Mechanical Circulatory Support for Advanced Heart Failure: Which, When and Where?
Heart Failure Epidemic: Estimate Number of Advanced HF Patients

300 Million US Population

HF = 2.6% of Population* or 7 Million Total

50-55% Systolic HF (3.0-3.5 Million)

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

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

Class IIIb + IV < 75 yrs
150-250,000 Pts
Heart Transplantation – The Global View

![Graph showing the number of heart transplants from 1982 to 2012. The graph illustrates a significant increase in the number of transplants, peaking around the mid-1990s and then stabilizing towards the end of the period.]
Therapeutic Strategies in Chronic Heart Failure

NYHA

I | EARLY | MID | LATE

II | Medical therapy + CRT | MCS HTx

III | Hospitalization

IV | Inotrope use

Time from diagnosis
VADs Overview
Classification of VADs

On the basis of period of use:

a) Short-Term VADs
b) Mid- and Long-Term VADs

On the basis of impaired ventricle:

a) LVAD
b) RVAD
c) Bi-VAD

On the basis of pumping mechanism:

a) Pulsatile
b) Non pulsatile
Short Term VADs

A  IABP  

B  Impella  

C  TandemHeart  

D  ECMO  

/ Werdan et al, EHJ, 2013
Indications for Short Term VADs

1. Cardiogenic Shock
   - Acute MI
   - AHF
   - Acute myocarditis
   - Post –cardiotomy
   - Acute rejection
2. High risk intervention
3. Bridge to LVAD or transplant
4. RV Failure
Short Term VADs: IABP – Pressure Unloading

Hemodynamic support = 0.5-1 L/min
Slightly increase coronary perfusion
Reduced Afterload

IABP Shock II Trial

P = 0.92 by log-rank test

Diastole  Systole
### Short Term VADs: Impella and Tandem Heart - Volume Unloading

**Hemodynamic support = 2.5-5 L/min**

**Increased Afterload**

<table>
<thead>
<tr>
<th></th>
<th>Tandem Heart™</th>
<th>Impella Recover® LP 5.0</th>
<th>Impella Recover® LP 2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter size (French)</td>
<td>—</td>
<td>9</td>
<td>—</td>
</tr>
<tr>
<td>Cannula size (French)</td>
<td>21 venous</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Flow (L/Min)</strong></td>
<td></td>
<td>Max. 5.0</td>
<td>Max. 2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max. 33 000</td>
<td>Max. 33 000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peripheral (femoral artery + left atrium after transseptal puncture)</td>
<td>Peripheral surgical cutdown (femoral artery)</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recommended duration of use</td>
<td>~14 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
<tr>
<td>Certification</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>FDA</td>
<td>PMN</td>
<td>IDE trial</td>
<td>IDE trial</td>
</tr>
<tr>
<td>Relative costs in comparison to intraaortic balloon pumping</td>
<td>++++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

- PMN, pre-market notification; IDE, investigational device exception.
- +, anticoagulation necessary; CE-certification present; ++++, high relative costs in comparison to ++++ very high relative costs in comparison to IABP.
Short Term VADs: ECMO
Mid- and Long Term VADs

Heartware (impeller)

Heartmate II (axial flow)

Syncardia TAH

AbioCor TAH
Once upon a time in 1969…
Liotta Heart – First Total Artificial Heart
REMATCH – Trial: Beginning of the Destination Therapy Era

Survival (%)

0 20 40 60 80 100
0 6 12 18 24 30

Months

LV assist device
Medical therapy

No. at Risk

LV assist device 68 38 22 11 5 1
Medical therapy 61 27 11 4 3 0

University Hospital Zurich

Rose et al., NEJM 2001
Advantages of Continuous Flow Devices

![Graph showing survival probability over months for continuous-flow and pulsatile-flow LVADs]

- **Continuous-flow LVAD**
- **Pulsatile-flow LVAD**

**No. at Risk**
- Continuous-flow LVAD: 133, 95, 82, 69, 62
- Pulsatile-flow LVAD: 59, 32, 19, 5, 2

*P = 0.008 by the log-rank test*
Newest LVADs

HeartWare HVAD
BTT in 2012

HeartMate II
BTT in 2008
DTT in 2010

MVAD

HeartMate III
VADs: Indications and Complications
### INTERMACS Profiles

<table>
<thead>
<tr>
<th>Level</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Critical cardiogenic shock</td>
<td>“Crash and burn”</td>
</tr>
<tr>
<td>2</td>
<td>Progressive decline</td>
<td>“Sliding fast”</td>
</tr>
<tr>
<td>3</td>
<td>Stable but inotrope dependent</td>
<td>Stable but dependent</td>
</tr>
<tr>
<td>4</td>
<td>Recurrent advanced HF</td>
<td>“Frequent flyer”</td>
</tr>
<tr>
<td>5</td>
<td>Exertion intolerant</td>
<td>“Housebound”</td>
</tr>
<tr>
<td>6</td>
<td>Exertion limited</td>
<td>“Walking wounded”</td>
</tr>
<tr>
<td>7</td>
<td>Advanced NYHA class III</td>
<td>Advanced NYHA class III</td>
</tr>
</tbody>
</table>
Indications Long Term VADs—What do the Guidelines Say

Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:

- LVEF <25% and, if measured, peak VO₂ < 12 mL/kg/min
- ≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause
- Dependence on i.v. inotropic therapy
- Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mm Hg and SBP ≤80–90 mmHg or CI ≤2 L/min/m²)
- Deteriorating right ventricular function
## Recognition of the growing use of VADs

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BTT:</strong> An LVAD or BiVAD is recommended in selected patients with end-stage HF despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>DT:</strong> An LVAD should be considered in highly selected patients who have end-stage HF despite optimal pharmacological and device therapy and who are not suitable for heart transplantation, but are expected to survive &gt;1 year with good functional status, to improve symptoms, and reduce the risk of HF hospitalization and of premature death.</td>
<td>IIA</td>
<td>B</td>
</tr>
</tbody>
</table>
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
## Increase in VAD for DT

### Table 2  CF and BiVAD Implants: April 2008 to December 2014 (n = 12,030)

<table>
<thead>
<tr>
<th>Device strategy at time of implant</th>
<th>2008 to 2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTT listed</td>
<td>1,529</td>
<td>404</td>
<td>623</td>
<td>734</td>
<td>3,290</td>
<td>27.3%</td>
</tr>
<tr>
<td>BTT likely</td>
<td>1,163</td>
<td>513</td>
<td>511</td>
<td>323</td>
<td>2,510</td>
<td>20.9%</td>
</tr>
<tr>
<td>BTT moderate</td>
<td>480</td>
<td>230</td>
<td>273</td>
<td>187</td>
<td>1,170</td>
<td>9.7%</td>
</tr>
<tr>
<td>BTT unlikely</td>
<td>164</td>
<td>73</td>
<td>67</td>
<td>54</td>
<td>358</td>
<td>3.0%</td>
</tr>
<tr>
<td>DT</td>
<td>1,355</td>
<td>983</td>
<td>1,152</td>
<td>1,108</td>
<td>4,598</td>
<td>38.2%</td>
</tr>
<tr>
<td>BTR</td>
<td>29</td>
<td>11</td>
<td>10</td>
<td>4</td>
<td>54</td>
<td>0.5%</td>
</tr>
<tr>
<td>Rescue therapy</td>
<td>15</td>
<td>7</td>
<td>6</td>
<td>10</td>
<td>38</td>
<td>0.3%</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>12</td>
<td>0.1%</td>
</tr>
<tr>
<td>Total</td>
<td>4,744</td>
<td>2,221</td>
<td>2,642</td>
<td>2,423</td>
<td>12,030</td>
<td>100%</td>
</tr>
</tbody>
</table>

BiVAD, biventricular assist device; BTR, bridge to recovery; BTT, bridge to transplant; CF, continuous flow; DT, destination therapy.
Overall Survival

Intermacs - Kaplan-Meier Survival for Intermacs Overall
Primary Prospective Implants: June 23, 2006 to September 30, 2015

Shaded areas indicate 70% confidence limits
p (log-rank) = N/A
Event: Death (censored at transplant or recovery)
Updated survival for CF-VAD

Era 1: LVAD 2008 – 2011
n=4588, deaths=1565

Era 2: LVAD 2012-2014
n=7084, Deaths=1400

P(overall) < .0001

Era 1: BiVAD 2008-2011
n=156, Deaths=82

Era 2: BiVAD 2012 – 2014
n=202, deaths=81

Event: Death (censored at transplant and recovery)

% Survival

0 6 12 18 24 30 36 42 48

Months post implant
Decision tree for elective mechanical circulatory support in advanced heart failure

1. HF Symptoms Limiting Daily Functioning and Quality of Life
2. Optimal Pharmacologic and Resynchronization Therapy >3 mos
   - Transplant Candidate
     - Low RV Failure Risk after LVAD: Consider LVAD as BTT
     - High RV Failure Risk after LVAD: Consider BiVAD or TAH as BTT
   - Not Eligible for Transplant
     - Low RV Failure Risk after LVAD
     - High RV Failure Risk after LVAD
       - Low LVAD Implant Risk: Supportive Cardiology
       - High LVAD Implant Risk
         - If reversible risk (eg, infection, AKI, malnutrition): Consider DT LVAD

Simplified 1-year outcomes using weighted averages for left ventricular assist device (LVAD; combined bridge-to-transplant and destination therapy)

Colleen K. McIlvennan CK et al. Circ Heart Fail. 2014
Complications

Infections
- Aggressive wound care
- Transcutaneous energy transfer technology
- Smaller lead diameter

Bleeding
- Gastrointestinal bleeding
  - CFVAD: acquired von Willebrand Factor

Thromboembolic complications

RV-Failure
Thromboembolic complications
RV-Failure after LVAD

- CI < 2.2 L/min/m² and CVP >18 mmHg
- Postoperative inotropic support > 14 days, NO >48 hrs
- Absence of other causes explaining circulatory failure
Biventricular Assist Device – Bi-VAD

