LVAD Update for Primary Care
A bit of past, present and Future

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Advanced Heart Failure / MCS Service
BSW Health
Disclosures

• I have no disclosures
Background

• AHF Problem
• Historical perspective
• Complications
• Referral for Advanced HF therapies
• Current Trends
• Future directions
# Implications of heart failure in the U.S. \(^1-4\)

| **5.7 million** | **Adults in the U.S. have heart failure**\(^1,2\)  
Up to 1.5 million are in the advanced stages |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At least 25,000</strong></td>
<td><strong>Patients are appropriate candidates for advanced heart failure therapies</strong>(^3)</td>
</tr>
</tbody>
</table>
| **Estimated 3,200** | **Donor hearts are available for heart transplants each year**\(^4\)  
Supply of donor hearts is limited and heart transplantation is not an option for all patients\(^3,4\) |
| **Over 270,000** | **Patients die of heart failure in the U.S. each year**\(^1,2\)  
About half of the people with heart failure die within 5 years of diagnosis\(^1,2\) |

Heart failure is the leading cause of death after cancer

Class IV heart failure mortality at 1 year is similar to that of aggressive malignancies

The Late Stage Heart Failure Patient

- Severe exercise intolerance
- Heart failure wasting syndrome
- Cardiorenal syndrome
- Right heart failure
- Inotrope dependence
## Defining Advanced Heart Failure

1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA class III or IV)

2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or reduced cardiac output at rest (peripheral hypoperfusion)

3. Objective evidence of severe cardiac dysfunction shown by at least 1 of the following:
   a. LVEF <30%
   b. Pseudonormal or restrictive mitral inflow pattern
   c. Mean PCWP >16 mm Hg and/or RAP >12 mm Hg by PA catheterization
   d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes

4. Severe impairment of functional capacity shown by 1 of the following:
   a. Inability to exercise
   b. 6-Minute walk distance ≤300 m
   c. Peak VO<sub>2</sub> <12 to 14 mL/kg/min

5. **History of ≥1 HF hospitalization in past 6 mo**

6. Presence of all the previous features despite “attempts to optimize” therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated
Clinical Course of Heart Failure

Transition to Advanced Heart Failure:
- Oral therapies failing
- A time for many major decisions
- Consider MCS and/or transplantation, if eligible
- Consider inversion of care plan to one dominated by a palliative approach, which may involve formal hospice
Survival after HF Hospitalization

Median survival (50% mortality) and 95% confidence limits in patients with HF after each HF hospitalization.

Setoguchi et al. Am Heart J 2007

MECHANICAL CIRCULATORY SUPPORT
A HISTORICAL PERSPECTIVE
First Heart Lung Machine model

John H. Gibbon, Jr. and the first successful heart-lung machine (images courtesy of the Thomas Jefferson University Library, Philadelphia, PA).
Domingo Liotta – The Argentinine

April 21, 1966,
the Liotta-DeBakey Paracorporeal Left Ventricular Assist Device (LVAD)

Department of Surgery of Baylor College of Medicine in Houston in 1961
August 6th 1966 – First Success

- Esperanza del Valle V
- Double valve replacement
- Post Cardiotomy shock with failure to wean from CPB
- Place on VAD for 10 days
- Complete recovery
Eligible population

1. New York Heart Association functional class IV for 60 days
2. LVEF <25%
3. Peak oxygen consumption <14 ml/min/kg (unless on balloon pump, intravenous inotropes, or physically unable to perform exercise test) or
4. intra-aortic balloon pump or
5. IV inotrope dependent for 14 days

Heartmate XVE vs. Medical Management

• DT

• N = 129

• Prospective 1:1
**REMATCH 2001**

<table>
<thead>
<tr>
<th>Event</th>
<th>Medical Therapy Group (N=60)</th>
<th>LVAD Group (N=67)</th>
<th>Rate Ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2.75</td>
<td>6.45</td>
<td>2.35 (1.86–2.95)</td>
</tr>
<tr>
<td>Neurologic dysfunction†</td>
<td>0.09</td>
<td>0.30</td>
<td>4.35 (1.31–14.50)</td>
</tr>
<tr>
<td>Supraventricular arrhythmia</td>
<td>0.03</td>
<td>0.12</td>
<td>3.92 (0.47–32.40)</td>
</tr>
<tr>
<td>Peripheral embolic event</td>
<td>0.06</td>
<td>0.14</td>
<td>2.29 (0.48–10.80)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0.30</td>
<td>0.60</td>
<td>2.03 (0.99–4.13)</td>
</tr>
<tr>
<td>Local infection</td>
<td>0.24</td>
<td>0.39</td>
<td>1.63 (0.72–3.70)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0.18</td>
<td>0.25</td>
<td>1.42 (0.54–3.71)</td>
</tr>
<tr>
<td>Miscellaneous adverse events</td>
<td>0.98</td>
<td>1.37</td>
<td>1.41 (0.93–2.12)</td>
</tr>
<tr>
<td>Syncope</td>
<td>0.03</td>
<td>0.04</td>
<td>1.31 (0.12–14.40)</td>
</tr>
<tr>
<td>Serious psychiatric disease</td>
<td>0.03</td>
<td>0.04</td>
<td>1.31 (0.12–14.39)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>0.18</td>
<td>0.12</td>
<td>0.65 (0.21–2.00)</td>
</tr>
<tr>
<td>Nonperioperative myocardial infarction</td>
<td>0.03</td>
<td>0.02</td>
<td>0.65 (0.04–10.30)</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>0.56</td>
<td>0.25</td>
<td>0.45 (0.22–0.90)</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>0.00</td>
<td>0.02</td>
<td>—</td>
</tr>
<tr>
<td>Event related to the LVAD</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>Suspected malfunction of LVAD</td>
<td>—</td>
<td>0.75</td>
<td>—</td>
</tr>
<tr>
<td>Perioperative bleeding</td>
<td>—</td>
<td>0.46</td>
<td>—</td>
</tr>
<tr>
<td>Infection of drive-line tract or pocket</td>
<td>—</td>
<td>0.41</td>
<td>—</td>
</tr>
<tr>
<td>Infection of pump interior, inflow tract, or outflow tract</td>
<td>—</td>
<td>0.23</td>
<td>—</td>
</tr>
<tr>
<td>Right heart failure</td>
<td>—</td>
<td>0.17</td>
<td>—</td>
</tr>
<tr>
<td>Failure of LVAD system</td>
<td>—</td>
<td>0.08</td>
<td>—</td>
</tr>
<tr>
<td>Thrombosis in LVAD</td>
<td>—</td>
<td>0.06</td>
<td>—</td>
</tr>
<tr>
<td>Perioperative myocardial infarction</td>
<td>—</td>
<td>0.00</td>
<td>—</td>
</tr>
</tbody>
</table>

