Long-Term Mechanical Circulatory Support (Destination Therapy) Should Move to NYHA Class III Patients

John C. Eun
PGY 3
University of Colorado Denver
Grand Rounds Presentation 11/17/2008
Heart Failure

- Prevalence in 2005
  - 5,300,000

- Incidence
  - 660,000/Year

- Mortality in 2004
  - 284,365

- Estimated Cost in 2008
  - $34.8 Billion

New York Heart Association (NYHA) Classification Scale for Heart Failure

- **Class I (Mild)**
  - No symptoms at any level of exertion and no limitation in ordinary physical activity.

- **Class II (Mild)**
  - Mild symptoms and slight limitation during regular activity.

- **Class IIIa (Moderate)**
  - Marked limitation of physical activity even during minimal activity.

- **Class IIIb (Moderate)**
  - Above with recent history of dyspnea at rest.

- **Class IV (Severe)**
  - Symptoms at rest.
Heart Failure

- Gold standard therapy for chronic end-stage HF is transplant.
- 2,192 heart transplants were performed in the United States in 2006 and 2,125 in 2005*.
- “Trivial” number of hearts vs. demand.
What is Destination Therapy?

- The use of mechanical circulatory support as a permanent therapy for patients in end-stage heart failure.
Indications for Destination Therapy

- NYHA Class IV for at least 90 days who are not a transplant candidate with a life expectancy of less than 2 years with all the following conditions.
  - failure to respond to optimal medical management for at least 60 of the last 90 days
  - Left Ventricular Ejection Fraction <25%
  - Demonstrated functional limitation with a peak oxygen consumption of <12 ml/kg/min OR continued need for IV inotropic therapy
  - Appropriate body size (≥1.5m²) to support VAD implantation
History\textsuperscript{4,5}

- 1963: D. Liotta (Houston) create the first left ventricular assist device (LVAD)
- 1966: DeBakey and Liotta achieved first successful implantation of a LVAD

Fig. 1. (A) DeBakey. (B) The first patient to survive after postcardiotomy support.
History$^{4,5}$

- 1969: Cooley and Liotta used the first total artificial heart (TAH) for a bridge to cardiac transplant.
LVAD

- First Generation: Pulsatile Pumps

Westaby S. Surg Clin N Am 2004

LVAD

- 2nd Generation: Axial Flow
LVAD

- 3rd Generation: Magnetic suspension mechanisms
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


- Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH)
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• Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH)

• May 1998-July 2001

• 20 Cardiac Transplant Centers

• Randomly assigned 129 pts with end-stage heart failure who were not candidates for transplant to:
  • LVAD-Heartmate VE (68)
  • Optimal Medical Management (61)
REMATCH²

- 48% reduction in the risk of death in LVAD vs. OMM from any cause (p=.001)
- Kaplan-Meier estimates of survival at 1 year 52% LVAD vs. 25% OMM (p=.002)
- Est. Survival at 2 years 23% LVAD vs. 8% OMM (p=.09)
- Median Survival 408 days LVAD vs. 150 days OMM
## REMATCH²

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Medical-Therapy Group</th>
<th>LVAD Group</th>
<th>Total</th>
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<tr>
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<td>no. of patients</td>
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<tr>
<td>Sepsis</td>
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<tr>
<td>Miscellaneous noncardiovascular causes</td>
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Destination Therapy

- FDA approved the Heartmate VE for Destination Therapy in November 2002 for Class IV HF patients.
Destination Therapy

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- Reimbursement for LVAD as Destination therapy by Medicare/Medicaid in October 2003
Why not class III?
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. Kfoury, 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

Circulation 2007;116;497-505


- “Patients...who are referred for DT before major complications of heart failure develop have the best chance of achieving an excellent 1-year survival with LVAD therapy”
Why not class III?
Why not class III?

- Current perception of current mechanical circulatory support.
- REMATCH shows only 52% survival at 1 year, 23% at 2 years
Why not class III?

- Current perception of current mechanical circulatory support.
- REMATCH shows only 52% survival at 1 year, 23% at 2 years
- Concern over device failure and complications (infection)
Reported initial experience with the HeartMate II (axial-flow pump).
Initial Clinical Experience with the HeartMate® II Axial-Flow Left Ventricular Assist Device

- Reported initial experience with the HeartMate II (axial-flow pump).
- 43 pts. underwent implantation of HeartMate II.
- 9/43 pts. died during the trial.
- 34 pts d/c’d home without major complications (mean hospital stay 36 days, range 14-106 days).
- 3 pts had subsequent transplant (175, 187, and 641 days)
- The 1st pt had to have the LVAD removed 2nd to infection at 749 days.
- 27 pts have ongoing support (longest duration >700 days)
Durability

Mechanical Reliability of the Jarvik 2000 Heart

Michael P. Siegenthaler, MD, O. H. Frazier, MD, Friedhelm Beyersdorf, MD, Jürgen Martin, MD, Hillel Laks, MD, John Elefteriades, MD, Asghar Khaghani, MD, Ulf Kjellman, MD, Bansi Koul, MD, John Pepper, MD, Robert Jarvik, MD, and Stephen Westaby, MD


• Retrospective study on 102 pts. between 2000 and 2004 with Jarvik 2000 (axial flow pump) implanted.

