Mechanical Circulatory Support for End Stage Heart Failure: Old Dogs and New Tricks

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Associate Professor of Surgery
Surgical Director, Cardiac Transplantation and Mechanical Circulatory Support
University of Colorado Denver
• Co-Principal Investigator (UCH), HM II Pivotal Study- Thoratec
• Principal Investigator (UCH), E-Valve Study, E-Valve, Inc.
• Principal Investigator (UCH), Heartnet Study, Paracor, Inc.
Figure VI-4. Number of Heart Transplants and Incidence of Transplant per Million Population, 1997-2006

Data From: 2007 OPTN/SRTR Annual Report, Tables 11.4 and 11.5.
Key Learning Objectives

- Patient Selection ←→ Device Selection
- Timing of implantation
- VAD Program requires extensive resources
Historical Overview

- Interest in MCS grew from successful use of cardiopulmonary bypass in 1950’s
- NHLBI – 1970’s – long term circulatory support
  - Heartmate LVAD
  - Novacor LVAD
  - Thoratec VAD
  - Cardiowest TAH
Utilization of MCS

• Bridge – to – Transplant (BTT)
  – Patient receiving the device is listed for transplant, or will be a transplant candidate

• Destination Therapy (DT)
  – Patient is not a candidate for heart transplantation and receives the pump as a lifetime therapy

• Bridge - to – Recovery
  – Patient has a potentially recoverable heart
    • Acute: Myocarditis, post-cardiotomy
    • Chronic: DCM (??)
Displacement Pumps
Thoratec Paracorporeal VAD
# Thoratec as Bridge-to-Transplant

Bridge = 60%  
Post-Card, Myocarditis = 40%

<table>
<thead>
<tr>
<th>Table III. Outcome</th>
<th>Bridging (n = 84)</th>
<th>Postcardiotomy heart failure (n = 17)</th>
<th>Miscellaneous (n = 13)</th>
<th>Total (n = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weaned</td>
<td>2 (68%)</td>
<td>1</td>
<td>—</td>
<td>3</td>
</tr>
<tr>
<td>Transplanted</td>
<td>57 (68%)</td>
<td>7 (41%)</td>
<td>4 (31%)</td>
<td>68 (60%)</td>
</tr>
<tr>
<td>Discharged</td>
<td>50 (60%)</td>
<td>8 (47%)</td>
<td>4 (31%)</td>
<td>62 (54%)</td>
</tr>
<tr>
<td>Death on support</td>
<td>25 (30%)</td>
<td>9 (53%)</td>
<td>9 (69%)</td>
<td>43 (38%)</td>
</tr>
</tbody>
</table>

## Table IV. Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>BTT (n = 84)</th>
<th>PC (n = 17)</th>
<th>Miscellaneous (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>26 (31%)</td>
<td>2 (12%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>20 (24%)</td>
<td>5 (29%)</td>
<td>4 (31%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>13 (16%)</td>
<td>6 (35%)</td>
<td>5 (39%)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>18 (21%)</td>
<td>2 (12%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>16 (19%)</td>
<td>3 (18%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>9 (11%)</td>
<td>2 (12%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>11 (13%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Exit site infection</td>
<td>11 (13%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>8 (10%)</td>
<td>2 (12%)</td>
<td>—</td>
</tr>
<tr>
<td>Right heart failure*</td>
<td>4 (12%)</td>
<td>1 (9%)</td>
<td>—</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>4 (5%)</td>
<td>2 (12%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Technical</td>
<td>3 (4%)</td>
<td>1 (6%)</td>
<td>—</td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>1</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*BTT, Bridge to transplant; PC, postcardiomy cardiogenic shock.

*In patients with Thoratec left ventricular support (bridging, n = 34; postcardiomy, n = 11).
Thoratec iVAD
Thoratec iVAD System
Heartmate XVE

Unique Technology Delivers Dramatically Low TE Rates

The HeartMate LVAS incorporates an exclusive proprietary textured blood-

Fig I. Schematic drawing of an implanted TCI HeartMate VE left ventricular assist system.
Heartmate XVE as BTT

- LVAD only
- Single pusher plate displacement device
  - CAM and bearings
- Unique coating of blood contact surface
  - Lowest thromboembolic rate of current devices (<5%)
  - Only device with Aspirin alone for anticoagulation
- Limitations
  - External driveline
  - Durability – bearings wear and limit device longevity (2 yrs.)
Bridging to transplant with the HeartMate left ventricular assist device: The Columbia Presbyterian 12-year experience

