Transfers, Facilitated and Rescue PCI for AMI

Michael J Cowley, M.D., FSCAI

Nothing to disclose
Primary PCI vs Lysis for STEMI
Meta-analysis of 23 trials

Short Term Events

<table>
<thead>
<tr>
<th>Event</th>
<th>PCI</th>
<th>Lysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5</td>
<td>7</td>
<td>p=0.0003</td>
</tr>
<tr>
<td>Re-MI</td>
<td>3</td>
<td>7</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Total CVA</td>
<td>1</td>
<td>2</td>
<td>p=0.0004</td>
</tr>
<tr>
<td>ICH</td>
<td>0.05</td>
<td>1</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Death, MI, CVA</td>
<td>8</td>
<td>14</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

Keeley EC Lancet 2003; 361: 13-20
Transfer for PCI is better than Lysis! (In a timely manner)
Lysis vs Transport for PCI
Meta-analysis of 5 RCT

Average transfer time = 39 min

Keeley EC Lancet 2003; 361: 13-20
Transfer for Primary PCI vs Lysis

Death, Re-MI, Stroke

Dalby M et al: Circ; 2003; 108: 1809

<table>
<thead>
<tr>
<th>Study</th>
<th>PCI</th>
<th>Lysis</th>
<th>Relative Risk</th>
<th>OR: 0.58 p&lt;0.001</th>
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<tbody>
<tr>
<td>Maastricht</td>
<td>8/75</td>
<td>14/75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRAGUE</td>
<td>8/101</td>
<td>23/99</td>
<td></td>
<td></td>
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<tr>
<td>Air-Pami</td>
<td>6/71</td>
<td>9/66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAPTIM</td>
<td>26/421</td>
<td>34/419</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DANAMI 2</td>
<td>63/790</td>
<td>107/782</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRAGUE 2</td>
<td>36/429</td>
<td>64/421</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>147/1887</strong></td>
<td><strong>251/1863</strong></td>
<td></td>
<td><strong>OR: 0.58 p&lt;0.001</strong></td>
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</tbody>
</table>
DANAMI-2
Primary Endpoint (Death, re-MI, CVA)

Average transfer time = 68 min

Fibrinolysis (front loaded tPA)

Log rank: p=0.002

PCI

NNT=18

Days

%
Time Delay Is Important with Primary PCI
Transfers, Facilitated and Rescue PCI

Delays due to Long Transfer Times are common

- Primary PCI is the preferred reperfusion strategy for STEMI if it can be done in a timely manner
- Only 25% of US hospitals are capable of Primary PCI
- 82% of STEMI pts transferred from non-PCI hospitals for Primary PCI have Door to Balloon times > 120 min (ACC/NCDR) Chakrabarti, JACC 2008
Primary PCI: Access in US

42% PCI hospital is closest facility
79% within 60 min prehospital time*

* Weather permitting

Nallamothu et al: Circulation 2006;113:1189
Relation Between D2B Times and In-Hospital Mortality in NRMI

Treatment Delays with 1° PCI

Cardiac Survival

Door–to–Balloon Time
- 0 – 1.4 hr
- 1.5 – 1.9 hr
- 2.0 – 2.9 hr
- ≥ 3.0 hr

p < 0.0001

n = 2,300

Transfer for Primary PCI

Only 36% <120 min

Chakrabarti A: J Am Coll Cardiol 51:2442, 2008
Door-In Door-Out Time at Referring Hospital

Median DIDO (IQR) = 74 min (45-132)
40% had DIDO >90 min

Ting HH: AHA 2009 (abstract)
Effect of Door-to-Balloon Time on Mortality in STEMI

N=29,222

P for trend < 0.001.