**No. at risk**

<table>
<thead>
<tr>
<th></th>
<th>LV assist device</th>
<th>Medical therapy</th>
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<tbody>
<tr>
<td>68</td>
<td>38</td>
<td>61</td>
</tr>
<tr>
<td>38</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td>22</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

**NEJM. 2001. 345(20):1435-1443.**
Pulsatile Generation: Rise of the machines
As of November 2019:
- 179 Active Sites
- 25,097 Patients Enrolled

May 2005
Is Pulse necessary? Maybe not...
HM II: Co-axial Flow CF-LVAD

B Control Device—Axial-Flow Pump

- Blood flow to aorta
- Outlet stator and diffuser
- Rotor bearing
- Motor
- Inlet stator and blood-flow straightener
- Rotor bearing
- Pump housing
- Percutaneous drive line
- Axial-flow pump designed for intraabdominal placement
- Outflow graft
- Diaphragm
- Heart
- Left ventricle
- Pericardial sac
- Inflow cannula

Rogers J et al NEJM 2017
Pumping Co-Axially

Archimedes Screw in Egypt

http://www.waterencyclopedia.com/Po-Re/Pumps-Traditional.html
HEARTMATE II : DT trial 2009

- Prospective randomized 2:1 HeartMate II vs. HeartMate XVE
- DT
- 1- and 2-yr HeartMate II survival

**Eligible population**
1. New York Heart Association functional class IIIB or IV symptoms for >45 of the last 60 days
2. LVEF <25%, and peak oxygen consumption <14 ml/min/kg (unless on balloon pump, intravenous inotropes, or physically unable to perform exercise test) or
3. IABP dependent for 7 days or
4. IV inotrope dependent for 14 days
HM DT Trial 2009

No. at risk
Continuous-flow LVAD 133 95 82 69 62
Pulsatile-flow LVAD 59 32 19 5 2

P = 0.008 by the log-rank test

## Adverse Effect Profile:

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Continuous-Flow LVAD (N=133) (211 patient-yr)</th>
<th>Pulsatile-Flow LVAD (N=59) (41 patient-yr)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. (%)</td>
<td>no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>no. of Events/Patient-Yr</td>
<td>no. of Events/Patient-Yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bump replacement</td>
<td>12 (9)</td>
<td>20 (34)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>24 (18)</td>
<td>8 (14)</td>
<td>0.22</td>
<td>0.21</td>
</tr>
<tr>
<td>Ischemic</td>
<td>11 (8)</td>
<td>4 (7)</td>
<td>0.10</td>
<td>0.38</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>15 (11)</td>
<td>5 (8)</td>
<td>0.12</td>
<td>0.33</td>
</tr>
<tr>
<td>LVAD-related infection</td>
<td>47 (35)</td>
<td>21 (36)</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Local non-LVAD infection</td>
<td>65 (49)</td>
<td>27 (46)</td>
<td>1.33</td>
<td>0.02</td>
</tr>
<tr>
<td>Sepsis</td>
<td>48 (36)</td>
<td>26 (44)</td>
<td>1.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding requiring PRBC</td>
<td>108 (81)</td>
<td>45 (76)</td>
<td>2.45</td>
<td>0.06</td>
</tr>
<tr>
<td>Bleeding requiring surgery</td>
<td>40 (30)</td>
<td>9 (15)</td>
<td>0.29</td>
<td>0.57</td>
</tr>
<tr>
<td>Other neurologic event</td>
<td>29 (22)</td>
<td>10 (17)</td>
<td>0.29</td>
<td>0.14</td>
</tr>
<tr>
<td>Right heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Managed with extended use of inotropes</td>
<td>27 (20)</td>
<td>16 (27)</td>
<td>0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Managed with RVAD</td>
<td>5 (4)</td>
<td>3 (5)</td>
<td>0.07</td>
<td>0.12</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>75 (56)</td>
<td>35 (59)</td>
<td>1.31</td>
<td>0.006</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>50 (38)</td>
<td>24 (41)</td>
<td>0.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal failure</td>
<td>21 (16)</td>
<td>14 (24)</td>
<td>0.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>3 (2)</td>
<td>0 (0)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>LVAD thrombosis</td>
<td>5 (4)</td>
<td>0 (0)</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>107 (94)</td>
<td>42 (96)</td>
<td>4.25</td>
<td>0.02</td>
</tr>
</tbody>
</table>

