ST Elevation MI
How far can we go?

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UC Davis Medical Center
Disclosures

● Speakers Bureau
  - Astra Zeneca
  - Bristol Myers/Sanofi
  - Daiichi Sankyo/Lilly
Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances

1954 - First open-heart procedure (Gibbon)
1958 - Coronary arteriography developed (Sones)
1961 - Risk factors defined
1962 - First beta-blocker developed (Black)
1969 - First description of CABG (Favaloro)
1972 - NHBPEP
1976 - First HMG CoA reductase inhibitor described (Endo)
1980 - First implantable cardioverter-defibrillator developed (Mirowski)
1979 - Coronary angioplasty developed (Grüntzig)
1985 - TIMI I
1985 - Superiority of primary PCI vs. fibrinolysis in acute MI noted
1986 - GISSI and ISIS-2
1987 - NCEP
1990 - 1992 - SAVE
1993 - Efficacy of drug-eluting vs. bare-metal stents determined
2000 - 2001 - ALLHAT
2002 - Genomewide association in early-onset MI described
2007 - Benefit of cardiac resynchronization therapy in heart failure demonstrated
2009 - Left-ventricular assist device as destination therapy shown to be effective
2009 - Deep gene sequencing for responsiveness to cardiovascular drugs performed

Nabel EG and Braunwald E. 2012;366:54-63
Emergency Department Visits Annually in the U.S.

- 95 MM visits
  - 8 MM for chest pain
    - 6.1 MM Non-cardiac
    - 0.6 MM for ST-segment Myocardial Infarction
    - 0.4 MM for Non-ST-segment Myocardial Infarction
    - 1.0 MM for Unstable Angina

1. Personal communication, W. Brian Gibler, MD, University of Cincinnati.
2. 2002 SMG Medicare Database.
Diagnostic Algorithm for Acute Coronary Syndrome Management

**Therapeutic goal:** rapidly break apart fibrin mesh to quickly restore blood flow

<table>
<thead>
<tr>
<th>ST-segment elevation MI</th>
<th>Non-ST Elevation ACS*</th>
<th>Non-ST Elevation MI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consider fibrinolytic therapy, if indicated, or primary percutaneous coronary intervention (PCI)</strong></td>
<td><strong>Therapeutic goal:</strong> prevent progression to complete occlusion of coronary artery and resultant MI or death</td>
<td><strong>Consider GP IIb-IIIa inhibitor + aspirin + heparin before early diagnostic catheterization</strong></td>
</tr>
</tbody>
</table>

**Non-ST Elevation MI**

+ Tn &/or + CK-MB

*ACS: Acute Coronary Syndrome*
Pathophysiology of Acute Coronary Syndromes
Pathogenesis of Acute Coronary Syndromes

- Plaque rupture
- Platelet adhesion
- Platelet activation and aggregation
- Partially occlusive arterial thrombosis & unstable angina
- Microembolization & non-ST-segment elevation MI
- Totally occlusive arterial thrombosis & ST-segment elevation MI

White HD. *Am J Cardiol* 1997;80 (4A):2B-10B.
Acute Myocardial Infarction
Role of the Platelet in Non-ST-Elevation Acute Coronary Syndromes

Generally caused by partially-occlusive, platelet-rich thrombus in a coronary artery.

Results from cross-linking of platelets by fibrinogen at platelet receptors GP IIb-IIIa at site of plaque rupture.

Role of the Thrombus in ST-segment Elevation MI (STEMI)

Generally caused by a completely occlusive thrombus in a coronary artery

Results from stabilization by fibrin mesh of a platelet aggregate at site of plaque rupture

Pathways to Platelet Activation

Thienopyridines (e.g., clopidogrel) only block one pathway to platelet activation

GP IIb-IIIa inhibitors displace fibrinogen in existing thrombi to disaggregate thrombus and prevent further platelet cross-linking and thrombosis

GP IIb-IIIa inhibitors prevent platelet activation by blocking GP IIb-IIa (outside-in signaling)

High-dose heparin stimulates PAF which activates platelets

Platelet Activating Factor

Fibrinogen (GP IIb-IIIa)

Aspirin only blocks one pathway to platelet activation

• GP IIb-IIIa inhibitors displace fibrinogen in existing thrombi to disaggregate thrombus and prevent further platelet cross-linking and thrombosis

• GP IIb-IIIa inhibitors prevent platelet activation by blocking GP IIb-IIa (outside-in signaling)

