Annual Admissions in US for Acute Coronary Syndromes (ACS)

- 240,000 ST-segment elevation MI (STEMI)
- 1.1 million Non-ST-segment elevation ACS

Spectrum of CAD

<table>
<thead>
<tr>
<th>Stable angina</th>
<th>Unstable angina</th>
<th>NSTEMI</th>
<th>STEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ST elevation</td>
<td>~1.1 Million Admissions Per Year</td>
<td>NSTEMI</td>
<td>STEMI</td>
</tr>
<tr>
<td>~0.24 Million Admissions Per Year</td>
<td>NSTEMI</td>
<td>STEMI</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CAD, coronary artery disease; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

Figures reproduced with permission from Davies MJ. *Heart*. 2000;83:361-366.
Importance of Speedy Reperfusion

SUMMARY

Occlusion of a large coronary artery (followed by reperfusion) was carried out in an anesthetized dog, and the heart examined 4 to 40 days later.

- Occlusion 5–20 min → No Infarction
- Occlusion 25–45 min → Infarction

Time to Treatment Is Critical in STEMI

0.24 million discharges per year for STEMI in US

Call 9-1-1
Call fast

Onset of symptoms of STEMI

9-1-1 EMS dispatch

EMS on-scene
- Encourage 12-lead ECGs
- Consider prehospital fibrinolytic if capable and EMS-to-needle within 30 min

EMS Transport

Golden hr = 1st 60 min

Total ischemic time: within 120 min

EMS to-needle within 30 min
EMS to-balloon within 90 min
Patient self-transport
Hospital door-to-balloon within 90 min

Patient EMS
Dispatch 1 min
Prehospital fibrinolysis
EMS-to-needle within 30 min

Not PCI capable
PCI capable

Inter-hospital transfer

GOALS

Time to reperfusion is a critical determinant of the extent of myocardial damage and clinical outcomes in patients with STEMI
Key factors in STEMI care are rapid, accurate diagnosis and keeping the encounter time to reperfusion as short as possible

Figure adapted with permission from Antman EM, et al.
Reperfusion of RCA

TIMI 1: SK vs t-PA

- Reperfusion of Occluded Arteries:
  - tPA: 60*%
  - SK: 35%

- Patency at 90 minutes:
  - tPA: 66*%
  - SK: 36%

*P < 0.001.

ISIS-2: SK + ASA

Placebo Infusion and Tablets: 568/4300 (13.2%)

Aspirin: 461/4295 (10.7%)

Streptokinase: 448/4300 (10.4%)

Streptokinase and Aspirin: 343/4292 (8.0%)

Cumulative Number of Vascular Deaths

Days From Randomization

The Modern Age of Reperfusion

A Comparison of Immediate Angioplasty with Thrombolytic Therapy for Acute Myocardial Infarction

Cindy L. Grines, M.D., Kevin F. Browne, M.D., Jean Marco, Donald Rothbaum, M.D., Gregg W. Stone, M.D., James O'Keefe, M.D., Paul Overlie, M.D., Bryan Donohue, M.D., Noah Chelliah, M.D., Gerald C. Timmis, M.D., Ronald E. Vlietsrta, M.D., Michelle Strezelecki, R.N., Sylvia Puchrowicz-Ochocki, M.D., and William W.O'Neill, M.D.,
for The Primary Angioplasty in Myocardial Infarction Study Group

NEJM 328:673, 1993

Platelet Glycoprotein IIb/IIa Inhibition with Coronary Stenting for Acute Myocardial Infarction

Gilles Montalescot, M.D., Ph.D., Paul Barragan, M.D., Oliver Wittenberg, M.D., Patrick Ecollan, M.D., Simon Elhadad, M.D., Philippe Villain, M.D., Jean-Marc Boulenc, M.D., Marie-Claude Morice, M.D., Luc Maillard, M.D., Michel Pansieri, M.D., Remi Choussat, M.D., and Philippe Pinton, M.D.,
for The ADMIRAL Investigators

