Heart Attack: The First 60 Minutes

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Disclosures

• Consultant to Bristol-Myers Squibb, Sanofi-aventis, The Medicines Company, Abbott Vascular, Medtronic, Boston Scientific, BSP Medical

• Research Grants from Abbott Vascular, Boston Scientific, Medtronic

• Off Label Utilization of Drug Eluting Stents and Bivalirudin will be discussed.
The Understanding of A Heart Attack:
First Year Medical School

Heart Attack=
Chest Pain and Heart Cracking
Open Due to Old Age
What is a Heart Attack?

• A Heart Attack is Damage to the Heart Muscle
• This usually results from a blocked artery on the outside of the heart
• A blocked heart artery is caused by Atherosclerosis
What Does A Heart Attack Look Like To An Interventional Cardiologist?
What Causes Atherosclerosis, Blocked Arteries and Heart Attack?

- Smoking
- Diabetes Mellitus
- Hypertension
- Hyperlipidemia
- Family History/Genetics
- Obesity/Sedentary
- ?
How Do We Diagnose a Heart Attack?

ST Elevation Acute Myocardial Infarction—EKG Diagnosis

- Chest Pressure, Heaviness, Pain.
- Location of chest symptoms are irrelevant (does not have to be over your heart).
- Weird variants—arm ache, tooth/jaw pain
- Shortness of breath, palpitations, loss of consciousness
A Different Lecture:
Prevention of Acute Myocardial Infarction with Risk Factor Modification
Question 1: If You Had A STEMI in 1975, What Was Your Chance of Dying In Hospital?

- A) 5%
- B) 10%
- C) 15%
- D) 20%
- E) 33%
Question 1: If You Had A STEMI in 1975, What Was Your Chance of Dying In Hospital?
Death From A Heart Attack

How Did We Get Here?

[Bar chart showing hospital mortality rates from 1975/1978 to FAHC 2009]

Dauerman, Am J Cardiol 2002: The Worcester Heart Attack Study
A 60 Year Old Woman Presents To a Vermont ED with New Onset Chest Pressure

- Hemodynamically stable, 6 hours of intermittent CP
- Do you have an algorithm or does the ED call and ask?
- Does the ED send right to cath lab or start meds?
- Which meds? Which Patients?
What Medication Can You Give at a wedding to save a heart attack patient’s life?

Ebers Papyrus ~ 1534 BC

- Recommended using the willow tree, known in Egyptian as tjeret, for internal use "to cause the heart to receive bread."
Aspirin

- From German acetylspirsaure + chemical suffix – in
- First synthesized in pure form by Friedr. Bayer & Co. in 1897.
- First pharmaceutical agent ever sold in pill form in early 1900’s.
Aspirin in Coronary Thrombosis

• “One aspirin a day.”

• “A regular aspirin is advised to all male patients in the age bracket between 45 and 65 years, and especially to those who are overweight, apparently have a tendency to overeat, and to lead a sedentary life with little or no physical activity.”

Mississippi Valley Medical Journal
1953;75:38-44

Experiences with Aspirin (Acetylsalicylic Acid) in the Nonspecific Prophylaxis of Coronary Thrombosis

Lawrence L. Craven, M.D.
Glendale, California

Coronary thrombosis is one of the principal causes of sudden death, prolonged morbidity, or permanent disability, and strikes especially often males in their late middle age, who to all appearances enjoyed the best of health. Ordinarily premonitory signs are absent, and it is therefore impossible to institute some form of specific preventive therapy. The possibility of general, nonspecific prophylaxis is hardly taken into consideration, and the medical profession tends to maintain a similarly fatalistic attitude toward episodes of coronary thrombosis as does the laity.

There can be no argument that any definitive plan of prophylaxis—specific or nonspecific—depends on continued research and a more complete understanding of the etiologic and pathologic aspects of coronary thrombosis. But in the meantime experiences which might have a bearing on the general prophylaxis of the disease may not be entirely without practical interest.

