LVAD and Destination Therapy vs Transplantation: Optimal Strategy?
Objectives:

Discuss the history of heart transplantation and mechanical circulatory support devices from the balloon pump to the first artificial hearts and destination VADs.

Describe the benefits and risks of today’s current technology and options in successful treatment of advanced heart therapy.

Describe the clinical status of devices, transplantation and probe the future of cardiac recovery.
ACC/AHA Stages:

A
Risk

B
Asx
Structural dx

C
Sx ever

D = IV sx
Refractory to
Optimal Med Rx

NYHA Symptom Class:
Back and forth

NYHA I

NYHA IV

INTERMACS Profiles

7 6 5 4 3 2 1

INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support
**Stage D CHF**

Screen for *Heart Transplant*
Exclude significant co-morbidities

- No
- Yes → List

Screen for Destination *LVAD*

- No
- Yes → Approved Device
  - Device Trials

Investigational Drug Trials
Chronic Infusion Therapy
Hospice
Population Estimate of Potential LVAD/Tx Patients

300 Million US Population

45-50% Preserved Systolic Function 3.0-3.5 M

HF = 2.6% Population* or 7 Million Total

35% Class I
35% Class II
25% Class III (5-10% IIIB)
2-5% Class IV

50-55% Systolic HF 3.0-3.5 Million

Class III B 100-150,000
Class IV 75-150,000

Theoretical Candidates for Mech Circ Support

Class IIIB+IV < 75 yrs 150-250,000 Pts

This represents approximate number of potential VAD candidates.
I have Heart Failure!

But now I have a VAD!
Never let the facts get in the way of a good story
THE PAST.
Conceptual eras of mechanical circulatory support..

1812 Le Gallois “parts of the body may be preserved by external perfusion”

Etienne-Jules Marey (Paris, 1881) – physician, inventor

.. the 1st “artificial heart

Guillotined head of a dog in perfusion experiments of Brukhonenko and Tchetchuline. This preparation relied on gas exchange from a second donor dog’s lungs. Diaphragm-like pumps pumped blood into the recipient dog’s carotid arteries. Dog heads perfused in this manner remained functional for a few hours. (Reprinted from Brukhonenko S, Tchetchuline S. Experiences avec la tete isolee du chien. 1. Technique et conditions des experiences. J Physiol Pathol Gen 1929;27:42)

.. a “biological oxygenator”
Intellectual origins of “mechanical assist” and “circulatory support”...

“Experimentally, it is possible to completely replace the heart with an artificial heart, and animals have been known to survive as long as 36 hours. This idea, I am sure, could be reached to full fruition if we had more funds to support more work, particularly in the bioengineering area.”
DeBakey (1963) Senator Lister Hill’s Subcommittee on Health

In Jan of 1964 James Hardy consented the sister of Boyd Rush – a 68 yo comatose deaf mute with ischemic heart failure and lower extremity gangrene – for “the insertion of a suitable heart transplant if such should be available. Rush decompensated and was placed on cardiopulmonary bypass. In the absence of a viable donor Hardy transplanted the heart of a 45 kg chimpanzee. The heart provided hemodynamic support for 90 minutes...

“...surgeons at Baylor hailed the Jackson transplant. The Baylor surgeons say there are two solutions for support of the failing heart...transplants from humans or animals and artificial hearts. The Baylor group is concentrating its efforts on developing an artificial heart.”
Associated Press, 25 Jan 1964
Shumway-Pioneer of Heart Transplantation

- Major experimental advances
- Autotransplants
- Developed atrial cuff technique
- 1960: 5 out of 8 dogs lived for 6-21 days
- 1965 Longer survival with 6MP, Steroids, AZA
- CAV

