Bridge to Transplant vs. Destination Therapy
Which Pathway?

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# Disclosure

Mayo Clinic Division of Cardiovascular Surgery

Research funding within the past year:

<table>
<thead>
<tr>
<th>AstraZeneca</th>
<th>Jarvik Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atricure</td>
<td>Medtronic</td>
</tr>
<tr>
<td>Avant Immunotherapeutics</td>
<td>St. Jude Medical</td>
</tr>
<tr>
<td>Baxter</td>
<td>Thoratec Corporation</td>
</tr>
<tr>
<td>Carbomedics/Sorin Group</td>
<td>TransTech Pharma</td>
</tr>
<tr>
<td>CryoLife</td>
<td>W.L. Gore and Associates</td>
</tr>
</tbody>
</table>

No personal equity, patents, licensing, or consulting agreements with the medical device or pharmaceutical industry to disclose
Heart Failure in the US

- 5.7 Million cases
- 500,000 new cases each year
- Prevalence is increasing
- At least 20% have end-stage HF
- Limited role for medical therapy for end-stage HF
High Risk for Developing HF

Asymptomatic HF

Symptomatic HF

Refractory End-Stage HF
Marked symptoms at rest despite maximal medical therapy

High Risk for Developing HF
• Hypertension
• CAD
• Diabetes mellitus
• Family history of cardiomyopathy

• Known structural heart disease
• Shortness of breath and fatigue
• Reduced exercise tolerance

• Previous MI
• LV systolic dysfunction
• Asymptomatic valvular disease

• Hypertension
• CAD
• Diabetes mellitus
• Family history of cardiomyopathy
Treatment Options

- Palliative Care
- Medical Therapy
- Transplantation
- LVAD (BTT vs. DT)
Kaplan-Meier cumulative mortality

Median survival (yr)

Kaplan-Meier cumulative mortality

Time since admission

1st admission (n=14,374)
2nd admission (n=3,358)
3rd admission (n=1,123)
4th admission (n=417)

Setoguchi: AHJ, 2007
Stage D Heart Failure
Treatment Options

Risks
Infection
Rejection
Immunosuppression

Risks
Thrombosis
Bleeding
Mechanical Failure
Treatment Options

- Palliative Care
- Medical Therapy
- Transplantation
- LVAD (BTT vs. DT)
Cardiac Transplantation

Selection Criteria

- End-stage heart disease (criteria necessary but not sufficient)
  - Life expectancy
  - Declining functional status V02 <50% predicted
  - Increasing requirements for medical therapy
  - EF <20%
  - Malignant arrhythmia
  - Not suitable for conventional therapy
- Age birth to ?
- Motivation and a functional support system
- Absence of contraindications
Cardiac Transplantation
Contraindications

- Age?
- Coexistent systemic illness
- Irreversible pulmonary vascular disease
- Parenchymal pulmonary disease
- Acute pulmonary emboli
- Severe peripheral vascular disease
- Irreversible renal or hepatic dysfunction
- Diabetes with severe end-organ disease
- Severe obesity
- Severe osteoporosis
- Active infection
- Psychosocial instability
- Unresolved addiction
Transplanted vs. Listed

The graph shows the number of patients transplanted and listed for transplant from 1988 to 2010. The line for transplanted patients (orange) and listed patients (teal) are plotted over time. The graph indicates a peak in the mid-1990s for the transplanted line, followed by a decline and then a steady increase towards 2010. The listed line also shows a consistent increase over the years.

Source: MAYO CLINIC

Graph: Transplanted vs. Listed
Treatment Options

- Palliative Care
- Medical Therapy
- Transplantation
- LVAD (BTT vs. DT)
The LVAD Candidate

- Decreasing LVEF
- Hyponatremia
- Worsening renal insufficiency
- Persistent congestion or low BP
- Recurrent ICD shocks
- Persistently increased BNP
- Recurrent hospitalizations
LVAD Indications

- Bridge to Transplant (BTT)
- Bridge to Decision or Recovery
- Destination therapy (DT)
FDA-Approved Indications for MCS

• **Bridge to Transplantation**
  - listed for heart transplantation
  - Advanced heart failure at risk of imminent death
  - Failing optimal medical management

• **Destination Therapy**
  - persistent NYHA class IV symptoms for 45 of the previous 60 days with optimal medical management
  - left ventricular ejection fraction $\leq 25\%$
  - peak oxygen consumption $<14 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ or dependent on inotropes for at least 14 days or IABP for at least 7 days if unable to exercise
  - not a candidate for heart transplantation
Mechanical circulatory support candidate selection

1. **Class III or IV HF with Optimal Medical Management**
   - Not Improved to NYHA I or II
     - Cardiac Resynchronization Therapy ± ICD Evaluation
       - CRT No
       - CRT Yes
         - No Improvement
         - Surgical Evaluation at MCS implant centre
   - Improved to NYHA I or II

