LVAD Destination Therapy
Now and the Future
Adel Abdulkader Tash
Prince Sultan Cardiac Centre
Its estimated that 500,000 patients in the USA are currently in the terminal phase of end stage heart failure and are refractory to maximized medical therapy (AHA Heart disease and stroke statistics 2007)

- Dismal prognosis (6% one year survival)
- Heart transplant
  - Donor heart shortage
  - Non transplant candidates
Permanant Implantation of LVAD as destination therapy could be a good alternative
• Feasibility trials were conducted for different device therapies in Europe and the US over the last 15 years.
• For these group of patients in refractory heart failure LVAD destination therapy has been proven to have better survival results then medical therapy
Clinical Trials of DT

- REMATCH
- INTrEPIID
- CUBS

INTERMACS registry
REMATCH

- Landmark trial in the history of clinical trials of heart failure
- 900 patients screened
- Randomized 129 patients with end stage heart failure ineligible for HT to either implantation of Heartmate XVE or optimal medical therapy
- 20 experienced transplant centres in the US
- OMT for at least 60 of the the last 90 days
- Thought to have a life expectancy of <2 years
REMATCH

- Entry criteria
  NYHA IV
  EF <25%
  peak O2 consumption < 12 ml/kg/min OR dependance on IV inotropes
REMATCH

- Use of LVAD improved functional class from IV—II
- 1 and 2 year survival on LVAD 52% and 23%
- 1 and 2 year survival on OMT 25% and 8%
  \[ p=0.009 \]

Median survival 408 days in the LVAD group and 150 in the OMT group

At the time of the final analysis there were 41 deaths out of 68 and the main cause was sepsis (41%) and device failure (17%)
LVAD Destination Therapy
• Majority of patients in REMATCH were on inotropic support, IABP support or both
• Randomizing “Titanic patients to a life boat or the sea”
• Apart from the primary outcomes, some of the outcomes were disappointing
  only 50% survived for 1 year
  QOL was not greatly improved on Minnesota scale
  many experienced chronic infections or neurological events, 10 of 68 LVADs were replaced, 2 patients had a
  3rd LVAD, long hospital stays for many.
REMATCH

- We have to keep in mind that this landmark trial was 10 years ago and the devices used were first generation LVADS with pulsatile flow. Now 2nd and 3rd generation devices are being used with evidence of better performance and longer durability.
INTrEPI

- Novacor LVAD for patients who were considered inotrope dependent in a prospective nonrandomized study
- 55 patients at 13 centers in the US and Canada
- Inclusion criteria
  - Adults, with inotrope dependent stage D heart failure, EF<25%, NYHA IV for the last 3 months before enrollment, non-transplant candidates
INTrEPI D

- Both groups had end organ hypoperfusion
- Survival at 6 months
  - LVAD 46%, OMT 22%

At 12 months
  - LVAD 27%, OMT 11%

Major cause of death in LVAD group
  - Stroke 34%, infection 24%

62% of patients in LVAD group developed a stroke especially in the 1st month of implant
INTrEPIID

- 85% of patients had no or minimal heart failure symptoms at the last assessment
- The survival rate was less in this study compared to REMATCH
- Device failure was lower in this study compared to REMATCH
CUBS Trial

• 1st European nonrandomized single arm observational study that evaluated the safety and performance of the Lion Heart 2000
• Fully implantable powered by transcutaneous energy transfer avoiding the external drive line which is a common source of infection
• 33 patients at 10 European centers and 1 US center
• All patients were NYHA IV and ineligible for HT
• The 1 and 2 year survival was 39% and 22%
• Inferior to the REMATCH but some of the enrolled candidates were high risk with end organ damage who would otherwise not have been enrolled in the REMATCH trial
Transition from clinical trials to broad clinical use

- 1st step is to assure that DT implants were performed safely
- SEPSIS and DEVICE FAILURE
- Difference between HM XVE and HM II
- Driveline immobilization
- Antibiotic prophylaxis
- ISHLT set clinical standards for the newly accredited DT programs
3rd INTERMACS Annual Report

