Percutaneous Management of Coronary Artery Disease

Angel E. Caldera, MD
Interventional Cardiology & Vascular Medicine
Disclosures

✓ None
Pathophysiology
Plaque Growth

Traditional Model

Current Model

Lesion progression

Years

Years
The First Coronary Angioplasty for Stable CAD; 1977

First coronary angioplasty lesion (circles) two days before (A) immediately after (B), and one month after (C) balloon dilation
Acute Coronary Syndromes
Acute Coronary Syndromes

- Unstable Angina
- NSTEMI
- STEMI

They are a SPECTRUM of the same disease process
Acute Coronary Syndromes

Inflammation in Plaque Rupture and Thrombosis

Atherosclerosis
Atherothrombosis
Vascular Spasm
Dissection
## ACS Spectrum

<table>
<thead>
<tr>
<th></th>
<th>UA</th>
<th>NSTEMI</th>
<th>STEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Ischemia without necrosis</td>
<td>Necrosis (nontransmural)</td>
<td>Transmural necrosis</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Negative Biomarkers</td>
<td>Positive biomarkers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No ECG ST-segment elevation</td>
<td></td>
<td>ECG ST-segment elevation</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Invasive or conservative depending on risk</td>
<td></td>
<td>Immediate reperfusion</td>
</tr>
</tbody>
</table>

*ACS Spectrum: Acute Coronary Syndromes Spectrum.*
Universal Definition Myocardial Infarction

- Plaque rupture with thrombus
  - MI Type 1
- Vasospasm or endothelial dysfunction
  - MI Type 2
- Fixed atherosclerosis and supply-demand imbalance
  - MI Type 2
- Supply-demand imbalance alone
  - MI Type 2
Universal Definition Myocardial Infarction

- Sudden cardiac death (MI Type 3)
- Peri-PCI MI (MI Type 4a)
- Stent thrombosis (MI Type 4b)
- Peri-CABG MI (MI Type 5)
Unstable Angina and NSTEMI
ACS Spectrum

5 million chest pain visits/yr with 1.57 million ACS admissions
Average age for first MI 65 yo in man and 71.8 in women
1 ACS every 30 seconds
1 Cardiac death every minute
1 in 6 death attributable to coronary heart disease

Chan, et al. Circ 2009;119
2013 AHA Heart and Stroke Statistics, cardiosource.org
All-Cause Mortality in STEMI vs NSTEMI

4606 AMI pts Undergoing Angiography

Chan, et al. Circ 2009; 119
Therapy in NSTEMI ACS is Complex

> 200 combinations with different effects on bleeding and thrombosis risk

Chan, et al. Circ 2009; 119
AHA/ACC Guideline

2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the Society for Cardiovascular Angiography and Interventions and Society of Thoracic Surgeons
Endorsed by the American Association for Clinical Chemistry

WRITING COMMITTEE MEMBERS*
Ezra A. Amsterdam, MD, FACC, Chair†; Nanette K. Wenger, MD, MACC, FAHA, Vice Chair*†; Ralph G. Brindis, MD, MPH, MACC, FSCAI‡; Donald E. Casey Jr, MD, MPH, MBA, FACP, FAHA§; Theodore G. Ganiats, MD∥; David R. Holmes Jr, MD, MACC†; Allan S. Jaffe, MD, FACC, FAHA*†; Hani Jneid, MD, FACC, FAHA, FSCAI†; Rosemary F. Kelly, MD¶; Michael C. Kontos, MD, FACC, FAHA*†; Glenn N. Levine, MD, FACC, FAHA†; Philip R. Liebson, MD, FACC, FAHA†; Debabrata Mukherjee, MD, FACC†; Eric D. Peterson, MD, MPH, FACC, FAHA*#; Marc S. Sabatine, MD, MPH, FACC, FAHA*†; Richard W. Smalling, MD, PhD, FACC, FSCAI***; Susan J. Zieman, MD, PhD, FACC†

