LVAD vs. Transplant: Who are the Patients and When to Refer?
Dimensions in Heart and Vascular Care
Hershey, PA
October 18, 2013

Disclosures:
Consultant: Thoratec Corporation
Principal Investigator, HeartWare ENDURANCE trial

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Associate Professor of Medicine
Senior Vice Chief for Clinical Affairs, Division of Cardiology
Medical Director, Cardiac Transplant and Mechanical Circulatory Support Program
Duke University

The Stage D Heart Failure Patient
- 5% of the heart failure population
- Intolerable symptoms
- Frequent hospitalizations
- Limited therapeutic options

Heart Failure Patients Underestimate Their Mortality Risk
Predictors of Higher Estimated Life Expectancy:
- Younger age
- Higher NYHA Class
- Lower EF
- Ischemic disease
- Less depression

JAMA 2008;299:2533-42
Heart Failure Risk Stratification

Defining the patient who is “in trouble”

- Signs, symptoms, and clinical course
- Etiology
- Ventricular structure and function
- Medication use and intolerance
- End-organ dysfunction
- Functional limitations
- Biomarkers

NYHA Functional Class is Insensitive to Mortality
Sub-stratification using Seattle HF Score

* Seven Subjects

The Impact of Heart Failure Hospitalization on Mortality Risk

A retrospective analysis of the CHARM Trial
The Prognostic Value of Functional Limitations

VO₂max = (AO₂ – VO₂) x CO

VO₂ ≥ 14 ml/kg/min
VO₂ ≤ 14 ml/kg/min (listed)*
VO₂ ≤ 14 ml/kg/min (not listed)*

* p<0.005 for VO₂ ≤ 14 vs > 14

Common Biomarkers Useful in Risk Stratification

- Natriuretic peptides
- Serum sodium
- BUN
- Creatinine
- Hemoglobin
- RDW
- Albumin

Is Physician Gestalt Important?

- ESCAPE Registry included 439 patients not randomized in trial but received a PAC
- No difference in hemodynamics except higher SVO₂ and CI in Trial patients
**Patient Preferences Impact Choices**

J Am Coll Cardiol 2008;52:1702-8

**Advanced Heart Failure Therapeutic Decision Tree**

Advanced Heart Failure on Optimal Therapy

- Palliative Care
  - Hospice
  - Appropriate for many
  - Very few come seeking

- Continued Therapy
  - Limited likelihood of improvement

- Inotropes
  - Symptom improvement
  - Short survival

- Transplant
  - Strict criteria
  - Limited resource

- VAD
  - Therapy for the masses?

**Prognosis on Chronic Dobutamine or Milrinone Infusions**

Special Considerations in Determining Eligibility for VAD or Transplant

- Age
- Duration and etiology of heart failure
- Urgency
- Baseline renal insufficiency, malignancy
- Right ventricular failure
- Ventricular arrhythmias

Simplified Risk Model for Continuous Flow LVADs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>SE</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 yrs)</td>
<td>0.274</td>
<td>0.12</td>
<td>1.32 (1.05-1.65)</td>
<td>0.018</td>
</tr>
<tr>
<td>Albumin (per g/dl)</td>
<td>-0.723</td>
<td>0.23</td>
<td>0.49 (0.31-0.78)</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine (per mg/dl)</td>
<td>0.740</td>
<td>0.22</td>
<td>2.10 (1.37-3.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>INR (per unit)</td>
<td>1.136</td>
<td>0.32</td>
<td>3.11 (1.66-5.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Center Volume &lt; 15</td>
<td>0.807</td>
<td>0.34</td>
<td>2.24 (1.15-4.37)</td>
<td>0.018</td>
</tr>
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Transplant generally limited to only very select patients > 65 years of age.

Clinical Strategies and Outcomes in Advanced Heart Failure Patients Older Than 70 Years of Age Receiving the HeartMate II Left Ventricular Assist Device

A Community Hospital Experience

Robert M. Ackerson, MD, Marina Sledzwick, RN, Steven E. Colton, MD, Sam Barriat, MD, Joseph Chavannes, MD, Rose Jaffe, MD, Peter Heagerty, MD, Walter Dostalik, MD

San Diego, California

Duke Clinical Research Institute
**Myocardial Recovery on MCS**

- 44 y/o with non-ischemic cardiomyopathy, cardiogenic shock, LVAD placed 2009
- Presented with recurrent driveline infection. Exit site had already been recreated and was close to pocket

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**Factors Associated with Functional Recovery**

- Younger age
- Shorter HF duration
- Non-ischemic etiology
- Minimal fibrosis
- If potential candidate, give max oral HF
- Needs to become a programmatic focus
- NEED PROSPECTIVE STUDIES

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**Are We Seeing Recovery in Clinical Trials and Registries?**

**INTERMACS Registry**

![Graphs showing recovery metrics over time](image)

*J Heart Lung Transplant 2012;31:117-26*
Use of LVADs for Recovery of LV Function: US Experience