Jeffrey A. Morgan, MDa
Ranjit John, MDa
Vivek Rao, MD, PhDb
Alan D. Weinberg, MSc
Brian J. Lee, BSa
Pamela A. Mazzeo, BAs
Margaret R. Flannery, ANPa
Jonathan M. Chen, MDa
Mehmet C. Oz, MDa
Yoshifumi Naka, MD, PhDa

J Thorac Cardiovasc Surg 2004
Heartmate BTT Columbia Outcomes

Bridge = 72%

<table>
<thead>
<tr>
<th>Device</th>
<th>PNEUM</th>
<th>DLVE</th>
<th>SLVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplanted</td>
<td>63.5</td>
<td>64.7</td>
<td>72.4</td>
</tr>
<tr>
<td>Expired</td>
<td>36.5</td>
<td>35.3</td>
<td>26.5</td>
</tr>
<tr>
<td>Explanted for Infection</td>
<td>3.8</td>
<td>11.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Explanted for Recovery</td>
<td>0</td>
<td>0</td>
<td>1.7</td>
</tr>
</tbody>
</table>

J Thorac Cardiovasc Surg 2004;
Heartmate BTT – LVAD vs. No LVAD
Heartmate BTT – LVAD Score

Figure 3. Bridging to transplant success based on preimplantation LVAD scores. LVAD scores were categorized as low (0-4), medium (5-7), and high (8-10).
LONG-TERM USE OF A LEFT VENTRICULAR ASSIST DEVICE FOR END-STAGE HEART FAILURE

ERIC A. ROSE, M.D., ANNETINE C. GELIJNS, PH.D., ALAN J. MOSKOWITZ, M.D., DANIEL F. HEITJAN, PH.D., LYNNE W. STEVENSON, M.D., WALTER DEMBITSKY, M.D., JAMES W. LONG, M.D., PH.D., DEBORAH D. ASCHEIM, M.D., ANITA R. TIERNEY, M.P.H., RONALD G. LEVITAN, M.SC., JOHN T. WATSON, PH.D., AND PAUL MEIER, PH.D., FOR THE RANDOMIZED EVALUATION OF MECHANICAL ASSISTANCE FOR THE TREATMENT OF CONGESTIVE HEART FAILURE (REMATCH) STUDY GROUP*
Figure 2. Kaplan–Meier Analysis of Survival in the Group That Received Left Ventricular (LV) Assist Devices and the Group That Received Optimal Medical Therapy.
# REMATCH

## Table 2. Causes of Death. *

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Medical-Therapy Group</th>
<th>LVAD Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular dysfunction</td>
<td>50</td>
<td>1</td>
<td>51</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Failure of LVAD</td>
<td><strong>0</strong></td>
<td><strong>7</strong></td>
<td><strong>7</strong></td>
</tr>
<tr>
<td>Miscellaneous noncardiovascular causes</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Miscellaneous cardiovascular causes</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac procedure</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Perioperative bleeding</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>54</strong></td>
<td><strong>41</strong></td>
<td><strong>95</strong></td>
</tr>
</tbody>
</table>

*LVAD denotes left ventricular assist device.
**TABLE 3. QUALITY OF LIFE AND FUNCTIONAL STATUS OF PATIENTS AT ONE YEAR.**

<table>
<thead>
<tr>
<th>Scale†</th>
<th>One Year</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO. ASSESSED/ TOTAL NO. (%)</td>
<td>SCORE</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD group</td>
<td>23/24 (96)</td>
<td>46±19</td>
</tr>
<tr>
<td>Medical-therapy group</td>
<td>6/11 (55)</td>
<td>21±21</td>
</tr>
<tr>
<td>Emotional role</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD group</td>
<td>23/24 (96)</td>
<td>64±45</td>
</tr>
<tr>
<td>Medical-therapy group</td>
<td>6/11 (55)</td>
<td>17±28</td>
</tr>
<tr>
<td>Minnesota Living with Heart Failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD group</td>
<td>23/24 (96)</td>
<td>41±22</td>
</tr>
<tr>
<td>Medical-therapy group</td>
<td>6/11 (55)</td>
<td>58±21</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD group</td>
<td>22/24 (92)</td>
<td>8±7</td>
</tr>
<tr>
<td>Medical-therapy group</td>
<td>5/11 (45)</td>
<td>13±7</td>
</tr>
<tr>
<td>Median NYHA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD group</td>
<td>24/24 (100)</td>
<td>II</td>
</tr>
<tr>
<td>Medical-therapy group</td>
<td>7/11 (64)</td>
<td>IV</td>
</tr>
</tbody>
</table>