HM II BTT/ DT: Effect on NYHA FC

The image shows bar charts for BTT and DT, illustrating the percentage of patients in different NYHA functional classes (I, II, III, IV) at various time points (baseline, 1 month, 3 months, 6 months, 12 months, 18 months, 24 months). The charts detail the percentage distribution across these classes, allowing for an analysis of the effect on NYHA functional classes over time.

JACC Volume 55, Issue 17, 27 April 2010, 1835-1836
HM II BTT/ DT: Effect on 6MWD

![Graph showing the effect of BTT and DT on 6MWD over time.](image-url)
HM II BTT/ DT: Effect on QoL

- Changes in quality of life assessed with the Minnesota Living With Heart Failure (MLWHF) Questionnaire
  - Lower values signify improved quality of life.
HVAD: Centrifugal Flow CF-LVAD

A Study Device—Centrifugal-Flow Pump

- Aorta
- Left ventricle
- Outflow graft
- Diaphragm
- Heart
- Percutaneous drive line connects to external battery pack and controller
- Centrifugal-flow pump designed for intrapericardial placement
- Blood flow from left ventricle
- Short inflow cannula
- Pump housing
- Blood flow to aorta
- Motor
- Percutaneous drive line
- Magnetic hydrodynamically levitated impeller

Rogers J et al NEJM 2017
Heartware DT trial - Endurance

Intention to Treat analysis

Survival at 24 months free of disabling stroke or reoperation to replace or remove the pump

P = 0.67 by log-rank test
P = 0.01 for noninferiority by Weibull model

No. at Risk
Study group 297 211 159
Control group 148 106 82

No. at Risk
Study group 296
Control group 149

CF-LVAD: Altering Physiology

- Doppler BP
- VAD “Hum”
- Driveline
- Pulse
- Controller/Alarms

Cardiac Output:
- 12,000 RPM: Cardiac Output = 5.1
  - Pulse Pressure = 6
  - Mean BP = 87
- 11,000 RPM: Cardiac Output = 4.9
  - Pulse Pressure = 9
  - Mean BP = 82
- 10,000 RPM: Cardiac Output = 4.8
  - Pulse Pressure = 12
  - Mean BP = 74
- 9,000 RPM: Cardiac Output = 4.7
  - Pulse Pressure = 16
  - Mean BP = 70
- 8,000 RPM: Cardiac Output = 4.5
  - Pulse Pressure = 25
  - Mean BP = 68

Cardiology Clinics 2007;25:553-64
Critical Role of Echo

- LVAD speed optimization
- Evaluation of pump function
- Evaluation of new symptoms
- Thrombus suspicion
# Understanding Advanced HF

**NYHA FC III-IV**: INTERMACS

**NEW YORK HEART ASSOCIATION CLASSIFICATIONS**

- **Class I**: Cardiac disease but no symptoms
- **Class II**: Mild symptoms and slight limitation during ordinary activity
- **Class III**: Marked limitation during any activity; comfortable only at rest
- **Class IV**: Severe limitations; symptoms even at rest; mostly bedbound

**INTERMACS Registry**

The Interagency Registry for Mechanically Assisted Circulatory Support is a US clinical registry that categorizes the clinical characteristics of device recipients.

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIIB/IV</td>
<td>1</td>
<td>Critical cardiogenic shock</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Progressive decline on inotropic support</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Inotrope dependent</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Resting symptoms</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Exertion intolerant</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Exertion limited</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>Advanced NYHA III symptoms</td>
</tr>
</tbody>
</table>

**INTERMACS Registry**

Registry provides even further detail on the advanced heart failure patient profile.

**Baylor Scott & White Health**

*INTERMACS Registry = Interagency Registry for Mechanically Assisted Circulatory Support*
# INTERMACS Profiles

<table>
<thead>
<tr>
<th>ADULT PROFILES</th>
<th>Current CMS - DT Functional Indication</th>
<th>IV INO*</th>
<th>Official Shorthand</th>
<th>NYHA CLASS Assumed</th>
<th>Modifier option</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS LEVEL 1</td>
<td>Met</td>
<td>X</td>
<td>“Crash and burn”</td>
<td>IV</td>
<td>TCS A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 2</td>
<td>Met</td>
<td>X</td>
<td>“Sliding fast” on inotropes</td>
<td>IV</td>
<td>TCS A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 3</td>
<td>Met</td>
<td>X</td>
<td>“Stable” continuous inotrope dependent * Can be in hospital or at home</td>
<td>IV</td>
<td>TCA if hosp FF if home A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 4</td>
<td>+ Peak VO₂ ≤ 12</td>
<td></td>
<td>Resting symptoms on oral therapy at home</td>
<td>AMB IV</td>
<td>FF A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 5</td>
<td>+ Peak VO₂ ≤ 12</td>
<td></td>
<td>“Housebound”, Comfortable at rest, symptoms with minimum activity ADL</td>
<td>AMB IV</td>
<td>FF A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 6</td>
<td></td>
<td></td>
<td>“Walking wounded”-ADL possible but meaningful activity limited</td>
<td>IIIB</td>
<td>FF A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 7</td>
<td></td>
<td></td>
<td>Advanced Class III</td>
<td>III</td>
<td>A only</td>
</tr>
</tbody>
</table>