NRMI: Advantage of PCI Compared With Fibrinolysis Decreases as PCI-Related Delay Increases

Odds of Death With Fibrinolysis

PCI Better

Fibrinolysis Better

PCI-Related Time Delay (Door-to-Balloon Minus Door-to-Needle), min

Interhospital Delay in Transfer Door-to-Door Times

1 year Mortality (n=616 pts)

- <30': 3.2%
- 30-60': 6.4%
- 60-90': 6.2%
- >90': 12.1%

p=0.01

De Luca G: AJC 2005; 95: 1361
US Transfer Delay for Primary PCI (NRMI 3 / 4)

- <16% < 2h
- 52% > 3h

Total Door to Balloon Time (h):
- <1
- 1 to 2: 15.1%
- 2 to 3: 32.4%
- 3 to 4: 22%
- 4 to 5: 14.1%
- 5 to 6: 8.2%
- 6 to 7: 4.7%
- >7: 3.2%

Nallamothu B: Circulation 2005; 111: 761
Rescue PCI is better than Lysis!
RESCUE PCI: REACT Trial

Primary End Point (D, re-MI, severe CHF, CVA) at 6 mo

Probability of Event-Free Survival

Days After Randomization

REACT= Rescue Angioplasty versus Conservative Treatment or Repeat Thrombolysis

Rescue Angioplasty or Repeat Fibrinolysis After Failed Fibrinolytic Therapy for ST-Segment Myocardial Infarction

A Meta-Analysis of Randomized Trials

Harindra C. Wijeysundera, MD,* Ram Vijayaraghavan, MD,* Brahmajee K. Nallamothu, MD, MPH,† JoAnne M. Foody, MD,‡§ Harlan M. Krumholz, MD, SM,‡∥ Christopher O. Phillips, MD, MPH,¶ Amir Kashani, MD, MS,‡ John J. You, MD,#†† Jack V. Tu, MD, PhD,**†† Dennis T. Ko, MD, MSc*††

Ontario, Canada; Ann Arbor, Michigan; New Haven and West Haven, Connecticut; and Cleveland, Ohio

JACC 2007; 49: 422-430
Rescue PCI vs Conservative Rx

Meta-analysis of 3 RCT (n=700 pts)

Wijeysundera HC: JACC 2007; 49:422-430
“Facilitated” PCI
Facilitated PCI

- Was inferior to pPCI with short transfer times
- Was harmful in ASSENT 4
  - Study had serious design flaws
- Did not address key question:
  - Best Rx for pts with long transfer delays?
Reperfusion Options for Transfer Patients with Expected Delays

- Primary PCI (no matter how long it takes)
- Lysis; ischemia-guided transfer for rescue PCI
- Lysis with transfer for immediate ("early" PCI): Pharmaco-invasive strategy
Facilitated or Pharmaco-invasive

- AMICO Registry
- CARESS-in-AMI
- TRANSFER-AMI
- NOR-DISTEMI
AMICO Registry: Pharmacoinvasive Rx
30 day Outcomes

Fast PCI

PPCI

Death

Stroke

re-MI

Any Event

Early Invasive vs Ischemia-guided Rx after Lysis for STEMI: Meta-analysis

### Death

<table>
<thead>
<tr>
<th>Study name</th>
<th>OR (95% CI)</th>
<th>Invasive</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEST</td>
<td>0.23 (0.03 – 2.12)</td>
<td>1 / 104</td>
<td>4 / 100</td>
</tr>
<tr>
<td>CAPITAL AMI</td>
<td>0.98 (0.19 – 4.97)</td>
<td>3 / 86</td>
<td>3 / 84</td>
</tr>
<tr>
<td>GRACIA 1</td>
<td>0.55 (0.24 – 1.27)</td>
<td>9 / 248</td>
<td>16 / 251</td>
</tr>
<tr>
<td>SIAM 3</td>
<td>0.41 (0.12 – 1.39)</td>
<td>4 / 82</td>
<td>9 / 81</td>
</tr>
<tr>
<td>PRAGUE 1</td>
<td>0.61 (0.28 – 1.35)</td>
<td>12 / 100</td>
<td>18 / 99</td>
</tr>
<tr>
<td>TOTAL</td>
<td>0.55 (0.34 - 0.90)</td>
<td>29 / 620</td>
<td>50 / 615</td>
</tr>
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</table>

