Circulatory Support in Acute Cardiogenic Shock: Continuum of Care

Mark B. Anderson, MD
Division of Cardiothoracic Surgery
UMDNJ / Robert Wood Johnson Medical School
New Brunswick, New Jersey
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Consulting Fees/Honoraria</td>
<td>Edwards Lifesciences</td>
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## Cardiogenic Shock: United States

<table>
<thead>
<tr>
<th></th>
<th>AMI</th>
<th>Post Cardiotomy</th>
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<tbody>
<tr>
<td>Admissions / Surgeries</td>
<td>746,000</td>
<td>528,000</td>
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<tr>
<td>Shock Incidence</td>
<td>6% (5-8%)</td>
<td>1.0% (0.5 - 1.5%)</td>
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<tr>
<td>Refractory IABP / Inotropes</td>
<td>40% (30 - 50%)</td>
<td>75% (70 - 80%)</td>
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<tr>
<td>Relative Incidence</td>
<td>1 : 40</td>
<td>1 : 150</td>
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<tr>
<td>Device Candidates</td>
<td>18,000</td>
<td>4,000</td>
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Currently Estimated Only 10-15% of Circulatory Support Candidates Are Being Treated
Inotropes in shock

Myocardial Protection?

The downward spiral of cardiogenic shock

Myocardial Ischemia Leads to Hypotension

Increased Ischemia

Pressor Added to Increase BP

Increased Oxygen Demand

Increased Cardiac Work

Increased Heart Rate & Contractility

Increased $\beta$P & SVRI

Circulatory Support

Positive inotropic agents

Energy-starved myocardium
Outcomes with Inotropes in Cardiogenic Shock

Pre-Shock
LV dysfunction, Borderline hemodynamics
- No Inotrope: 2%
- Low-Dose: 3%
- Moderate-Dose: 7.5%

Shock
LV dysfunction, Borderline hemodynamics, On IABP, inotropes
- One High-Dose: 21%
- Two High-Dose: 42%

Profound Shock
Severe LV dysfunction, poor hemodynamics, refractory IABP, inotropes
- Three High-Dose: 80%

Mortality Risk with Inotrope Dosing

The reduction of hemodynamic loading assists self-regeneration of the injured heart by increasing cell proliferation, inhibiting cell apoptosis, and inducing stem cell recruitment.

• Injured heart may have regenerative function
• Excessive loss of myocytes may be induced by mechanical stresses
• Self repair possible under favorable conditions

Equate Healing With Promoting Recovery
More Potent Devices (LVAD) are Invasive and Used Too Late or not at all

The solution: Minimally Invasive Circulatory Support

Reason:

• Facilitates early device implantation in treatment cascade
  - Improved ease of use (device: < 10min implantation)
  - Reduced invasiveness (device: percutaneous)
  - Reduced comorbidities (device: AE comparable to IABP)
  - Demonstrated effectiveness (device: improved patient outcomes)

• Helps build clinical awareness:
  - Best Practices for Myocardial Protection and Recovery

Goal is the early treatment of cardiogenic shock!
Beneficial Effects of Impella Technology

- **Inflow (ventricle)**
  - **Outflow (aortic root)**

  **Mechanical Work**
  - **Wall Tension**

  **EDV, EDP**

  **O₂ Demand**

  **O₂ Supply**

  **Cardiac Power Output**

  **AOP**

  **Flow**

  **Microvascular Resistance**

  **Coronary Flow**
IABP - most frequently applied circulatory assist device

**Meta-analysis of IABP in ST-elevation MI ... change guidelines?**
*Sjauw et al., Eur Heart J (2009)*

**Scope of Review**
- 804 articles reviewed
- 340 relevant articles identified
- 79 retrospective articles
- 16 series

**Final Study**
- 9 cohort studies and 7 randomized clinical trials of IABP in STEMI:
  - NRMI-2PCI, AMC CS, GUSTO-I, Shock Trial, Waksman, Ohman, PAMI-II, Van t’Hof, TACTICS
Impella vs IABP in AMI Cardiogenic Shock

