STEMI, Cardiac Arrest and Cardiogenic Shock: Advanced Therapies During Therapeutic Hypothermia

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MANAGING SIMULTANEOUS INSULTS TO THE BRAIN, THE HEART, and Preservation of End-organ Function
RECENT MHI@ANW DATA
1/1/08-10/31/09

760 “LEVEL ONE” ST ELEVATION MIs

- CARDIAC ARREST—80 (10.5%)
- CARDIAC ARREST + CARDIOGENIC SHOCK—30 (4%)
- “COOL IT” 14/30 (46.6%) (Median age 64.5, 56.6% male, Culprit artery-LAD 11, RCA 5, LCX 2, None 7, Unknown 5)
- Avg Stents 1.1
- IABP 12/30 (40%)
- In-Hospital MORTALITY 16/30 (53.3%)

CARDIOGENIC SHOCK
Scope of the Problem

Diverse etiology
- Acute MI 7-10%
- Cardiac Arrest 40-50%
- Post-cardiotomy 0.2-0.5%
- Decompensated CHF
- Acute fulminating myocarditis
CARDBIOGENIC SHOCK

Presence of all of the following criteria immediately before or during the first 24 hours:

- **Arterial hypotension** (systolic arterial blood pressure below 90 mmHg or mean arterial blood pressure below 70 mmHg for 30 minutes or longer with or without therapy);
- **PCWP >18 mmHg** (in patients with a pulmonary artery catheter) or an acute decrease of the left ventricular ejection fraction below 40% (in patients without a pulmonary artery catheter);
- **Need for a continuous infusion of inotropic drugs**
- **IABP**


SHOCK TRIAL

Early Revascularization v.s. Medical Treatment

- Randomized prospective trial
  - Mean age 66 yrs
  - 152 emergent revascularization (PTCA or CABG)
  - 150 medical treatment
    - 63% thrombolytic therapy
    - 86% IABP
    - 25% late revascularization

SHOCK Investigators NEJM 1999;341:625-34
SHOCK Trial: 30-Day and 1-year Survival Based on Type of Urgent Revascularization

30-Day Survival (p=0.86)

- PCI: 55.6%
- CABG: 57.4%

1-Year Survival (p=0.71)

- PCI: 51.9%
- CABG: 46.8%

PCI=percutaneous coronary intervention; CABG=coronary artery bypass graft surgery

PCI for Cardiogenic Shock
ACC/AHA Guidelines

1. Primary PCI is recommended for patients <75 years old with ST elevation or left bundle branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock, unless further support is futile because of the patient's wishes or contraindications/unsuitability for further invasive care.

2. Primary PCI is reasonable for selected patients ≥75 years with ST elevation or left bundle branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock. Patients with good prior functional status who are suitable for revascularization and agree to invasive care may be selected for such an invasive strategy.
Any revascularization, (angioplasty or CABG), in the AMI - cardiogenic shock patient population currently carries a 40% in-hospital mortality!

86% of patients had an IABP inserted

Hochman JS, et al. NEJM 1999 Aug; 341:625-634
BE AGGRESSIVE EARLY

- SBP < 100mmHg on two episodes within first 6 hours independently associated with death
- Appropriate fluids
- Drugs (Dobutamine, Vasopressin, ? NE)
- Mechanical Support


Limitations of Conventional Therapy

- IABP decreases LV workload and increase C.O. by 10-15%
- Need for high dose inotropic support increases myocardial oxygen demand
- Mortality for cardiogenic shock remains >50%

? Could more powerful mechanical support have improved outcomes
Emerging Role of Early Mechanical Circulatory Support

- Hemodynamic stabilization
- Normalization of end organ perfusion
- Potential for Cardiac recovery and weaning
- **Time for evaluation of other options**
  - Transplant
  - Long-term Mechanical Therapy (Destination Therapy)

Timing is Critical

**Early intervention increases the probability of survival:**

*In Acute Settings, Cardiac Function is RECOVERABLE*
LV “Recovery” Goals

- To decompress the ventricle(s).
- Wean toxic levels of inotropes.
- Allow ATP stores to return.
- Allow cytokines to be metabolized.
- Preserve end organ function.