* Intravenous inotropic therapy only approved for refractory Class IV symptoms
Patient Profile/ Status: INTERMACS Levels

1. Critical cardiogenic shock
2. Progressive decline
3. Stable but inotrope dependent
4. Recurrent advanced HF
5. Exertion intolerant
6. Exertion limited
7. Advanced NYHA III

Degrees of Class IV

AMBULATORY HEART FAILURE PATIENTS
INTERMACS : A Guide to Timing for therapy

<table>
<thead>
<tr>
<th>NYHA Class III</th>
<th>Class IIIB</th>
<th>Class IV (Ambulatory)</th>
<th>Class IV (On Inotropes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS Profiles</td>
<td>7</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>1.0% Percent of current implants in INTERMACS</td>
<td>1.4%</td>
<td>3.0%</td>
<td>14.6%</td>
</tr>
<tr>
<td>CURRENTLY NOT APPROVED</td>
<td>LIMITED ADOPTION</td>
<td>GROWING ACCEPTANCE</td>
<td></td>
</tr>
</tbody>
</table>

FDA Approval: Class IIIB/IV
MECHANICAL CIRCULATORY SUPPORT COMPLICATIONS
IS THE BENEFIT REALLY WORTH THE RISK?
LVAD: Complications

- Hemotocompatibility
  - CVA (Hemorrhagic and Thrombotic)
  - Pump thrombus
  - GI bleeding

- Device malfunction
  - Driveline infection
  - Sepsis/ Pump infection
  - Short to shield

- RV dysfunction
- Arrhythmias
- New de novo AR
LVAD: GI Bleeding

- AVM angiogenesis
- 100% loss of HMW vWF factor

<table>
<thead>
<tr>
<th>Implant duration</th>
<th>Nonpulsatile</th>
<th>Pulsatile</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 55)</td>
<td>(n = 46)</td>
<td></td>
</tr>
<tr>
<td>First bleeding event after 15 d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events/100 patient-y</td>
<td>47.7</td>
<td>7.3</td>
<td>.0036</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>3</td>
<td>.0013</td>
</tr>
<tr>
<td>First bleeding event after 30 d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events/100 patient-y</td>
<td>46.5</td>
<td>4.7</td>
<td>.0028</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>2</td>
<td>.0114</td>
</tr>
<tr>
<td>All bleeding events after 15 d</td>
<td>(events/100 patient-y)</td>
<td>63</td>
<td>6.8</td>
</tr>
</tbody>
</table>

## HVAD : Stroke

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>HVAD (n=296)</th>
<th>Control (n=149)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>No. of events</td>
</tr>
<tr>
<td>Stroke</td>
<td>85 (28.7%)</td>
<td>110</td>
</tr>
<tr>
<td>Ischemic CVA</td>
<td>50 (16.9%)</td>
<td>65</td>
</tr>
<tr>
<td>Hemorrhagic CVA</td>
<td>42 (14.2%)</td>
<td>45</td>
</tr>
<tr>
<td>TIA</td>
<td>24 (8.1%)</td>
<td>27</td>
</tr>
</tbody>
</table>

### Ischemic Stroke

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA (≤ 81 mg)</td>
<td>7.059</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>2.915</td>
<td>0.0176</td>
</tr>
</tbody>
</table>

### Hemorrhagic Stroke

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (&gt; 90 mmHg)</td>
<td>9.901</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ASA (≤ 81 mg)</td>
<td>6.825</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>INR (&gt; 3)</td>
<td>5.051</td>
<td>0.0073</td>
</tr>
</tbody>
</table>
LVAD therapy: Complications

*Major Event: First occurrence of infection, bleeding, device malfunction, stroke or death

Patients 5436, Events = 3611

<table>
<thead>
<tr>
<th>Months</th>
<th>% Freedom</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>48%</td>
</tr>
<tr>
<td>6</td>
<td>40%</td>
</tr>
<tr>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>24</td>
<td>19%</td>
</tr>
<tr>
<td>36</td>
<td>14%</td>
</tr>
</tbody>
</table>

Months post implant
LVAD Therapy
CURRENT DEVICES
LVAD: Evolution

HeartMate VE™ LVAD

1998
BTT
1998
DT
1998
2002

Pulsatile flow

First LVAD FDA approved for DT

HeartMate II™ LVAD

2008
BTT
2008
DT
2010

Continuous flow (axial)

Over 26,600 patients implanted with patients on therapy out to 5 and 10+ years\(^1\)

HeartMate 3™ LVAD

2017
ST (BTT)
2017
LT (DT)
2018

Continuous flow (centrifugal) with Full MagLev™ Flow Technology

The best published outcomes for continuous-flow LVADs\(^2\)\(^-\)\(^6\)