Norman Shumway
Heart Transplantation

- December 2, 1967
- **Donor:** Denise Davall (24 year-old female MVA)
- **Recipient:** Louis Washkansky (53 year-old male with ischemic cardiomyopathy)
- Azathioprine, Steroids, Local radiation
- **POD#9** Rejection
- **POD#18** Death (Pneumonia)
Barnard did prove that heart transplants are possible- he also became world-famous and started dating movie stars. The recipient of the heart, on the other hand, died within three weeks. And for years, heart transplants suffered from casualty rates that would have appalled a Civil War surgeon: Of the first 175 recipients, 152 were dead within three years.
# Heart Transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Survival</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53</td>
<td>18 days</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>18 months</td>
<td>CAV</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>20 months</td>
<td>Gastric CA</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>64 days</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>5</td>
<td>37</td>
<td>12.5 years</td>
<td>CAV</td>
</tr>
</tbody>
</table>
Chemical Structure of Cyclosporin-A
NUMBER OF HEART TRANSPLANTS REPORTED BY YEAR

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.
Now, cardiac transplantation is epidemiologically trivial in heart failure management.
We are both the product and prisoners of our successes.

There Are Not Enough Donor Hearts
Indications and Contraindications for Heart Transplantation

Absolute indications in appropriate patients

- For hemodynamic compromise caused by HF
- Refractory cardiogenic shock
- Documented dependence on intravenous inotropic support to maintain adequate organ perfusion
- Peak $V^\prime O_2$ 10 mL kg$^{-1}$ min$^{-1}$ with achievement of anaerobic metabolism
- Severe symptoms of ischemia that consistently limit routine activity and are not amenable to coronary artery bypass surgery or percutaneous coronary intervention
- Recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities

Relative indications

- Peak $V^\prime O_2$ 11 to 14 mL kg$^{-1}$ min$^{-1}$ (or 55% predicted) and major limitation of the patient’s daily activities
- Recurrent unstable ischemia not amenable to other intervention
- Recurrent instability of fluid balance/renal
- Insufficient indications

Low left ventricular ejection fraction
- History of functional class III or IV symptoms of HF
- Peak $V^\prime O_2$ 15 mL kg$^{-1}$ min$^{-1}$ (and 55% predicted) without other indications

Relative contraindications

- Age _72 y
- Severe peripheral vascular or cerebrovascular disease
- Diabetes mellitus with end-organ damage
- Severe lung, liver, or renal disease
- Uncorrected abdominal aortic aneurysm (_4–6 cm)
- Systemic infection (HIV, hepatitis B, Hepatitis C)
- Psychosocial impairment

Absolute contraindications

- Systemic illness that will limit survival despite heart transplantation
- HIV/AIDS (definition: CD4 count _200 cells/mm$^3$)
- Neoplasm other than skin or low-grade prostate cancer that has not been cured or is not in remission
- Systemic lupus erythematosus or sarcoid with multisystem involvement
- Fixed pulmonary hypertension
- Pulmonary vascular resistance _6 Wood units
- Transpulmonary gradient _15 mm Hg
LVADs Address Significant Unmet Needs for Stage Four Patients

Transplantation - Constrained Supply of Donor Hearts

- Current U.S. heart transplant wait list at ~10,000 patients; ~2500 hearts available for transplantation per year

U.S. Heart Transplants

Rapid Growth in VAD Acceptance and Utilization

Chronic VADs – Worldwide Implants

Thoratec Estimates

<table>
<thead>
<tr>
<th>Year</th>
<th>U.S. Heart Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>~2,000</td>
</tr>
<tr>
<td>2010</td>
<td>~4,000</td>
</tr>
<tr>
<td>2015</td>
<td>Approaching 10,000</td>
</tr>
</tbody>
</table>

US Market Opportunity - Chronic VADs

Eligible for Chronic VADs

NYHA Class IV

CHF

5.8m patients
670k new cases annually

1 American Heart Association Heart Disease and Stroke Statistics, 2010 Update; AHA website
2 Organ Procurement and Transplantation Network, www.optn.org
3 NIH Estimate
VAD Program Circa 1998

Cardiologist

Not a candidate!

Surgeon
Evolution of implantable mechanical cardiac assist technologies....

