LVAD As Destination Therapy
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No Disclosures

Circulatory Support Strategies

- Intra-aortic balloon pump (IABP)
- Percutaneous Ventricular Assist Device (pVAD)
  Tandem Heart
  Impella Recovery System
- Extracorporeal Membrane Oxygenation (ECMO)
Components of the Ventricular Assist Device

Traditional Terminology

- **Destination Therapy (DT)**
  longterm mechanical circulatory assist device for patients who have contraindications to cardiac transplantation
- **Bridge to Transplant**
- **Bridge to Recovery**
- **Bridge to Candidacy**

- But, Bridge to Decision preferred
The New England Journal of Medicine

LONG-TERM USE OF A LEFT VENTRICULAR ASSIST DEVICE FOR END-STAGE HEART FAILURE

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REMATCH Trial

Magnitude of Survival Benefit with LVAD DT Therapy

NEJM 2009; 361(23): 2241-51
NEJM 2001; 345(20): 1435-43
200 patients randomized in 2:1

continuous flow (n=134) vs pulsatile flow (n=64) device

transplant ineligible; refractory symptoms; optimal medical therapy
DT Trial CAP: Conclusions & Inference

Conclusions

- Trend towards improving survival
  - Fewer deaths from hemorrhagic stroke
- Significant reductions in adverse events:
  - Hemorrhagic stroke >50% reduction
  - Device related infections >35% reduction
  - Sepsis >25% reduction
- Both QoL measures (KCCQ and MLWHF) demonstrated significant improvement over baseline values

Source: Park SJ, AHA 2010

What is the magnitude of absolute survival benefit with LVAD DT therapy?

LVAD in the Real World
Interagency Registry for Mechanically Assisted Circulatory Support

- National Heart Lung & Blood Institute (NHLBI)–sponsored collaborative database

- collects information on durable mechanical circulatory support (MCS) device implants in the United States.

- prospective patient enrollment & data collection June 23, 2006

- June 23, 2006 - September 30 2010

  **2868 patients implanted with 1 or more MCS devices**

- data from 79 MCS centers; 69 designated as DT MCS centers
Current actuarial survival with continuous-flow pumps:

- > 80% at 1 year
- > 70% at 2 years

The Selection Process: Risk Stratification

- REMATCH: LVAD benefit up to 2 years for most populations.
- More people can benefit due to the availability of devices.
- Most of the mortality occurred during the initial hospitalization for LVAD surgery.

  - Degree of organ compromise
  - Urgency at the time of implantation
  - Associated with irreversible organ dysfunction.

*Can we identify the patient heading towards early death but not yet dying?*
INTERMACS: Indications for Destination Therapy

Table 6: Patient Profile Levels—Adult Primary Implants: INTERMACS, June 2006–June 2010

<table>
<thead>
<tr>
<th>Level</th>
<th>DT patients No. (%)</th>
<th>All other LVADs No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Critical cardiogenic shock</td>
<td>36 (9)</td>
<td>467 (22)</td>
</tr>
<tr>
<td>2. Progressive decline</td>
<td>159 (41)</td>
<td>947 (44)</td>
</tr>
<tr>
<td>3. Stable but inotrope-dependent</td>
<td>101 (26)</td>
<td>374 (18)</td>
</tr>
<tr>
<td>4. Recurrent advanced HF</td>
<td>57 (15)</td>
<td>233 (11)</td>
</tr>
<tr>
<td>5. Exertion Intolerant</td>
<td>19 (5)</td>
<td>51 (2)</td>
</tr>
<tr>
<td>6. Exertion limited</td>
<td>7 (2)</td>
<td>34 (2)</td>
</tr>
<tr>
<td>7. Advanced NYHA class III</td>
<td>6 (2)</td>
<td>28 (1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>385 (100)</td>
<td>2,134 (100)</td>
</tr>
</tbody>
</table>

DT, destination therapy; HF, heart failure; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; NYHA, New York Heart Association. P < 0.0001.