White HD. *Am J Cardiol* 1997; 80:2B-10B.
Phillips DR, Scarborough RM. *Am J Cardiol* 1997;80(4A):11B-20B.
Inf MI, Wenckebach

** ** ACUTE MI ** **

Abnormal ECG

Technician: rena
Test ind: chest pain

Referred by: dr menon

Unconfirmed
Treatment of STEMI - Thrombosis

TPA

PCI
Fibrinolytic therapy

Did save lives compared to placebo, **BUT**
- At best, restored TIMI 3 flow in 55% (rt-PA), +
- Incidence of recurrent ischemia and reinfarction ↑

ICH 0.5-1.0% of pts

2 hours after t-PA

6 hours after t-PA
Coronary Angiography – Occluded RCA

Aspiration Thrombectomy
Coronary Angiography - RCA

Angiosculpt Scoring
Severe residual lesion
Coronary Angiography - RCA

Stent deployment and post dilations
Coronary Angiography - RCA

Final Angiograms
Adjunctive Medical Management of AMI Patient
# Anti-Ischemic Treatment Options to Help Stabilize ACS Patients

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nitrates</strong></td>
<td>Dilate blood vessels; relax and expand arteries, increasing blood flow</td>
</tr>
<tr>
<td><strong>Morphine</strong></td>
<td>Provides pain relief; dilates blood vessels; relaxes and expands artery, increasing blood flow</td>
</tr>
<tr>
<td><strong>Beta blockers</strong></td>
<td>Slow pumping action of heart; reduce oxygen requirements</td>
</tr>
<tr>
<td><strong>ACE inhibitors</strong></td>
<td>Dilate blood vessels; prevent fluid retention; ease the workload of the heart</td>
</tr>
<tr>
<td><strong>Calcium blockers</strong></td>
<td>Dilate blood vessels; reduce vascular smooth-muscle contraction</td>
</tr>
</tbody>
</table>
Target Directed Therapy
Antiplatelet Agents

- ticagrelor
- prasugrel
- clopidogrel
- ticlopidine

ADP = adenosine diphosphate, TXA2 = thromboxane A2, COX = cyclooxygenase.
Currently Available Antiplatelet Therapies

**Oral**
- Aspirin
- Dipyridamole
- Cilostazol
- Thienopyridines: P$2Y_{12}$ inhibitor of platelet function
  - Clopidogrel (Plavix)
  - Ticlopidine (Ticlid)
  - Prasugrel (Effient)
- Ticagrelor (Brilinta)

**Intravenous**
- Glycoprotein (GP) IIb/IIIa inhibitor of platelet function
  - ReoPro (abciximab)
  - Integrilin (eptifibatide)
  - Aggrastat (tirofiban)
IIb/IIIa Inhibitors with UFH in PCI and ACS

Death/MI at 30 Days

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Odds Ratio &amp; 95% CI</th>
<th>Placebo</th>
<th>IIb/IIIa</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIC</td>
<td>2,099</td>
<td></td>
<td>10.1%</td>
<td>7.0%</td>
</tr>
<tr>
<td>IMPACT-II</td>
<td>4,010</td>
<td></td>
<td>8.4%</td>
<td>7.1%</td>
</tr>
<tr>
<td>EPILOG</td>
<td>2,792</td>
<td></td>
<td>9.1%</td>
<td>4.0%</td>
</tr>
<tr>
<td>CAPTURE</td>
<td>1,265</td>
<td></td>
<td>9.0%</td>
<td>4.8%</td>
</tr>
<tr>
<td>RESTORE</td>
<td>2,139</td>
<td></td>
<td>6.3%</td>
<td>5.1%</td>
</tr>
<tr>
<td>EPISTENT</td>
<td>2,399</td>
<td></td>
<td>10.2%</td>
<td>5.2%</td>
</tr>
<tr>
<td>PRISM</td>
<td>3,231</td>
<td></td>
<td>7.0%</td>
<td>5.7%</td>
</tr>
<tr>
<td>PRISM PLUS</td>
<td>1,570</td>
<td></td>
<td>11.9%</td>
<td>8.7%</td>
</tr>
<tr>
<td>PARAGON</td>
<td>2,282</td>
<td></td>
<td>11.7%</td>
<td>11.3%</td>
</tr>
<tr>
<td>PURSUIT</td>
<td>10,948</td>
<td></td>
<td>15.7%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Overall</td>
<td>30,336</td>
<td></td>
<td>11.1%</td>
<td>9.0%</td>
</tr>
</tbody>
</table>

