End-stage Heart Failure
Left Ventricular Assist Devices

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November 3, 2009
Heart Failure: LVAD Therapy

- **Background**

- Heart transplantation

- Mechanical support

- Specific Devices
# Heart Failure

<table>
<thead>
<tr>
<th>Age</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>50-64</td>
<td>5-7%</td>
</tr>
<tr>
<td>65-74</td>
<td>10-12%</td>
</tr>
<tr>
<td>&gt;75</td>
<td>15%</td>
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</tbody>
</table>
End Stage Heart Failure

- Refractory symptoms
- Intolerance of standard medical treatments
- Poor hemodynamics with end-organ dysfunction
- Frequent hospitalizations
End Stage Heart Failure

- 5-10% of total heart failure population
- >60% of health care expenditures for heart failure
- One-year survival 10-20%
End Stage Heart Failure: Treatments

- Defibrillator
- Bi-Ventricular Pacing
- Intravenous Inotropes
- Heart Transplantation
- Mechanical Circulatory Support
Mortality on Intravenous Inotropes

Stevenson, L. W. Circulation 2003;108:492-497

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Heart Failure: LVAD Therapy

- Background
- Heart transplantation
- Mechanical support
- Specific devices
Heart Transplantation


Half-life = 10.0 years

N=78,050
Heart Transplantation


Survival (%) vs. Years

- 1982-1991 (N=18,846)
- 1992-2001 (N=35,238)
- 2002-6/2007 (N=15,620)
LVAD Terminology

- Temporary support
- Bridge to transplantation
- Destination therapy
Heart Failure: LVAD Therapy

- Background
- Heart transplantation
- Mechanical support
- Abiomed Impella
Abiomed Impella 2.5

Clinical Adoption in US

FDA Clearance in June’08

1000+ patients treated

300+ US Centers

2 Trials Open
USpella Registry

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Abiomed Impella 2.5
Impella 2.5

- High-risk angioplasty
- Acute myocardial infarction
Others includes Elective CABG, Myocarditis with shock, Post-cardiotomy shock, septic shock, toxic shock, post partum cardiomyopathy, other cardiomyopathies with shock

Main Indications For Support

- Elective (37%)
- Without Shock (20%)
- With Shock (14%)
- Acute Myocardial Infarction (34%)
- Other (5%)
- Urgent (18%)
- ADHF w/ Shock (6%)

High Risk PCI (55%)
Impella Improves Hemodynamics in AMI Shock

Cardiac Index

\[ \text{Cardiac Index (l/min/m}^2 \] = 1.9±0.5 \quad \text{Pre Impella*} \\
= 2.5±0.6 \quad \text{On Impella}

\[ p=0.02 \]

Mean Arterial Pressure

\[ \text{MAP (mmHg)} \] = 62±19 \quad \text{Pre Impella*} \\
= 87±16 \quad \text{On Impella}

\[ p=0.003 \]

SVR

\[ \text{SVR (x 1000 dynes/sec x cm}^2 \] = 1.8±0.7 \quad \text{Pre Impella*} \\
= 1.3±0.5 \quad \text{On Impella}

\[ p=0.01 \]

Wedge Pressure

\[ \text{PCWP (mmHg)} \] = 28±8 \quad \text{Pre Impella*} \\
= 20±10 \quad \text{On Impella}

\[ p=0.001 \]

*Pre-Impella measurements were recorded with optimal medical management measures (inotropes + IABP)
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%

Therapy Usage Pre-Impella Support

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*N=25 subjects have LVEF measurements available Pre and Post PCI
** Longest available follow-up from PCI

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Survival to Discharge

AMI with No Shock: 89% (n=36)
AMI with Shock: 58% (n=26)

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Heart Failure: LVAD Therapy

• Background
• Heart transplantation
• Mechanical support
  • Heartmate II
REMATCH

Survival (%)

Months

NO. AT RISK
LV assist device 68 38 22 11 5 1
Medical therapy 61 27 11 4 3 0


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**Table 6. Hospitalization Experience.**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th><strong>Medical-Therapy Group</strong></th>
<th><strong>LVAD Group</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Days alive</td>
<td>150</td>
<td>408</td>
</tr>
<tr>
<td>Days spent out of the hospital</td>
<td>106</td>
<td>340</td>
</tr>
<tr>
<td>Days spent in the hospital</td>
<td>24</td>
<td>88</td>
</tr>
<tr>
<td>Days spent in the hospital for medical management or implantation of LVAD</td>
<td>5</td>
<td>29</td>
</tr>
</tbody>
</table>

*LVAD denotes left ventricular assist device.*
Conclusions: REMATCH

- LVAD resulted in survival advantage
- Improved quality of life
- Morbidity and mortality is substantial in LVAD group
Follow up to REMATCH

- FDA approval of HeartMate XVE
- CMS reimbursement approval
- Designated DT LVAD centers
- Mandatory post-approval FDA registry
Thoratec HeartMate II
HeartMate II LVAS

Key Design Features

- Relatively Simple Design
  - Valveless
  - Only one moving part, the rotor
  - Blood immersed bearings designed for minimization of blood damage
  - All motor drive and control electronics are outside of the implanted blood pump

- Speed range: 6,000 to 15,000 rpm

- Flow range: 3 – 10 L/min
HM II Pump External View

- Inflow Conduit (20 mm)
- Flex Section:
  - Woven polyester graft
  - Titanium ring
  - Preclotting slots
  - Silastic sleeve
- Outflow Graft (16 mm)
- Bend Relief
- Percutaneous lead (8 mm)
- Blood Pump
More than 3,000 patients worldwide have now been implanted with the HeartMate II LVAS

