Cardiogenic Shock

Nick Tehrani, MD
Classic Criteria for Diagnosis of Cardiogenic Shock

1. Systemic Hypotension
   systolic arterial pressure < 80 mmHg

2. Persistent Hypotension
   at least 30 minutes

3. Reduced Systolic Cardiac Function
   Cardiac index < 1.8 l x m²/ min

4. Tissue Hypoperfusion
   Oliguria, cold extremities, confusion

5. Increased Left Ventricular Filling
   Pulmonary capillary wedge pressure > 18 mmHg
### Spectrum of Clinical Presentations

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Respiratory Distress</th>
<th>Hypotension</th>
<th>Hypoperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>21%</td>
<td></td>
<td>1.4%</td>
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<tr>
<td>22%</td>
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<td>5.6%</td>
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<tr>
<td>70%</td>
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<td>28%</td>
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<tr>
<td>60%</td>
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<td>65%</td>
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Risk Factors for Cardiogenic Shock Due to AMI-mediated LV Dysfunction…

- Age > 65
- Female gender
- Large infarction
- Anterior infarction
- Prior infarction
- DM
- Prior HTN
Post-mortem study of Shock hearts

- At least 40% of the myocardium infarcted in the aggregate (old and new injury)
- 80% have significant LAD disease
- 2/3 have severe 3Vdz
Outcomes of Cardiogenic Shock

- Historic mortality 60-80%

- More recently reported mortality numbers
  - 67% in the SHOCK trial registry
  - 56% in GUSTO-I
  (v.s. 3% in Pts. without shock)
Outcomes of Cardiogenic Shock

- The ST pattern in Cardiogenic shock:
  - 15-30% $\rightarrow$ Non-ST elevation MI
    - Older
    - Mortality: 77%
  - 70-85% $\rightarrow$ ST elevations MI/ New LBBB
    - Mortality: 53-63%

SHOCK registry findings on this point...
Outcomes of Cardiogenic Shock

The SHOCK registry

- **Similar mortality** in the two groups
  - 62.5% in non-ST elevation
  - 60.4% with ST elevation
Pathophysiology of Shock

- **Effect of Hypotension**
  - Flow in *normal coronary*:
    - Regulated by microvascular resistance
    - Coronary flow may be preserved at AO pressures as low as 50 mm Hg
  - In coronary vessel with *critical stenosis*:
    - Vasodilator reserve of microvascular bed is exhausted
    - Decrease in AO pressure $\Rightarrow$ Coronary hypoperfusion
Pathophysiology of Shock

Effect of Hypotension (continued…)

Normal heart extracts 65% of the O2 present in the blood

→

Little room for augmentation of O2 extraction
Pathophysiology of Shock

Effect of:
Elevated LVEDP on coronary flow

*Graph depicting the effect of LVEDP on coronary flow.*
Pathophysiology of Shock

Hypotension $+ \uparrow$ LVEDP and critical stenosis $\rightarrow$ Myocardial Hypoperfusion $\rightarrow$ LV dysfunction $\rightarrow$ Systemic lactic acidosis $\rightarrow$ Impairment of non-ischemic myocardium $\rightarrow$ worsening hypotension.
- LVEDP elevation
- Hypotension
- Decreased coronary perfusion
- Ischemia
- Further myocardial dysfunction
- Neurohormonal activation → Vasoconstriction
- Endorgan hypoperfusion
Medical Stabilization of Shock Pts.

- Figure out the volume status, Swan if in doubt
- Air way
- Judicious afterload reduction
- Maintain AV synchrony
  - Don’t tolerate Afib
  - Dual chamber pacing if A-V block present
- Correct Acid-Base disturbances
- Maintain BP (→IABP and/or Pressors)....
Physiologic Effect of IABP in-vivo

- Decreased afterload $\rightarrow$ LV O2 consumption
  
  Williams, et.al., Circulation 1982

- Kern, et.al., Circulation 1993
  - Coronary blood flow velocity was measured using doppler-wire in nine patients with critical stenotic lesions.
  - Peak diastolic coronary flow velocity beyond the stenosis was unaffected by intra-aortic balloon pumping.
  - There was unequivocal IABP-mediated augmentation of both proximal and distal coronary blood flow velocities post PTCA.
Physiologic Effect of IABP in-vivo