0.79 (0.73, 0.85)  
\[ p < 10^{-9} \]

Topol EJ Lancet 1999;353:227-231
Aspirin

- The simplest drug available in cardiology
  - Old and oral, once a day
- One of the most efficacious
- The cheapest available
- Therefore:
  - The most cost-effective
Aspirin in Acute MI: ISIS-2

Placebo alone:
568/4300 (13.2%)

Aspirin alone:
461/4295 (10.7%)

Streptokinase alone:
448/4300 (10.4%)

Streptokinase plus aspirin:
343/4292 (8.0%)
# Dose-Dependence and Aspirin Efficacy

## Aspirin Dose and Efficacy

<table>
<thead>
<tr>
<th>Aspirin Dose</th>
<th># Trials</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>500–1500 mg</td>
<td>34</td>
<td>19</td>
</tr>
<tr>
<td>160–325 mg</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>75–150 mg</td>
<td>12</td>
<td>32</td>
</tr>
<tr>
<td>&lt;75 mg</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Any aspirin</td>
<td>65</td>
<td>23</td>
</tr>
</tbody>
</table>

*ASA Better ASA Worse*

**BMJ. 2002;324:71-86.**
Rationale for Newer Antiplatelet and Antithrombotic Therapies

- Despite treatment with aspirin and heparin, the incidence of MI and CV death during hospitalization remains high at 6-8%.
- Long term, the incidence of these events remains high at 6-8% per year.
- Majority of patients who enter the hospital for acute coronary syndrome (ACS) are already on aspirin therapy.

# Clopidogrel Across Spectrum of CAD

<table>
<thead>
<tr>
<th>Acute STEMI</th>
<th>UA/NSTEMI</th>
<th>PCI</th>
<th>Long-term 2° (1°) prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLARITY*</td>
<td>CURE†</td>
<td>CREDO†</td>
<td>CAPRIE§</td>
</tr>
<tr>
<td>COMMIT†</td>
<td></td>
<td></td>
<td>CHARISMA† (Lancet 1996)</td>
</tr>
</tbody>
</table>

98,809 Patients Enrolled in Randomized Clinical Trials

<table>
<thead>
<tr>
<th>STEMI</th>
<th>UA/NSTEMI</th>
<th>PCI</th>
<th>MI/Stroke/PAD</th>
<th>High-Risk Vascular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days + Benefit</td>
<td>1 Year + Benefit</td>
<td>1 Year + Benefit</td>
<td>1-3 Years + Benefit</td>
<td>Up to 3.5 years Benefit in symptomatic patients only</td>
</tr>
</tbody>
</table>

*Clopidogrel vs. placebo. †Clopidogrel + ASA. §Clopidogrel vs. ASA.

Is aspirin and clopidogrel enough for everyone? Do we have a need for newer agents?
Prasugrel (Effient)

- Hydrolysis by intestinal carboxylesterases
- Oxidation by intestinal and hepatic CYP-450
- Increased potency > 75% inhibition
Ticagrelor (Brilinta): an oral reversible P2Y\textsubscript{12} antagonist

Ticagrelor is a cyclo-pentyl-triazolo-pyrimidine (CPTP)

- **Direct acting**
  - Not a prodrug; does not require metabolic activation
  - Rapid onset of inhibitory effect on the P2Y\textsubscript{12} receptor
  - Greater inhibition of platelet aggregation than clopidogrel

- **Reversibly bound**
  - Degree of inhibition reflects plasma concentration
  - Faster offset of effect than clopidogrel
  - Functional recovery of all circulating platelets
The therapeutic target for thienopyridines and CPTPs is the platelet P2Y$_{12}$ receptor.
Inhibition of Platelet Aggregation (IPA): Prasugrel and Clopidogrel Loading Dose

The relationship between IPA and clinical activity has not been established.

*Represents healthy subjects in a crossover study who were not on concurrent ASA therapy (n=64).

