Rise of the Machines: Outcomes of Left Ventricular Assist Devices

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Heart Failure: A Growing Global Epidemic

• By 2030 in US → 10 million
• Limited donor organ availability
• Durable, implantable ventricular assist devices (LVADs) to overcome the shortage


Projected Mortality for AHF Exceeds Other Terminal Diseases

• For patients with irreversible biventricular failure
• BSA 1.7 – 2.5 m²
Or
• >10 cm from ant vert body to inner sternum at T10

Exponential Rise in VAD Implantation

2006: N=100
2013: N=2500
* 2500% INCREASE

JHLT. 2013 Oct; 32(10): 951-964
79% Survival to Transplant w/ TAH

REMATCH: Better Survival with LVAD

P=0.0001
1yr = 52%
2yr = 29%
P=0.0003
2yr* = 8%

Growing Experience, Improving Survival with Implantable VAD Therapy

Patient Selection is Key

Also Improved:
- QOL
- Functional capacity

INTERMACS, Interagency Registry for Mechanical Circulatory Support

4/24/2017
Survival Inversely Related to INTERMACS Score

Pulsatile, Volume Displacement Pumps – Constraints
- Provides excellent pulsatile hemodynamic support
- Approved for bridge-to-transplantation and destination therapy
- Large size
  - Minimum BSA requirement of 1.5 m²
- Extensive surgical dissection
- Limited durability
- Requirement for venting of air
  - Large percutaneous lead
- Noisy operation

Kaplan-Meier Estimates of Survival from the As-Treated Analysis, According to Treatment Group

HeartMate II LVAS System Components
- Flexible inflow conduit
- Textured surfaces
  - Inlet cannula, inflow and outflow elbows
  - Thrombo-resistant
- Outflow graft with bend relief
- Anastomosed to LV apex and ascending aorta

Pulsatile-Flow (Panel A) and Continuous-Flow (Panel B) Left Ventricular Assist Devices (LVADs)

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Kaplan-Meier Estimates of Survival from the As-Treated Analysis, According to Treatment Group

Pulsatile-Flow (Panel A) and Continuous-Flow (Panel B) Left Ventricular Assist Devices (LVADs)
More than 20,000 patients worldwide have now been implanted with the HeartMate II LVAS. Over 7,000 patients on ongoing support.

There is now a patient from the Pivotal Trial who has been on support with HeartMate II for over a decade.
A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure

Mandip R. Mehra, M.D., Yoshifumi Naka, M.D., Na Li, M.D., David J. Goldsmith, M.D., Joseph C. Cleveland, M.D., Rocco Celentano, M.D., Mary N. Walsh, M.D., Camilo A. Mello, M.D., Christian Patel, M.D., Ulrich P. Linde, M.D., Francis P. Pagani, M.D., Keith D. Aurigemma, M.D., David A. Oyer, M.D., Kelly McCants, M.D., Akira Inoue, M.D., Gregory A. Bivard, M.D., Douglas Hernandez-Goel, M.D., James W. Long, M.D., and Christopher Sullivan, M.D., for the MOMENTUM 3 Investigators.

Patient meets MOMENTUM 3 eligibility criteria?

Short Term (ST) Cohort
N=294
6-month follow-up
Randomization 1:1

Long Term (LT) Cohort
N=366
24-month follow-up

Full Study Cohort
N=1028
24-month follow-up for powered secondary endpoint

HeartMate 3
N=152
HeartMate II
N=142

Treatment failures (not treated with study device)
N=4
No LVAD implant: 1
Withdrawal of consent: 1
Transplant: 1
Implanted with non-study LVAD: 1

Primary Endpoint Analysis (ITT)
Survival at 6 months free of disabling stroke or reoperation to replace or remove the pump

Non-inferiority Analysis
Absolute difference: 4.7% (95% LCB -10.0%, P=0.004)