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

Continuous-flow Rotary Devices

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
  - Magnetic Levitation
  - Axial Blood Flow Path
  - InCor

Centrifugal Blood Flow Path
- Magnetic Levitation
- External Motor Drive System
- DuraHeart
- Levacor
- HeartMate III
- HVAD (HeartWare)

Axial Blood Flow Path
- Magnetic Levitation
- Bearingless Motor Drive System
- VentrAssist

Hydrodynamic Levitation
- Bearingless Motor Drive System

II

Flow diagram:
- Outflow Stator
- Outflow Bearing
- Rotor
- Inflow Stator
- Inflow Bearings

III

A
- Magnetic coupling
- Rotor and permanent magnet
- Levitation coil
- Drive coil
Heartware (impellar)

Left ventricular assist vs. biventricular replacement...

Durable vs non-durable applications

Heartmate II (axial flow)

Syncardia TAH

AbioCor TAH
Study Outcomes

- 90% of patients were transplanted, recovered or had ongoing support at 6 months.
- Operative 30-day survival was 96%.
- Survival was superior to that which has been previously reported with LVAD usage.
HeartMate II BTT

### Baseline INTERMACS Profiles

<table>
<thead>
<tr>
<th>INTERMACS Profile</th>
<th>HeartMate II (n=169)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>41 (24%)</td>
</tr>
<tr>
<td>2</td>
<td>63 (37%)</td>
</tr>
<tr>
<td>3</td>
<td>33 (20%)</td>
</tr>
<tr>
<td>4</td>
<td>21 (12%)</td>
</tr>
<tr>
<td>5-7</td>
<td>11 (7%)</td>
</tr>
</tbody>
</table>

61% of patients in the study were in profile 1 or 2.

<table>
<thead>
<tr>
<th>Profile</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Critical cardiogenic shock</td>
</tr>
<tr>
<td>2</td>
<td>Progressive decline</td>
</tr>
<tr>
<td>3</td>
<td>Stable, but inotrope dependant</td>
</tr>
<tr>
<td>4</td>
<td>Recurrent advanced heart failure</td>
</tr>
<tr>
<td>5</td>
<td>Exertion tolerant</td>
</tr>
<tr>
<td>6</td>
<td>Exertion limited</td>
</tr>
<tr>
<td>7</td>
<td>Advanced NYHA III</td>
</tr>
</tbody>
</table>
Functional Status

% NYHA Class I or II

- p<0.001 over time
- Both treatments

6 Minute Walk Distance

- p<0.001 over time
- Both treatments

n= 126; 55
n= 50; 19

CF LVAD
PF LVAD

NEJM 2009;361(23):2241-51
"Every new day is the best day of my life," says Ally (at her fitting May 17). Right: her battery pack. Below: the "phantom limb" pump.

Ally Smith sees herself in her taffeta gown, staring back in the mirror—and tears up. "I thought," she says, "this was never going to happen."

Just last year Ally, 22, was planning her future: A strep throat had led to a broader infection that left the Richmond, Texas, student in advanced heart failure. In an eight-hour surgery, doctors implanted a revolutionary new version of a lifesaving heart pump. Miniaturized with a lightweight and extra-long-lasting battery pack, it has helped some 4,000 patients like Ally resume their lives; otherwise she might be dead. Now she has a great life.

THE BIONIC BRIDE

Thanks to a powerful new heart pump, Ally Smith has a second lease on life—and big plans for her wedding day.

By Alicia Dennis and Daria Atlas

Photographs by Matthew Harnon
ARE WE THERE YET?
ROADMAP Patient Population

<table>
<thead>
<tr>
<th>NYHA Class III</th>
<th>Class IV (Ambulatory)</th>
<th>Class IV (On Inotropes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS Profiles</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Percent of current implants in INTERMACS¹</td>
<td>1.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Currently Not Approved</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDA Approval: Class III/IV</td>
<td>Limited Adoption</td>
<td>Growing Acceptance</td>
</tr>
</tbody>
</table>

¹Kirklin et al J Heart Lung Transplant 2014; 33:555-64
Primary End-Point
Alive at 12 months on original therapy with increase in 6MWD by 75m