Potential reduction in infarct size
LAD occlusion model

Massive Myocardial damage

Up to 5-times Reduction in infarct size over base line

Impella study – Flameng et al 2000
Impella 2.5 Technology

Clinical Adoption in US
- FDA Clearance in June’08
- 1000+ patients treated
- 300+ US Centers
- 2 Trials Open
- USpella Registry

Impella® 5.0

- Miniaturized Blood Pump Technology
  - 21 Fr micro-axial pump (requires 22-24 Fr Sheath)

- High-Flow Circulatory Support
  - Delivers up to 5 L/min blood flow support

- Directly Unloads Left Ventricle
  - Actively unloads up to 5 L/min from LV

- Peripheral Placement
  - Single peripheral insertion point
  - Femoral Artery Cut-down/ Axillary artery approach
### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>No Shock Mean ± SD or %</th>
<th>Shock Mean ± SD or %</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>74 ± 10</td>
<td>64 ± 16</td>
<td>0.003</td>
</tr>
<tr>
<td>Gender (Male in %)</td>
<td>72 %</td>
<td>92 %</td>
<td>0.04</td>
</tr>
<tr>
<td>STEMI (NSTEMI)</td>
<td>3% (97%)</td>
<td>69% (31%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>33 ± 15</td>
<td>31 ± 14</td>
<td>0.6</td>
</tr>
<tr>
<td>Unprotected LM or LPC</td>
<td>50 %</td>
<td>50 %</td>
<td>0.9</td>
</tr>
<tr>
<td>Multivessel Disease</td>
<td>75 %</td>
<td>91 %</td>
<td>0.2</td>
</tr>
<tr>
<td>Revasc (PCI/CABG/None)</td>
<td>100% / 0 / 0</td>
<td>65% / 23% / 12%</td>
<td>0.002</td>
</tr>
<tr>
<td>Impella placement Pre-PCI</td>
<td>95%</td>
<td>14%</td>
<td>0.001</td>
</tr>
<tr>
<td>Pump Flow (L/min)</td>
<td>2.2 ± .3</td>
<td>2.2 ± .4</td>
<td>0.9</td>
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</table>
USpella AMI Shock Patients

Impella Used After Failed Conventional Therapies (i.e., Revascularization, Inotropes and IABP)

- Emergent Revascularization: 88%
- High Dose Inotropes: 88%
- Already on IABP: 68%

Impella Improves Hemodynamics in AMI Shock

- Cardiac Index: Pre-Impella* 1.9±0.5, On Impella 2.5±0.6, p=0.02
- Mean Arterial Pressure: Pre-Impella* 62±19, On Impella 87±16, p=0.003
- SVR: Pre-Impella* 1.8±0.7, On Impella 1.3±0.5, p=0.01
- Wedge Pressure: Pre-Impella* 28±8, On Impella 20±10, p=0.001

*Pre-Impella measurements were recorded with optimal medical management measures (inotropes + IABP)
Survival to Discharge By Indication

USpella

<table>
<thead>
<tr>
<th>AMI with No Shock</th>
<th>AMI with Shock</th>
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</thead>
<tbody>
<tr>
<td>89% (n=36)</td>
<td>58% (n=26)</td>
</tr>
</tbody>
</table>

TandemHeart® PTVA

- Removes oxygenated blood from the LA via a transeptal cannula
- Returns blood to the femoral artery
- Continuous flow, centrifugal pump 4-5 LPM
TandemHeart® PTVA

Transseptal Cannulation

21 Fr. Transseptal Cannula for venous return
15 or 17 Fr. Arterial Cannula
Lubrication and Pump Controller Line

Blood Pump
Blood Pump Holster
Leg Wrap
Highlights of Texas Heart Institute Experience

<table>
<thead>
<tr>
<th>Refractory Cardiogenic Shock</th>
<th>Pre TandemHeart</th>
<th>Post TandemHeart</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI (lpm)</td>
<td>0.7 +/- 0.5</td>
<td>2.79 +/- 0.97</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SVO2 (%)</td>
<td>39 +/- 10</td>
<td>66 +/- 8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>29 +/- 9</td>
<td>14 +/- 5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>79 +/- 20</td>
<td>101 +/- 13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lactic acid (mg/dl)</td>
<td>64 +/- 54</td>
<td>27 +/- 30</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>2.3 +/- 1.3</td>
<td>1.5 +/- 0.7</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