Consider Bi-VAD:
- Extended infarct areas
- Malignant arrhythmias
- Prolonged cardiogenic shock
- Two-or multi-organ failure
Timing is everything…

<table>
<thead>
<tr>
<th>NYHA</th>
<th>EARLY</th>
<th>MID</th>
<th>LATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Medical therapy</td>
<td>+CRT</td>
<td>MCS HTx</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Early: Medical therapy
- Mid: +CRT
- Late: MCS HTx

Outpatient clinic
Hospitalization
Inotrope use

Time from diagnosis
Survival and INTERMACS Level

Survival by Levels

<table>
<thead>
<tr>
<th>Levels</th>
<th>n</th>
<th>deaths</th>
<th>6 mths</th>
<th>12 mths</th>
<th>36 mths</th>
<th>48 mths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>1803</td>
<td>507</td>
<td>82%</td>
<td>76%</td>
<td>58%</td>
<td>50%</td>
</tr>
<tr>
<td>Levels 2 &amp; 3</td>
<td>7978</td>
<td>2054</td>
<td>87%</td>
<td><strong>80%</strong></td>
<td>58%</td>
<td>48%</td>
</tr>
<tr>
<td>Levels 4-7</td>
<td>2194</td>
<td>561</td>
<td>89%</td>
<td>82%</td>
<td>61%</td>
<td>49%</td>
</tr>
<tr>
<td>Not Specified</td>
<td>55</td>
<td>6</td>
<td>94%</td>
<td>90%</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

Event: Death – censored at transplant, recovery and device exchange

P(overall) = .0001
p(1 vs. 2 & 3) = .001
p(1 vs. 4-7) < .0001
p(2&3 vs. 4-7) = .06

JHLT. 2015, 7th INTERMACS
### INTERMACS Profile at Implant

**Table 3** CF LVAD/BiVAD Implants: April 2008 to December 2014 ($n = 12,030$)

<table>
<thead>
<tr>
<th>Patient profile at time of implant</th>
<th>2008 to 2011</th>
<th>2012 to 2014</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1—Critical cardiogenic shock</td>
<td>465</td>
<td>961</td>
<td>1,803</td>
<td>15.0%</td>
</tr>
<tr>
<td>2—Progressive decline</td>
<td>1,249</td>
<td>2,416</td>
<td>4,507</td>
<td>37.5%</td>
</tr>
<tr>
<td>3—Stable but inotrope-dependent</td>
<td>660</td>
<td>1,987</td>
<td>3,471</td>
<td>28.8%</td>
</tr>
<tr>
<td>4—Resting symptoms</td>
<td>372</td>
<td>968</td>
<td>1,646</td>
<td>13.7%</td>
</tr>
<tr>
<td>5—Exertion-intolerant</td>
<td>83</td>
<td>198</td>
<td>331</td>
<td>2.7%</td>
</tr>
<tr>
<td>6—Exertion-limited</td>
<td>48</td>
<td>81</td>
<td>141</td>
<td>1.2%</td>
</tr>
<tr>
<td>7—Advanced NYHA Class III</td>
<td>29</td>
<td>44</td>
<td>76</td>
<td>0.6%</td>
</tr>
<tr>
<td>Not specified$^a$</td>
<td>0</td>
<td>46</td>
<td>55</td>
<td>0.5%</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>2,906</td>
<td>6,701</td>
<td>12,030</td>
<td>100%</td>
</tr>
</tbody>
</table>

CF, continuous flow; NYHA, New York Heart Association.

$^a$Due to change in web-based data entry capture in Protocol v3.0 (May 2012).
Triggers for Referral for VAD Evaluation

- Inability to wean inotropes or frequent inotrope use
- Peak V02 max < 14-16 ml/kg/min or <50% predicted
- Two or more HF admissions in 12 months
- Worsening right heart function and secondary pulmonary hypertension
- Worsening renal failure
- Diuretic refractoriness associated with worsening renal function
- NYHA class IV on most days
- Recurrent, refractory VT
VADs – not for all

**Contraindications**

**Absolute**
- Irreversible hepatic disease
- Irreversible renal disease
- Irreversible neurological disease
- Medical nonadherence
- Severe psychosocial limitations

**Relative**
- Age >80 y for DT
- Obesity or malnutrition
- MS disease that impairs rehabilitation
- Active systemic infection or prolonged intubation
- Untreated malignancy
- Severe PVD
- Active substance abuse
- Impaired cognitive function
- Unmanaged psychiatric disorder
- Lack of social support
Key to successful circulatory Support

- PATIENT SELECTION
- Timing of Implantation
- Meticulous surgical technique
- Appropriate Device Selection
- Avoid RV Failure
Heart Team

Prof. Dr. med. 
Frank Ruschitzka
Leiter Herzinsuffizienz
- 

Dr. med. Stefano Benussi
Leitender Arzt

Prof. Dr. med. Francesco Maisano
Klinikdirektor

PD Dr. med. 
Andreas Flammer
Oberarzt

Prof. Dr. med. 
Markus Wilhelm
Oberarzt

PD Dr. med. Frank Enseleit
Oberarzt

Dr. med. Michelle Frank
Oberärztin
HTX ?  DT ?