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Patient Selection: Risk Stratification

### Individual Predictors of Poor Operative Outcome
- age
- female
- DM2
- prior CV surgery
- pre-existing RHF
- coagulopathy
- target organ failure (renal; liver; respiratory)

### Risk Scores Predict Overall Outcome
- INTERMACS
- Leitz-Miller
- Columbia
- Apache II
- Seattle Heart Failure Score
Risk Score Limitations

• Lack prospective independent validation
• Outcome data only short-term
• Derived mainly in pts with *first generation* devices
• Under-representation of
  women
  African-Americans
  recidivism of drugs / alcohol
  DM2
  extremes of BMI

Who Should Get a VAD?
LVAD DT: Indications

- NYHA IV
- Life expectancy < 2 yrs
- Transplant ineligible
- Failure to respond to optimal medical management for > 60 of the last 90 days
- LVEF ≤ 25%
- Refractory cardiogenic shock or cardiac limitation
- Peak VO2 ≤ 12 mL·kg⁻¹·min⁻¹
- Inotropic dependence
- Recurrent symptomatic VT, Vfib with an untreatable arrhythmogenic substrate

LVAD DT: Contraindications

- Potentially reversible HF
- High surgical risk
- Recent or evolving stroke
- Neurological deficits impairing the ability to manage device
- Coexisting terminal condition (eg, metastatic cancer, cirrhosis)
- Abdominal aortic aneurysm 5 cm
- Biventricular failure in patients older than 65 years
- Active systemic infection or major chronic risk for infection
- Fixed pulmonary or portal hypertension
- Severe pulmonary dysfunction (eg, FEV1 ≤1 L)
- Impending renal or hepatic failure
- Multisystem organ failure
- Inability to tolerate anticoagulation
- HIT
- Psychiatric illness or lack of social support that may impair ability to maintain and operate VAD
LVAD DT: Relative Contraindications

- Age > 65 years, unless minimal or no other clinical risk factors
- CRF with serum creatinine > 3.0 mg/dL
- Severe chronic malnutrition
  - BMI < 21 kg/m² in males; <19 kg/m² in females
- Morbid Obesity
  - BMI > 40 kg/m²
- Mechanical ventilation
- Severe MS; moderate to severe AI; uncorrectable MR

LVAD: The Ideal Candidate?
LVADs: The Ideal Candidate?

3rd INTERMACS Annual Report:
Primary Cause of Mortality in DT VAD

<table>
<thead>
<tr>
<th>Primary cause of death</th>
<th>Early (&lt;1 mo)</th>
<th>Later (&lt;1 mo)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% of 35</td>
<td>n</td>
</tr>
<tr>
<td>Cancer</td>
<td>0</td>
<td>0%</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac Failure</td>
<td>2</td>
<td>5%</td>
<td>7</td>
</tr>
<tr>
<td>Cardiovascular: Other</td>
<td>4</td>
<td>11%</td>
<td>4</td>
</tr>
<tr>
<td>Device Malfunction</td>
<td>0</td>
<td>0%</td>
<td>3</td>
</tr>
<tr>
<td>Hematologic: Other</td>
<td>0</td>
<td>0%</td>
<td>1</td>
</tr>
<tr>
<td>Hemorrhage: Disseminated</td>
<td>2</td>
<td>5%</td>
<td>0</td>
</tr>
<tr>
<td>Intravas Coagulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage: Post-Operative</td>
<td>4</td>
<td>11%</td>
<td>0</td>
</tr>
<tr>
<td>surgery related</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage: Pulmonary</td>
<td>2</td>
<td>5%</td>
<td>0</td>
</tr>
<tr>
<td>Hemorrhage: Other</td>
<td>0</td>
<td>0%</td>
<td>3</td>
</tr>
<tr>
<td>Infection</td>
<td>1</td>
<td>2%</td>
<td>5</td>
</tr>
<tr>
<td>Other chronic illness</td>
<td>1</td>
<td>2%</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary: Respiratory Failure</td>
<td>2</td>
<td>5%</td>
<td>2</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>1</td>
<td>3%</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>11%</td>
<td>10</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>11%</td>
<td>11</td>
</tr>
<tr>
<td>CNS cause of death</td>
<td>4</td>
<td>11%</td>
<td>5</td>
</tr>
<tr>
<td>MOF</td>
<td>5</td>
<td>14%</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>62%</td>
<td>97</td>
</tr>
</tbody>
</table>

CNS, central nervous system: LVAD, left ventricular assist device.
Cardiac Failure includes RV Failure and VT/VF.