*Plus–minus values are means ±SD. Only patients who completed testing were included in the analysis. There were too few patients for an analysis of two-year data. LVAD denotes left ventricular assist device.
Heartmate XVE Pump and Valve Wear

Figure 2. Severe destruction of the XVE inflow valve (morphologic damage score = 3) in a 38-year-old man who died after 486 days of uneventful mechanical support due to sudden device failure. Note the...
Heart Failure

Outcomes of Left Ventricular Assist Device Implantation as Destination Therapy in the Post-REMATCH Era

Implications for Patient Selection

Katherine Lietz, MD, PhD; James W. Long, MD, PhD; Abdallah G. Kfouri, MD; Mark S. Slaughter, MD; Marc A. Silver, MD; Carmelo A. Milano, MD; Joseph G. Rogers, MD; Yoshifumi Naka, MD, PhD; Donna Mancini, MD; Leslie W. Miller, MD

Methods and Results—The present study included 280 patients who underwent HeartMate XVE LVAD implantation between November 2001 and December 2005. A preoperative risk score for in-hospital mortality after LVAD implantation was established in 222 patients with complete data. All patients were followed up until death or December 2006. The 1-year survival after LVAD implantation was 56%. The in-hospital mortality after LVAD surgery was 27%. The main causes of death included sepsis, right heart failure, and multiorgan failure. The most important determinants of in-hospital mortality were poor nutrition, hematological abnormalities, markers of end-organ or right ventricular dysfunction, and lack of inotropic support. Stratification of DT candidates into low (n=65), medium (n=111), high (n=28), and very high (n=18) risk on the basis of the risk score calculated from these predictors corresponded with 1-year survival rates of 81%, 62%, 28%, and 11%, respectively.

Circulation. 2007;116:497-505
Post REMATCH DT Survival

**Figure 1.** Survival after LVAD implantation as DT in the post-REMATCH era.
<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Odds Ratio (CI)</th>
<th>P</th>
<th>Weighted Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count ≤148×10³/µL</td>
<td>7.7 (3.0 to 19.4)</td>
<td>&lt;0.001</td>
<td>7</td>
</tr>
<tr>
<td>Serum albumin ≤3.3 g/dL</td>
<td>5.7 (1.7 to 13.1)</td>
<td>&lt;0.001</td>
<td>5</td>
</tr>
<tr>
<td>International normalization ratio &gt;1.1</td>
<td>5.4 (1.4 to 21.8)</td>
<td>0.01</td>
<td>4</td>
</tr>
<tr>
<td>Vasodilator therapy</td>
<td>5.2 (1.9 to 14.0)</td>
<td>0.008</td>
<td>4</td>
</tr>
<tr>
<td>Mean pulmonary artery pressures ≤25 mm Hg</td>
<td>4.1 (1.5 to 11.2)</td>
<td>0.009</td>
<td>3</td>
</tr>
<tr>
<td>Aspartate aminotransferase &gt;45 U/mL</td>
<td>2.6 (1.0 to 6.9)</td>
<td>0.002</td>
<td>2</td>
</tr>
<tr>
<td>Hematocrit ≤34 %</td>
<td>3.0 (1.1 to 7.6)</td>
<td>0.02</td>
<td>2</td>
</tr>
<tr>
<td>Blood urea nitrogen &gt;51 U/dL</td>
<td>2.9 (1.1 to 8.0)</td>
<td>0.03</td>
<td>2</td>
</tr>
<tr>
<td>No intravenous inotropes</td>
<td>2.9 (1.1 to 7.7)</td>
<td>0.03</td>
<td>2</td>
</tr>
</tbody>
</table>
Figure 2. Survival after LVAD implantation as DT by the candidate’s operative risk.
REMATCH Conclusions

• Sickest group of patients with HF ever studied in RCT
• Survival and QOL benefit demonstrated with LVAD
• Infectious/Pump failure issues limited widespread adoption
• Infectious issues: patient selection
• Pump failure: Technology/innovation
RV Function/Dysfunction in LVAD
The Forgotten Ventricle in LVAD