It should be pointed out that only ten years ago the prophylactic use of anticoagulants in the presence of impending venous thrombosis or following coronary occlusion was still considered to be hypothetical or controversial. Nowadays sufficient experience has been accumulated to establish precise indications and dosages for this type of medication, which is well on its way to becoming a standardized procedure.

The value of anticoagulant therapy using heparin and dicumarol in the prevention of embolism and repeated coronary occlusion has been demonstrated beyond any reasonable doubt. Thus the question arises whether the salicylates, which have essentially the same effect as the dicumarols, are less powerful, do not deserve a place in the general nonspecific prophylaxis of coronary occlusion, Because of their lesser potency these drugs can be more freely prescribed, and may prove useful if administered to subjects most likely to experience coronary thrombosis, before the first episode has taken place.

More particularly, the value of aspirin (acetylsalicylic acid) in the general prophylaxis of coronary occlusion is suggested by observations accumulated during the past seven years. Concededly, the effectiveness of any type of prophylactic treatment is difficult to prove, and this applies especially to a procedure aiming merely at nonspecific prevention. Observations on healthy subjects can never be made under strictly scientific conditions, and resulting figures are often within limits suitable for statistical evaluation. Such findings may therefore either be substantiated or refuted by subsequent clinical research. But as long as the field of general prophylaxis of coronary thrombosis is still outside the limits of present-day research procedures, preliminary observations may still be of practical importance provided:

1. The measure is safe in all subjects and throughout the entire extended period of medication;
2. The observations are not in opposition to the trends and results of clinical and experimental research; and
3. It is well understood that the findings were not arrived at under strictly scientific conditions.

Aspirin (acetylsalicylic acid) was suggested as a general prophylactic of coronary thrombosis to 1400 healthy male subjects, mainly between the ages of 45 and 68 years, who were overweight and known to lead a sedentary life. It is common knowledge that individuals of this type are more frequently and earlier in their lives exposed to the dangers of sudden episodes of coronary thrombosis. But the precise cause of such attacks cannot be ascertained with any degree of certainty, and it must be assumed that a multitude of factors contribute to the development of coronary thrombosis. Undeniably, atherosclerosis plays a considerable part, but even most recent authors on the subject are unable to account for the occurrence of specific episodes which are described as spontaneous events. Despite all electrocardiographic observations, and findings at autopsy, the matter is far from being resolved. How could it otherwise be explained that many persons with advanced atherosclerosis of the entire arterial tree live to a ripe old age, and then die of something else than "heart disease". There must be other factors which enter into the picture and are responsible for "heart attacks".

It is in this respect of interest to note that the incidence of postoperative

Placebo alone: 13.2%
Aspirin alone: 9.4%
Streptokinase alone: 9.2%
Streptokinase plus aspirin: 8.0%
Evolution of STEMI Patient Management

- STEMI management has evolved over the past 2 decades based on new clinical data involving technologic and pharmacologic advances.

**Primary Lytic Therapy**
- **ISIS-2** (N=17,187)
- **GUSTO-I** (N=41,021)
- **RAPID I** (N=606)
- **RAPID II** (N=324)

**Combination Therapy**
- **LYTIC + GPI, LMWH, or DTI**
- **GUSTO-III** (N=15,059)
- **RAPPORT** (N=483)
- **ISAR-2** (N=401)
- **ASSENT-3** (N=6095)
- **CADILLAC** (N=2082)

**Primary PCI**
- **HERO-2** (N=17,073)
- **COMMENT** (N=409)
- **FINESSE** (N=3602)
- **FINESSE-6** (N=12,092)
- **On-Time 2** (N=984)

- **TAPAS** (N=1,071)
- **HORIZONS AMI** (N=3602)
- **OASIS-6** (N=2452)
- **FASTER** (N=409)
- **BIAMI** (N=201)
- **BRAVE-3** (N=800)
Are Medications Enough?
Mechanical Solutions for Coronary Blockage
Primary PCI/Stenting for STEMI