- The Interagency for Mechanically Assisted Circulatory Support (INTERMACS)
- Prospective data and patient enrollment started June 23, 2006—September 2010
- The 1st continuous-flow axial pump HM II was approved for DT Jan 2010
- 2868 patients received implantation
- 79 centers in US of which 69 were designated as DT centers by CMS
**INTERMACS**

**intermacs**: June 2006 – June 2010

**Adult Primary LVAD Enrollment:** n=2325

<table>
<thead>
<tr>
<th>Year</th>
<th>Continuous Flow Intracorporeal Pump</th>
<th>Pulsatile Intracorporeal Pump</th>
<th>Pulsatile Paracorporeal Pump</th>
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<tbody>
<tr>
<td>2006 Jul-Dec</td>
<td>1</td>
<td>121</td>
<td>71</td>
</tr>
<tr>
<td>2007 Jan-Jun</td>
<td>0</td>
<td>0</td>
<td>103</td>
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<tr>
<td>2007 Jul-Dec</td>
<td>0</td>
<td>0</td>
<td>109</td>
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<tr>
<td>2008 Jan-Jun</td>
<td>103</td>
<td>44</td>
<td>44</td>
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<tr>
<td>2008 Jul-Dec</td>
<td>326</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>2009 Jan-Jun</td>
<td>392</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>2009 Jul-Dec</td>
<td>320</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2010 Jan-Jun</td>
<td>614</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

**Implants per 6 months**

- **Cont Intra Pump**: 1, 0, 0, 103, 326, 392, 320, 614
- **Puls Intra Pump**: 71, 121, 68, 109, 44, 23, 13, 3
- **Puls Para Pump**: 10, 10, 16, 17, 8, 10, 11, 5
INTERMACS

Device type Adult primary implant: INTERMACS Jun 2006 - Jun 2010
LVAD 2325 (87%)
BIVAD 277 (10%)
TAH 78 (3%)

The overall survival in the LVAD group was
3 months 89%, 6 months 85%, 12 months 79%, 24 months 66%
INTERMACS

- The transition from PFP to CFP was dramatic starting in 2008
- From Jan – June 2010 CFP 98% of adult primary LVAD implants
- CFP has provided a significant survival advantage to PFP
Overall Survival

INTERMACS: June 2006 – September 2010
Adult Primary LVADs: n=2506

Continuous Flow Pump, n=1936, deaths=272
Pulsatile Flow Pump, n=570, deaths=177

By Pump Type

% Survival

<table>
<thead>
<tr>
<th>Month</th>
<th>CFP</th>
<th>PFP</th>
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<tbody>
<tr>
<td>3 mo</td>
<td>91%</td>
<td>83%</td>
</tr>
<tr>
<td>6 mo</td>
<td>88%</td>
<td>76%</td>
</tr>
<tr>
<td>12 mo</td>
<td>83%</td>
<td>67%</td>
</tr>
<tr>
<td>24 mo</td>
<td>75%</td>
<td>45%</td>
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</tbody>
</table>

Event: Death (censored at transplant or explant recovery)

p < .0001

Months after Device Implant
INTERMACS

- Device strategy at the time of implant—many patients receiving the device before a final decision about transplant
- Strategy change in the last 5 years toward DT
  - BTT 1161 (43%)
  - BTC 1131 (42%)  DT 309 (11%)
  - likely 759 (28%)
  - moderate 280 (10%)
  - unlikely 92 (3.4%)
INTERMACS

- DT increased from
  jun 2006—dec 2008  96 (8.4%)
  Jan 2009– jun 2010 213 (13.8%)
Long Term Left Ventricular Assist Device as Bridge to Heart Transplantation: De Facto Destination Therapy in Many?