• 83 as bridge to transplant

• 19 as destination therapy

• Studied the mechanical reliability of the Jarvik 2000
Durability

- No failures of the internal components
  - Longest survivor remains on support for almost 5 years.
- 18 devices were removed
  - Sent back to manufacturing site
  - Benchtop-tested (mean 2.8 years)
  - No mechanical failures
Durability

- Case report of 5 pts. with greater than 4 years with destination therapy.
- These patients spent over 90% of the time at home.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Sex</th>
<th>Age</th>
<th>Type of surgery</th>
<th>Device</th>
<th>Reason for long-term support</th>
<th>Current status</th>
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<td>Urgent</td>
<td>Novacor</td>
<td>Own wishes</td>
<td>Alive</td>
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<td>Emergency</td>
<td>Novacor</td>
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<tr>
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<td>EXCOR</td>
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<tr>
<td>5</td>
<td>ICMP</td>
<td>Male</td>
<td>68</td>
<td>Rescue</td>
<td>EXCOR</td>
<td>Age</td>
<td>Alive</td>
</tr>
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All patients on inotropic support prior to LVAD implantation.
DCMP—dilative cardiomyopathy, ICMP—ischaemic cardiomyopathy.
The Jarvik 2000 is associated with less infections than the HeartMate left ventricular assist device

M.P. Siegenthaler*, J. Martin, K. Pernice, T. Doenst, S. Sorg, G. Trummer, O. Friesewinkel, F. Beyersdorf

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• Retrospective study from 2000-2002 comparing HeartMate (pneumatic) vs. Jarvik 2000.

• Jarvik 2000: 1/6 (16%) pts had an infection
  • after 270 days of LVAD support
  • infection resolved with IV Abx

• HeartMate: 7/11 (64%) pts had an infection
First experiences with a novel magnetically suspended axial flow left ventricular assist device

Roland Hetzer*, Yuguow Weng, Evgenij V. Potapov, Miralem Pasic, Thorsten Drews, Michael Jurmann, Ewald Hennig, Johannes Müller


- 24 pts. had and Incor LVAD (axial flow with magnetic suspension ) from 2002-2003.

- Cumulative time on the device 6.9 years
  - Longest time on LVAD 12.6 month

- No reported infections.
Successful Experience in Bridging Patients to Heart Transplantation With the MicroMed DeBakey Ventricular Assist Device
Ettore Vitali, MD, Marco Lanfranconi, MD, Elena Ribera, MD, Giuseppe Bruschi, MD, Tiziano Colombo, MD, Maria Frigerio, MD, and Claudio Russo, MD
Ann Thorac Surg 2003;75:1200–4

- DeBakey LVAD (axial flow) was given to 11 pts from 2000 to 2001.
- Used as bridge to transplant
- Mean duration of LVAD therapy was 51 days
- No reported infections
Infection

- Results of these trials show that while infection is still a major problem, they are far lower than the REMATCH trail would suggest.

- Use of appropriate antibiotic therapy is needed as well as aggressive diagnosis and treatment of infections.

- Further trials with newer devices are needed.
Quality of Life

“patient(s) with NYHA class III HF takes several minutes to recover from tying their shoelaces. Furthermore, many patients classified as being in NYHA class IV are house-bound and do not wear shoes because of swollen feet and ankles. There are no ethical dilemmas surrounding destination therapy—the target population has short wretched lives.”
Quality of Life

- Survey of 102 pts
  - Mean age 58
  - Mean LVEF 21%
  - Median HF duration 5 years
  - 37% NYHA class III

- Of pts with life expectancy <1 year
  - 50% would consider LVAD

- Of pts who could not walk 1 block
  - 40%+ would consider LVAD

- Conclusions:
  - “one block or one year”
99 patients with HF took quality of life surveys:

• “Minnesota living with heart failure”
• “Dyspnea scale”
• Length vs. Quality
Quality of Life

• HF patients express meaningful preferences about quality vs. length of life.

• Higher dyspnea scores
• Worse HF scores
  • Preference for quality of life vs. length of life

Conclusion

• Newer LVAD technology has greater mechanical durability

• There are fewer infections today than during the REMATCH trial

• Quality of Life is better with DT.

• Patients can determine if they want longer life, or better quality of life.
References


4) http://echo.gmu.edu/bionics/exhibits.htm


6) Hoshi, H., Shinshi T., et al. Third-generation blood pumps with mechanical noncontact magnetic bearings. Artif Organs 2006;30(5);324-338.


11) Potapov E.V., Jurmann M. J., et al. Patients supported for over 4 years with left ventricular assist devices [case report]. European Journal of Heart Failure 2006;8;756-759.