- 1108 patients from HeartMate II Clinical Trials database
- Only 20/1108 (1.8%) recovered
- Age Mean: 33 yrs
- HF Duration < 1 yr in 65% of recovered
- Median support time = 324 days

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<th>Patients</th>
<th>Recovery</th>
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<tr>
<td>Non-ischemic</td>
<td>531</td>
<td>18</td>
<td>3.4</td>
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<td>Ischemic</td>
<td>577</td>
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<td>Total</td>
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<td>&lt; 40</td>
<td>147</td>
<td>12</td>
<td>8.2*</td>
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<tr>
<td>≥ 40</td>
<td>384</td>
<td>6</td>
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Myocardial Functional Recovery on a Pulsatile Device: The Harefield Experience

- Adjunctive Clenbuterol
- Adjunctive Cell Therapy

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Urgency of Advanced Heart Failure Therapy

- Status 1A:
  - Mechanical ventilation
  - IABP
  - Cardiogenic shock with PAC and 2 inotropes in ICU
  - Dysfunctional VAD
- Status 1B:
  - Stable inotropes
  - Stable VAD

<table>
<thead>
<tr>
<th>All Time</th>
<th>&lt; 30 d</th>
<th>3 Mo</th>
<th>6 Mo</th>
<th>12 Mo</th>
<th>24 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status 1A</td>
<td>409</td>
<td>92</td>
<td>85</td>
<td>63</td>
<td>70</td>
</tr>
<tr>
<td>Status 1B</td>
<td>1099</td>
<td>95</td>
<td>165</td>
<td>194</td>
<td>229</td>
</tr>
<tr>
<td>Status 2</td>
<td>970</td>
<td>61</td>
<td>116</td>
<td>112</td>
<td>172</td>
</tr>
</tbody>
</table>
Post-Transplant Renal Dysfunction

- Complex pathology
- Multifactorial
- Related to underlying conditions
- Mediated by immunosuppression
- 5-10% of patients are on dialysis 10 yrs following heart transplant

Importance of RV Function

- Pre-implant diagnosis is challenging and there is a lack of consensus regarding diagnostic criteria
- Limits function of device
- Associated with end-organ dysfunction
- Associated with prolonged length of stay
- Right ventricular failure following LVAD implantation is an important cause of post-implant morbidity and mortality

Predictors of RV failure during LVAD support

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Desirable Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVSWI ([(mPA - mCVP) x SV/BSA])</td>
<td>&gt; 300 mmHg x mL/m²</td>
</tr>
<tr>
<td>CVP</td>
<td>&lt; 15 mmHg</td>
</tr>
<tr>
<td>Presence of tricuspid regurgitation</td>
<td>Minimal to moderate</td>
</tr>
<tr>
<td>PVR and TPG</td>
<td>PVR &lt; 4 Woods Units and TPG &lt; 15 mmHg</td>
</tr>
<tr>
<td>RV size</td>
<td>RV DIA &lt; 25 cm and BSALV &lt; 177 cm</td>
</tr>
<tr>
<td>Need for preoperative support</td>
<td>None</td>
</tr>
</tbody>
</table>
The Impact of LVAD on Ventricular Arrhythmias

- 100 consecutive VAD patients
- Mean age=51 yrs, 63% ischemic

<table>
<thead>
<tr>
<th>Ventricular Arrhythmias</th>
<th>Patients With LVAD &amp; Ventricular Arrhythmia</th>
<th>Patients With IVAD &amp; Ventricular Arrhythmia</th>
<th>Patients With LVAD &amp; No Ventricular Arrhythmia</th>
<th>Patients With IVAD &amp; No Ventricular Arrhythmia</th>
<th>Rate of New Onset Ventricular Arrhythmias</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT/VTW</td>
<td>20</td>
<td>17</td>
<td>14</td>
<td>10</td>
<td>38/16; p = 0.17</td>
</tr>
<tr>
<td>PVC/PVCW</td>
<td>28</td>
<td>24</td>
<td>16</td>
<td>10</td>
<td>38/16; p = 0.17</td>
</tr>
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J Am Coll Cardiol 2005;45:1428-34

Issues of Nutrition

Markers of Poor Nutrition
- BMI < 20 kg/m²
- Pre-albumin < 15 mg/dl
- Transferrin > 250 mg/dl
- Total Cholesterol < 130 mg/dl
- Lymphocyte Count < 100
- PO supplements
- Enteral nutrition
- TPN (last resort)

Obesity not a contraindication
- Devices can provide adequate support
- Has not impacted outcomes
- May be contraindication for transplant
- Patients not losing weight on VAD support
Summary and Conclusions

- Risk stratification is a critical component of selecting patients for advanced heart failure therapy. It requires integration of multiple data points.
- The short- and intermediate-term results with DT VAD and transplant are similar. Longer term results and data from a clinical trial would be helpful in clinical decision-making.
- Consider VAD for:
  - Urgent need for support
  - Patients who may recover
  - Patients with baseline renal insufficiency or high likelihood of malignancy
- Consider transplant for:
  - Patients with right heart failure
  - Patients with VT