- **Fuchs, et.al., Circulation, 1983**

- Great cardiac vein flow was measured in seven patients receiving maximal drug therapy and requiring balloon pumping for unstable angina.
- All patients had greater than 90% stenosis of the proximal LAD coronary artery.
- Increased great cardiac vein flow correlated with increased mean aortic diastolic pressure across changes in balloon volumes (off, 20 cc, 30 cc, and 40 cc) and changes in assist ratio (off, 1:4, 1:2, and 1:1) \( (p = .02) \).
Physiologic Effect of IABP in-vivo

Thus balloon pumping increased flow to a bed fed by the critical stenosis, or **collateral vessels**
Results of a Randomized Prospective Trial of Intraaortic Balloon Counterpulsation and Intravenous Nitroglycerin in Patients With Acute Myocardial Infarction

JOHN T. FLAHERTY, MD, FACC, LEWIS C. BECKER, MD, FACC, JAMES L. WEISS, MD, FACC, JEFFREY A. BRINKER, MD, FACC, BERNADINE H. BULKLEY, MD, FACC, GARY GERSTENBLITH, MD, FACC, CLAYTON H. KALLMAN, ScM, MYRON L. WEISFELDT, MD, FACC

Baltimore, Maryland
IABP in Acute MI

- Pre-thrombolytic era
- **No Lytics**, ASA, or Lopressor
- 20 patients with Acute MI and “extensive myocardium at risk per baseline Thalium” were Randomized.
- Pt.s in Shock were excluded

Std. Rx:
- O2, MSO4, Lido, Heparin

Std Rx +
- IABP Plus IV NTG
IABP in Acute MI

- Patients had repeat Thalium scan on Day-4
- No differences were observed between the two groups regarding:
  - Thalium defect score comparing days 1 and 4
  - The ejection fraction comparing days 1 and 4

=> “Unlikely that a mortality benefit is conferred by the IABP/NTG combination”
Utility of IABP in Shock Pts.

- Observed clinical benefits:
  - Improved acid-base status
  - Improved urine output
  - Improved mentation
  - Improved overall hemodynamics

All this, however, does not add up to improved survival without *Flow Restoration*
Thrombolysis in Cardiogenic Shock

- Rates of Reperfusion Lower, and
- Rates of Reocclusion Higher
  Than in non-shock pts

Possible Reason:

Diffusion of thrombolytic agent into the thrombus may be PRESSURE DEPENDENT.
BP Effect on efficacy of lytics in Shock

Dog data

- LAD occlusion by thrombus
- Hypotension induced by phlebotomy

Prewitt
JACC 1994; 23:784
Any Randomized Trials of Thrombolysis in Cardiogenic Shock???

- Most thrombolytic trials specifically excluded patients in cardiogenic shock

- The only large placebo-controlled thrombolytic study specifically examining Pts. presenting with shock was GISSI-1
  - Streptokinase

=> No Benefit
Combined IABP and Thrombolysis

**Observational Data:**

**GUSTO-I:**
IABP in 62 of the 310 lytic Rx’d Pts. in shock
Combined IABP and Thrombolysis

- Kovack, et. al., JACC 1997
- Stomel, et. al., Chest 1994

Two retrospective observational series from community hospitals:

*Improved survival* from combination Rx.
Combined IABP and Thrombolysis

Observational Data from SHOCK Registry:

- Cardiogenic shock (LV Failure)
  - No Thrombolytic
    - No IABP: n=285, 77% (n=233, 83%; n=52, 48%)
    - IABP: n=279, 52% (n=84, 76%; n=195, 41%)
  - Thrombolytic
    - No IABP: n=132, 63% (n=105, 74%; n=27, 19%)
    - IABP: n=160, 47% (n=51, 69%; n=109, 37%)

- p = .005
- p < .0001
Combined IABP and Thrombolysis
-Barron, et.al., AHJ June 2001
-National Registry of MI-2, Data base
-21,178 pts. Presenting with or developing post-MI shock
-32% Received IABP

The younger pts., twice as likely to get TT => Selection Bias
Combined IABP and Thrombolysis

Accompanying Editorial by Magnus Ohman, and Judith Hochman:

“Although, there is a wealth of physiologic and outcomes data to support the use of early IABP therapy in cardiogenic shock (in conjunction with lytics), randomized trials are clearly needed….”
Combined IABP and Thrombolysis

The only randomized trial on the subject:

Thrombolysis and Counterpulsion to Improve Cardiogenic Shock Survival (TACTICS): Results of a Prospective Randomized Trial.