Test for heterogeneity: Q-value 1.35 df 4 (p 0.85) I² 0

### Reinfarction

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<thead>
<tr>
<th>Study name</th>
<th>OR (95% CI)</th>
<th>Invasive</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEST</td>
<td>0.62 (0.21 – 1.81)</td>
<td>6 / 104</td>
<td>9 / 100</td>
</tr>
<tr>
<td>CAPITAL AMI</td>
<td>0.37 (0.12 – 1.10)</td>
<td>5 / 86</td>
<td>12 / 84</td>
</tr>
<tr>
<td>GRACIA 1</td>
<td>0.59 (0.25 – 1.38)</td>
<td>9 / 248</td>
<td>15 / 251</td>
</tr>
<tr>
<td>SIAM 3</td>
<td>0.99 (0.14 – 7.18)</td>
<td>2 / 82</td>
<td>2 / 81</td>
</tr>
<tr>
<td>PRAGUE 1</td>
<td>0.46 (0.17 – 1.29)</td>
<td>6 / 100</td>
<td>12 / 99</td>
</tr>
<tr>
<td>TOTAL</td>
<td>0.53 (0.33 - 0.86)</td>
<td>28 / 620</td>
<td>50 / 615</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Q-value 1.01 df 4 (p 0.91) I² 0

Wijeysundera HC: AHJ 2008; 156: 564-572
Early Routine PCI vs Standard Rx after Lysis
7 RCT (n=2961 pts)
30 Day Clinical Outcomes

- Death re-MI: Early PCI 3.3%, Standard Rx* 3.8%, p=0.51
- re-MI: Early PCI 2.8%, Standard Rx* 4.7%, p=0.003
- D, MI: Early PCI 5.6%, Standard Rx* 8.3%, p=0.004
- re-lisch: Early PCI 1.9%, Standard Rx* 7.1%, p=0.001
- Major Bleed: Early PCI 4.9%, Standard Rx* 5.5%, p=ns

* Rescue PCI: 20%

Borgia F: EHJ 2010; 31: 2156-2169
CARESS in AMI: Design

- **Reteplase**
  - UFH bolus (max 3000 + IV at 7 U/kg/h)
  - Abciximab bolus + IV
  - ASA 300-500 mg iv

Facilitated PCI:
- UFH (7 U/Kg/h) for transfer
- PCI: ACT adjusted to 200-250” ; UFH stopped after PCI

Medical Treatment/Rescue:
- UFH (7 U/Kg/h for 24 hrs) If
- Rescue PCI: ACT adjust to 200-250”; UFH stopped after PCI

Clopidogrel for 1-12 mo after stenting (514 pts; 82%)
CARESS IN AMI
Primary Outcome at 30 days

Death, re-MI, refractory ischaemia

OR 0.34 (95% CI 0.17-0.68)

p = 0.001

Rescue 11.1%

‘Facilitated’ 4.1%

DiMario C: Lancet 2008; 371:559-568
Transfer-AMI

‘High Risk’ STEMI < 12 hrs

- TNK + ASA + UFH / Enoxaparin + Clopidogrel

Community Hospital Emergency Department

“Pharmacoinvasive Strategy”
- Urgent Transfer to PCI Centre

PCI Centre Cath Lab

Cath / PCI ≤ 6 hrs (+ reperfusion)
- Cath + Rescue PCI ± GPI
- Elective Cath ± PCI > 24 hrs later

Assess chest pain, ST↑ resolution at 60-90 min after Rx

Failed Reperfusion*

Successful Reperfusion

Repatriation of stable pts 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
Pharmacoinvasive vs Lysis for high risk STEMI

Primary Endpoint* at 30 Days

N=1,004 pts

OR=0.54 (0.37, 0.78)

\[ p=0.0013 \]

Days from Randomization

*Primary EP: Death, re-MI, CHF, Severe re-Ischemia, Shock
**PCI in STEMI* 2011 Guidelines**

**Indications**

<table>
<thead>
<tr>
<th></th>
<th>CO</th>
<th>LOE</th>
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<tbody>
<tr>
<td><strong>Non-Primary PCI (Delayed PCI)</strong></td>
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<td></td>
</tr>
<tr>
<td>Evidence of lytic failure or IRA reocclusion</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>Patent IRA 3 - 24 h after lytic therapy</td>
<td>IIA</td>
<td>B</td>
</tr>
</tbody>
</table>

*Systems goal for primary PCI:
  - < 90 min of first medical contact at hospital with PCI capability (Class I, LOE: B)
  - < 120 min when the pt presents to hospital without PCI capability (Class I, LOE: B)
Transfer, Facilitated and Rescue PCI