2. **Destination Therapy Evaluation**
   - FDA Criteria:
     - NYHA Class III or IV HF
     - Have received optimal medical therapy for at least 45 of the last 60 days
     - Not a candidate for cardiac transplantation
   - VAD
     - Yes: Destination Therapy
     - No: Palliative Care
     - Continuous IV Inotrope Therapy
     - Hospice

3. **Cardiac Transplant Evaluation**
   - Criteria:
     - Refractory HF
     - Acceptable comorbidities
     - Adequate psychosocial support
     - Medical compliance
   - VAD
     - Bridge-to-Transplantation Therapy
     - Transplant
Ventricular Assist Device Innovation

1st Generation

Pulsatile Technology

FDA Approved
BTT 1998
DT 2002

Bearings with stator

2nd Generation

Continuous Flow Technology
Axial Design

FDA Approved
BTT 2008
DT 2010

Bearingless with magnetic and hydrodynamic levitation

3rd Generation

Continuous Flow Technology
Centrifugal Design

FDA Approved
BTT 2013
DT Pending

○ Minaturization
○ Durability
Ventricular Assist Device Innovation

- **Thoratec HeartMate III**
  - Centrifugal flow pump design with magnetic levitation of impellor

- **HeartWare MVAD**
  - Axial flow pump design with hydromagnetic levitation of impellor

- **Terumo DuraHeart II**
  - Centrifugal flow pump design with magnetic levitation of impellor

- **HeartMate X**
  - Axial flow pump design with advanced bearing support of impellor
INTERMACS - Implants per Year by Device Type
Primary Prospective Implants: June 23, 2006 to December 31, 2012

Number of Implants per Year

Year
2006 (Jun-Dec) 2007 2008 2009 2010 2011 2012 (Jan-Dec)
LVAD BiVAD TAH
81 72 79 93 80 94 62
20 22 23 24 29 24 36
2 2 2 2 2 2 2
INTERMACS - Kaplan-Meier Survival for INTERMACS Overall
Primary Prospective Implants: June 23, 2006 to December 31, 2012

Event: Death (censored at transplantation or recovery)

<table>
<thead>
<tr>
<th>MONTHS</th>
<th>SURVIVAL</th>
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<tbody>
<tr>
<td>1</td>
<td>94%</td>
</tr>
<tr>
<td>3</td>
<td>89%</td>
</tr>
<tr>
<td>6</td>
<td>85%</td>
</tr>
<tr>
<td>12</td>
<td>78%</td>
</tr>
<tr>
<td>24</td>
<td>66%</td>
</tr>
<tr>
<td>36</td>
<td>56%</td>
</tr>
<tr>
<td>48</td>
<td>47%</td>
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<tr>
<td>60</td>
<td>43%</td>
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</tbody>
</table>

Shaded areas indicate 70% confidence limits

INTERMACS Overall (n = 7913, deaths = 1880)
INTERMACS - Kaplan-Meier Survival for Continuous Flow LVADs (with or without RVAD implant at time of LVAD operation) by Pre-Implant Device Strategy

Primary Prospective Implants: June 23, 2006 to December 31, 2012

Event: Death (censored at transplantation or recovery)

Pre-Implant Device Strategy
- Bridge to Transplant (n = 4457, deaths = 862)
- Destination Therapy (n = 2246, deaths = 605)

p (overall) = <.0001

Shaded areas indicate 70% confidence limits
EQ5D Visual Analog Scale (VAS) across time (mean ± SE)

<table>
<thead>
<tr>
<th>EQ5D VAS</th>
<th>Pre-implant</th>
<th>3 month</th>
<th>6 month</th>
<th>12 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best</td>
<td>100</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>90</td>
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<td>70</td>
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<td>20</td>
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</tr>
<tr>
<td></td>
<td>10</td>
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<tr>
<td>Worst</td>
<td>0</td>
<td></td>
<td></td>
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</tbody>
</table>

(N = 852)  (N = 628)  (N = 466)  (N = 281)

CF LVAD, n = 1694

P < 0.0001 (pre vs 3 mo)

P < 0.0001 (pre vs 6 mo)

P < 0.0001 (pre vs 12 mo)
June 2006 – June 2012: Destination Therapy

EQ5D Dimension: Self Care

<table>
<thead>
<tr>
<th>% With Problems</th>
<th>Pre-Implant</th>
<th>3 Month</th>
<th>6 Month</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=88</td>
<td>N=12</td>
<td>N=5</td>
<td>N=4</td>
</tr>
<tr>
<td>(N=852)</td>
<td>(N=528)</td>
<td>(N=466)</td>
<td>(N=281)</td>
<td></td>
</tr>
</tbody>
</table>

Some Problems | Extreme Problems

CF LVAD, n = 1694

p < 0.0001
1. Critical cardiogenic shock
2. Progressive decline, on inotropes
3. Stable, but inotrope dependent
4. Recurrent advanced HF
5. Exertion intolerant
6. Exertion limited
7. Advanced NYHA III
Survival to Dismissal