2. Effient Full Prescribing Information.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Class</th>
<th>IPA (20 uM ADP mean)</th>
<th>Time to peak onset</th>
<th>Reversibility (d/c before CABG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticlopidine 250 mg bid</td>
<td>thienopyridine (pro-drug)</td>
<td>25%</td>
<td>48 hrs</td>
<td>non reversible</td>
</tr>
<tr>
<td>Clopidogrel 300 mg LD</td>
<td>thienopyridine (pro-drug)</td>
<td>30% - 40%</td>
<td>12 hrs</td>
<td>non reversible</td>
</tr>
<tr>
<td>Clopidogrel 600 mg LD</td>
<td>thienopyridine (pro-drug)</td>
<td>35% - 50%</td>
<td>6 hrs</td>
<td>non reversible</td>
</tr>
<tr>
<td>Clopidogrel 75 mg qd</td>
<td>thienopyridine (pro-drug)</td>
<td>30% - 35%</td>
<td>-</td>
<td>non reversible</td>
</tr>
<tr>
<td>Clopidogrel 150 mg qd</td>
<td>thienopyridine (pro-drug)</td>
<td>45% - 50%</td>
<td>-</td>
<td>non reversible</td>
</tr>
<tr>
<td>Prasugrel 60 mg LD*</td>
<td>thienopyridine (pro-drug)</td>
<td>80%</td>
<td>1-2 hrs</td>
<td>non reversible</td>
</tr>
<tr>
<td>Prasugrel 10 mg qd*</td>
<td>thienopyridine (pro-drug)</td>
<td>60%</td>
<td>-</td>
<td>non reversible</td>
</tr>
<tr>
<td>Prasugrel 5 mg qd*</td>
<td>thienopyridine (pro-drug)</td>
<td>40%</td>
<td>-</td>
<td>non reversible</td>
</tr>
<tr>
<td>Ticagrelor 180 mg LD*</td>
<td>cyclo-pentyl-triazolo-pyrimidine*</td>
<td>80%</td>
<td>1-2 hrs</td>
<td>reversible</td>
</tr>
<tr>
<td>Ticagrelor 90 mg bid*</td>
<td>cyclo-pentyl-triazolo-pyrimidine*</td>
<td>70%</td>
<td>-</td>
<td>reversible</td>
</tr>
</tbody>
</table>

*Less affected by genetic polymorphisms and drug interactions (e.g. PPIs)

**not a pro-drug
Prasugrel and Ticagrelor in STEMI
Stent Thrombosis (definite or probable)

**TRITON-TIMI-38 Primary PCI (<12°)**
- **15 months**
  - Clopidogrel (n=1235)
  - Prasugrel (n=1203)

**PLATO Primary PCI (<24°)**
- **12 months**
  - Clopidogrel (n=3792)
  - Ticagrelor (n=3752)

**HR [95%CI]**
- **TRITON-TIMI-38**
  - HR = 0.55 [0.30-1.00]
  - P = 0.048

- **PLATO**
  - HR = 0.74 [0.55-1.00]
  - P = 0.05

Steg PG et al. Circulation 2010;122:2131-41*
Prasugrel and Ticagrelor in STEMI
Cardiovascular Death

TRITON-TIMI-38 Primary PCI (<12°)
15 months
- Clopidogrel (n=1765)
- Prasugrel (n=1767)

HR[95%CI] = 0.69 [0.43-1.11]
P=N/A

N=1235

PLATO Primary PCI (<24°)
12 months
- Clopidogrel (n=3792)
- Ticagrelor (n=3752)

HR[95%CI] = 0.83 [0.67–1.02]
P=0.07

N=1203

Personal communicatoin, Eli Lilly
Steg PG et al. Circulation 2010;122:2131-41
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzylo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*
CV Death, MI or Stroke at 15 Months

HR = 0.79 (0.65–0.97)  
NNT = 42  
RRR = 21%  
p = 0.02

Stent Thrombosis: All ACS

Any Stent Post-Randomization

HR = 0.48 (95% CI, 0.4–0.6)
P < 0.0001

Stent Thrombosis* (%)

<table>
<thead>
<tr>
<th>Days After Randomization</th>
<th>Prasugrel % (n/N) 1.1 (68/6422)</th>
<th>Clopidogrel % (n/N) 2.2 (142/6422)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>150</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>200</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>250</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>300</td>
<td>2</td>
<td>3</td>
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<tr>
<td>350</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>400</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>450</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*Stent thrombosis defined as Academic Research Consortium definite or probable.
†Observed data.