What is a Stent: Stainless Steel + Polymer + Protective Drug
Aspirin and/or Fibrinolysis Can Open an Artery, but only a Stent Can Relieve the Blockage
Heart Attack, Reperfusion and Time: The First 60 Minutes

- American College of Cardiology National Cardiovascular Data Registry: an analysis of 43,801 STEMI patients undergoing primary PCI between 2005-2006

In-hospital Mortality

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>In-hospital Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>3.0</td>
</tr>
<tr>
<td>60</td>
<td>3.5</td>
</tr>
<tr>
<td>90</td>
<td>4.3</td>
</tr>
<tr>
<td>120</td>
<td>5.6</td>
</tr>
<tr>
<td>150</td>
<td>7.0</td>
</tr>
<tr>
<td>180</td>
<td>8.4</td>
</tr>
</tbody>
</table>

1st Challenge: Fix the Internal System—On Site Patients

- **FAHC**
- **National Average**

Single Point of Activation—E.D in Control

Uniform Approach For All Practitioners: Cardiac Trauma

The 30 minute response rule: Same as for any other trauma team
Door To Balloon Time:
Goal 90 minutes maximum time to open artery

- 1 Phone Call System
- ED Attendings Take Control—No Cardiology Consult
- No Pharmacology Delays
- Provide Real Time Feedback to ED, Cath Lab, EMS
Should All Patients with STEMI Get Transferred for an Immediate Stent?
High-risk ST elevation MI patients (>4 mm elevation), Sx < 12 hrs
5 PCI centers (n=443) and 22 referring hospitals (n=1,129), transfer in < 3 hrs

DANAMI 2:
Should Transfer Patients Get Primary PCI for STEMI?

Lytic therapy
Front-loaded tPA
100 mg
(n=782)

Primary PCI with transfer
(n=567)

Primary PCI without transfer
(n=223)

Death / MI / Stroke at 30 Days

Stopped early by safety and efficacy committee

HR Anderson, NEJM 2003
Longest transport = 95 miles

Mean transport = 35 miles
Transfer is Better than Lytics if D2B < 120 Minutes

- **Combined**: P=0.0003
  - Lytic: 14% RRR 45%
  - Primary PCI: 8%

- **Transfer Sites**: P=0.002
  - Lytic: 14% RRR 40%
  - Primary PCI: 9%

- **Non-Transfer Sites**: P=0.048
  - Lytic: 12% RRR 45%
  - Primary PCI: 7%

Median D2B=114 minutes for transfers
It Can Be Done in The U.S.: The Minnesota Experience

- 30 hospitals, up to 210 miles from PCI center
- 1,345 STEMI from 2003-2006, all patients, all primary PCI
- **Zone 1**—Less than 60 miles, ASA/Plavix/UFH. (D2B=95 minutes)
- **Zone 2**—half dose lytics and 94% air transport (D2B=120 minutes)

T. Henry, Circulation 2007
Primary PCI for STEMI: Pharmacology Algorithm
ASA, Clopidogrel and UFH and
Avoiding Pharmacology Related Delays in D2B

Time from ED Presentation at NWMC to Open Artery at FAHC: 88 Minutes

27 miles, on interstate highway
What if STEMI was a Gun Shot Wound to the Heart?