Magnus Ohman, et.al.,

TACTICS

- ST elevation MI patients, presenting within 12 hours of Sx, and Cardiogenic shock
- 57 Patients were randomized

- Thrombolytic Therapy alone
- Thrombolytic Therapy + IABP
TACTICS

- The **primary endpoint** of 6 month mortality **was not** statistically significant, $P=0.3$

- Subgroup analysis:
  - For KILLIP classes III and IV, $P=0.07$
PATIENT IS IN SHOCK w/ ST elevations, and < 12 hrs Sx onset

If **EARLY REVASCULARIZATION** is not to be pursued:

Administration of Lytics **should not be delayed** in anticipation of placement of IABP despite **lack of randomized data** proving efficacy.

- IABP
- Pressors **May** increase the efficacy of Lytics
SHOCK Trial

Whether EARLY REVASCULARIZATION improves survival among patients with cardiogenic shock?
SHOCK Trial

302 Pts. with ST elevation (or new LBBB) and cardiogenic shock

- Immediate Revascularization (CABG/PTCA)
- Late revascularization (if indicated) deferred for at least 54 hours

• Within 36 hrs. of MI onset
• Within 12 hrs. of Shock onset
SHOCK Trial:
Primary end point, 30 days mortality

**30 days mortality**
- Diff. = 9%
- P = 0.11

**6 Months mortality**
- Diff. = 13%
- P = 0.027

**12 Months mortality**
- Diff. = 14%
- P < 0.02
SHOCK Trial
Why wasn’t the Primary end-point met?

- Low mortality in the initial medical mgt gp.

- High rates of
  - IABP use, 86%
  - TT use, 63%
  - Delayed revascularization, 21%
    - Median of 104 hrs post randomization

30 days mortality
SHOCK Trial: Subgroup analysis, Age less than 75

Mortality

<table>
<thead>
<tr>
<th></th>
<th>30 days</th>
<th>6 months</th>
<th>12 Months</th>
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<tbody>
<tr>
<td>Revasc.</td>
<td>41%</td>
<td>45%</td>
<td>48.4%</td>
</tr>
<tr>
<td>Med Rx</td>
<td>56%</td>
<td>65%</td>
<td>66.7%</td>
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P=0.02 CI<1.0
P=0.002 CI<1.0
P<0.02 CI<1.0
SHOCK Trial:
What to do with Pt.s older than 75

- Total no. of Pt.s older than 75 y.o. = 56 (/302)

- The early revascularization groups had worse outcome at:
  - 30 days (CI >> 1.0)
  - 6 months (CI >> 1.0)
  - 12 months, no difference in outcome
What to do with Pt.s older than 75

- SHOCK Registry results is **in contrast** to the SHOCK Trial findings in this subgroup.

  - Those older than 75 y.o., selected to undergo ERV had a survival advantage.
  - *Case by case assessment* in this population, and **not across the board exclusion** is called for.
## Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

**SHOCK Trial:**

<table>
<thead>
<tr>
<th></th>
<th>Revascularization (N=152)</th>
<th>Medical Treatment (N=150)</th>
</tr>
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<tbody>
<tr>
<td>IIb/IIIa Antagonist</td>
<td>41.7%</td>
<td>25%</td>
</tr>
<tr>
<td>Stent Placement</td>
<td>35.7%</td>
<td>52.3%</td>
</tr>
</tbody>
</table>
Role of IIb/IIIa inhibitors in Cardiogenic Shock

- Retrospective subgroup analysis from the PURSUIT trial Hassade, et.al., JACC, 2000

  - Randomization to eptifibatide did not affect the incidence of shock
  - Patients randomized to eptifibatide who developed shock had a significantly reduced incidence of death at 30 days
  - A possible mechanism of benefit is relief of microvascular obstruction
Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