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Lars Wallentin, M.D., Ph.D., Richard C. Becker, M.D., Andrzej Budaj, M.D., Ph.D., Christopher P. Cannon, M.D., Håkan Emanuelsson, M.D., Ph.D., Claes Held, M.D., Ph.D., Jay Horrow, M.D., Steen Husted, M.D., D.Sc., Stefan James, M.D., Ph.D., Hugo Katus, M.D., Kenneth W. Mahaffey, M.D., Benjamin M. Scirica, M.D., M.P.H., Allan Skene, Ph.D., Philippe Gabriel Steg, M.D., Robert F. Storey, M.D., D.M., and Robert A. Harrington, M.D., for the PLATO Investigators*
Time to first primary efficacy event (composite of CV death, MI or stroke)

Cumulative incidence (%)

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9,333</td>
<td>9,291</td>
</tr>
<tr>
<td>60</td>
<td>8,628</td>
<td>8,521</td>
</tr>
<tr>
<td>120</td>
<td>8,460</td>
<td>8,362</td>
</tr>
<tr>
<td>180</td>
<td>8,219</td>
<td>8,124</td>
</tr>
<tr>
<td>240</td>
<td>6,743</td>
<td>6,743</td>
</tr>
<tr>
<td>300</td>
<td>5,161</td>
<td>5,096</td>
</tr>
<tr>
<td>360</td>
<td>4,147</td>
<td>4,047</td>
</tr>
</tbody>
</table>

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval

HR 0.84 (95% CI 0.77–0.92)

p=0.0003

NNT=54
Antiplatelet Guideline Recommendations for STEMI Patients

- **Aspirin**
  - Load with 325 mg
  - Maintenance 75-325 mg daily

- **Clopidogrel**
  - Load with 300-600 mg
  - Maintenance 75 mg daily

- **Prasugrel**
  - Load with 60 mg
  - Maintenance 10 mg daily, 5 mg if < 60kg

- **Ticagrelor**
  - Load with 180 mg
  - Maintenance with 90 mg BID (aspirin <100 mg)
Emerging Therapies
Factor Xa Inhibitors and Direct Thrombin Inhibitors

Bivalirudin
Bivalent Synthetic Direct Thrombin Inhibitor

- Specifically inhibits
  - Fluid phase thrombin
  - Clot-bound thrombin
  - Thrombin-mediated platelet aggregation

- Reversible
- $T_{0.5} = 25$ minutes
- No HIT or HITTS

Topol EJ: Textbook of Interventional Cardiology
Harmonizing Outcomes with Revascularization and Stents in AMI

3602 pts with STEMI with symptom onset ≤12 hours

Aspirin, thienopyridine

R 1:1

UFH + GP IIb/IIIa inhibitor (abciximab or eptifibatide)  Bivalirudin monotherapy (± provisional GP IIb/IIIa)

Emergent angiography, followed by triage to...

CABG  –  Primary PCI  –  Medical Rx

3006 pts eligible for stent randomization

R 3:1

Paclitaxel-eluting TAXUS stent  Bare metal EXPRESS stent

Clinical FU at 30d, 6 mo, 1 yr, and then yearly through 3 yrs; angio FU at 13 mo

Stone GW et al
HORIZONS
Three-Year All-Cause Mortality

- Bivalirudin alone (n=1800)
- Heparin + GPIIb/IIIa (n=1802)

30-day HR [95%CI]=
0.66 [0.44, 1.00]
P=0.048

3-yr HR [95%CI]=
0.75 [0.58, 0.97]
P=0.03

Is there any way to further reduce mortality in STEMI?

Reduce infarct size!
## Partial list of Pharmacologic Studies to Reduce Reperfusion Injury Which Have Failed!

<table>
<thead>
<tr>
<th>Trial</th>
<th>Agent</th>
<th>Proposed mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAMI 9</td>
<td>Fluosol</td>
<td>Inhibit neutrophils, enhance O$_2$</td>
</tr>
<tr>
<td>ISIS-4, MAGIC</td>
<td>Magnesium</td>
<td>Membrane stabilization</td>
</tr>
<tr>
<td>CORE</td>
<td>RheothRx</td>
<td>Enhance O$_2$ delivery</td>
</tr>
<tr>
<td>EMIP-FR</td>
<td>Trimetazidine</td>
<td>Less H$^+$, free radicals, neutrophils</td>
</tr>
<tr>
<td>Flaherty</td>
<td>hSOD</td>
<td>Free radical scavenger</td>
</tr>
<tr>
<td>CALYPSO</td>
<td>Cylexin</td>
<td>Inhibit p-selectin, neutrophils</td>
</tr>
<tr>
<td>AMISTAD I, II</td>
<td>Adenosine</td>
<td>Inhibits neut., vasodilates, metab.</td>
</tr>
<tr>
<td>HALT, LIMIT</td>
<td>Anti-CD18</td>
<td>Inhibit neutrophils</td>
</tr>
<tr>
<td>ESCAMI</td>
<td>Eniporide</td>
<td>Na+/H$^+$ exchange inhibitor</td>
</tr>
<tr>
<td>APEX-AMI</td>
<td>Pexelizumab</td>
<td>C5b-9b complement inhibition</td>
</tr>
<tr>
<td>TRIUMPH</td>
<td>Tilarginine</td>
<td>Nitric oxide donor</td>
</tr>
<tr>
<td>REVIVAL-3, HEBE-3, REVEAL</td>
<td>EPO</td>
<td>Enhances O$_2$ delivery</td>
</tr>
<tr>
<td>PROTECTION AMI</td>
<td>Delcasertib</td>
<td>Inhibits mitochondrial δ-protein kinase C</td>
</tr>
</tbody>
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Relationship Between Myocardial Salvage and Survival: 2005