1 phone call only

EMS Arrives; Automatic Algorithm—Transfer to Level 1 Trauma Center (GW Medical Center)

Ambulance Activates Surgical Trauma Team: Joe Giordano and his team awaits Reagan’s arrival Directly To the O.R to remove bullet and stop bleeding
Is A Rapid Cardiac Trauma System Important: Time and Death

**Figure 3.** Kaplan-Meier Cumulative Mortality Estimates for Patients With ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention (N=6209)

<table>
<thead>
<tr>
<th>System delay, min</th>
<th>No. at risk</th>
<th>Follow-up, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-60</td>
<td>347</td>
<td>1</td>
</tr>
<tr>
<td>61-120</td>
<td>2843</td>
<td>1</td>
</tr>
<tr>
<td>121-180</td>
<td>2092</td>
<td>1</td>
</tr>
<tr>
<td>181-360</td>
<td>1127</td>
<td>1</td>
</tr>
</tbody>
</table>

Stratified according to intervals of system delay (time from contact with the health care system to the time of primary PCI). PCI indicates percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

Terkelson, Danish Registry, JAMA 2010
The Northwest Medical Center Model:
Achieving Door to Balloon Times of Less Than 90 Minutes for STEMI Patients Transferred for Primary PCI
Bina Ahmed, Stefan Lischke, Faye Straight, Prospero B. Gogo, Stephen Leffler, Marc Kutler, David J. Schneider, Harold L. Dauerman
University of Vermont, Burlington Vermont
ACC, 2009

3% 70% 24% 6%
0% 10% 20% 30% 40% 50% 60% 70%
<60 <90 90-120 120-150
Minutes

Total D2B times in STEMI patients transferred for PPCI

Figure: Distribution of D2B times in STEMI patients transferred for PPCI. Total D2B time is time from arrival to first hospital to balloon inflation. 70% of patients achieved the recommended D2B time of 90 minutes.

- “New cardiac program treats patients faster

System ensures care given within 90 minutes of arrival in ER”

AP November 16, 2008, MSNBC.com, Newark Starledger, Orlando Sentinel….. Beijing, News, Korea
The Vermont Zone 1 STEMI Program:
A Coordinated Regional Primary PCI Program

Draw a 35 mile radius:
DANAMI 2 Trial
Median Travel Distance
Change in STEMI Care since Jan 1, 2007: UVM Uses the Zone 1 Primary PCI Approach

- 75 woman presents to a STEMI PCI Referral Center. Chest pain x 4 hours. Nearest cath lab is 45 minutes away.
- Do you have a ready ambulance that can defibrillate? **YES**
- Is patient DNR? **NO**
- Is patient willing to undergo cath? **YES**
- ASA 325, clopidogrel 600 po, and bolus UFH—Transfer Always and Immediately for Primary PCI.
- Goal—90 minutes to open artery.
Mean Door to Balloon for Zone 1 STEMI PCI Program in 2009

All patients

- PCI: 66.6 minutes
- Non-PCI: 100.7 minutes

Closest and farthest transfers

- Closest, 37km
- Farthest, 101km
Outcomes for Vermont Regional Zone 1 STEMI PCI Program: 2009

ASA 325 mg po, Plavix 600 mg po (and switch to prasugrel 10 po selectively) UFH upstream and switch to bivalirudin in cath lab

**Continue bivalirudin for 2 hours post PCI**
Bailout use of GPI only (9% of STEMI patients)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N=128</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality*</td>
<td>5.5%</td>
</tr>
<tr>
<td>ARC-defined prob/definite stent thrombosis, in-hospital</td>
<td>0.8%</td>
</tr>
<tr>
<td>Major bleeding^</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

* 5 of the 7 deaths presented in shock/arrest
^ Major bleeding was defined as need for any transfusion, hematoma >5cm, or vascular repair during the hospitalization.

Anderson PA, Gogo PB, Dauerman HL, J. Thromb. Thrombolysis 2010
Door to Balloon Times 2009: Significant Transfer Improvement after STEMI Nursing Feedback Program Initiated

K McKenney and HL Dauerman, Euro PCR 2010
Question: If You Had A STEMI While Skiing at Stowe in the winter, what would you want to happen?