NEJM 344:1895, 2001
Primary PCI vs Thrombolysis in STEMI: Quantitative Analysis (23 RCTs, N=7739)

Short-term outcomes (4–6 wk)

- Death: PCI > Thrombolytic
- Nonfatal MI: PCI > Thrombolytic
- Recurrent Ischemia: PCI > Thrombolytic
- Hemorrhagic Stroke: PCI > Thrombolytic
- Major Bleed: PCI > Thrombolytic
- Death, Nonfatal Reinfarction, or Stroke: PCI > Thrombolytic

Fibrinolysis or angioplasty
Time and TIMI flow

Earlier reperfusion vs. better reperfusion

Lysis
Time: 60+ minutes
TIMI 3 flow: 50-60%

PCI
Time: 90+ minutes
TIMI 3 flow: 80-90%
Mortality With Primary PCI vs Lysis by Relative Timing

For every 10-min delay to PCI: 0.94% reduction in mortality difference vs lytics.

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

Odds of Death With Fibrinolysis

PCI Better

Fibrinolysis Better

PCI-Related Delay (door-to-balloon minus door-to-needle time), min

### D2B: Strategies Associated With a Significant Reduction in Door-to-Balloon Time (“Code 90”)

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Mean reduction in door-to-balloon time (min)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Having emergency medicine physicians activate the cath lab</td>
<td>8.2</td>
</tr>
<tr>
<td>Having a single call to a central page operator activate the cath lab</td>
<td>13.8</td>
</tr>
<tr>
<td>Having the ED activate the cath lab while patient is still en route</td>
<td>15.4</td>
</tr>
<tr>
<td>Expecting staff to arrive at the cath lab within 20 minutes after page</td>
<td>19.3</td>
</tr>
<tr>
<td>Having an attending cardiologist always on site</td>
<td>14.6</td>
</tr>
<tr>
<td>Having staff in the ED and cath lab use and receive real-time feedback</td>
<td>8.6</td>
</tr>
</tbody>
</table>

*P<.05 for all.

RACE: Door-to-Device Times in PCI Hospitals and Reperfusion Times in Non-PCI Hospitals

**Median times, min**

<table>
<thead>
<tr>
<th></th>
<th>Direct presenters, primary PCI</th>
<th>All transfers, primary PCI</th>
<th>Fibrinolysis, door-to-needle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-</td>
<td>85</td>
<td>165</td>
<td>35</td>
</tr>
<tr>
<td>Post-</td>
<td>74</td>
<td>128</td>
<td>29</td>
</tr>
</tbody>
</table>

**P-values:**

- Direct presenters, primary PCI: $P < .001$
- All transfers, primary PCI: $P < .001$
- Fibrinolysis, door-to-needle: $P = .002$


**RACE**, Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Department.
RUSH Door to Balloon Time (goal <90min)
Evolution of Guidelines for ACS

1990
ACC/AHA
AMI
R. Gunnar

1992
ACC/AHA
AMI
R. Gunnar

1994
AHCPR/NHLBI
UA
E. Braunwald

1996
Rev
Upd
ACC/AHA
AMI
T. Ryan

1999
Rev
Upd
ACC/AHA
AMI
E. Braunwald

2000
Rev
Upd
ACC/AHA
UA/NSTEMI
E. Braunwald

2002
Rev
Upd
ACC/AHA
STEMI
E. Antman

2004
Rev
Upd
ACC/AHA
STEMI/PCI
E. Antman

2007
Upd
ACC/AHA
STEMI/PCI
F. Kushner

ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation;JACC.