A Randomized Clinical Trial to Evaluate the Safety and Efficacy of a Percutaneous Left Ventricular Assist Device Versus Intra-Aortic Balloon Pumping for Treatment of Cardiogenic Shock Caused by Myocardial Infarction

Melchior Seyfarth, MD,*† Dirk Sibbing, MD,* Iris Bauer, MS,* Georg Fröhlich, MD,† Lorenz Bott-Flügel, MD,† Robert Byrne, MB, MRCPI,* Josef Dirschinger, MD,† Adnan Kastrati, MD,* Albert Schömig, MD†

Munich, Germany

Objectives
The aim of this study was to test whether the left ventricular assist device (LVAD) Impella LP2.5 (Abiomed Europe GmbH, Aachen, Germany) provides superior hemodynamic support compared with the intra-aortic balloon pump (IABP).

Background
Cardiogenic shock caused by left ventricular failure is associated with high mortality in patients with acute myocardial infarction (AMI). An LVAD may help to bridge patients to recovery from left ventricular failure.

Methods
In a prospective, randomized study, 26 patients with cardiogenic shock were studied. The primary end point was the change of the cardiac index (CI) from baseline to 30 min after implantation. Secondary end points included lactic acidosis, hemolysis, and mortality after 30 days.

Results
In 25 patients the allocated device (n = 13 IABP, n = 12 Impella LP2.5) could be safely placed. One patient died before implantation. The CI after 30 min of support was significantly increased in patients with the Impella LP2.5 compared with patients with IABP (Impella: ΔCI = 0.49 ± 0.46 l/min/m²; IABP: ΔCI = 0.11 ± 0.31 l/min/m²; p = 0.02). Overall 30-day mortality was 46% in both groups.

Conclusions
In patients presenting with cardiogenic shock caused by AMI, the use of a percutaneously placed LVAD (Impella LP 2.5) is feasible and safe, and provides superior hemodynamic support compared with standard treatment using an intra-aortic balloon pump. (Efficacy Study of LV Assist Device to Treat Patients With Cardiogenic Shock [ISAR-SHOCK]; NCT00417378) (J Am Coll Cardiol 2008;52:1584–8) © 2008 by the American College of Cardiology Foundation.
Coronary Perfusion with Impella Benchmark Trial Data from Koenig et al, Univ. of Louisville

Improved perfusion in non-ischemic area

Improved perfusion adjacent to ischemic area
Myocardial Infarction and Impella

Unloading Reduces Infarct Size … Impella vs IABP
Meyns et al., JACC (2003)
RECOVER I: A Safety and Feasibility Study for IMPELLA RECOVER 5.0 Device

Postcardiotomy patients who after CPB continue to present with marginal or low cardiac output despite conventional therapy.
Hemodynamic Improvement during and after Impella 5.0 Support

Cardiac Index

Cardiac Index (l/min/m²)

- **Pre Impella**: 1.4 ± 0.1
- **On Impella**: 3.0 ± 0.4
- **Post Impella**: 2.6 ± 0.3

*p < 0.05

Pump Flow: 4.2 ± 0.8 [3.0-5.2] l/min
Hemodynamic Improvement during and after Impella 5.0 Support

Data of UMDNJ. Subset of RECOVER I.

**Pulmonary Art. Diastolic Pressure**

<table>
<thead>
<tr>
<th></th>
<th>Pre Impella</th>
<th>On Impella</th>
<th>Post Impella</th>
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<tbody>
<tr>
<td>PAD (mmHg)</td>
<td>30±5</td>
<td>20±2</td>
<td>18±3</td>
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*p <0.05*

**Central Venous Pressure**

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<tr>
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<th>On Impella</th>
<th>Post Impella</th>
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<tbody>
<tr>
<td>CVP (mmHg)</td>
<td>14±4</td>
<td>12±2</td>
<td>12±1</td>
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</table>