827 references

Circulation. 2014;130;e344–e436
1. **Likelihood** of symptoms representing an ACS?
   - High, Intermediate, Low
   - Tools:
     - History, Exam, ECG, Biomarkers
     - Score (AHA/ACC Risk, HEART, etc)

2. **Prognosis** if ACS is likely?
   - Guide treatment intensity
   - Tools:
     - ECG within 10 min, repeat q 15-30 min
     - Biomarkers (Troponin), repeat 3-6 hrs
     - Risk Score (TIMI, GRACE, PURSUIT, other)

*Farkouh ME, et al. Medicine 2009*
Prognosis in ACS

Antman E, et al. NEJM 1996; 335:1342-1349
Prognosis in ACS

TIMI Risk Score
14-Day Event Rates

- Age ≥65
- ≥3 CAD risk factors
- Prior CAD (cath stenosis ≥ 50%)
- Aspirin use in past 7 days
- ≥2 angina episodes within 24 hrs
- ST-segment deviation
- Elevated cardiac biomarkers

Death, MI, Ischemia requiring revascularization at 14 days (%)

0 10 20 30 40 50

0~1 2 3 4 5 6~7

4.7 8.3 13.2 19.9 26.2 40.9

P<0.01

Antman E, et al. JAMA 2000; 284:835-842
Prognosis in ACS

GRACE Risk Model
Probability of In-Hospital Death

www.outcomes.umassmed.org/grace
NSTEMI ACS – Management Strategy

Definite/Possible ACS
Initiate Aspirin, betablockers (po), Statins, Nitrates, Anticoagulants, Telemetry

Early Invasive Strategy
- Electrical or mechanical instability
- Refractory, resistant, recurrent angina
- Elevated Risk Score (Grace>140, TIMI>4)
- Abnormal Biomarkers (>20% change)
- New ST segment depression
- PCI in the past 6 months or prior CABG
- DM or CKD (Stage II or III)
- LVEF < 40%
- Mod Risk Score (GRACE 109-140,TIMI ≥ 2)

Ischemia-Guided Strategy
- TIMI Risk ≤ 2
- No ST segment deviation
- Negative Biomarkers

Coronary Angiography

Stable
Assessment of LVEF
Stress test
LVEF < 40
Recurrent symptoms
Heart Failure
Serious Arrhythmia
Worsening MR
STEMI
ACCF/AHA Guideline

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction: Executive Summary

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions

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Patrick T. O’Gara, MD, FACC, FAHA, Chair†;
Frederick G. Kushner, MD, FACC, FAHA, FSCAI, Vice Chair*†; Deborah D. Ascheim, MD, FACC†;
Donald E. Casey, Jr, MD, MPH, MBA, FACP, FAHA‡; Mina K. Chung, MD, FACC, FAHA*†;
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Y. Joseph Woo, MD, FACC, FAHA†; David X. Zhao, MD, FACC*†

228 references + 2 Updates

Circulation. 2013.127;529–555
STEMI

1.7 million Americans per year suffer from an AMI, 290,000 of which are STEMIs
It is estimated that the number of years of life lost due to an AMI is 14.2 years
12% of those who make it to the hospital will die from their STEMI

AHA Statistical update 2006
Mortality in STEMI

<table>
<thead>
<tr>
<th>Killip class</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6</td>
</tr>
<tr>
<td>II</td>
<td>17</td>
</tr>
<tr>
<td>III</td>
<td>38</td>
</tr>
<tr>
<td>IV</td>
<td>60</td>
</tr>
</tbody>
</table>

Cornwell JACS 1998;187:123
Survival Benefit of Fibrinolytics

N: 58,600 (9 Randomized Trials)