Summary

- Primary PCI is preferred for STEMI
- Primary PCI preferred if transfer times are short
- Pharmacoinvasive strategy is preferred for when transfer times are long
- Early “routine” PCI after lysis is preferred over rescue strategy (particularly in high risk pts)
  - Includes rescue PCI for failed reperfusion
  - Prevents early reocclusion after successful lysis
Relationship Between Myocardial Salvage and Survival

Median U.S. Sx-ER: 2°
Goal U.S. PCI Sx-bal: 3.5°

Modifying factors
- Collaterals
- Ischemic preconditioning
- MVO₂

90' DBT

Time to treatment is critical
Opening the IRA (PCI > lysis)

Gersh, Stone, Holmes. JAMA 2005
2012: Do whatever it takes to reduce time from symptom onset to ER arrival and time from ER arrival to PCI!

↑ Public awareness of MI Sx

Chest pain centers of excellence with lower DBTs and excellent outcomes

Regional coordination

Ambulance ECG telemetry

Ambulance/ER CCL activation

ICs sleep in hospital

Continual QI
Relationship Between Myocardial Salvage and Survival

- Median U.S. Sx-ER: 1.75°
- Goal U.S. PCI Sx-bal: 2.75°
- 60' DBT

Modifying factors:
- Collaterals
- Ischemic preconditioning
- MVO$_2$

Treatment objectives:
- Time to treatment is critical
- Opening the IRA (PCI > lysis)

Gersh, Stone, Holmes. *JAMA* 2005
Door-to-balloon time <90 mins at CMS hospitals

Percentage of patients with D2B time < 90 minutes

N pts 2005 2006 2007 2008 2009 2010
48,977 52,028 51,298 53,032 53,682 42,150

Median 96 mins
Median 64 mins
44.2%
91.4%
Relationship Between Myocardial Salvage and Survival

- Time to treatment is critical
- Opening the IRA (PCI > lysis)
- Extent of salvage (% of area at risk)
- Treatment objectives
- Modifying factors
  - Collaterals
  - Ischemic preconditioning
  - MVO₂

Gersh, Stone, Holmes. *JAMA* 2005

- Median U.S. Sx-ER: 1.5°
- 45' DBT
- Goal U.S. PCI Sx-bal: 2.25°
- Mortality reduction (%)
- Hours: 1, 3, 6, 12, 24
- Extent of salvage (% of area at risk)
Relationship Between Myocardial Salvage and Survival: The future?

- Median U.S. Sx-ER: 1.5°
- Goal U.S. PCI Sx-bal: 2.25°
- 45’ DBT

Interventions to improve:
- Reperfusion injury
- Microcirculatory function

Modifying factors:
- Collaterals
- Ischemic preconditioning
- MVO₂

Treatment objectives:
- Time to treatment is critical
- Opening the IRA (PCI > lysis)
Interhospital Delay in Transfer Door-to-Door Times

1 year Mortality (n=616 pts)

<table>
<thead>
<tr>
<th>Delay (sec)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>3.2</td>
</tr>
<tr>
<td>30-60</td>
<td>6.4</td>
</tr>
<tr>
<td>60-90</td>
<td>6.2</td>
</tr>
<tr>
<td>&gt;90</td>
<td>12.1</td>
</tr>
</tbody>
</table>

p=0.01

De Luca G: AJC 2005; 95: 1361
Interhospital Delay in Transfer Door-to-Door Times
1 year Mortality (n=616 pts)

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30'</td>
<td>3.2%</td>
</tr>
<tr>
<td>30-60'</td>
<td>6.4%</td>
</tr>
<tr>
<td>60-90'</td>
<td>6.2%</td>
</tr>
<tr>
<td>&gt;90'</td>
<td>12.1%</td>
</tr>
</tbody>
</table>

\[ p = 0.01 \]

De Luca G: AJC 2005; 95: 1361
US Transfer Delay for Primary PCI (NRMI 3 / 4)

- <16% < 2h: 0.3%
- 2 to 3: 32.4%
- 3 to 4: 22%
- 4 to 5: 14.1%
- 5 to 6: 8.2%
- 6 to 7: 4.7%
- >7: 3.2%

Total Door to Balloon Time (h)