References:
Heartmate 3: Fully Magnetically Levitated LVAS

Wide blood flow passages to reduce shear stress
Frictionless with absence of mechanical bearings
Intrinsic Pulse designed to reduce stasis and avert thrombosis

Heartmate 3: Fully Magnetically Levitated LVAS

- KEY DESIGN FEATURE
  Large and Consistent Gaps designed to minimize shear stress and blood component activation.
  - Secondary flow paths ~0.5 mm along the side, and ~1.0 mm above and below the rotor.
  - Pump surfaces flat and flow is undisturbed.
Heartmate 3:
Fully Magnetically Levitated LVAS

- **KEY DESIGN FEATURE:** Fluid Dynamics designed to minimize shear stress and activation of blood components.
  - The HeartMate 3™ rotor and inlet have been designed to minimize shear and avoid stasis over the entire range of operation (2.5 to 10 L/min).
  - The relatively large secondary flow paths facilitate smooth flow transitions, generous washing, and low shear.
Study Aim of the full cohort analysis was to:

- Confirm findings from the earlier pivotal trial cohorts (short-term and long-term)
- Provide additional statistical power to show superiority for the primary endpoint
- Power the principal secondary endpoint for pump replacement

Primary Endpoint:

- Survival at 2 years free of disabling stroke (>3 mRS) or reoperation to replace or remove a malfunctioning device

Principal Secondary Endpoint:

- Pump replacement at 2 years

Other Secondary Endpoints:

- Actuarial survival, rehospitalizations, functional status, and quality of life
MOMENTUM 3: Final Report 2019
Study Design and Net Trial Experience

**Short Term (ST) Cohort**
- N=294
- 6-month follow-up

**Randomization**
- 1:1

Patient meets MOMENTUM 3 eligibility criteria?

**Long Term (LT) Cohort**
- N=366
- 2-year follow-up

**Additional 72 patients enrolled**

**Full Cohort**
- N=1028
- 2-year follow-up

**Additional 662 patients enrolled**

3rd and final analysis at 2-years (100%)

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>ST cohort analysis at 6-months</th>
<th>LT cohort analysis at 2-years</th>
<th>Full cohort analysis at 2-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>294</td>
<td>(7.1%)</td>
<td>(35.6%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>366</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1028</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**References:**

SJM-HM3-0319-0191 | Item approved for Global use.
## Baseline Characteristics

**INTERMACS‡ Profile**

### INTERMACS‡ Profile for MOMENTUM 3 Cohort

<table>
<thead>
<tr>
<th>INTERMACS profile (definition)</th>
<th>HeartMate 3™ LVAD (N=516)</th>
<th>HeartMate II™ LVAD (N=512)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong> Critical cardiogenic shock</td>
<td>11 (2.1)</td>
<td>18 (3.5)</td>
</tr>
<tr>
<td><strong>2</strong> Progressive decline on inotropic support</td>
<td>156 (30.2)</td>
<td>146 (28.5)</td>
</tr>
<tr>
<td><strong>3</strong> Stable, but inotropic dependent</td>
<td>272 (52.7)</td>
<td>251 (49.0)</td>
</tr>
<tr>
<td><strong>4</strong> Resting symptoms</td>
<td>67 (13.0)</td>
<td>82 (16.0)</td>
</tr>
<tr>
<td><strong>5-7</strong> or not provided*</td>
<td>10 (1.9)</td>
<td>15 (2.9)</td>
</tr>
</tbody>
</table>

*Assessments not performed in two (2) HeartMate 3 and five (5) HeartMate II LVAD patients.*

SJM-HM3-0319-019 1 Item approved for Global use.

Survival at 2 Years
HeartMate 3™ LVAD continues to show the highest survival for a LVAD at 2 years in a randomized controlled clinical trial.

HR = 0.88 (95%CI: 0.67-1.16)
P = 0.37 by log-rank test

No. at Risk:

<table>
<thead>
<tr>
<th></th>
<th>Months After Implant</th>
</tr>
</thead>
<tbody>
<tr>
<td>HeartMate 3™ LVAD</td>
<td>515 447 383 322 289</td>
</tr>
<tr>
<td>HeartMate II™ LVAD</td>
<td>505 414 339 285 248</td>
</tr>
</tbody>
</table>
Primary Endpoint Met, and Clinical Superiority Demonstrated Event-Free Survival at 2 Years*

![Event-Free Survival Graph]

Superiority Analysis

HR = 0.60 (95% CI: 0.47-0.75)

P <0.0001 by log-rank test

No. at Risk:

<table>
<thead>
<tr>
<th>Device</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>HeartMate III™ LVAD</td>
<td>516</td>
<td>438</td>
<td>373</td>
<td>313</td>
<td>280</td>
</tr>
<tr>
<td>HeartMate II™ LVAD</td>
<td>512</td>
<td>401</td>
<td>321</td>
<td>264</td>
<td>223</td>
</tr>
</tbody>
</table>

*Survival at 2 years free of disabling stroke (>3 mRS) or reoperation to replace or remove a malfunctioning device
Powered Secondary End Point Analysis
Significantly lower rate of pump replacement at 2 years

**11.3%**

HR = 0.19 (95%CI: 0.10-0.35)

