tbody>
</table>
ExTRACT- TIMI 25:-

Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction
ExTRACT TIMI-25
Protocol Design

N = 20,497

STEMI < 6 h
Lytic eligible

ASA

Lytic choice by MD
(TNK, tPA, rPA, SK)

Double-blind, double-dummy

ENOX

< 75 y: 30 mg IV bolus
SC 1.0 mg / kg q 12 h (Hosp DC)
≥ 75 y: No bolus
SC 0.75 mg / kg q 12 h (Hosp DC)
CrCl ≤ 30: 1.0 mg / kg q 24 h

UFH

60 U / kg bolus (4000 U)
Inf 12 U / kg / h (1000 U / h)
Duration: at least 48 h
Cont’d at MD discretion

Day 30

1° Efficacy Endpoint: Death or Nonfatal MI
1° Safety Endpoint: TIMI Major Hemorrhage

through 30 days, death or non-fatal MI was significantly reduced with enoxaparin by 17%, corresponding to 2.1% absolute risk difference.
ExTRACT-TIMI 25: Major Secondary End Point

Death, Nonfatal MI, or Urgent Revascularization

UFH

14.5%
(1479)

Enoxaparin

11.7%
(1199)

↓ 280 Events
19% RRR

RR 0.81
(95% CI, 0.75-0.87)
P < .001

Days After Randomization

Patients (%)

48 hours

6.1%

5.3%
12% RRR

RR 0.88
(0.79-0.98)
P = .02

ExTRACT TIMI-25: Bleeding Endpoints at 30 Days

ARD 0.7%
RR 1.53
P < 0.0001

ARD 0.1%
RR 1.27
P = 0.14

ARD 0.5%
RR 1.50
P < 0.0001

ARD = absolute risk difference.
Fondaprinux

pure Xa inhibitor

OASIS-6 Trial
OASIS-6 Trial

- Objective: evaluate the effect of fondaparinux compared with control (UFH or placebo) when initiated early and given for up to 8 days
- Patients separated into stratum 1 (control group in whom UFH was not indicated; thus, fondaparinux was compared to placebo) and stratum 2 (fondaparinux compared to UFH)
- PCI substudy assessed efficacy of fondaparinux in both strata in primary PCI setting
- 12,092 patients with STEMI from 447 hospitals in 41 countries (enrolled September 2003 – January 2006)
OASIS-6: Study Design

12,000 Patients with STEMI < 12 hours of symptom onset

Lytics (SK, tPA, TNK, rPA), Primary PCI or No Reperfusion (eg, late)

Stratification

UFH not indicated

Randomization
Fondaparinux
Placebo

UFH indicated
Randomization
Fondaparinux
UFH X 24-48 hrs

Primary Outcome: Death/MI at 30 Days

OASIS-6 Trial: Study Design

12,092 patients presenting with STEMI within 24 hours of symptom onset (shortened to 12 hours of symptom onset midway through trial)

Randomized, Blinded, Factorial.
28% female, mean age, 62 years, mean follow-up, 3-6 months

Stratum 1 (No UFH)
N=5658

- Fondaparinux
  N=2823
  2.5 mg/day for up to 8 days or hospital DC

- Placebo
  N=2835

Stratum 2 (UFH)
N=6434

- Fondaparinux
  N=3213
  2.5 mg/day for up to 8 days or hospital DC

- UFH
  N=3221

* Primary end point: Composite of death or reinfarction at 30 days
* Secondary end point: Composite of death or reinfarction at 9 days and at final follow-up

## OASIS-6: Severe Bleeding at 9 Days

<table>
<thead>
<tr>
<th></th>
<th>Fondaparinux</th>
<th>Placebo/UFH</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cases</td>
<td>1.0%</td>
<td>1.3%</td>
<td>0.77</td>
<td>.13</td>
</tr>
<tr>
<td>Stratum 1 vs</td>
<td>1.0%</td>
<td>1.6%</td>
<td>0.63</td>
<td>.06</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratum 2 vs</td>
<td>1.1%</td>
<td>1.1%</td>
<td>0.95</td>
<td>.82</td>
</tr>
<tr>
<td>UFH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HR = hazard ratio.
OASIS-6 Trial: Results