Current Uses for TandemHeart®

- High Risk PCI
- Acute MI with Shock
- Cardiogenic Shock, Bridge to Recovery
- Cardiogenic Shock, Bridge to Implanted LVAD (Bridge to a Bridge)
- Support During High Risk Surgery
- Right Ventricular Assistance
Case #2: 47yo male cauc

- Known cardiac history and prior PCI
- Sudden severe, retrosternal CP while at his local McDonalds
- EKG – Acute ant MI, Level I Protocol initiated
- Transported to ANW
- V Fib arrest outside of ANW ED, 2 min CPR, defibrillation
- Initial Troponin T 4.69

Catheterization Lab

- Intubated
- Emergent angio:
  - Total occlus prox LAD, 90% stenosis 1st diagonal
  - Patent stents RCA, Circ and 2nd marginal
- PCI to prox LAD with DES, balloon dilation of 1st diagonal
- RHC:
  - PA 42/22, mean 29; PCWP 21
- LVEF 30%
- IABP inserted, remained hypotensive BP 70/53
- Impella 2.5 inserted
Return to ICU

- BP 94/63, mean 76; HR 74 SR
- PA 30/20, mean 26, PW 14, CVP 15, CO 5.89, CI 3.01
- Anticoagulation: heparin infusion
- Echo: LVEF 30-35% with significant anterior and septal WMA, mod decreased RV systolic function
- WBC 12.8, Hgb 12.4, BUN 13, Cr 0.93

Hosp Day #2-3

- Remained intubated, sedated
- Continued Impella support, dopamine, dobutamine
- BP 95/59, mean 73, HR 76 SR
- PA 27/13, mean 18, PW 8, CVP 6, CO 3.5, CI 1.73
- WBC 11.5, Hgb 11.4, Bili 3.9, BUN 19, Cr increased to 1.21
- Gross hematuria. Plasma Hgb 475. Hemolysis 2° Impella?
- Decision to change VAD to TandemHeart
Hosp Day #3 (cont)

- Hemodynamics improved post-TandemHeart: BP 97/67, mean 77, P 69 SR, PA 30/12, mean 18, PW 18, CVP 9, CO 6.38, CI 3.16
- Dopamine and Dobutamine off. Levophed weaned from 9 to 4
- Urine noted to be less bloody. Plasma Hgb 110 → 68

Hosp Days #4 - #7

- Remains intubated, sedated with Fentanyl and Propofol.
- BP 108/68, mean 80, P 79 SR, PA 30/15, mean 20, PW 15, CVP 10, CO 6.91, CI 3.42
- Levophed off
- Urine output > 100cc/hr, Cr decreased to 1.2
- Remained intermittently febrile, T Max 101-102. BCx, UCx, Sputum Cx all remained negative. CXR no significant infiltrates. Continued antibiotics.
- Bili cont to rise, peaked at 9.9 before slowly decreasing. US gallbladder: no obstruction.
Hosp Day #8

- Sedation weaned, neurologically responsive
- Vent weaned, extubated
- TandemHeart weaned and removed, repair R fem artery and vein. Total duration of TandemHeart support: 5 days, 45 minutes
- Hemodynamics post TandemHeart removal: BP 120s, P 80s SR, PA 22/13, mean 16, PW 13, CVP 11, CO 5.3, CI 2.62 Discharged to home on day #16. Outpatient rehab arranged in local community.

ALGORITHM

Cardiogenic Shock

Initial resuscitation/hypothermia

Cath Lab/PCI

Mechanical Support

Wean mechanical support

Transplant evaluation
Assess neuro status
Metabolic support

Alternative Therapy
DECISION MAKING

- TEE
- Attempt to wean
- End Organ Function
- Transplant candidacy

What If ......

Weaning impossible ??
Alternative Treatment Options
Heart Transplantation

- Organ function preserved
- Neuro status intact
- Donor available in timely fashion

Indications strict
Transplantation in Pts on short term LVAD … Rare

pVAD as a Bridge to LVAD in Cardiogenic Shock pts
Long-term VAD Support

- Improved Biocompatibility
- Improved Durability
  - VAD Internal components
  - Mechanics of flow generation
- Improved VAD External components
- Freedom from major infections complications and Strokes

2nd-Generation Devices
Axial Flow Pumps

- Continuous flow, rotary pump
  - Axial design
- Small
  - Length 7 cm
  - Diameter 4 cm
  - 280 gm
- Quiet operation
- Single internal moving part
  - Potential for long-term durability