*p <0.05*
# Clinical Outcomes-Recover 1

## Primary Endpoints:
- Death: 2 (12%)
- CVA (Pre/On/Post?): 1 (6%)

## Secondary Endpoints:
- Aortic Insufficiency: 0 (0%)
- Aortic Valve Injury: 0 (0%)
- Bleeding requiring Re-op: 3 (17%)
- Failure to implant device: 1 (6%)
- Device Failure (stoppage): 1 (6%)
- Insertion Site Infection: 1 (6%)
- Vascular Injury: 1 (6%)
- Hemolysis: 1 (6%)
- Renal Failure: 1 (6%)
- Hepatic Failure: 1 (6%)
- Sepsis: 2 (12%)

## Observed In-hospital Mortality
- 12%

## Predicted In-hospital Mortality
- 34%

## Support Time
- Mean ± SD = 3.5 ± 3.0 days
- Range = [1.7 – 13 days]

*The adverse events have not been all monitored and adjudicated as of 10/8/08. The results may vary after the adjudication.*
Medium Term Surgical VAD

• Para-corporeal, pulsatile, uni or bi-ventricular support
• Atrial or Ventricular cannulation
• No Coring of the Ventricle required
• Average Length of support = 22 days (Longest = 312 days)
• Early Ambulation, Excellent Hemocompatibility, Lower Anticoagulation

ABIOMED AB5000®
Recovery of Left Ventricular Function in AMI Cardiogenic Shock After Temporary LVAD: AB5000
A U.S. Multicenter Experience

Mark Anderson¹, Michael Madani², Yoshifumi Naka³, Daniel Raess⁴, Louis Samuels⁵, Benjamin Sun⁶, Lynn Sleeper⁷, Karim Benali on behalf of all participating centers

¹Robert Wood Johnson Medical School, New Brunswick, ²University of California San Diego, San Diego, CA; ³Columbia University Medical Center, New York, NY; ⁴Saint Francis Hospital, Indianapolis, IN; ⁵Lankenau Medical Science Hospital, Philadelphia, PA; ⁶Ohio State University Medical Center, Columbus, OH; ⁷New England Research Institute, Watertown, MA, ⁷ABIOMED
63% of the Survivors Recovered Their Native Heart Function

Average Time of VAD Support to Achieve Recovery = 25 days [range 2-95 days]

30-day Survival (N=100)

- Recovered (63%)
- Transplanted (20%)
- Other Device (17%)

Data Registry for All US patients with AMI Cardiogenic Shock implanted with ABIOMED AB5000 between October 1st 2003 and June 30 2006
ACUTE CARDIOGENIC SHOCK STRATEGIES

Medical

- Acute MI
- Acute Viral Myocarditis
- Acute Postpartum Coronary Dissection
- Intractable Ventricular Arrhythmia
- Trauma

Cardiogenic Shock

↓CI, ↓MAP, ↑PCWP, ↑CVP

Surgical

- s/p CABG
- s/p Valve Replacement
- s/p Failed Transplant
- s/p Implantable LVAD
- s/p LVA Repair
- s/p Post-Infarct VSD

Inotropes

+-/- IABP

CI < 2.2

Impella

+-/- rvad

wean trial

Low Output with 2 Med Dose Inotropes

Enzymes, TEE, hemodynamics, biopsy?

30 min. of wean from CPB or PCI

3d-2weeks From event

Persistent Cardiac Dysfunction

After LVAD  ↑CVP  ↓LVAD flow

After RVAD  ↑PAP  ↓MAP

Bi-Ventricular Support

Medium Term VAD

AB5000

wean trial

2wks-3 mos from event

Recovery likely

Recovery unlikely

Recovery

No Recovery

Transplant

Destination

Implantable VAD

HM II

Cath Lab

OR

Swan Ganz

Recovery likely

Recovery unlikely
Conclusions

Management of Cardiogenic Shock Requires a Strategy that Includes:

- Early, aggressive approach, using less invasive technology
- IABP / inotropes ineffective, dangerous?
- Collaboration between cardiology / cardiac surgery
- Adequate opportunity for recovery
- Continuum strategy with devices
Paradigm Shift

Failure of acute support does not equal transplantation

Mechanical Circulatory Support

Bridge to Transplant  Bridge to Recovery
Door to Balloon     Door to Unloading

Everyone is a recovery candidate until proven otherwise!
Thank You