P < 0.0001 by log-rank test

**2.3%**

RR (95%CI) = 0.21 (0.11 – 0.38)
P<0.0001

Only 3 HeartMate 3™ LVAD exchanges for suspected pump thrombosis or elevated LDH

**No. at Risk:**

<table>
<thead>
<tr>
<th>HeartMate 3</th>
<th>515</th>
<th>444</th>
<th>379</th>
<th>317</th>
<th>283</th>
</tr>
</thead>
<tbody>
<tr>
<td>HeartMate II</td>
<td>505</td>
<td>403</td>
<td>322</td>
<td>264</td>
<td>226</td>
</tr>
</tbody>
</table>

SJM-HM3-0319-0191 | Item approved for Global use
Key Adverse Event: Pump Thrombosis
Significantly higher freedom from suspected or confirmed pump thrombosis

No. at Risk:

<table>
<thead>
<tr>
<th></th>
<th>HeartMate 3™ LVAD</th>
<th>HeartMate II™ LVAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>515</td>
<td>505</td>
</tr>
<tr>
<td>6</td>
<td>447</td>
<td>399</td>
</tr>
<tr>
<td>12</td>
<td>382</td>
<td>317</td>
</tr>
<tr>
<td>18</td>
<td>320</td>
<td>263</td>
</tr>
<tr>
<td>24</td>
<td>287</td>
<td>229</td>
</tr>
</tbody>
</table>

HR = 0.09 (95% CI: 0.04-0.19)
P < 0.0001 by log-rank test

Only 7 cases out of 515 of suspected or confirmed pump thrombosis (1.4%)

FREEDOM FROM PUMP THROMBOSIS

99%
Key Adverse Event: Stroke
Significantly higher freedom from all stroke in HeartMate 3™ LVAD than control

Freedom from all stroke (%)

No. at Risk:
HeartMate 3™ LVAD
HeartMate II™ LVAD

<table>
<thead>
<tr>
<th>Months After Implant</th>
<th>HeartMate 3™ LVAD</th>
<th>HeartMate II™ LVAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>515</td>
<td>505</td>
</tr>
<tr>
<td>6</td>
<td>429</td>
<td>384</td>
</tr>
<tr>
<td>12</td>
<td>361</td>
<td>299</td>
</tr>
<tr>
<td>18</td>
<td>304</td>
<td>252</td>
</tr>
<tr>
<td>24</td>
<td>270</td>
<td>210</td>
</tr>
</tbody>
</table>

HR = 0.47 (95%CI: 0.34-0.66)
P < 0.0001 by log-rank test

Adverse event rate for stroke: 9.9%
2-yr Stroke Rates in Contemporary Randomized Clinical Trials

HeartMate 3™ LVAD patients had the lowest stroke rates at 2 years

Stroke Rate at 2 Years in MOMENTUM 3¹, ENDURANCE Supplemental², and ENDURANCE³

Results are from different trials, with different cohorts, and cannot be compared directly.

Key Adverse Event: GI Bleeding
Significantly higher freedom from GI bleeding in HeartMate 3™ LVAD patients than control

HR = 0.72 (95%CI: 0.57-0.90)
P = 0.005 by log-rank test

No. at Risk:
HeartMate 3™ LVAD
515 381 308 251 204
HeartMate II™ LVAD
505 325 248 202 167
GI Bleeding Rates in Contemporary Randomized Clinical Trials

HeartMate 3™ LVAD patients had the lowest GI bleeding rates at 2 years.

GI Bleeding Rate at 2 Years in MOMENTUM 3¹, ENDURANCE Supplemental², and ENDURANCE³

<table>
<thead>
<tr>
<th>Device</th>
<th>MOMENTUM 3 Full Cohort</th>
<th>ENDURANCE Supplemental</th>
<th>ENDURANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HeartMate 3</td>
<td>25%</td>
<td>45%</td>
<td>34%</td>
</tr>
<tr>
<td>HeartMate II</td>
<td>31%</td>
<td>39%</td>
<td>35%</td>
</tr>
<tr>
<td>HVAD</td>
<td>45%</td>
<td>34%</td>
<td>35%</td>
</tr>
</tbody>
</table>

Results are from different trials, with different cohorts, and cannot be compared directly.

Hospitalization rates and Duration of Hospitalization
Significantly fewer days in hospital for HeartMate 3™ LVAD patients than control

In a 2 year economic analysis of the MOMENTUM 3 trial, HeartMate 3™ LVAD demonstrated:

- **51% reduction** in average cumulative cost per patient-year\(^1\)
- **Fewer total hospitalizations** per patient year\(^1\)
- **8.3 fewer hospital days** per-patient year on average\(^1\)

LVAD: INDICATIONS AND TIMING
Time to Transition: Clinical Cues

- Repeated (≥2) hospitalizations or ED visits for HF in the past year
- Progressive deterioration in renal function
- Weight loss without other cause (e.g. cardiac cachexia)
- Intolerance to ACE inhibitors due to hypotension and/or worsening renal function
- Intolerance to beta blockers due to worsening HF or hypotension
- Frequent systolic blood pressure < 90 mmHg
- Persistent dyspnea with dressing or bathing requiring rest
- Inability to walk 1 block on the level ground due to dyspnea or fatigue
- Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose > 160 mg/d and/or use of supplemental metolazone therapy
- Progressive decline in serum sodium, usually to < 133 mEq/L
- Frequent ICD shocks