Group 1: INTERMACS 1: crash and burn
Group 2: INTERMACS 2 and 3: hospitalized and inotrope-dependent
Group 3: INTERMACS 4 – 7: poor functional capacity

Group 3 vs. Group 1: $p < 0.01$
Group 3 vs. Group 2: $p = 0.73$
Group 2 vs. Group 1: $p < 0.01$

Boyle A et al. ESC HF Congress Milan, Italy 2008.
Survival by INTERMACS

Survival by INTERMACS

Survival (%)

Months from VAD Insertion

p = .02

Pagani et al. ISHLT 2008
Group 1: INTERMACS 1: 
crash and burn
Group 2: INTERMACS 2 and 3: hospitalized and inotrope-dependent
Group 3: INTERMACS 4 – 7: 
poor functional capacity

Group 3 vs. Group 1: p < 0.001
Group 3 vs. Group 2: p < 0.001
Group 2 vs. Group 1: p = ns

Boyle A et al. ESC HF Congress Milan, Italy 2008.
Patient Selection

- Don’t wait for progressive renal dysfunction
- Don’t wait until multiple pressors are required
- Don’t wait for cardiac cachexia
- Infections need to be resolved before implant
- Patients with poor functional capacity and frequent decompensations
- Patients with frequent life-threatening ventricular arrhythmias
Patient Selection

• Best done electively; crisis management should be as a bridge to decision

• VADs should not be an alternative to death but rather a bridge to life: wait too long and pay a heavy price
# Pre-Implantation Goals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Desirable Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Renal</strong></td>
<td>BUN &lt; 50 mg/dL</td>
</tr>
<tr>
<td></td>
<td>SCr &lt; 2.5 mg/dL</td>
</tr>
<tr>
<td><strong>Hematologic</strong></td>
<td>INR &lt; 1.2</td>
</tr>
<tr>
<td></td>
<td>Hb &gt; 10 g/dL</td>
</tr>
<tr>
<td></td>
<td>PLT &gt; 150,000/ml</td>
</tr>
<tr>
<td><strong>Nutritional</strong></td>
<td>Albumin &gt; 3 g/dL</td>
</tr>
<tr>
<td></td>
<td>Pre-albumin &gt; 15 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Transferrin &gt; 250 mg/dL</td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td>TB &lt; 2.5 mg/dL</td>
</tr>
<tr>
<td></td>
<td>ALT, AST &lt; 2 times normal</td>
</tr>
<tr>
<td><strong>Hemodynamic</strong></td>
<td>RAP &lt; 15 mmHg</td>
</tr>
<tr>
<td></td>
<td>PCWP &lt; 24 mmHg</td>
</tr>
</tbody>
</table>
Candidates for Bridge

Current or Ongoing Definite Contraindications for Permanent Support

- uncertain neurological status (cardiac arrest, prolonged CPR)
- major end organ dysfunction (renal and hepatic dysfunction)
  - severe hemodynamic instability
  - major coagulopathy
  - active, untreated infections

“Relative” Contraindications for Permanent Support

- high-risk social situations
  - mechanical ventilation

Intra-aortic Balloon Pump
Impella

Motor

Impeller Pump

Blood Outlet Area

Blood Inlet Area
Tandem Heart
Bilateral Centrimag
Acute Refractory Cardiogenic Shock (Multiple Inotropes & Pressors, IABP) with Multisystem Organ Failure +/- Prior Cardiac Arrest Uncertain Neurologic Status

Transfer to our institution

CentriMag Biventricular Support

(Monitor End-organ Function, Nutritional Support, Wean Sedation, Echocardiography)

End-organ Functional Recovery
Neurological Recovery
Cardiac Recovery

CentriMag Explant

End-organ Functional Recovery
Neurological Recovery
No Cardiac Recovery

HeartMate Implantation

End-organ Functional Recovery +/- No Neurological Recovery
Cardiac Recovery +/-

Neurology Consult
CT Scan, EEG

Poor Neurological Prognosis

CentriMag Support Withdrawn
LVAD Current Practice

Multidisciplinary Working Environment

Administration
- DOS
- CVS Division
- CV Disease
- Transplant Center

Clinical Teams
- VAD Coordinators
- CVS NPs/PAs

Nursing
- Clinical Nurse Specialists
- Nursing Education Specialists
- CV Surgery Clinical Nurse Specialists

Cardiovascular Surgery
- Surgical Services

Cardiovascular Disease
- Transplant Service
- Heart Failure Clinic

Mechanical Device Support
- Palliative Care
- Pharmacy
- Rehabilitation
- ECHO
- Social Services
- Psychiatry
- Dietetic/Food Services
- Flight Team
- AHFC
- Anesthesia
Q32. If a patient who presented in refractory cardiogenic shock and was placed on temporary MCS has end-organ and neurological recovery, but not cardiac recovery, what clinical pathway is most appropriate for definitive management?

a. MCS wean and explant
b. Long-term implantable LVAD
c. Withdrawal of support
d. None of the above
Thank You!