<table>
<thead>
<tr>
<th>End Point</th>
<th>LVAD (n=85)</th>
<th>OMM (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive at 12 months on original therapy with increase in 6MWD by 75m</td>
<td>33 (39%)</td>
<td>17 (21%)</td>
</tr>
<tr>
<td>Components that prevented success:</td>
<td>N=52 (61%)</td>
<td>N=64 (79%)</td>
</tr>
<tr>
<td>Death within 1 year</td>
<td>17 (20%)</td>
<td>17 (21%)</td>
</tr>
<tr>
<td>Delayed LVAD</td>
<td>NA</td>
<td>18 (22%)</td>
</tr>
<tr>
<td>Delta 6MWT&lt;75m</td>
<td>33 (39%)</td>
<td>29 (36%)</td>
</tr>
<tr>
<td>Urgent Tx</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

O.R. = 2.4 [1.2-4.8]; P=0.017

Excluded LVAD patients: 3 withdrawn, 8 missing 6MWD
Excluded OMM patients: 9 withdrawn, 13 missing 6MWD
Including 1 TAH
Intent-to-Treat Survival

H.R. = 0.98 [0.57 - 1.70] P = 0.946

Survival (%)

Remaining at risk:

<table>
<thead>
<tr>
<th>Intent</th>
<th>At 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVAD:</td>
<td>74 on LVAD</td>
</tr>
<tr>
<td></td>
<td>3 HTx</td>
</tr>
<tr>
<td>OMM:</td>
<td>59 on OMM</td>
</tr>
<tr>
<td></td>
<td>17 with delayed LVAD(^1)</td>
</tr>
</tbody>
</table>

\(^1\)TAH pt censored alive and withdrawn
Survival As-Treated on Original Therapy

LVAD 30 day mortality: 1%
LOS: 17 [13, 22] days

H.R. = 1.67 [1.04 - 2.66] P = 0.033

Remaining at risk:

<table>
<thead>
<tr>
<th>Time Post-Enrollment (Months)</th>
<th>LVAD Patients</th>
<th>OMM Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>97</td>
<td>103</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>77</td>
</tr>
<tr>
<td>4</td>
<td>74</td>
<td>59</td>
</tr>
</tbody>
</table>
## Risk-Benefit Analysis

### Primary End Point
Alive at 12 mo with
\( \Delta6\text{MWD} > 75\text{m} \)

### Survival
Intent-to-treat
As treated on original therapy

### NYHA Class, HRQoL, and Depression
Alive at 12 mo with
\( \Delta\text{NYHA} \geq 1 \text{ class} \)
\( \Delta\text{EQ-5D VAS} > 20 \text{ points} \)
\( \Delta\text{PHQ-9} \geq 5 \text{ points} \)

### Adverse Events
Composite

### Risk-Benefit Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ratio [LCI, UCI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>O.R</td>
<td>2.40 [1.2, 4.8]</td>
<td>0.017</td>
</tr>
<tr>
<td>H.R</td>
<td>0.98 [0.57, 1.70]</td>
<td>0.946</td>
</tr>
<tr>
<td>O.R</td>
<td>1.67 [1.04, 2.66]</td>
<td>0.033</td>
</tr>
<tr>
<td>O.R</td>
<td>8.8 [4.4, 17.5]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>O.R</td>
<td>4.1 [1.9, 8.9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>O.R</td>
<td>4.2 [1.7, 10.2]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R.R</td>
<td>0.44 [0.34, 0.55]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

1. In patients with baseline VAS < 68 (lowest 3 quartiles)
2. In patients with baseline PHQ-9 > 5 (mild or worse severity of depression)
Unexpected Abrupt Increase in Left Ventricular Assist Device Thrombosis

Randall C. Starling, M.D., M.P.H., Nader Moazami, M.D., Scott C. Silvestry, M.D.,
Gregory Ewald, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D.,
J. Eduardo Rame, M.D., Michael A. Acker, M.D., Eugene H. Blackstone, M.D.,
John Ehrlinger, Ph.D., Lucy Thuita, M.S., Maria M. Mountis, D.O.,
Edward G. Soltesz, M.D., M.P.H., Bruce W. Lytle, M.D.,
and Nicholas G. Smedira, M.D.
Problems?