Primary End Point: Death/Reinfarction

Reduction in Death/MI at 30 days:
- Stratum 1 (no UFH indicated)
  - Fondaparinux: 11.2%
  - Placebo: 14%
  - P < 0.05

- Stratum 2 (UFH indicated)
  - Fondaparinux: 8.3%
  - UFH: 8.7%
  - P = NS

NS = not significant.
OASIS-6: Conclusions

- Strategy of fondaparinux is clearly superior to placebo for treatment of STEMI.
- In patients treated with UFH (75% <48hrs), fondaparinux appears at least as effective as UFH.
- In patients treated with primary PCI, there was no benefit with fondaparinux due to an excess of catheter thrombosis.
- Strong evidence for a “margin of safety” with respect to bleeding.

Antithrombin Therapy in STEMI

- Acute therapy in STEMI focuses on reperfusion and antithrombotic therapy.
- Current ACC/AHA STEMI guidelines recommend IV UFH as adjunctive therapy to reperfusion therapy (Class I).
- ExTRACT-TIMI 25 showed enoxaparin superior to current standard of UFH as the antithrombin to support fibrinolysis.
- Fondaparinux effective in STEMI without increasing risk of bleeding or stroke (OASIS-6), but some subsets did not benefit:
  - Patients undergoing PCI
  - Patients in whom UFH, not placebo, was the control.
**HERO-2 trial**

which evaluated the intravenous direct thrombin inhibitor Bivalirudin, which was evaluated against unfractionated heparin along with streptokinase
HERO-2 trial

- **Bivalirudin**, showed a moderate reduction in recurrent MI from 2.3% to 1.6% with an increase in moderate to mild bleeding.

- These data have supported our guideline recommendations that **bivalirudin** may be used as an alternative for patients with **STEMI** who have a history of heparin-induced thrombocytopenia.
HERO-2: Bivalirudin vs. UFH with SK for STEMI

- Death: UFH 10.9%, Bivalirudin 10.8%, P = NS
- Re-MI: UFH 2.3%, Bivalirudin 1.6%, P < 0.001
- Severe Bleeding: UFH 0.5%, Bivalirudin 0.7%, P = 0.07
- Moderate Bleeding: UFH 1.1%, Bivalirudin 1.4%, P = 0.05
- Mild Bleeding: UFH 9%, Bivalirudin 12.8%, P < 0.001

Trials of Facilitated PCI

ASSENT-4 PCI
- STEMI
  - TNK
    - UFH
      - Angio + Primary PCI
        - Death/HF
  - None

FINESSE
- STEMI
  - rPA + Abciximab
    - UFH or LMWH
      - Angio + Primary PCI
        - Abciximab
          - Death/Shock/HF/VF

CARESS
- High-Risk STEMI
  - rPA + Abciximab
    - Resuscitate PCI
      - UFH
        - Immediate PCI
          - Death/MI/Refractory Ischemia

CARESS = Combined Abciximab Retreplase Stent Study; rPA = reteplase; TNK = tenecteplase; UFH = unfractionated heparin; LMWH = low-molecular-weight heparin; HF = heart failure; VF = ventricular fibrillation.
FINESSE

Trial Design:
A randomized, double-blind trial of abciximab with half-dose of the thrombolytic reteplase (n = 828), abciximab alone (n = 818), or placebo (n = 806) in patients undergoing PCI for STEMI. All patients received IV infusion of abciximab in the cath lab and continued for 12 hours.