Nir Uriel, Sang-Woo Pak, Mauer Biscotti, Bartlomiej Kachnjarz, Paolo C. Colombo, Daniel Sims, Hiroo Takayama, Yoshifumi Naka, Donna Mancini and Ulrich P. Jorde
Medicine, Columbia University, New York, NY
Surgery, Columbia University, New York, NY

(Journal of Cardiac Failure vol 16 No.8S August 2010)
• Retrospective chart review off all patients receiving LVAD BTT 10 years, single center
• 224 LVAD implants, 166 (74%) were transplanted, 25 (11%) are still listed, 33 (15%) were delisted due to mortality or advanced morbidity
• There is a 30 day grace period where the patient is upgraded to UNOS 1A then goes to 1B status
• So many LVAD BTT patients are unlikely to be transplanted (only 44 patients were transplanted as a 1B status)
Also noticed was the gradual change in the severity of illness of the patients --- the proportion of patients in critical cardiogenic shock has decreased from 35% to 17%
### INTERMACS profiles

<table>
<thead>
<tr>
<th>level</th>
<th>Jun 06—dec 08</th>
<th>Jan 09—jun 10</th>
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<tbody>
<tr>
<td>1. Cardiogenic shock</td>
<td>395 (34.7%)</td>
<td>267 (17.3%)</td>
</tr>
<tr>
<td>2. Progressive decline</td>
<td>457 (40.2%)</td>
<td>697 (45.2%)</td>
</tr>
<tr>
<td>3. Stable but inotrope dependent</td>
<td>148 (13%)</td>
<td>300 (19.5%)</td>
</tr>
<tr>
<td>4. Recurrent advanced HF</td>
<td>96 (8.4%)</td>
<td>178 (11.5%)</td>
</tr>
<tr>
<td>5. Exertion intolerant</td>
<td>15 (1.3%)</td>
<td>51 (3.3%)</td>
</tr>
<tr>
<td>6. Exertion limited</td>
<td>11 (1%)</td>
<td>32 (2.1%)</td>
</tr>
<tr>
<td>7. Advanced NYHA III</td>
<td>16 (1.4%)</td>
<td>17 (1.1%)</td>
</tr>
<tr>
<td>total</td>
<td>1138 (100%)</td>
<td>1542 (100%)</td>
</tr>
</tbody>
</table>
INTERMACS

Intermacs: June 2006 – June 2010
Adult Primary LVAD Enrollment, Destination Therapy: n=298

- Pulsatile Intracorporeal Pump
- Continuous Flow Intracorporeal Pump

<table>
<thead>
<tr>
<th>Year</th>
<th>Cont Intra Pump</th>
<th>Puls Intra Pump</th>
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<tbody>
<tr>
<td>2006 Jul-Dec</td>
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<td>15</td>
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<tr>
<td>2007 Jan-Jun</td>
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<td>21</td>
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<tr>
<td>2007 Jul-Dec</td>
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<tr>
<td>2008 Jan-Jun</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>2008 Jul-Dec</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>2009 Jan-Jun</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>2009 Jul-Dec</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>2010 Jan-Jun</td>
<td>176</td>
<td>0</td>
</tr>
</tbody>
</table>
INTERMACS

- The most common contraindication of HT was advanced age followed by renal dysfunction and a high BMI.
- 50% of the contraindications were considered “modifiable” leaving the possibility open for eventual HT.
INTERMACS

- The overall survival for DT LVAD is 67% 1 year and 46% 2 years,
INTERMACS

- The conversion from PFP to CFP the 1 year survival improved from 61% to 74%
INTERMACS

- Of 385 primary DT patients, 13 received a temporary RVAD for unexpected RV failure at the time of LVAD implant---→ for these patients the outcome was poor
- By multivariate analysis only higher RA pressure was identified as a possible risk factor for the need for RVAD support
INTERMACS

- Risk factors for death in DT patients
  - Older age
  - Critical cardiogenic shock
  - Diabetes
  - PHT
  - Higher BUN
  - Lower sodium
  - Concomitant surgery
  - BiVAD, and PFP
Better Patient Selection
Better Device technology
Are the key points for a successful DT LVAD implant
Better Technology

- PFP have significant disadvantages → large pump size that requires extensive surgical dissection, and the requirement of a large body habitus and the presence of a large percutaneous lead for venting of air and audible pump operation.
- REMATCH had a rate of these device failures and 65% of patients alive at 2 years needed a device change.
- 2nd and 3rd Generation CFP
Development of CFP