HeartMate II Clinical Trial
Phase II – Pivotal Study

FDA approved IDE for 2 Clinical Trials

1. Bridge to Transplant -133 pts at 26 sites
   Enrollment: March 2005 to May 2006

2. Destination Therapy
   - 200 patients, at 40 sites
   - Randomized 2:1; HM II vs HM XVE
   - Ongoing: 151 patients (Enrollment complete)
Heartmate II BTT Trial

Results

HeartMate II Clinical Trial
Cause of Death (n=28/133, 21%)

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>N</th>
<th>% of deaths</th>
<th>% of implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>6</td>
<td>21%</td>
<td>5%</td>
</tr>
<tr>
<td>Ischemic CVA</td>
<td>5</td>
<td>17%</td>
<td>4%</td>
</tr>
<tr>
<td>MOF</td>
<td>4</td>
<td>14%</td>
<td>3%</td>
</tr>
<tr>
<td>Hemorrhagic CVA</td>
<td>3</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>Right heart failure</td>
<td>2</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>Anoxic brain injury¹</td>
<td>2</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>Inflow graft twisted</td>
<td>1</td>
<td>3%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Other²</td>
<td>5</td>
<td>17%</td>
<td>4%</td>
</tr>
</tbody>
</table>

¹After protamine reaction, hemothorax
²Cardiac arrest, adenocarcinoma, central line exanguination, support withdrawn, and unknown
Updated HeartMate II BTT Outcomes (n=281)

Outcomes at 18 months

- Transplantation, Recovery or Ongoing Support: 222 (79%)
- Transplantation: 157 (56%)
- Ongoing device support: 58 (20.6%)
- Death: 56 (20%)
- Recovery: 7 (2.5%)
- Withdrawn: 3 (1%)

Pagani et al.

Actuarial Survival
HeartMate II Destination Therapy Trial

As-treated analysis
Log-rank Test p=0.008

Duration of support (yrs):
- CF LVAD
  - Median: 1.7
  - Longest: 3.7
- PF LVAD
  - Median: 0.6
  - Longest: 2.1

Remaining at risk:
- CF LVAD
  - 193
  - 69
  - 32
  - 19
  - 9
  - 5
- PF LVAD
  - 95
  - 32
  - 19
  - 5
  - 2

2010 Miracle on Ice Conference
© Minneapolis Heart Institute® at Abbott Northwestern Hospital
Functional Status
HeartMate II Destination Therapy Trial

% NYHA Class I or II

6 Minute Walk Distance

p<0.001†
p<0.001†

100
80
60
40
20
0

Percent of patients

LVAD Duration

Baseline 3 mo 12 mo 24 mo

CF LVAD
PF LVAD

† over time for both treatments

Quality of Life
HeartMate II Destination Therapy Trial

MLWHF

KCCQ

p<0.001†
p<0.001†

p<0.05 between treatments at 12 mo
† over time for both treatments
Heartmate 2 Received FDA Approval for BTT 2009 and Destination Therapy in January of 2010
Summary

BRIDGE to BRIDGE STRATEGY

- Optimizes patient survival
- Short-term VAD
  - Provides prompt resuscitation
  - Resolution of organ injury
  - Gives time for transplant or Long-term LVAD pt. evaluation
  - Conserves long-term VAD resources
  - Avoids implant of patients unlikely to survive
- Long-term VAD provides
  - Lower risk Compared to immediate TX
  - Long-term circulatory support in pts unlikely to recover for TX
  - Rehabilitation and Discharge Home

2010 Miracle on Ice Conference
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Summary—Cardiogenic Shock Post Arrest

- Continuum of aggressive care (pre-hospital, ER, definitive correction of initial insult (when possible), and aggressive, ongoing “Code Status” in first 36 hours is critical for successful outcomes.
- Many of our current medical therapies may not be as efficacious as we thought and perhaps may increase mortality—*the rules are different post arrest*
- High Risk Group (4% of MIs)—pooled results from “Resusitation Centers” will be needed to guide future care.

CONCLUSION

To improve early survival in Cardiogenic Shock

- Immediate establishment of mechanical support
- Early transition to chronic cardiac support if recovery and weaning not possible
“It is not the strongest of the species that survives nor the most intelligent, but the one who is most responsive to change”

Charles Darwin