- A) EMS to Copley Hospital, 12 Lead EKG, Give Full Dose Lytics and Transfer to PCI Center if Ongoing CP
- B) EMS to Copley Hospital, 12 Lead EKG, Give Full Dose Lytics and Transfer Automatically to PCI Center
- C) EMS to Copley Hospital, Get 12 Lead EKG, and transfer for Primary PCI after starting GPI
- D) EMS to Copley Hospital, 12 Lead EKG, transfer for Primary PCI after aspirin, clopidogrel and heparin only
- E) EMS to get 12 lead EKG at scene and if automated reading says “STEMI”, transfer directly from mountain to PCI Center for Primary PCI.
Are There Complications of STEMI PCI? Bleeding and Vascular Complications Are Getting Better

**Figure 1A**

- **P < 0.001 for temporal trends in both men and women**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Vascular Complication Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50</td>
<td>2.1</td>
</tr>
<tr>
<td>50-59</td>
<td>2.85</td>
</tr>
<tr>
<td>60-69</td>
<td>4.37</td>
</tr>
<tr>
<td>70-79</td>
<td>5.03</td>
</tr>
<tr>
<td>&gt;80</td>
<td>7.03</td>
</tr>
</tbody>
</table>

- **P < 0.001 for trend**

- Major Vascular Complications, %
  - Arterial injury and/or arterial injury related bleeding among Women
  - N = 13,653 Patients Undergoing PCI

Newer STEMI PCI Pharmacology: Decreases Bleeding and Mortality

- **Heparin + GPIIb/IIIa inhibitor (n=1802)**
- **Bivalirudin monotherapy (n=1800)**

**Death (%)**

- **3.1%**
- **2.1%**

**HR [95%CI] = 0.66 [0.44, 1.00]**

**P=0.048**

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**Number at risk**

- Bivalirudin: 1800, 1758, 1751, 1746, 1742, 1729, 1666
- Heparin + GPIIb/IIIa: 1802, 1764, 1748, 1736, 1728, 1707, 1630

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*Stone GW et al. NEJM 2008*
Strategies to Reduce Bleeding and Improve Patient Comfort after PCI

No More Sand Bags: Femoral Closure Devices

Clip on Common Femoral Artery

Access via the Wrist
Can We Reduce Other STEMI PCI Complications—Clotting/Stent Thrombosis

What about our Zone 2 hospitals (60-120 miles): Impossible to get D2B < 120 minutes
For Patients > 60 minutes away, Primary PCI delay to greater than 120 minutes unacceptable

- American College of Cardiology National Cardiovascular Data Registry: an analysis of 43,801 STEMI patients undergoing primary PCI between 2005-2006

The Pharmacoinvasive Strategy: Thrombolytics are the Wire, But We Still Need the Stent
We need both rapid reperfusion and complete artery opening: The Birth of Pharmacoinvasive Therapy

Synergistic Treatment of ST-Segment Elevation Myocardial Infarction With Pharmacoinvasive Recanalization

Harold L. Dauerman, MD, FACC, Burton E. Sobel, MD, FACC

Burlington, Vermont

Both pharmacologic and mechanical approaches designed to limit infarct size by recanalization of infarct-related arteries have reduced mortality associated with ST-segment elevation myocardial infarction (STEMI). Early efforts to combine the two were attenuated because of complications encountered. Primary percutaneous coronary intervention (PCI) and thrombolysis became viewed as alternative rather than complementary modalities. Time to recanalization and adequacy of restoration of perfusion were found to be pivotal determinants of a favorable outcome with either approach. Because pharmacologic intervention can be initiated immediately in virtually any hospital, it is a promising initial step. Because PCI proffers more complete recanalization, it may be a particularly salutary initial or subsequent step. Because of unavoidable delay often confronting implementation of PCI, optimal advantage may accrue from the use of both approaches in combination. We seek to emphasize the potential synergy by referring to the combined approach as “pharmacoinvasive recanalization” rather than by the conventional term “facilitated PCI.” Virtually all patients with STEMI can benefit from prompt, sustained, and complete coronary recanalization. Thus, investigations focusing on identification of pharmacologic regimens that can safely initiate recanalization as early as possible, minimize bleeding, and broaden the temporal window available for efficacy of subsequent, optimally timed PCI should provide particularly valuable information. (J Am Coll Cardiol 2003;42:646–51) © 2003 by the American College of Cardiology Foundation
The Basis of Pharmacoinvasive Therapy