Driveline  Thrombus  Transfusion
The data we need to truly compare the therapies does not exist.

Perhaps
Heart Transplant vs Left Ventricular Assist Device in Heart Transplant-Eligible Patients

Matthew L. Williams, MD, Jaimin R. Trivedi, MD, MPH, Kelly C. McCants, MD, Sumanth D. Prabhu, MD, Emma J. Birks, MD, Laurie Oliver, RN, and Mark S. Slaughter, MD

Division of Thoracic and Cardiovascular Surgery and Division of Cardiovascular Medicine, University of Louisville, and Jewish Hospital Transplant Center, Louisville, Kentucky

Table 3. Index Hospitalization and Rehospitalization Costs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>No.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index hospitalization cost, $</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BTT</td>
<td>196,707</td>
<td>37,858.62</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>HTx</td>
<td>127,978</td>
<td>44,117.61</td>
<td>13</td>
<td>0.0001</td>
</tr>
<tr>
<td>Presurgical hospital, days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BTT</td>
<td>10.6</td>
<td>10.06</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>HTx</td>
<td>3.9</td>
<td>13.25</td>
<td>13</td>
<td>0.07</td>
</tr>
<tr>
<td>Post index hospitalization cost, $</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BTT</td>
<td>33,302</td>
<td>70,098.41</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>HTx</td>
<td>38,437</td>
<td>48,268.28</td>
<td>13</td>
<td>0.81</td>
</tr>
</tbody>
</table>

![Survival Analysis Graph]

Survival Probability

- BTT
- HTx

Survival

- Type

P = 0.38

P = 0.2
Left Ventricular Assist Device Destination Therapy Versus Extended Criteria Cardiac Transplant
Mani A. Daneshmand, Keshava Rajagopal, Brian Lima, Nikta Khorram, Laura J. Blue, Andrew J. Lodge, Adrian F. Hernandez, Joseph G. Rogers and Carmelo A. Milano
Ann Thorac Surg 2010;89:1205-1210
DOI: 10.1016/j.athoracsur.2009.12.058

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>EC-AL (n = 93)</th>
<th>DT-LVAD (n = 60)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>74% (69/93)</td>
<td>78% (47/60)</td>
<td>0.6993</td>
</tr>
<tr>
<td>Age, years</td>
<td>65 (56, 68)</td>
<td>60 (52, 69)</td>
<td>0.742</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>25.7 (22.8, 29.8)</td>
<td>28.7 (26.0, 33.5)</td>
<td>0.0028</td>
</tr>
<tr>
<td>Serum creatinine, mg/dL</td>
<td>1.4 (1.1, 1.8)</td>
<td>1.6 (1.2, 2.0)</td>
<td>0.1202</td>
</tr>
<tr>
<td>Organ wait time, days</td>
<td>24.5 (10.5, 74.0)</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous inotropes</td>
<td>51% (47/93)</td>
<td>87% (52/60)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>22% (20/93)</td>
<td>30% (18/60)</td>
<td>0.2548</td>
</tr>
<tr>
<td>Oliguria</td>
<td>22% (20/93)</td>
<td>32% (19/60)</td>
<td>0.1854</td>
</tr>
<tr>
<td>Elevated CVP, &gt;16 mm Hg</td>
<td>23% (21/93)</td>
<td>42% (25/60)</td>
<td>0.0184</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>15% (14/93)</td>
<td>8% (5/60)</td>
<td>0.3158</td>
</tr>
<tr>
<td>Elevated PT, &gt;16 s</td>
<td>30% (28/93)</td>
<td>37% (22/60)</td>
<td>0.4805</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>61% (57/93)</td>
<td>40% (24/60)</td>
<td>0.0128</td>
</tr>
<tr>
<td>LVAD score</td>
<td>2 (1, 3)</td>
<td>3 (1, 4.5)</td>
<td>0.1283</td>
</tr>
</tbody>
</table>
Left Ventricular Assist Device Destination Therapy Versus Extended Criteria Cardiac Transplant