Long-Term Mortality Benefit With the Combination of Stents and Abciximab for Cardiogenic Shock Complicating Acute Myocardial Infarction

[Coronary Artery Disease]

Chan, Albert W. MD, MS; Chew, Derek P. MBBS; Bhatt, Deepak L. MD; Moliterno, David J. MD; Topol, Eric J. MD; Ellis, Stephen G. MD

AJC Jan. 15, 2002
Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

- Single center, non-randomized
- Data collected: Jan. 1993 and June 2000
- Thirty month follow-up available

96 Pt.s w/ Cardiogenic Shock

- Stent + Reopro N=27
- Stent Only N=14
- PTCA + Reopro N=18
- PTCA Only N=37
Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

On Univariate analysis:

Absence of Stent use:
HR 2.39, 95% CI 1.22 to 4.67, p = 0.01

Absence of Abciximab use:
HR 1.95, 95% CI 1.03 to 3.71, p = 0.04

EF \leq 30%:
HR 3.44, 95% CI 1.35 to 8.78, p = 0.01
Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

Use of Stents
- 29% Absolute mortality reduction
- 1 additional life saved for each 3-4 treated Patients.

Abciximab + Stenting
- 10% Absolute mortality reduction
- 1 additional life saved for each 10 patients treated.
Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

Results of Primary Percutaneous Transluminal Coronary Angioplasty Plus *Abciximab* With or Without Stenting for Acute Myocardial Infarction Complicated by Cardiogenic Shock

Giri, Satyendra MD, MPH, MRCP; Mitchel, Joseph DO; Azar, Rabih R. MD, MSc; Kiernan, Francis J. MD; Fram, Daniel B. MD; McKay, Raymond G. MD; Mennett, Roger MSc; Clive, Jonathan PhD; Hirst, Jeffrey A. MD, MS

*AJC*, 15 January 2002
This was a nonrandomized, prospective observational study.

113 (13.9%) were diagnosed with cardiogenic shock from 8/95 to 8/99.
Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

No Reopro

With Reopro

Cumulative Event Free Survival

- Stent use
- No Stent use

Log rank 5.50, p value 0.01
# Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

## Multivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI grade flow &lt; 3</td>
<td>9.8</td>
<td>2.4–40</td>
<td>0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>3.5</td>
<td>1.2–2.1</td>
<td>0.024</td>
</tr>
<tr>
<td>Total ischemic time</td>
<td>1.6</td>
<td>1.2–2.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Abciximab use</td>
<td>0.24</td>
<td>0.06–0.97</td>
<td>0.04</td>
</tr>
<tr>
<td>Abciximab/stent interaction</td>
<td>0.18</td>
<td>0.04–0.81</td>
<td>0.02</td>
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Role of IIb/IIIa Inhibitors and Stents in Cardiogenic Shock

Speculation:

Greater use of Abxicimab, and Stents in the SHOCK Trial may well have resulted in a positive primary endpoint.

The age cutoff of 75 may or may not have retained its significance vis-à-vis increased mortality.
Reversal of Cardiogenic Shock by Percutaneous Left Atrial-to-Femoral Arterial Bypass Assistance

- VADs were implanted in 18 consecutive patients who had cardiogenic shock after myocardial infarction.
- A 21F venous cannula into the left atrium by transseptal puncture using TEE.
- Pts served as their own controls.
- All hemodynamic parameters showed significant improvement.
- “The influence of this device on long-term prognosis warrants further investigation.”
Take Home Points

- Combining Reopro with Stenting *is likely* to enhance the benefit of early revascularization.

- IABP helpful in stabilizing the Pt.
  - Mitigates clinical signs of SHOCK
  - *May* improve outcome with concurrent Lytics

- No definitive evidence *(randomized trials)* showing improved outcomes with IABP/Lytic combination.
Take Home Points

- Nothing magical about the age cut off of 75, case by case assessment in this population is called for.

- If pt. is not a candidate for early revascularization, but is within 12 hrs. of MI onset, administration of lytics (subject to risk-benefit assessment, age, grafts,…) should not be delayed in anticipation of placement of IABP.