- Time and Flow Both Matter
- Initial Flow Matters
- Keeping the artery open matters
'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

Failed Reperfusion*

Cath / PCI within 6 hrs regardless of reperfusion status

Cath and Rescue PCI ± GPI Agent

Successful Reperfusion

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
## TRANSFER-AMI

### 30-day Primary End Point and Components

<table>
<thead>
<tr>
<th>End point</th>
<th>Standard (%)</th>
<th>Pharmacoinvasive (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point</td>
<td>16.6</td>
<td>10.6</td>
<td>0.0013</td>
</tr>
<tr>
<td>Death</td>
<td>3.6</td>
<td>3.7</td>
<td>0.94</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>6.0</td>
<td>3.3</td>
<td>0.044</td>
</tr>
<tr>
<td>Recurrent ischemia</td>
<td>2.2</td>
<td>0.2</td>
<td>0.019</td>
</tr>
<tr>
<td>Death/MI/ischemia</td>
<td>11.7</td>
<td>6.5</td>
<td>0.004</td>
</tr>
<tr>
<td>New/worsening CHF</td>
<td>5.2</td>
<td>2.9</td>
<td>0.069</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>2.6</td>
<td>4.5</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Cantor WJ. American College of Cardiology 2008 Scientific Sessions/i2 Summit-SCAI Annual Meeting; March 30, 2008; Chicago, IL.
## TRANSFER-AMI
### 30-day Bleeding End Points

<table>
<thead>
<tr>
<th>End point</th>
<th>Standard (%)</th>
<th>Pharmacoinvasive (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial hemorrhage</td>
<td>1.2</td>
<td>0.2</td>
<td>0.066</td>
</tr>
<tr>
<td>TIMI major</td>
<td>4.6</td>
<td>4.3</td>
<td>0.88</td>
</tr>
<tr>
<td>TIMI major*</td>
<td>3.2</td>
<td>2.2</td>
<td>0.33</td>
</tr>
<tr>
<td>GUSTO moderate</td>
<td>2.2</td>
<td>3.5</td>
<td>0.26</td>
</tr>
<tr>
<td>GUSTO severe*</td>
<td>1.2</td>
<td>0.6</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Non–CABG-related

Cantor WJ. American College of Cardiology 2008 Scientific Sessions/i2 Summit-SCAI Annual Meeting; March 30, 2008; Chicago, IL.
Recommendations for Triage and Transfer for PCI (for STEMI) (cont.)

NEW Recommendation

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.

ACC/AHA STEMI Guidelines, JACC December 2009
STEMI:
Within 24 Hours CP

PCI Capability or
< 60 minute Transfer Time

UFH or Bivalirudin:
GPI Optional: Avoid if High Bleed Risk
B Blockers ONLY if HTN

90 minutes
To Open Artery

Primary PCI with Stenting:
GPI/Thrombectomy if Large Thrombus
or as Bailout; Otherwise, Bivalirudin Alone

Continue bivalirudin for
2 hours after PCI

ASA/Clopidogrel
Or ASA/Prasugrel
Statin
Groin Closure
Cardiac Rehab
Lopressor 12.5 bid