Mani A. Daneshmand, MD, Keshava Rajagopal, MD, PhD, Brian Lima, MD, Nikta Khorram, BS, Laura J. Blue, NP, Andrew J. Lodge, MD, Adrian F. Hernandez, MD, Joseph G. Rogers, MD, and Carmelo A. Milano, MD

Departments of Surgery and Medicine, Duke University Medical Center, Durham, North Carolina
In conclusion, patients offered DT-LVAD had more decompensated heart failure preoperatively. Despite this, perioperative (30-day) and short-term (1-year) survival are similar for DT-LVAD and EC-AL. Unlike EC-AL patients, DT-LVAD patients do not have to wait for organ availability; therefore, they avoid important “waiting list mortality.” Finally, although midterm (2 to 3 years) DT-LVAD survival is inferior to EC-AL survival, newer, more durable LVAD designs may provide superior survival for these patients. Moreover, even with the use of marginal donor organs, the overall pool of hearts is inadequate to address the population of end-stage heart failure. Therefore, from an epidemiologic perspective, improving DT-LVAD outcomes represents the greatest hope for addressing end-stage heart failure.
Comparison of functional status between patients with ventricular assist devices and patients after heart transplantation.

I D Laoutaris¹, S Adamopoulos¹, A Manginas¹, L Louca¹, MS Kallistratos¹, A Gkouziouta¹, V Vartela¹, A Dritsas¹, ¹Onassis Cardiac Surgery Center - Athens – Greece

Patients with VADs were matched for age, gender and BMI to HTx patients.

Fifteen patients with VAD:
LVAD [n=7]/ BiVAD [n=8], Berlin Heart (Bridged to HTx)
14 males, 1 female
Age 38.3±15.9 yrs,
BMI 23.6±4.2 kg/m2

Fourteen patients after OHTx
12 males, 2 females
Age 43±11 years
BMI=24±4.9 kg/m2

Exercise capacity was tested using cardiopulmonary exercise testing on a treadmill using the Dargie protocol and the 6-min walk-test (6MWT) at least 3 months post-surgery. Dyspnea was measured using the Borg scale at the end of the 6MWT.

EUROprevent 2011
Comparison of functional status between patients with ventricular assist devices and patients after heart transplantation

I D Laoutaris¹, S Adamopoulos¹, A Manginas¹, L Louca¹, MS Kallistratos¹, A Gkouziouta¹, V Vartela¹, A Dritsas¹, ¹Onassis Cardiac Surgery Center - Athens - Greece,

**Conclusions:** Patients after HTx present with a higher maximal exercise capacity and less dyspnea in comparison to patients with VADs. However, submaximal exercise capacity which may be more important in determining daily activities does not differ significantly between HTx and VAD patients. Exercise training may contribute to a further improvement in the functional status of VAD recipients especially in cases of permanent assisting.
Heart Replacement Therapy in Patients > 65 Yrs