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VAD-Related Infections

Fig 1. Severe wound infection of the lateral wall uncovering the pump chamber and drive line.

Fig 2. Severe median wound infection with a visible outflow conduit.

*Ann Thorac Surg* 2000;70:538-541
VAD-Related Infections

- Prevalence 14% to 72%
- Drive line infections seed other parts of the LVAD including the pocket
- Antibiotic goal ideally bactericidal; typically bacteriostatic
- Biofilm forming bacteria & fungi

Strategies:

- Improvements in perioperative care
- Smaller blood pumps
- Better patient selection
- Future directions include fully implantable pumps

Ventricular Arrhythmia

Figure 1. Twelve-lead electrocardiogram showing ventricular fibrillation.
Patient was in VF for 12 hours!

**Ventricular Arrhythmia**

**VAD-Related Bleeding**

- **Hct / Hgb**
  - **Hemolysis**
    - Jaundice
    - ↑ Bili, LDH, pHgb
  - **Anatomical Bleed**
    - Pallor
    - Bili, LDH, pHgb
  - **Thrombosis**
    - Jaundice
    - ↑ Bili, LDH, pHgb

**GI Bleed**
- Guaiac Stools
- Endoscopy
- Capsulosity
- Body Imaging

**VAD CTA**
Mechanisms of GI Bleeding

- Increased intraluminal pressure
- Lowered pulse pressure; hypoperfusion

Axial Flow Device

- Decrease in HMW multimers leading to impaired coagulation

Acquired vWD

- vWF fragments
- Impaired platelet aggregation

Angiodysplasia

- GI Bleeding

VAD-Related Bleeding

Clinical Dilemma

Antithrombotic Strategy:
- ASA 81 – 325 mg daily
- Coumadin INR:
  - 1.5 - 2.0
  - 2.0 - 2.5 atrial fibrillation
  - hypercoagulability
  - thrombosis

What to do if recurrent bleeding?
What to do if recurrent thrombosis?

Stroke

Bleed
VAD-Related Syncope

- Syncope
  - Pump Obstruction
  - Pump Failure
    - Septal Suction
    - Pump Thrombosis
    - Poor intrinsic contractility
    - Fusion of aortic valve

Key Study: Ramp Echo

Ominous Sign #4: VAD-Related Syncope

Ramp Echocardiogram:
Limited study to evaluate ventricular chamber size and valvular hemodynamics in response to changes in VAD speed

Mechanical unloading of the ventricle increases with increasing VAD rpm

- **VAD Too fast**
  - Septal shift (leftward)
  - Aortic Valve closed
  - Worsening TR
  - Decreasing RV function

- **VAD Too Slow**
  - Ventricle dilated
  - Aortic valve opens w/ each beat
  - Worsening MR
Summary

- Despite best medical therapy, Stage D HF portends a poor prognosis

- LVADs provide mortality & quality of life improvement

- Longterm Challenges:
  - Patient Selection
  - Timing of intervention
  - Cost & accessibility
  - Ethics

Conclusions

- VADs have demonstrated significant mortality benefits in patients with end-stage cardiomyopathy

- Significant & varied morbidity

- Common chief complaints have more profound VAD-related diagnoses

- Management for optimal care continues to evolve with our understanding of VAD-related complications
Is there a New Dawn?

*What have VADs taught us about the end-stage heart failure?*

- VAD physiology & hemodynamics
- Potential Insights into Myocardial Recovery
- Future Directions

Heart Failure: Epidemiological Significance

- prevalence ~5 million Americans
- 500-600 000 new cases diagnosed annually
- annual costs range from $10 billion to $40 billion
- annual mortality rate for advanced disease > 50%
- aggregate 5 yr survival rate 50%
Non-Optimal Optimal Therapy

The Therapeutic Ceiling of Medical Therapy
Best Therapy ≠ Ideal Outcome

The “Economics” of Cardiac Transplantation
Demand >>> Supply

250-500,000 patients in the US are in Stage D HF (refractory; endstage)

mean survival of 3.4 months

one-year rate of 6% for patients who reach inotrope dependence.

80,000 to 150,000 patients with advanced heart failure could potentially benefit from HT in the United States every year