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

- **Modifying factors**
  - Collaterals
  - Ischemic preconditioning
  - MVO₂

- **U.S. Goal:** Symptoms to balloon: 3.5°

- **Median U.S. Sx-ER:** 2°

- **90’ DBT**

- **Mortality reduction (%):**
  - 90' DBT: U.S. Goal: Symptoms to balloon: 3.5°

Gersh, Stone, Holmes. JAMA 2005
2010+: Do whatever it takes to reduce time from symptom onset to ER arrival and 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
“TIME IS MUSCLE”
Relationship Between Myocardial Salvage and Survival: 2010

Extending of salvage (% of area at risk)

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

Treatment objectives

Modifying factors
- Collaterals
- Ischemic preconditioning
- MVO₂

Median U.S. Sx-ER: 1.75°
U.S. Symptoms to balloon: 2.75°

Gersh, Stone, Holmes. JAMA 2005
Door-to-balloon Time <90 Mins at US Hospitals

Relationship Between Myocardial Salvage and Survival: 2015?

- Extent of salvage (% of area at risk)
- Hours

Mortality reduction (%)
- Median U.S. Sx-ER: 1.5°
- 45' DBT
- U.S. Symptoms to balloon: 2.25°

Modifying factors
- Collaterals
- Ischemic preconditioning
- MVO₂

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

Gersh, Stone, Holmes. JAMA 2005
Mechanical Approaches to Thrombus

Thrombus aspiration
(Rinspirator, Pronto, Export, Rescue, Diver CE, etc.)

Distal protection (GuardWire, FilterWire, AngioGuard, etc.)

Thrombectomy
(AngioJet, X-Sizer)
Distal Protection and Thrombectomy in AMI

Macroscopic embolic debris can be retrieved from >75% of cases
TAPAS: 1,071 pts with STEMI undergoing primary PCI randomized in the ER to manual aspiration


30 days
4.0% vs. 2.1%
P=0.07

1 year
7.6% vs. 4.0%
P=0.04
MGuard Concept

STENT + EMBOLIC PROTECTION
Myocardial Preservation

**Therox** → Supersaturated aqueous oxygen infusion

(PO$_2$ 760-1000 mmHg)
TherOX: Hyperoxemic Perfusion

90’ IC infusion of hyperoxemic blood immediately following successful primary PCI

Spears RS.
High Complexity PCI –
Ventricular Assist Devices

- Cardiogenic shock
- Severe LV dysfunction
- Severe multivessel disease
- Unprotected LM disease
- Complex bifurcation disease
History of Cath Lab Ventricular Support

- ECMO
- IABP
- CPS
- Hemopump
- TandemHeart
- Impella

Decades:
- 70’s
- 80’s
- 90’s
- 00’s
TandemHeart pVAD System

- Removes oxygenated blood from left atrium via transeptal cannula inserted via the femoral vein
- Centrifugal external pump "aspirates" the blood outside the body
- Returns blood via femoral artery
- Provides continuous flow to systemic circulation
Impella pVAD System

- Directly unloads the left ventricle
- Rotary pump provides axial blood flow to ascending aorta
- Ease of placement in the cath lab
STEMI Summary

How can we improve outcomes further?

- ACS encompasses a broad spectrum of pts
  - STEMI, NSTEMI, UA
- STEMI requires early aggressive medical management for ischemia – Time is muscle!
- Target directed therapy for both platelet and thrombin formation
- Aspiration thrombectomy should be routine
- Hemodynamic support early in the course of CS
- New therapies are on the horizon
Thank You