- Evaluated all patients undergoing DT LVAD, BTT LVAD, or OHT alone at CPMC between 2005-2012
- Included all patients aged 65-72 years who underwent LVAD or isolated OHT
- Stratified patients according to treatment strategy
  - Group DT: Destination therapy LVAD
  - Group BTT: Bridge to Transplant LVAD
  - Group HTx: isolated heart transplant without mechanical support
- Time zero was on day of implant for patients receiving an LVAD and day of transplant for patients receiving heart transplant
- Primary outcome of interest was 2 year overall survival
## Baseline Group Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DT</th>
<th>BTT</th>
<th>HTx</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, n</td>
<td>24</td>
<td>43</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>69.7 ± 2.2</td>
<td>67.2 ± 2.1</td>
<td>67.1 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>20 (83.3)</td>
<td>38 (88.4)</td>
<td>46 (97.9)</td>
<td>0.09</td>
</tr>
<tr>
<td>Ischemic etiology, n (%)</td>
<td>21 (87.5)</td>
<td>24 (55.8)</td>
<td>29 (61.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>NYHA class</td>
<td>3.5 ± 0.5</td>
<td>3.5 ± 0.7</td>
<td>3.47 ± 0.5</td>
<td>0.99</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>19.5 ± 5.2</td>
<td>20.4 ± 4.4</td>
<td>21.9 ± 9.1</td>
<td>0.33</td>
</tr>
<tr>
<td>LVEDD, cm</td>
<td>6.4 ± 0.9</td>
<td>6.8 ± 0.8</td>
<td>6.2 ± 1.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean PAP, mmHg</td>
<td>41.5 ± 7.5</td>
<td>35.5 ± 9.7</td>
<td>30.3 ± 9.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCWP, mmHg</td>
<td>27.5 ± 7.4</td>
<td>25.3 ± 9.0</td>
<td>20.2 ± 7.2</td>
<td>0.001</td>
</tr>
<tr>
<td>PVR, dyn*s/cm(^5)</td>
<td>445.5 ± 165.5</td>
<td>284.1 ± 136.7</td>
<td>288.3 ± 184.4</td>
<td>0.005</td>
</tr>
<tr>
<td>Inotrope dependence, n (%)</td>
<td>18 (75.0)</td>
<td>41 (95.3)</td>
<td>39 (83.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Pre-op MCS</td>
<td>7 (29.2)</td>
<td>16 (37.2)</td>
<td>0 (0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
# Outcomes

<table>
<thead>
<tr>
<th></th>
<th>DT</th>
<th>BTT</th>
<th>HTx</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to discharge, n (%)</td>
<td>21 (87.5)</td>
<td>36 (83.7)</td>
<td>41 (87.2)</td>
<td>0.87</td>
</tr>
<tr>
<td>Reoperation for bleed, n (%)</td>
<td>3 (12.5)</td>
<td>8 (18.6)</td>
<td>11 (23.4)</td>
<td>0.54</td>
</tr>
<tr>
<td>Need for CRRT, n (%)</td>
<td>3 (12.5)</td>
<td>7 (16.3)</td>
<td>7 (14.9)</td>
<td>0.92</td>
</tr>
<tr>
<td>Respiratory failure, n (%)</td>
<td>3 (12.5)</td>
<td>6 (14.0)</td>
<td>8 (17.0)</td>
<td>0.86</td>
</tr>
<tr>
<td>Any infection, n (%)</td>
<td>6 (25.0)</td>
<td>14 (32.6)</td>
<td>12 (25.5)</td>
<td>0.71</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>2 (8.3)</td>
<td>2 (4.7)</td>
<td>2 (4.3)</td>
<td>0.75</td>
</tr>
<tr>
<td>Post-op MCS, n (%)</td>
<td>1 (4.2)</td>
<td>4 (9.3)</td>
<td>4 (8.5)</td>
<td>0.74</td>
</tr>
<tr>
<td>Follow-up time, years</td>
<td>1.7 ± 1.1</td>
<td>2.5 ± 2.0</td>
<td>4.2 ± 2.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Two Year Survival

log-rank p=0.47

# at risk
DT: 21 19 13 9
BTT: 35 33 27 20
HTx: 41 40 35 33
Conclusions

• No difference in survival to discharge or 2-year survival between DT, BTT, or HTx groups
• No difference in rates of major complications
• There is a need for a multi-center trial in elderly ESHF patients to determine optimal heart replacement therapy
Outcomes Critical to the Success of LVAD Patients

• Survival (near term and long term)
• Quality of Life
• Freedom from Adverse Events
  – Drive application and cost in part by accounting for readmissions
• Available to the appropriate patients.
Although Adverse Events Remain a Barrier to Future Growth

Patient survival has improved slightly despite a higher mix of sicker DT patients...

...although total readmission rates remain a burden.

Top drivers of readmissions:
- Bleeding
- Stroke
- Thrombus

Source: INTERMACS data for HeartMate II through 2Q14
What do Patients want?