Cornwell JACS 1998;187:123
Time Matters

2. Minimal Additional benefit after 3 hours.

Cornwell JACS 1998;187:123
# Contraindications to Fibrinolytics

## Absolute Contraindications

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any prior intracranial hemorrhage</td>
</tr>
<tr>
<td>Known structural cerebral vascular lesion</td>
</tr>
<tr>
<td>Known intracranial neoplasm</td>
</tr>
<tr>
<td>Ischemic stroke within the past 3 months (except for acute stroke within 3-4.5 hours)</td>
</tr>
<tr>
<td>Suspected aortic dissection</td>
</tr>
<tr>
<td>Active bleeding or bleeding diathesis (excluding menses)</td>
</tr>
<tr>
<td>Significant closed-head or facial trauma within 3 months</td>
</tr>
</tbody>
</table>
Fibrinolytics vs Primary PCI

(23 Trials, N=7739)

Cornwell JACS 1998;187:123
Timing in PCI

Each 30 minute delay in Primary PCI results in a 7.5% relative increase in 1 year mortality

Circulation 2004;109:1223
Competing Reperfusion Strategies

Fibrinolysis
- 100% Available
- 50-60% Eligible
- 55% Reperfuse
- 10-20% Reooclusion
- 2% Stroke

Primary PCI
- <1% Stroke
- 5% Reooclusion
- <25% Availability
- >90% Reperfuse
- 100% Eligible
Competing Reperfusion Strategies

2. Minimal Additional benefit after 3 hours.

Each 30 minute delay in Primary PCI results in a 7.5% relative increase in 1 year mortality.
Guideline Recommendations

Lytic Eligible?

No

Transfer for Primary PCI

Yes

Anticipated Time from FMC to PCI

<120 Minutes

<3 Hours

Transfer for Primary PCI

3-12 Hours

Transfer for Primary PCI

>120 Minutes

Transfer for Primary PCI

Lytics and Transfer*

Transfer for Primary PCI

Time of Symptoms
Stable Coronary Artery Disease
Goals of Therapy

- Improve symptoms and QOL
- Improve Prognosis (likelihood of survival)
- Prevent non-fatal endpoints
  - MI
  - HF
  - VT/VF
Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*
North American Trial

19 US Non-VA Hospitals
15 VA Hospitals
16 Canadian Hospitals

50 Hospitals
2,287 patients enrolled between 6/99-1/04
3,071 Patients met protocol eligibility criteria

2,287 Consented to Participate (74% of protocol-eligible patients)

1,149 Were assigned to PCI group
  46 Did not undergo PCI
  27 Had a lesion that could not be dilated
  1,006 Received at least one stent

1,149 Were included in the primary analysis

784 Did not provide consent
  - 450 Did not receive MD approval
  - 237 Declined to give permission
  - 97 Had an unknown reason

1,138 Were assigned to medical-therapy group

1,138 Were included in the primary analysis

107 Were lost to follow-up

97 Were lost to follow-up
Exclusion Criteria

- Uncontrolled unstable angina
- Complicated post-MI course
- Revascularization within 6 months
- Ejection fraction <30%
- Cardiogenic shock/severe heart failure
- History of sustained or symptomatic VT/VF
Survival Free of Death from Any Cause and Myocardial Infarction

Number at Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
<th>Year 6</th>
<th>Year 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Therapy</td>
<td>1138</td>
<td>1017</td>
<td>959</td>
<td>834</td>
<td>638</td>
<td>408</td>
<td>192</td>
</tr>
<tr>
<td>PCI</td>
<td>1149</td>
<td>1013</td>
<td>952</td>
<td>833</td>
<td>637</td>
<td>417</td>
<td>200</td>
</tr>
</tbody>
</table>

Optimal Medical Therapy (OMT)

PCI + OMT

Hazard ratio: 1.05
95% CI (0.87-1.27)
P = 0.62
Survival Free of Myocardial Infarction

Number at Risk

<table>
<thead>
<tr>
<th>Therapy</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<td>833</td>
<td>637</td>
<td>418</td>
<td>200</td>
<td>134</td>
</tr>
</tbody>
</table>