High-risk clinical triggers for referral for evaluation for advanced heart failure therapies

<table>
<thead>
<tr>
<th>I</th>
<th>IV inotropes</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>NYHA IIIB/IV or persistently elevated natriuretic peptides</td>
</tr>
<tr>
<td>E</td>
<td>End-organ dysfunction (Cr &gt; 1.8 mg/dL or BUN &gt; 43 mg/dL)</td>
</tr>
<tr>
<td>E</td>
<td>Ejection fraction ≤ 35%</td>
</tr>
<tr>
<td>D</td>
<td>Defibrillator shocks</td>
</tr>
<tr>
<td>H</td>
<td>Hospitalizations &gt; 1</td>
</tr>
<tr>
<td>E</td>
<td>Edema (or elevated PA pressure) despite escalating diuretics</td>
</tr>
<tr>
<td>L</td>
<td>Low blood pressure, high heart rate</td>
</tr>
<tr>
<td>P</td>
<td>Prognostic medication — progressive intolerance or down-titration GDMT</td>
</tr>
</tbody>
</table>

Additional patient considerations for referral:
- CRT non-responder
- Physical activity limited or impaired quality of life

Review before LVAD Implant

- Hepatic Function
- Pulmonary Function
- Neurologic Function
- Renal Function
- Multiorgan Failure
- Age
- Body Size
- Malignancy
- Nutritional Status
- Psychological and Psychiatric Conditions
- Infectious Disease

Cardiovascular Considerations
- Intracardiac Shunt
- Arrhythmias
- Inotropic Support
- Valvular Disease
- Ischemic Heart Disease
- Right Ventricular Function

Non-Cardiovascular Considerations
Why patients chose a LVAD?
Survival vs Quality Living
Frailty and the Selection of Patients for Destination Therapy Left Ventricular Assist Device

*Circ Heart Failure* 2012; 5:286

Kelsey M. Flint, MD; Daniel D. Matlock, MD, MPH; JoAnn Lindenfeld, MD; Larry A. Allen, MD, MHS

A

Frailty

*Increased Vulnerability to Stress*

LVAD-Responsive Frailty

- Systolic and diastolic dysfunction
- ↑ PCWP and CVP
- ↓ Cardiac output

LVAD-Independent Frailty

- Inflammation
- Anorexia
- Polypharmacy
- Deconditioning

- Sarcopenia
- Malnutrition
- Cognitive deficits
- Injurious falls

- Aging
- COPD / lung disease
- Cancer
- Diabetes
- Osteoporosis
- Peripheral vascular disease
- Cirrhosis
- Neurologic disease

Post-Operative Complications

- Prolonged LOS
- Need for ICU care

Impaired Health Status

- Disability
- Loss of ADLs
- Institutionalization

Reduced Survival
When late may be too late...

Continuous Flow LVAD/BiVAD Implants: 2013 – 2016, n= 10,726

Survival by Intermacs Profiles*

% Survival

<table>
<thead>
<tr>
<th>Intermacs Profiles</th>
<th>n</th>
<th>deaths</th>
<th>6 mths</th>
<th>12 mths</th>
<th>36 mths</th>
<th>48 mths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profile 1</td>
<td>1629</td>
<td>477</td>
<td>79%</td>
<td>74%</td>
<td>52%</td>
<td>51%</td>
</tr>
<tr>
<td>Profiles 2 &amp; 3</td>
<td>7437</td>
<td>1716</td>
<td>88%</td>
<td>82%</td>
<td>61%</td>
<td>53%</td>
</tr>
<tr>
<td>Profiles 4-7</td>
<td>1651</td>
<td>376</td>
<td>89%</td>
<td>84%</td>
<td>67%</td>
<td>57%</td>
</tr>
</tbody>
</table>

Event: Death – censored at transplant, recovery and device exchange

Months post implant

P(overall) < .0001
p(Profile 1 vs. Profiles 2 & 3) < .0001
p(Profile 1 vs. Profiles 4-7) < .0001
p(Profiles 2&3 vs. Profiles 4-7) = .02
# INTERMACS PROFILES: LVAD Timing