Nallamothu B: Circulation 2005; 111: 761
Reperfusion Options for Transfer Patients with Expected Delays

- Lysis; ischemia-guided transfer for rescue PCI
- Lysis, routine transfer for aggressive rescue PCI
- Primary PCI (no matter how long it takes)
- Lysis with transfer for immediate ("early" PCI): Pharmaco-invasive strategy
Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a meta-analysis

Francesco Borgia¹, Shaun G. Goodman², Sigrun Halvorsen³, Warren J. Cantor⁴, Federico Piscione⁵, Michel R. Le May⁶, Francisco Fernández-Avilés⁷, Pedro L. Sánchez⁷, Konstantinos Dimopoulos¹, Bruno Scheller⁸, Paul W. Armstrong⁹, and Carlo Di Mario¹*
Acute Ischemic Heart Disease

An early invasive strategy versus ischemia-guided management after fibrinolytic therapy for ST-segment elevation myocardial infarction: A meta-analysis of contemporary randomized controlled trials

Harindra C. Wijeysundera, MD, a John J. You, MD, b,c,d Brahmanee K. Nallamothu, MD, MPH, c
Harlan M. Krumholz, MD, SM, e,g Warren J. Cantor, MD, h and Dennis T. Ko, MD, MSc a,d Toronto, Hamilton, and Newmarket, Ontario, Canada; Ann Arbor, MI; and New Haven, CT

Background Although the use of an early invasive strategy among patients with ST-segment elevation myocardial infarctions (STEMI) who are treated initially with fibrinolytic therapy is common, the safety and efficacy of this approach remains uncertain. We performed a meta-analysis to best estimate the benefits and harms of an early invasive strategy in STEMI patients treated initially with full-dose intravenous fibrinolytic therapy, as compared to a traditional strategy of ischemia-guided management.

Methods We included contemporary randomized controlled trials, defined a priori as those with >50% stent use during percutaneous coronary intervention (PCI). Outcomes extracted from the published results of eligible trials included all-cause mortality, reinfarction, stroke, and in-hospital major bleeding.

Results We identified 5 contemporary trials enrolling 1,235 patients who met our inclusion criteria. Of the patients randomized to an early invasive strategy, 86% underwent PCI with 87% receiving stents. Follow-up duration ranged from 30 days to 1 year. An early invasive strategy was associated with significant reductions in mortality (odds ratio [OR] 0.55, 95% CI 0.34-0.90) and reinfarction (OR 0.53, 95% CI 0.33-0.86) compared with ischemia-guided management. There were no significant differences in the risk of stroke (OR 1.31, 95% CI 0.42-4.10) or major bleeding (OR 1.41, 95% CI 0.74-2.69).

Conclusions An early invasive strategy after fibrinolytic therapy is associated with significant reductions in mortality and reinfarction. Our results suggest a potentially important role for this strategy in the management of STEMI patients but should be confirmed by large randomized trials. (Am Heart J 2008;156:564-572.e2)
AMICO: Alliance for Myocardial Infarction Care Optimization

Ali. E. Denktas, MD, Haris Athar, MD, Stefano Sdringola, MD, H. Vernon Anderson, MD, Richard W. Smalling, MD, CHUL Ahn, PhD

Raymond G. McKay, MD
Primary Endpoint: 30-Day Death, re-MI, CHF, Severe Recurrent Ischemia, Shock

N=1,004 pts

OR=0.54 (0.37, 0.78)

p=0.0013

Standard (n=496)
Pharmacoinvasive (n=508)
Primary Endpoint: 30-Day Death, re-MI, CHF, Severe Recurrent Ischemia, Shock

N=1,004 pts

OR=0.54 (0.37, 0.78)
p=0.0013

Days from Randomization

<table>
<thead>
<tr>
<th>Days</th>
<th>Standard (n=496)</th>
<th>Pharmacoinvasive (n=508)</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>422</td>
<td>468</td>
</tr>
<tr>
<td>5</td>
<td>415</td>
<td>466</td>
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<tr>
<td>10</td>
<td>415</td>
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<td>20</td>
<td>414</td>
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<tr>
<td>25</td>
<td>412</td>
<td>457</td>
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<tr>
<td>30</td>
<td>16.6</td>
<td>10.6</td>
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