Harvard Partners Ambulatory HF
2 Centers 2008

MedaMACS Screening Pilot
10 Centers - 2011

Patient Priorities

Stewart et al, JHLT 2009

5 hospitalizations in the 6 months prior to LVAD
1583 days on HMII

Easily 416 rounds of golf
2 hospitalizations since LVAD

Eagle?
Adult Heart Transplants
Kaplan-Meier Survival by Age Group
(Transplants: January 1982 – June 2012)

Median survival (years): 18-39=12.6; 40-59=10.7; 60-69=9.1; 70+=8.2

All pair-wise comparisons were significant at p < 0.05 except 60-69 vs. 70+. 
Adult Heart Transplants
Kaplan-Meier Survival by Age Group
(Transplants: January 2006 – June 2012)

No pair-wise comparisons were significant at p < 0.05 except
18-39 vs. 60-69: p = 0.0010
40-59 vs. 60-69: p < 0.0001.
Next Generation VADs
Heartmate III

- Fully Magnetically Levitated
  - Large pump gaps designed to reduce blood trauma
- Artificial pulse
- Textured blood contacting surfaces
- Wide range of operation
  - Full support (2 – 10 L/min)
- Advanced Design for Surgical Ease
HeartMate 3: Artificial Pulse

Caution: Investigational Device. Limited by federal (US) law to investigational use.
HeartMate III: Artificial Pulse

**Key Potential Benefits**

- **Artificial Pulse**
  - Full Magnetic Bearing permits sharp speed changes and ability to implement an artificial pulse
  - Potential clinical advantages / reduced adverse events\(^1\)-\(^4\)
    - Aortic insufficiency
    - Bleeding
    - Thrombosis & stroke

2. Letsou G, et.al. *Improved left ventricular unloading and circulatory support with synchronized pulsatile left ventricular assistance compared with continuous-flow left ventricular assistance in an acute porcine left ventricular failure model*. J Card Surg 2010;140:1181-8.

*In development. Not approved for sale.*
Heartmate fully implanted system*

Flexible Lifestyle: Eliminates the driveline and “around the clock” worn equipment.
LVAD induced remodeling: Basic science and clinical implications for recovery

* biomarkers of recovery (genetic, structural, metabolic)
* therapeutic intervention (pre, post, and peri)
* etiology of CHF (sequential tissue)

Leftward shift of the EDPVR (structural “reverse remodeling”)

Time dependent reduction in heart size (EDP of 30 mmHg, V_{30})

Regression of cellular hypertrophy

![Images of chest X-rays and ultrasound scans showing LVAD implantation and recovery over time.](image)
Marginal donor criteria included age greater than 55 years old, hepatitis C positive, cocaine use, ejection fraction less than 0.45, or donor to recipient (BMI) greater mismatch of 20%
Cold Ischemia Limitations

- Ischemic Injury
- No Resuscitative Capabilities
- No Assessment Capabilities
- Time and Distance Limitation
- Limits Utilization of Donor Hearts
Warm Preservation Transmedics

- Physiologic Preservation
- Resuscitative Capabilities
- Metabolic Assessment
- Expand Time & Distance
- Improve Utilization
Decision tree for elective mechanical circulatory support in advanced heart failure.

Stewart G, Givertz M. Circulation 2012;125:1304-1315

Copyright © American Heart Association
DICk Cheney 
CHANGED THE FACE OF 
TRANSPLANT
HE’S NOT THE ONLY ONE.

1189 days on HMII started as DT.
Tx 12/29/13
Oldest OHT in MO. 75 years old
Adult Heart Transplants

% of Patients Bridged with Mechanical Circulatory Support*  
(Transplants: January 2000 – December 2013)

* LVAD, RVAD, TAH, ECMO

JHLT. 2015 Oct; 34(10): 1244-1254
Conclusion

• Device technology continues to evolve
• Patient Survival is improving for transplantation and MCS
• Many Device Complications remain
• Future clinical trials will identify those patients who benefit more from device therapy than transplant
The problem is not the problem. The problem is your attitude about the problem.

Do you understand?

- Captain Jack Sparrow