- RV Failure complicates 10-30% of LVAD implants
- RV failure is multifactorial
  - Secondary Pulmonary Hypertension
  - RV contractile dysfunction
  - Bleeding, acidosis, acute lung injury
- Previously identified risk factors: RVSWI, female sex, small BSA, non-ischemic CM
The Right Ventricular Failure Risk Score

A Pre-Operative Tool for Assessing the Risk of Right Ventricular Failure in Left Ventricular Assist Device Candidates

Jennifer Cowger Matthews, MD,* Todd M. Koelling, MD,* Francis D. Pagani, MD, PhD,† Keith D. Aaronson, MD, MS*

Ann Arbor, Michigan

J Am Coll Cardiol 2008;51:2163–72

Table 6

Right Ventricular Failure Risk Score and Likelihood of RV Failure by Score Strata

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>n</th>
<th>RV Failure (n)</th>
<th>No RV Failure (n)</th>
<th>Likelihood Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3.0</td>
<td>142</td>
<td>29</td>
<td>113</td>
<td>0.49 (0.37–0.64)</td>
</tr>
<tr>
<td>4.0–5.0</td>
<td>25</td>
<td>15</td>
<td>10</td>
<td>2.8 (1.4–5.9)</td>
</tr>
<tr>
<td>≥5.5</td>
<td>30</td>
<td>24</td>
<td>6</td>
<td>7.6 (3.4–17.1)</td>
</tr>
</tbody>
</table>

Risk Score is derived by summing points awarded for the presence of a vasopressor requirement (4 points), AST ≥80 IU/l (2 points), bilirubin ≥2.0 mg/dl (2.5 points), and creatinine ≥2.3 mg/dl (3 points).

Abbreviations as in Table 1.
Displacement Pumps
Rotary/Continuous Flow/Axial Pumps
Heartmate II
Pump Rotor and Stators

Flow

Outflow Stator
Outflow Bearings
Rotor
Inflow Bearings
Inflow Stator
Use of a Continuous-Flow Device in Patients Awaiting Heart Transplantation

Leslie W. Miller, M.D., Francis D. Pagani, M.D., Ph.D., Stuart D. Russell, M.D., Ranjit John, M.D., Andrew J. Boyle, M.D., Keith D. Aaronson, M.D., John V. Conte, M.D., Yoshifumi Naka, M.D., Donna Mancini, M.D., Reynolds M. Delgado, M.D., Thomas E. MacGillivray, M.D., David J. Farrar, Ph.D., and O.H. Frazier, M.D., for the HeartMate II Clinical Investigators*

ABSTRACT
Figure 1. Components of the Continuous-Flow Left Ventricular Assist Device (LVAD).

The inflow cannula is inserted into the apex of the left ventricle, and the outflow cannula is anastomosed to the ascending aorta. Blood exits through the left ventricular apex and into the left ventricular assist device, which pumps throughout cardiac diastole and systole into the ascending aorta, with the rotor being the only moving part. The left ventricular assist device pump is placed within the abdominal wall or peritoneal cavity. A percutaneous lead carries the electrical cable to an electronic controller and battery packs, which are worn on a belt and shoulder holster, respectively.
Figure 1. The bearingless motor combines drive, magnetic bearing and rotor function into a single unit. The motor generates the magnetic bearing force that is levitating the rotor into the pump housing and it also generates the torque necessary to produce the uni-directional flow. Copyright IHC 2004.
The Jarvik 2000 pump is implanted inside the left ventricle of the patient’s heart.

A fabric tube from the outflow end of the pump connects it to the aorta.

Depending on the heart’s condition and the patient’s level of activity, the output of the Jarvik 2000 can be adjusted to accommodate patient needs using a small, external controller.