If Reperfusion Fails,
Emergent PCI with stent

ASA/Clopidogrel
Or ASA/Prasugrel
Statin

No PCI Capability and
> 60 minute Transfer Time

UFH (60 U/Kg)
Beta Blockers only if HTN

Lytic Contraindicated

Transfer: 30 Minute
Rule for EMS Cath
Team Activation

Pharmacoinvasive
PCI:
4-24 hours after lytics

Transfer from
Community ER
To PCI site ER

If no CP and less than 50%
ST Elevations, PCI at 4-24
Hours with Stent

**No Prasugrel if
CVA/TIA or lytics**

Rescue PCI:
Class I Indication

Transfer from
Community ER
To PCI site ER

If no CP and less than 50%
ST Elevations, PCI at 4-24
Hours with Stent

90 minutes
To Open Artery

ASA 325 po

Lyric Contraindicated
Improving Technology: 2003 and forward
Drug Eluting Stents, Thrombectomy and Left Ventricular Assist Devices
Drug Eluting Stents Are Not Good For STEMI Due to Increased Risk of Stent Thrombosis (Blood Clots)?

- A) True
- B) False
Bare Metal Stents = Restenosis (Scar Tissue);
Drug Eluting Stents = Thrombosis (Blood Clots).
A New Technology Scare in 2007

Drug Eluting Stents Improve Outcomes: HORIZONS Trial

Ischemic TLR (%)

- TAXUS DES (n=2257)
- EXPRESS BMS (n=749)

Months

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>TAXUS DES</th>
<th>EXPRESS BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2257</td>
<td>749</td>
</tr>
<tr>
<td>3</td>
<td>2105</td>
<td>677</td>
</tr>
<tr>
<td>6</td>
<td>2041</td>
<td>654</td>
</tr>
<tr>
<td>9</td>
<td>1949</td>
<td>611</td>
</tr>
<tr>
<td>12</td>
<td>1618</td>
<td>507</td>
</tr>
</tbody>
</table>

1-yr HR [95%CI] = 0.58 [0.44, 0.76]
P < 0.001
New Technologies: Future Directions

Addressing Thrombus Mechanically

Other Areas of Development

- Support for the sickest patient—cardiogenic shock and left ventricular assist devices
- Support for the sickest patients---cardiac arrest and cooling
- Improved drug eluting stents
## New Devices for STEMI: Thrombus Removal

<table>
<thead>
<tr>
<th></th>
<th>Aspiration (n = 535)</th>
<th>Convention al PCI (n = 536)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Mortality</td>
<td>4.7%</td>
<td>7.6%</td>
<td>1.67 (1.02-2.75)</td>
<td>0.042</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>3.6%</td>
<td>6.7%</td>
<td>1.93 (1.11-3.37)</td>
<td>0.020</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>2.2%</td>
<td>4.3%</td>
<td>1.97 (0.98-3.96)</td>
<td>0.05</td>
</tr>
<tr>
<td>Cardiac Death or Non-Fatal Reinfarction</td>
<td>5.6%</td>
<td>9.9%</td>
<td>1.81 (1.16-2.84)</td>
<td>0.009</td>
</tr>
<tr>
<td>MACE</td>
<td>16.6%</td>
<td>20.3%</td>
<td>1.26 (0.95-1.67)</td>
<td>NS</td>
</tr>
</tbody>
</table>


The Medicines Company does not recommend the use of products outside their approved FDA labeling. For more information about ANGIOMAX, please see the representative for full Prescribing Information.
Improving Trends in All-Cause Mortality, Length of Stay, and AMI Hospitalizations for over 2.7 Million Medicare Patients