<table>
<thead>
<tr>
<th>INTERMACS profile descriptions</th>
<th>Time frame for Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Profile 1: Critical cardiogenic shock</strong>&lt;br&gt;Patients with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, often confirmed by worsening acidosis and/or lactate levels. <em>“Crash and burn.”</em></td>
<td>Definitive intervention needed within hours.</td>
</tr>
<tr>
<td><strong>Profile 2: Progressive decline</strong>&lt;br&gt;Patient with declining function despite intravenous inotropic support, may be manifest by worsening renal function, nutritional depletion, inability to restore volume balance <em>“Sliding on inotropes.”</em> Also describes declining status in patients unable to tolerate inotropic therapy.</td>
<td>Definitive intervention needed within few days.</td>
</tr>
<tr>
<td><strong>Profile 3: stable but inotrope dependent</strong>&lt;br&gt;Patient with stable blood pressure, organ function, nutrition, and symptoms on continuous intravenous inotropic support (or a temporary circulatory support device or both), but demonstrating repeated failure to wean from support due to recurrent symptomatic hypotension or renal dysfunction <em>“Dependent stability.”</em></td>
<td>Definitive intervention elective over a period of weeks to few months.</td>
</tr>
<tr>
<td><strong>Profile 4: Resting symptoms</strong>&lt;br&gt;Patient can be stabilized close to normal volume status but experiences daily symptoms of congestion at rest or during ADL. Doses of diuretics generally fluctuate at very high levels. More intensive management and surveillance strategies should be considered, which may in some cases reveal poor compliance that would compromise outcomes with any therapy. Some patients may shuttle between 4 and 5.</td>
<td>Definitive intervention elective over period of weeks to few months.</td>
</tr>
<tr>
<td><strong>Profile 5: Exertion Intolerant</strong>&lt;br&gt;Comfortable at rest and with ADL but unable to engage in any other activity, living predominantly within the house. Patients are comfortable at rest without congestive symptoms, but may have underlying refractory elevated volume status, often with renal dysfunction. If underlying nutritional status and organ function are marginal, patient may be more at risk than INTERMACS 4, and require definitive intervention.</td>
<td>Variable urgency, depends upon maintenance of nutrition, organ function, and activity.</td>
</tr>
<tr>
<td><strong>Profile 6: Exertion limited</strong>&lt;br&gt;Patient without evidence of fluid overload is comfortable at rest, and with activities of daily living and minor activities outside the home but fatigues after the first few minutes of any meaningful activity. Attribution to cardiac limitation requires careful measurement of peak oxygen consumption. In some cases with hemodynamic monitoring to confirm severity of cardiac impairment. <em>“Walking wounded.”</em></td>
<td>Variable, depends upon maintenance of nutrition, organ function, and activity level.</td>
</tr>
<tr>
<td><strong>Profile 7: Advanced NYHA III</strong>&lt;br&gt;A placeholder for more precise specification in future, this level includes patients who are without current or recent episodes of unstable fluid balance, living comfortably with meaningful activity limited to mild physical exertion.</td>
<td>Transplantation or circulatory support may not currently be indicated.</td>
</tr>
</tbody>
</table>

## Modifiers for Profiles

- **TCS** – Temporary Circulatory Support can modify only patients in hospital (other devices would be INTERMACS devices) includes IABP, ECMO, TandemHeart, Levitronix, BVS 5000 or AB5000, Impella.

- **Arrhythmia** – can modify any profile. Recurrent ventricular tachyarrhythmias that have recently contributed substantially to clinical compromise. This includes frequent ICD shock or requirement for external defibrillator, usually more than twice weekly.

- **FF** – Frequent Flier – can modify only outpatients, designating a patient requiring frequent emergency visits or hospitalizations for diuretics, ultrafiltration, or temporary intravenous vasoactive therapy.

**Possible Profiles to Modify**

- 1, 2, 3 In hospital.
- Any profile.
- 3 if at home. 4, 5, 6. A frequent flyer would rarely be profile 7.
LVAD: FUTURE DIRECTIONS
Future Directions

• Further miniaturization
• Improved Connectivity
• Remote monitoring
• Transcutaneous Transmission ~ 5 yrs
HeartMate™ LVAS Equipment
Overview

HM Touch: New Wireless Communication System

14 V Li-Ion Batteries and Clips:
Power the system when patients are active or outdoors for up to 17 hours. 2 batteries are used at a time with clips.

Battery Charger:
Charges, calibrates, and tests the batteries.

Mobile Power Unit:
Connects to the System Controller to transfer power from AC outlet.

Go Gear Wearables:
Organizes the System Controller and batteries for patients to wear and carry.

Power Module and Wireless Adapter
Provides power to the system from AC outlet and also connects to the System Monitor via Wireless Adapter.

App and Tablet
Provides clinicians with the ability to wirelessly program and monitor system parameters, track alarm conditions, and view and save data.
HeartMate Touch™ Communication System Introduction

System Overview

HeartMate™ Touch

Controller

AC Power Supply

External Battery

Battery Charger

Controller Power Cable

Battery Cable

Edison Driveline Connection

HM3 LVAD

Future Compatibility - Merlin.Net™

Software Embedded

Future Compatibility - Wearables

Bluetooth

System Overview

Transport

Wearables
HeartMate Touch™ Communication System Introduction

1. Tablet installed in a protective case

2. HeartMate Touch™ App

3. Wireless Adapter

4. Power Adapter & Apple Travel adapter kit for international markets

5. External Memory Drive
Next Generation Wearables and Transport Solutions

Belt
Vest
Daily Bag
Shower Bag
Transport
LVAD: Take Home Points

• Advanced Heart Failure has a poor prognosis without early recognition and treatment
• After survival, functional Status and QOL improvements are Important factors for patients
• LVAD technology has come a long way and continues to evolve with improved durability and side effect profile
• Early patient referral to an advanced center for shared decision making with patients is recommended for optimal outcomes
Our future?

The Borg: From the Star Trek television series. The Borg represented a hybrid of humans and machines.

Elon Musk Announces Plan to 'Merge' Human Brains With AI

Neuralink wants to start by treating brain injuries, eventually "achieve a symbiosis with artificial intelligence."

By Mitch Bowman and Jason Koebler | Jul 17 2019, 11:59am

The inhibitor chip...gone...
Thank you for your Attention