Source: Texas Heart Institute

The News & Observer
HMII Pivotal Study
## Study Objective and Design

(Rev 18)

<table>
<thead>
<tr>
<th></th>
<th>BTT</th>
<th>DT</th>
</tr>
</thead>
</table>
| **Entry criteria**   | Traditional study criteria                           | Similar to Rematch; slightly less sick: Class IIIB or IV, OMM 45 out of 60  
|                      | BSA $\geq 1.5$                                       | BSA $\geq 1.5$                                      |
| **Controls**         | Historic Thoratec data (>3,500 pts)                  | Randomized 2:1                                      |
|                      |                                                      | (HMII vs. XVE)                                      |
| **Success criteria:**| Performance standard:                                | 2 year composite endpoint.                          |
| **Primary objectives**| 75% of pts reach transplant or 180 days of support while  | Survival at 2 yrs and free from clinically relevant stroke (Rankin score $> 3$) and re-operation to repair or replace the device |
|                      | remaining listed 1A or 1B                           |                                                      |
| **# Patients/sites** | 133 patients; 25 sites                               | 200 total patients; 40 sites: (UCH)                 |
|                      |                                                      | 133 HMII vs. 67 HMI                                 |
University of Colorado VAD Experience

• Program incepted in October 2000
• 56 VADs implanted in 54 Patients (10/00-10/08)
• 29 patients were Bridge-to-Transplant with Heartmate LVAD
• 7 patients were Destination Therapy with Heartmate LVAD
• 1 patient (DT) for Exchange of LVAD at End-of-Life
• 3 patients were Hybrid Heartmate LVAD + Thoratec RVAD as Bridge-to-Transplant
• 6 patients with Thoratec either LVAD, RVAD or LVAD + RVAD
• 8 Patients with Heartmate II LVAD
  – 3 DT
  – 1 XVE Exchange
  – 4 Bridge-to-Transplant
University of Colorado Heartmate Bridge-to-Transplantation

- 23 of 28 patients bridged successfully to transplant
- 82% Bridge-to-Transplant at UCH vs. 70% ISHLT
Left ventricular assist device as bridge to transplantation does not adversely affect one-year heart transplantation survival

Joseph C. Cleveland, Jr, MD, a Frederick L. Grover, MD, a David A. Fullerton, MD, a David N. Campbell, MD, a Max B. Mitchell, MD, a JoAnn Lindenfeld, MD, b Eugene E. Wolff, MD, b Brian D. Lowes, MD, b Simon F. Shakar, MD, b Andreas Breike, MD, b Anne Cannon, RN, BSN, a and Alastair D. Robertson, PhD b

Objective: Left ventricular assist devices are increasingly used as a bridge to transplantation. It remains unclear whether the use of pretransplant left ventricular assist devices adversely affects short-term survival after cardiac transplantation.

Methods: A retrospective review of 317 consecutive patients undergoing cardiac transplantation at an academic center between 1986 and 2006 was undertaken. Left ventricular assist devices were used pretransplant in 23 of these 317 patients, and 294 patients did not require left ventricular assist device support. Patients with a left ventricular assist device were supported with a Heartmate VE or Heartmate XVE (Thoratec Corp, Pleasanton, Calif). Kaplan–Meier survival estimates were compared between the left ventricular assist device group and the non-left ventricular assist device group using the log-rank test. In addition, occurrence of death was analyzed between the 2 groups with a chi-square analysis. The results are expressed as 1-year survival with 95% confidence intervals in parentheses.

Results: The 1-year survival for all 317 patients was 0.86 (0.82–0.90). The patient survival for the group without a left ventricular assist device before cardiac transplant was 0.87 (0.83–0.90), and the survival for the group with a left ventricular assist device as bridge to transplantation was 0.83 (0.67–0.98; P = .77). For the deaths that occurred in all 317 patients, 19% of the patients without left ventricular assist devices died within 30 days of transplant, whereas 80% of the patients with left ventricular...
UCHSC OHTX Patient Survival - All

UCHSC OHTX Survival with LVAD

ADULT HEART TRANSPLANTATION


- Pulsatile flow (N=1,813)
- No LVAD (N=14,154)

Survival (%)

Years

Note: Only 42 transplants involving continuous flow devices; too few to analyze.

p < 0.0001

ISHLT 2006

J Heart Lung Transplant 2006;25:869-79
University of Colorado VAD Program

• One of 65 CMS certified programs for VAD as Destination Therapy in US

• Recently received Joint Commission Certification for the University of Colorado VAD program – July 22, 2008 (14th site in US)
Bridge-to-Recovery
Reverse Remodeling with LVAD

Before HM II LVAD

After HM II LVAD
LVAD – Bridge to Recovery

**The NEW ENGLAND JOURNAL of MEDICINE**

**ORIGINAL ARTICLE**

**Left Ventricular Assist Device and Drug Therapy for the Reversal of Heart Failure**

Emma J. Birks, M.R.C.P., Ph.D., Patrick D. Tansley, F.R.C.S.,
James Hardy, M.B., B.S., B.Sc., Robert S. George, M.R.C.S., B.Sc.,
Christopher T. Bowles, Ph.D., Margaret Burke, F.R.C.Path.,
Nicholas R. Banner, F.R.C.P., Asghar Khaghani, F.R.C.S.,
and Magdi H. Yacoub, F.R.S.