Hazard ratio: 1.13
95% CI (0.89-1.43)
P = 0.33
COURAGE

Rates of Death or MI by Residual Ischemia – 314 Patients

- 0% (n=23): 0.0%
- 1%–4.9% (n=141): 15.6%
- 5%–9.9% (n=88): 22.3%
- ≥10% (n=62): 39.3%

p=0.002

Shaw et al. Circ 2008;117
COURAGE
Ischemia Reduction – PCI vs MT – 314 Patients
International Study Of Comparative Health Effectiveness With Medical And Invasive Approaches (ISCHEMIA):

Primary Report of Clinical Outcomes

Funded by the National Heart, Lung and Blood Institute
Judith S. Hochman, MD
NYU School of Medicine
On behalf of the ISCHEMIA Research Group
# Eligibility Criteria

## Clinical and Stress Test Eligibility Criteria

### Inclusion Criteria
- Age ≥21 years
- Moderate or severe ischemia*
  - Nuclear ≥10% LV ischemia (summed difference score ≥7)
  - Echo ≥3 segments stress-induced moderate or severe hypokinesis, or akinesia
  - CMR
    - Perfusion: ≥12% myocardium ischemic, and/or
    - Wall motion: ≥3/16 segments with stress-induced severe hypokinesis or akinesia
- Exercise Tolerance Testing (ETT) ≥1.5mm ST depression in ≥2 leads or ≥2mm ST depression in single lead at <7 METS, with angina

### Major Exclusion Criteria
- NYHA Class III-IV HF
- Unacceptable angina despite medical therapy
- EF < 35%
- ACS within 2 months
- PCI or CABG within 1 year
- eGFR <30 mL/min or on dialysis

## CCTA Eligibility Criteria

### Inclusion Criteria
- ≥50% stenosis in a major epicardial vessel (stress imaging participants)
- ≥70% stenosis in a proximal or mid vessel (ETT participants)

### Major Exclusion Criteria
- ≥50% stenosis in unprotected left main

*Ischemia eligibility determined by sites. All stress tests interpreted at core labs.*
Study Flow

Enrolled (8518)

Randomized (5179)
Study CCTA in 73% of randomized participants

Screen Failure (3339)
Major Reasons:
• Insufficient ischemia (N = 1350)
• No obstructive CAD (N = 1218)
• Unprotected LMD (N = 434)

Randomized to INV (2588)

Median follow-up for survivors 3.3 years
(IQR 2.2 to 4.3 years)
Proportion of follow-up completed: 99.4%

Randomized to CON (2591)

Median follow-up for survivors 3.3 years
(IQR 2.2 to 4.4 years)
Proportion of follow-up completed: 99.7%

Ischemia, Symptoms + Non-Obstructive CAD
66% Women
Primary Outcome: CV Death, MI, hospitalization for UA, HF or resuscitated cardiac arrest

Adjusted Hazard Ratio = 0.93 (0.80, 1.08)
P-value = 0.34

Absolute Difference INV vs. CON

6 months:
$\Delta = 1.9\% \,(0.8\%,\, 3.0\%)$

4 years:
$\Delta = -2.2\% \,(-4.4\%,\, 0.0\%)$

Subjects at Risk

<table>
<thead>
<tr>
<th></th>
<th>CON</th>
<th>INV</th>
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<tr>
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<tr>
<td>1</td>
<td>2431</td>
<td>2364</td>
</tr>
<tr>
<td>2</td>
<td>1907</td>
<td>1908</td>
</tr>
<tr>
<td>3</td>
<td>1300</td>
<td>1291</td>
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<tr>
<td>4</td>
<td>733</td>
<td>730</td>
</tr>
<tr>
<td>5</td>
<td>293</td>
<td>271</td>
</tr>
</tbody>
</table>
Conclusion

- Revascularization provides a mortality benefit in patients with STEMI and most patients with ACS

- Early revascularization is critical in patients with STEMI and high risk NSTEMI

- In patients with Stable Coronary Artery Disease an initial invasive strategy did not reduce the risk of CV death, MI or Hospitalization