1st Generation: Pulsatile, Volume Displacement Devices
- HeartMate XVE
- Thoratec IVAD
- Thoratec pIVAD
- Novacor

2nd Generation: Continuous-flow Rotary Devices
- Contact Bearing Design
- Axial Blood Flow Path
- HeartMate II
- DeBakey
- Jarvik Flowmaker

3rd Generation: Continuous-flow Rotary Devices
- Non-contact Bearing Design
- Centrifugal Blood Flow Path
- Axial Blood Flow Path
  - Magnetic Levitation
  - Direct-drive Motor System
  - Incor

- Hydrodynamic Levitation
- Bearingless Motor Drive System
- VentrAssist

- Magnetic Levitation
- External Motor Drive System
- DuraHeart®
- HeartMate III
- HVAD (HeartWare)®
2\textsuperscript{nd} generation $\rightarrow$ CFP with an axial flow which have an internal rotor within the blood flow path that is suspended by the contact bearings.
• 3rd generation CFP → with an impelllar or rotor suspended in the blood flow path using a “noncontact” bearing design
• Utilizing a centrifugal blood flow path and incorporates either magnetic and/or hydrodynamic levitation of the internal impeller
3rd Generation

- Levitation systems utilized in the 3rd generation rotary pumps suspend the moving impeller within the blood field without any mechanical contact.
- Reducing wear and tear
- Reducing heat generation
- Achieved through magnetic or hydrodynamic bearing design
- “Washing” of the impeller → less thromboembolic complications
3rd Generation

- Centrifugal design → more sensitive pressure flow relationship than axial design
- This greater sensitivity increases the margin of safety from creating suction events and improves pump flow during LA return “exercise response”
VentrAssist

- Centrifugal noncontact bearing device
- Wt 298 gm 60 mm diam
- Hydrodynamic levitation
DuraHeart

- CFRP, noncontact bearing centrifugal design
- Wt 540 gm displacement volume of 180 cm³
- Active magnetic levitation
Levacor

- CFRP with centrifugal and noncontact bearing design
- Wt 440 gm
- Both passive and active magnetic levitation design
Incor

- CFRP with axial design
- Magnetic levitation using a direct drive mechanism
- Wt 200 gm volume displacement of 80 ml
HVAD

- Small CFRP with centrifugal and noncontact bearing design, Magnetic and hydrodynamic levitation
- Displacement volume 45 ml Wt 145 gm with a flow capacity of 10 L/min
- Completely in pericardial cavity with out the need for pocket formation
HVAD

- Wide blade impeller
- Better hemocompatibility
- Impeller suspension by both passive magnetic and hydrodynamic bearing systems
• 3rd generation CFP with noncontact bearing design offer the potential of enhanced durability and safety
• Early clinical experience demonstrate efficacy with regard to hemodynamic support
• Further clinical evaluation will be needed to determine if the improved hydrodynamic properties of centrifugal pumps and potential enhanced durability of a noncontact bearing design are associated with improvements in patient outcomes
Better patient selection

- Procedural risk of LVAD therapy\(\rightarrow\) stable HF patients with life expectancy\(>2\) years should not be offered
- Patients who have progressed to secondary organ dysfunction may have missed the optimal treatment window
- The current guidelines for patient selection for DT are very broad
- In all the clinical trials of DT the operative mortality has been strikingly high exceeding that for patients BTT
• Death usually occurred with a functioning device and were due to consequences of operative complications
• Two thirds of the deaths in the post-REMATCH era occurred before discharge (76 of 120)
Worsening of nutritional state, end-organ and right ventricular function with progressive heart failure
Risk prediction models

- DT risk score Leitz Miller (LM)
- The Seattle Heart Failure Model SHFM
- INTERMACS levels for HF
- Columbia score
- APACHE II
Evaluation of Risk Indices in Continuous-Flow Left Ventricular Assist Device Patients

Justin M. Schaffer MS\textsuperscript{a}, Jeremiah G. Allen MD\textsuperscript{a}, Eric S. Weiss MD, MPH\textsuperscript{a}, Nishant D. Patel MD\textsuperscript{a}, Stuart D. Russell MD\textsuperscript{b}, Ashish S. Shah MD\textsuperscript{a} and John V. Conte MD\textsuperscript{a}.