**METHODS**

We enrolled 15 patients with severe heart failure due to nonischemic cardiomyopathy and with no histologic evidence of active myocarditis. All had markedly reduced cardiac output and were receiving inotropes. The patients underwent implantation of left ventricular assist devices and were treated with lisinopril, carvedilol, spironolactone, and losartan to enhance reverse remodeling. Once regression of left ventricular enlargement had been achieved, the $\beta_2$-adrenergic–receptor agonist clenbuterol was administered to prevent myocardial atrophy.
Device Explantation Criteria

- LVEDD < 60 mm
- LVESD < 50 mm
- LV EF > 45%
- PCWP < 12
- Resting Cardiac Index > 2.8 l/min/m2
- Max VO2 uptake > 16 ml/kg/min
- Device off for 15 minutes
Cumulative Rate of Freedom from Recurrence of Heart Failure among the 11 Surviving Patients Who Underwent Explantation

Ejection Fraction (Panel A), Left Ventricular End-Diastolic Diameter (Panel B), and Left Ventricular End-Systolic Diameter (Panel C) before Implantation and after Explantation, and Maximal Oxygen Consumption (VO₂ Max) (Panel D) with Exercise before and after Explantation.

MECHANICAL CIRCULATORY SUPPORT

Assist Devices Fail to Reverse Patterns of Fetal Gene Expression Despite $\beta$-Blockers

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Background: Heart failure is associated with reversal to a fetal gene expression pattern of contractile and metabolic genes. Substantial recovery of ventricular function with assist devices is rare. Our goal was to evaluate the effects of assist devices on fetal gene expression and hypoxia inducible factor-1$\alpha$ (HIF-1$\alpha$), a transcriptional factor in hypoxic signaling.

Methods: Human heart tissue was obtained from the left ventricular apex at the time of assist device implantation and again from the left ventricular free wall during cardiac transplantation. Non-failing tissue was obtained from unused hearts from human donors. Gene expression was measured with the Affymetrix 133 plus 2 Array. HIF-1$\alpha$ was measured by Western blotting with commercially available antibodies.

Results: Heart failure was associated with a decrease in $\alpha$-myosin heavy chain and sarcoplasmic reticulum-$Ca^{2+}$ adenosine triphosphatase messenger RNA expression along with an increase in skeletal tropomyosin. This pattern persisted after assist device therapy. Heart failure was also associated with abnormalities in regulatory metabolic genes including glucose transporter 1 (GLUT1). These patterns also persisted after assist device therapy despite a reduction in atrial natriuretic peptide expression and normalization of HIF-1$\alpha$.

Conclusions: Failure of assist devices to produce sustained recovery of myocardial contractile function may be due in part to persistent fetal transcriptional patterns of contractile and metabolic genes. J Heart Lung Transplant 2007;26:1170–6. Copyright © 2007 by the International Society for Heart and Lung Transplantation.

Cardiac assist devices are effective for bridging patients to The Journal of Heart and Lung Transplantation

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Figure 2. Transcriptional profiles of contractile genes are presented with the standard error (*p < 0.05 vs non-failing; #p < 0.1) SRCaATPase, sarcoplasmic reticulum calcium adenosine triphosphatase; LVAD, left ventricular assist device.
VAD – Future Considerations

• Axial flow?
  – Trials with HM II and Jarvik 2000 Flowmeter ongoing

• Durability
  – HM II more durable than HM XVE
  – Jarvik 2000 implanted > 6 years in one patient

• Completely contained system with portability
  – No external driveline
Summary and Key Points

- Patient/Device Selection
- Timing of Implantation
- Multidisciplinary Program
  - CT Surgery
  - Cardiology
  - Nursing
  - Coordinator
  - Referring Physicians
  - ICU/Anesthesia
SURVIVAL

When you are in deep trouble, say nothing, and try to look like you know what you're doing.