Primary endpoint was death or complications of MI (cardiogenic shock, heart failure, or resuscitated ventricular fibrillation) by 90 days.
Results

- No difference in primary endpoint of death or complications of MI between the three groups

**Death or Complications of MI by 90 Days**

- Reteplase + Abciximab + Facilitated PCI: 9.8%
- Abciximab + Facilitated PCI: 10.5%
- Placebo + Primary PCI: 10.7%

*p = NS*
Conclusions

- Among patients undergoing PCI for STEMI, there was no difference in frequency of death or complications of MI by 90 days when comparing facilitated PCI strategy of abciximab and half-dose thrombolytic (reteplase), facilitated PCI strategy with abciximab alone, or placebo with primary PCI.

- However, both facilitated PCI strategies were associated with increased risk of bleeding.
Summary

- **Time is Muscle**

- **Reperfusion Therapy:**
  - Time from symptom onset & time to PCI vs. clinical risk of bleeding

- **New Advances in Adjunctive Rx:**
  - ASA + clopidogrel in lytic treated pts
  - LMWH or fondaparinux: superior to placebo
  - Enoxaparin superior to UFH

- **Future may be pharmacoinvasive strategy**
Thank You
Table 3 ECG manifestations of acute myocardial ischaemia (in absence of LVH and LBBB)

ST elevation
New ST elevation at the J-point in two contiguous leads with the cut-off points: ≥ 0.2 mV in men or ≥ 0.15 mV in women in leads V₂–V₃ and/or ≥ 0.1 mV in other leads

ST depression and T-wave changes
New horizontal or down-sloping ST depression ≥ 0.05 mV in two contiguous leads; and/or T inversion ≥ 0.1 mV in two contiguous leads with prominent R-wave or R/S ratio >1

Table 4 ECG changes associated with prior myocardial infarction

Any Q-wave in leads V₂–V₃ ≥ 0.02 s or QS complex in leads V₂ and V₃
Q-wave ≥ 0.03 s and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF, or V₄–V₆ in any two leads of a contiguous lead grouping (I, aVL, V₆; V₄–V₆; II, III, and aVF)¹
R-wave ≥ 0.04 s in V₁–V₂ and R/S ≥ 1 with a concordant positive T-wave in the absence of a conduction defect

¹The same criteria are used for supplemental leads V₇–V₉, and for the Cabrera frontal plane lead grouping.
The results are impressing :-) 

The 30 day mortality in the prehospital thrombolysis arm is only 3.8%. But if the delay between pain to prehospital thrombolysis is under 2 hours this 30 day mortality fall down to 2.2%.

Also the occurrence of cardiogenic shock in favor of prehospital thrombolysis 1.3%.

This is better result than all recent trials published comparing on site thrombolysis to primary angioplasty (DANAM11, C Port, PRAGUE 11)
Ways to improve the Time-to-Treatment

- Information of the patients.
- Shortening of the intra-hospital delays by better organization & more importantly prehospital triage and treatment.

Efficacy and safety of prehospital triage is now recognized world wide. It should involve emergency physicians and cardioligist in a real local task-force to join and coordinate their efforts.

That is the way to open more arteries earlier, that is to say to save myocardium and more lives.
The primary efficacy end point was the composite of an occluded infarct-related artery (TIMI 0 or 1 on angiography) or death or recurrent MI before angiography.
OASIS-6: Efficacy of Fondaparinux by Strata on Death/MI at 30 Days

<table>
<thead>
<tr>
<th>Stratum</th>
<th>No. of Events (%)</th>
<th>Fondaparinux vs. Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Fonda</td>
</tr>
<tr>
<td>I</td>
<td>14.0</td>
<td>11.2</td>
</tr>
<tr>
<td>(n = 5658)</td>
<td>(Fonda vs. Placebo)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>8.7</td>
<td>8.3</td>
</tr>
<tr>
<td>(n = 6434)</td>
<td>(Fonda vs. UFH)</td>
<td></td>
</tr>
</tbody>
</table>

Stratum I: No indication for UFH
Stratum II: Indication for UFH
Interaction p value 0.01 = statistical significance

HR = hazard ratio.