- Patients supported ≥ 1 year: 471
- Patients supported ≥ 2 years: 188
- Patients supported ≥ 3 years: 42
- Patients supported ≥ 4 years: 3
- Patients supported ≥ 5 years: 1

*As of 6/30/09
HeartMate II LVAD
Blood Flow Path

- **Inflow from LV**

- **Inlet Stator**
  - 3 vanes “straighten” the flow before it enters the rotor

- **Rotor**
  - Propel blood toward outflow & spins it radially imparting kinetic energy

- **Outlet stator**
  - “Straightens” flow as leaves rotor and pressure is further increased

- **Outflow to ascending aorta**
HeartMate II LVAD
Clinical Experience
HeartMate II Pivotal Trial

FDA approved Investigational Device Exemption (IDE) for two clinical studies:

1. Bridge to Transplantation (BTT) – patients enrolled at 33 sites

2. Destination Therapy (DT) – patients enrolled at 40 sites
   - Randomized 2:1; HeartMate II vs. HeartMate I
   - Enrollment completed May, 2007
   - Two year follow-up completed May, 2009
HeartMate II BTT Clinical Study
Entry Criteria

• New York Heart Association Class IV heart failure symptoms
• Transplant listed 1A or 1B (if 1B meet hemodynamic criteria)
• On inotropic support
• No severe end-organ dysfunction/failure
• Ability to tolerate anticoagulant or antiplatelet therapies
• No moderate to severe aortic insufficiency without plans for correction
HM2 Clinical Trial
Patient Demographics

• Median Age: 55 years (18-69)
• Etiology: 37% Ischemic
• 21% Female, 79% Male
• BSA
  ➢ Female 1.65 m² (1.33-2.45)
  ➢ Male 2.10 m² (1.53-2.62)
• UNOS 1A 48%, 1B 52%
HeartMate II Clinical Study
BTT Trial Design

- Multicenter, non-blinded, non-randomized, prospective study

- Primary outcomes
  - Death
  - Transplantation
  - Myocardial recovery
  - Survival to 180 days on LVAS support
<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td>16 ± 6</td>
</tr>
<tr>
<td>Cardiac Index</td>
<td>2.0 ± 0.6</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>26.2 ± 7.9</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>95.7 ± 14.6</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.4 ± 0.5</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>104 ± 286</td>
</tr>
<tr>
<td>Intravenous Inotropes</td>
<td>89%</td>
</tr>
<tr>
<td>≥ 2 Inotropes</td>
<td>25%</td>
</tr>
<tr>
<td>IABP</td>
<td>41%</td>
</tr>
</tbody>
</table>
Duration of Support

- Median duration: 155 days (longest: 3.2 yr)
- Average duration: 237 days
- 181 pt-years cumulative support
- 87% patients discharged
  - 78% on device support
  - 10% following transplant (prior to index discharge)
- 77% of time (140 pt-years) spent out of hospital
Primary Outcomes at 18 months (n=281)

- Transplanted: 55.8% (157)
- Ongoing Support > 180 Days: 20.6% (58)
- Cardiac Recovery with Device Explant: 2.5% (7)

Kaplan-Meier Survival (N=281)

Number at risk:
- 281
- 1 month: 281
- 6 months: 133
- 12 months: 77
- 18 months: 58

Survival %:
- 1 month: 92 ± 2%
- 6 months: 82 ± 3%
- 12 months: 73 ± 3%
- 18 months: 72 ± 3%

HeartMate II Clinical Trial

Percent of patients

Baseline 1 mo 3 mo 6 mo

0% 59% 79% 85%

NYHA II NYHA I

P < 0.001

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HeartMate II Clinical Trial

Functional Status – 6 minute walk

Meters

Baseline 1 mo 3 mo 6 mo

42 ± 98 197 ± 171 297 ± 211 346 ± 215

P < 0.001
HeartMate II Clinical Trial
Summary of QoL Findings

• At three and six months, 72% and 85% of patients, respectively, were NYHA Class I or II

• Average distance covered during 6-minute walk test improved 4.5x in one month and 8x in 6 months

• Patients reported significant improvement in quality of life
# Adverse Event Rates

<table>
<thead>
<tr>
<th>Event</th>
<th>Continuous Flow HM II (62 pt yrs) (n=133)</th>
<th>Pulsatile Flow HM VE¹ (86 pt yrs) (n=280)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>0.78</td>
<td>1.47</td>
</tr>
<tr>
<td>Driveline infection</td>
<td>0.37</td>
<td>3.49</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.19</td>
<td>0.44</td>
</tr>
<tr>
<td>Non-stroke neurological</td>
<td>0.26</td>
<td>0.67</td>
</tr>
<tr>
<td>RV failure</td>
<td>0.08</td>
<td>0.30</td>
</tr>
</tbody>
</table>

¹Frazier OH, Rose EA, Oz MC, et al; J Thor CV Surg 2001
HeartMate II Clinical Study

Actuarial survival during support

Percent Survival

Months Post Enrollment

HMII (n=194)

HM VE (n=280)
Lessons from BTT with Implantable LVADs

- Advanced heart failure can be treated with LVAD only
- Most device malfunctions are treatable and nonfatal
- Extended periods of support possible
- Reasonable quality of life
Left ventricular assist device therapy is a safe and effective treatment for patients awaiting heart transplantation.
Destination therapy provides superior survival and quality of life in patients with end-stage heart failure
How to help

• Support measures which allow for these life-saving therapies

• Support funding for biomedical research