Improving the System of Care for STEMI Patients
### Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefit &gt;&gt;&gt; Risk</strong></td>
<td><strong>Benefit &gt;&gt; Risk</strong></td>
<td><strong>Benefit ≥ Risk</strong></td>
<td><strong>Risk ≥ Benefit</strong></td>
</tr>
<tr>
<td>Procedure/Treatment <strong>SHOULD</strong> be performed/administered</td>
<td>Additional studies with focused objectives needed</td>
<td>Additional studies with broad objectives needed; Additional registry data would be helpful</td>
<td>No additional studies needed</td>
</tr>
<tr>
<td><strong>IT IS REASONABLE to perform procedure/administer treatment</strong></td>
<td><strong>IT IS REASONABLE to perform procedure/administer treatment</strong></td>
<td><strong>IT IS REASONABLE to perform procedure/administer treatment</strong></td>
<td><strong>IT IS REASONABLE to perform procedure/administer treatment</strong></td>
</tr>
<tr>
<td><strong>MAY BE CONSIDERED</strong></td>
<td><strong>MAY BE CONSIDERED</strong></td>
<td><strong>MAY BE CONSIDERED</strong></td>
<td><strong>MAY BE CONSIDERED</strong></td>
</tr>
<tr>
<td><strong>should</strong></td>
<td><strong>is reasonable</strong></td>
<td><strong>may/might be considered</strong></td>
<td><strong>is not recommended</strong></td>
</tr>
<tr>
<td><strong>is recommended</strong></td>
<td><strong>can be useful/effective/beneficial</strong></td>
<td><strong>may/might be reasonable</strong></td>
<td><strong>is not indicated</strong></td>
</tr>
<tr>
<td><strong>is indicated</strong></td>
<td><strong>is probably recommended or indicated</strong></td>
<td><strong>usefulness/effectiveness is unknown/unclear/uncertain or not well established</strong></td>
<td><strong>should not</strong></td>
</tr>
<tr>
<td><strong>is useful/effective/beneficial</strong></td>
<td></td>
<td></td>
<td><strong>is not useful/effective/beneficial</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>may be harmful</strong></td>
</tr>
</tbody>
</table>

**ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation; JACC.**

Improving the System of Care for STEMI Patients
### Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk Additional studies with focused objectives needed</td>
<td>Benefit ≥ Risk Additional studies with broad objectives needed; Additional registry data would be helpful</td>
<td>Risk ≥ Benefit No additional studies needed</td>
</tr>
<tr>
<td>Procedure/ Treatment SHOULD be performed/administered</td>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
<td>Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</td>
</tr>
</tbody>
</table>

### Level of Evidence

<table>
<thead>
<tr>
<th>Level A:</th>
<th>Level B:</th>
<th>Level C:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation based on evidence from multiple randomized trials or meta-analyses. Multiple (3-5) population risk strata evaluated; General consistency of direction and magnitude of effect</td>
<td>Recommendation based on evidence from a single randomized trial or non-randomized studies Limited (2-3) population risk strata evaluated</td>
<td>Recommendation based on expert opinion, case studies, or standard-of-care Very limited (1-2) population risk strata evaluated</td>
</tr>
</tbody>
</table>
Recommendations for Triage and Transfer for PCI

ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation;JACC.
Reperfusion

STEMI patients presenting to a hospital with PCI capability should be treated with primary PCI within 90 minutes of first medical contact.

*Modified recommendation*

STEMI patients presenting to a hospital without PCI capability and who cannot be transferred to a PCI center for intervention within 90 minutes of first medical contact should be treated with fibrinolytic therapy within 30 minutes of hospital presentation, unless contraindicated.

*Modified recommendation*

Recommendations for Triage and Transfer for PCI

1. Each community should develop a STEMI system of care following the standards at least as stringent as those developed for Mission Lifeline to include:
   - destination protocols to STEMI Receiving Centers
   - transfer protocols for patients who arrive at STEMI Referral Centers and are primary PCI candidates, and/or are fibrinolytic ineligible and/or in cardiogenic shock

ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation;JACC.
Recommendations for Triage and Transfer for PCI

1. It is reasonable to transfer high risk patients who receive fibrinolytic therapy as primary reperfusion therapy at a non-PCI capable facility to a PCI-capable facility as soon as possible where either PCI can be performed when needed or as a pharmacoinvasive strategy.