### Table 2. Trend in All-Cause Mortality, Length of Stay, and AMI Hospitalizations

<table>
<thead>
<tr>
<th>Year</th>
<th>In-Hospital</th>
<th>30-d</th>
<th>30-d Risk-Standardized</th>
<th>Length of Stay, d</th>
<th>AMI Hospitalizations, No.</th>
<th>AMI Discharges per Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed, Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td>Total Hospitals</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Range</td>
<td>IQR</td>
<td>Mean (SD)</td>
<td>Median (IQR)</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>14.6 (5.9)</td>
<td>18.9 (6.8)</td>
<td>18.8 (2.1)</td>
<td>10.4-27.5</td>
<td>17.3-20.1</td>
<td>7.9 (6.3)</td>
</tr>
<tr>
<td>1996</td>
<td>13.8 (5.8)</td>
<td>18.4 (6.7)</td>
<td>18.2 (2.2)</td>
<td>9.1-26.7</td>
<td>16.8-19.6</td>
<td>7.5 (6.0)</td>
</tr>
<tr>
<td>1997</td>
<td>13.2 (5.6)</td>
<td>18.0 (6.7)</td>
<td>17.7 (2.2)</td>
<td>9.0-26.5</td>
<td>16.3-19.2</td>
<td>7.3 (6.8)</td>
</tr>
<tr>
<td>1998</td>
<td>12.8 (5.4)</td>
<td>17.9 (6.3)</td>
<td>17.8 (1.7)</td>
<td>12.3-25.3</td>
<td>16.7-18.8</td>
<td>7.2 (6.8)</td>
</tr>
<tr>
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<td>14.1 (5.7)</td>
<td>19.5 (6.7)</td>
<td>19.3 (1.7)</td>
<td>14.4-25.4</td>
<td>18.3-20.3</td>
<td>7.3 (5.9)</td>
</tr>
<tr>
<td>2000</td>
<td>13.5 (5.3)</td>
<td>18.9 (6.4)</td>
<td>18.8 (1.7)</td>
<td>12.9-27.0</td>
<td>17.8-19.8</td>
<td>7.2 (6.0)</td>
</tr>
<tr>
<td>2001</td>
<td>13.2 (5.5)</td>
<td>18.7 (6.4)</td>
<td>18.5 (1.7)</td>
<td>13.1-26.1</td>
<td>17.5-19.5</td>
<td>7.1 (6.0)</td>
</tr>
<tr>
<td>2002</td>
<td>12.6 (5.0)</td>
<td>18.1 (6.2)</td>
<td>17.9 (1.7)</td>
<td>13.1-25.0</td>
<td>16.8-18.9</td>
<td>7.1 (5.9)</td>
</tr>
<tr>
<td>2003</td>
<td>12.0 (5.1)</td>
<td>17.8 (6.5)</td>
<td>17.6 (1.7)</td>
<td>12.1-24.1</td>
<td>16.4-18.6</td>
<td>7.2 (6.3)</td>
</tr>
<tr>
<td>2004</td>
<td>11.4 (5.1)</td>
<td>17.2 (6.6)</td>
<td>17.0 (1.5)</td>
<td>12.3-22.9</td>
<td>16.0-17.9</td>
<td>7.2 (6.4)</td>
</tr>
<tr>
<td>2005</td>
<td>10.8 (5.2)</td>
<td>16.5 (6.9)</td>
<td>16.5 (1.6)</td>
<td>11.0-24.8</td>
<td>15.5-17.5</td>
<td>7.1 (6.1)</td>
</tr>
<tr>
<td>2006</td>
<td>10.1 (5.2)</td>
<td>16.1 (7.0)</td>
<td>15.8 (1.7)</td>
<td>10.6-21.6</td>
<td>14.7-16.8</td>
<td>7.0 (6.0)</td>
</tr>
</tbody>
</table>

Abbreviations: AMI, acute myocardial infarction; IQR, interquartile range.

*Hospital has at least 1 case of AMI within an index year.*
The field of STEMI Management has evolved and we have come a long way since 1989 and the birth of reperfusion era with aspirin.

- Regional systems of care focusing on primary PCI (if D2B < 120 minutes) are feasible and effective
- Regional systems of care (Zone 2) focusing on initial lytics followed by same day PCI (pharmacoinvasive therapy) are especially important for rural areas
- STEMI technology has improved: drug eluting stents, thrombectomy, left ventricular assist devices