Superiority Analysis
HR 0.55, (95% CI 0.32-0.95), P=0.037

Key Adverse Events:
Pump Thrombosis, Neurological Events, Bleeding

<table>
<thead>
<tr>
<th>Event</th>
<th>HeartMate 3 (n=151)</th>
<th>HeartMate II (n=138)</th>
<th>RR 95% CI for RR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected or Confirmed Pump Thrombosis</td>
<td>0 (0)</td>
<td>0</td>
<td>N/A</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>All Stroke</td>
<td>12 (7)</td>
<td>19 (13)</td>
<td>0.66</td>
<td>0.39</td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>4 (2)</td>
<td>9 (6)</td>
<td>0.56</td>
<td>0.18</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>8 (5)</td>
<td>9 (6)</td>
<td>0.81</td>
<td>0.66</td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>9 (6)</td>
<td>13 (9)</td>
<td>1.75</td>
<td>0.36</td>
</tr>
<tr>
<td>Other Neurological Events*</td>
<td>9 (6)</td>
<td>8 (6)</td>
<td>1.03</td>
<td>0.95</td>
</tr>
<tr>
<td>Bleeding</td>
<td>16 (11)</td>
<td>32 (23)</td>
<td>0.50</td>
<td>0.29</td>
</tr>
<tr>
<td>Bleeding Requiring Surgery</td>
<td>7 (5)</td>
<td>11 (8)</td>
<td>0.66</td>
<td>0.18</td>
</tr>
<tr>
<td>Gastrointestinal Bleeding</td>
<td>24 (16)</td>
<td>39 (28)</td>
<td>0.64</td>
<td>0.12</td>
</tr>
</tbody>
</table>

No Pump Thrombosis in the HeartMate 3 LVAS group
Similar Stroke and Bleeding rates in both groups

Unplanned Hospital Readmissions After HeartMate II Implantation

Frequency, Risk Factors, and Impact on Residence Use and Survival

Nichole E. Swiford, M.D., Katherine J. Horowitch, R.N., Brian Liner, M.D., Maria M. Moncure, D.O., Rushid C. Shingko, M.B.B.S., Lucy Thom, M.B., Dheeraj M. Sheth, M.D., Eugene H. Beckson, M.D.*
Cleveland Clinic


N=48 (52%) w/ 177 unplanned hospital readmissions
– 87 non-LVAD related
– 90 LVAD associated
Long Term Mortality Contributors

- Thrombosis
- Stroke - ischemic or hemorrhagic
- RV Failure
- MSOF
- Infection/Sepsis
- Device malfunction
- Bleeding

Reoperation

Cumulative Incidence of HMII Device Thrombosis

Neurologic Events

Boyle et al: Retrospective analysis of BTT (956) and DT (551) HMII trial+CAP patients

- Hemorrhagic stroke, 8% cumulative incidence (0.05 events ppy)
- Ischemic stroke, 6% cumulative incidence (0.04 events ppy)

Boyle JACC 2014;63:880

Bleeding on HMII

Early bleeding:
- Thoracic (42% of major bleeds)
- Undetermined

Late bleeding:
- GI (21% of major bleeds) and recurrent
- CNS

Boyle JACC 2014;63:880

Risk factors for bleeding

Boyle et al: (JACC 2014;63:880)

- Age >65 yrs (HR 1.3 [1.1-1.6])
- Preop HCT <31% (HR 1.31 [1.0-1.6])
- ISCM (HR 1.35 [1.1-1.7])
- Female sex (HR 1.45 [1.1-1.8])

Major Bleeding During HMII

Bunte et al (n=145)
- Single center study of HMII pts
- >3 u first postop week or any thereafter-1.1 events ppy

Boyle et al (n=956)
- BTT and DT HMII trial pts
- Bleeding > 2u-0.67 events ppy

Vicious Interdependent Cycle

Major obstacle to VAD as long term cardiac replacement therapy
If I only had an LVAD...

• Trends point towards an ever increasing proportion of “heart failure” patients requiring conventional & advanced cardiac care
• Mechanical circulatory support will continue to evolve and provide the greatest hope for the greatest number of heart failure patients
• Some of the most impactful and newest advances in the field will be trialed here by Baylor Scott & White Health
• Many of these patients will have VAD related and non-related ER visits and rehospitalizations