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

ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation;JACC.
Routine Early Angioplasty after Fibrinolysis for Acute Myocardial Infarction

Warren J. Cantor, M.D., David Fitchett, M.D., Bjug Borgundvaag, M.D., John Ducas, M.D., Michael Heffernan, M.D., Eric A. Cohen, M.D., Laurie J. Morrison, M.D., Anatoly Langer, M.D., Vladimir Dzavik, M.D., Shamir R. Mehta, M.D., Charles Lazzam, M.D., Brian Schwartz, M.D., Amparo Casanova, M.D., Ph.D., and Shaun G. Goodman, M.D., for the TRANSFER-AMI Trial Investigators*
TRANSFER-AMI: Study Design

High-risk ST-elevation MI within 12 hrs of symptom onset

TNK + ASA + Heparin or Enoxaparin + Clopidogrel

Randomization

Pharmacoinvasive Strategy
Urgent Transfer to PCI Center

Standard Treatment
Assess chest pain, ST↑ resolution at 60-90 min after randomization

Failed Reperfusion
Successful Reperfusion

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

a ST-segment resolution <50% and persistent chest pain, or hemodynamic instability.

Cantor WJ. Presented at: American College of Cardiology 2008 Scientific Sessions/i2 Summit-SCAI Annual Meeting; March 30, 2008; Chicago, IL.
Figure 2. Kaplan–Meier Curves for the Primary End Point at 30 Days.

The primary end point was the composite of death, reinfarction, worsening heart failure, or cardiogenic shock within 30 days. PCI denotes percutaneous coronary intervention.
**TRANSFER-AMI**

**Trial design:** Patients with STEMI who presented to centers where timely primary PCI was not feasible were randomized to a pharmacoinvasive strategy (emergent transfer for PCI within 6 hours of fibrinolysis) or to standard treatment after fibrinolysis.

**Preliminary Results**
- Primary end point (death, MI, heart failure, severe recurrent ischemia, or shock): 10.6% in pharmacoinvasive arm vs 16.6% in standard treatment arm ($P=0.0013$)
- Reinfarction: 3.3% vs 6.0% ($P=0.044$)
- Recurrent ischemia: 0.2% vs 2.2% ($P=0.02$)

**Conclusions**
- Pharmacoinvasive approach safe and efficacious compared with treatment with thrombolytics and transfer for rescue PCI only
- Optimal window: 6 hours

Cantor WJ. Presented at: American College of Cardiology 2008 Scientific Sessions/i2 Summit-SCAI Annual Meeting; March 30, 2008; Chicago, IL.

www.cardiosource.com
1. Patients who are not high risk who receive fibrinolytic therapy as primary reperfusion therapy at a non-PCI capable facility may be considered for transfer to a PCI-capable facility as soon as possible where either PCI can be performed when needed or as a pharmacoinvasive strategy.

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

ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation;JACC.
Triage and Transfer for PCI: STEMI Patients Who Are Candidates for Reperfusion

- 2007 STEMI Focused Update describes several strategies for reperfusion: “facilitated PCI” and “rescue PCI.”
- These terms are no longer used for the recommendations in this update.
- The contemporary therapeutic choices leading to reperfusion for the treatment of patients presenting with STEMI can be described without these potentially misleading labels.

ACC/AHA 2009 Joint STEMI/PCI Focused Update. On Line Circulation;JACC.
Reperfusion Rx For STEMI

Improved Outcome

1976

i.c. SK

i.v. SK

SK + ASA

tPA + ASA + hep

1º PTCA

Stent + IIb/IIIa

Future Directions

Drug Eluting Stents
Thrombus Aspiration
Bivalirudin
Improving Systems of Care
Stem Cells?

↓ Time to Rx, Beta Blockade, ACEI
Open Heart Surgery Programs (adult)

Chicago 15
Chicago suburbs 31
NW Indiana 10
Total 54

Population ~9 million
Scatterplot Showing the Relationship Between Hospital Primary Angioplasty Volume and In-Hospital Mortality

Reperfusion Rx For STEMI

Systems of STEMI Care

Improved Outcome

1976

Time to Rx, Beta Blockade, ACEI

2010
RUSH Door to Balloon Time
(goal <90min)

Begin QI Initiative

Door to balloon