Conclusions

Among the LM, COL, APACHE II, INTERMACS, and SHFM scores, the best predictor of mortality in a single institutional cohort of continuous-flow LVAD patients was the SHFM score.

## Survival Statistics

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>80%</td>
<td>94%</td>
</tr>
<tr>
<td>2 year</td>
<td>64%</td>
<td>89%</td>
</tr>
<tr>
<td>5 year</td>
<td>33%</td>
<td>75%</td>
</tr>
<tr>
<td>Mortality</td>
<td>20%</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>36%</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>67%</td>
<td>25%</td>
</tr>
<tr>
<td>Mean life expectancy</td>
<td>4.1 years</td>
<td>9.7 years</td>
</tr>
</tbody>
</table>

## Baseline Characteristics

### Clinical
- **Age**: 65
- **Gender**: Male
- **NYHA Class**: 3
- **Weight (kg)**: 80
- **EF**: 20
- **Syst BP**: 120

### Medications
- **ACE-I**
- **Beta-blocker**
- **ARB**
- **Statin**
- **Allopurinol**
- **Aldosterone blocker**

### Diuretics
- **Lasix**
- **Bumex**
- **Demadex**
- **Metolazone**
- **HCTZ**

### Lab Data
- **Hgb**: 13.4
- **Lymphocytes**: 24
- **Uric Acid**: 7
- **Total Chol**: 190
- **Sodium**: 137

### Devices
- **None**
- **BiV Pacer**
- **ICD**
- **BiV ICD**
- **QRS >120 msec**

### Interventions
- **ACE-I**
- **Beta-blocker**
- **Statin**
- **Aldosterone Blocker**

Copyright 2004–2005 Wayne Levy & David Linker
Clinical outcomes for CF LVAD stratified by pre op INTERMACS classification

<table>
<thead>
<tr>
<th>Profile 1</th>
<th>Critical cardiogenic shock</th>
<th>Life threatening hypotension, inotropic support, organ hypoperfusion, acidosis, lactate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profile 2</td>
<td>Progressive decline</td>
<td>Decline, inotropes, worsening RF, nutritional, inability to restore volume balance</td>
</tr>
<tr>
<td>Profile 3</td>
<td>Stable but inotrope dependent</td>
<td>Stable on inotropes</td>
</tr>
<tr>
<td>Profile 4</td>
<td>Resting symptoms</td>
<td>Daily sym of congestion at rest or during activities of daily living ADL</td>
</tr>
<tr>
<td>Profile 5</td>
<td>Exertion intolerant</td>
<td>Comfortable at rest or ADL unable to engage with other activities</td>
</tr>
<tr>
<td>Profile 6</td>
<td>Exertion limited</td>
<td>No overload, comfortable with minor activity</td>
</tr>
<tr>
<td>Profile 7</td>
<td>Advanced NYHA III</td>
<td>Comfortable with meaningful activity, limited to mild physical activity</td>
</tr>
</tbody>
</table>
• 101 patients with BTT and DT LVAD
• 3 groups ➔ group 1 “profile 1”
  group 2 “profile 2 and 3”
  group 3 “profiles 4-7”
Survival to discharge post LVAD

Series 1

- Group 1
- Group 2
- Category 3

Series 1
INTERMACS classification is a useful metric for risk stratifying candidates for MCS. Less acutely ill but functionally impaired HF patients receiving CF LVADs had longer short and long term survival and shorter lengths of stay compared with patients who were more acutely ill.

(Andrew J. Boyle et al. the Journal of Heart and Lung Transplantation 2011)
DT Therapy Future Frontiers

- Thromboembolism and bleeding
- Biocompatible surfaces or coatings
- The use of endothelial progenitor cells and seeding the LVAD materials
- Infections ➔ transcutaneous energy transmission to avoid the drive line
- Reverse ventricular remodelling and recovery of ventricular function
Thank you