Mechanical Circulatory Support in Advanced Heart Failure and Cardiogenic Shock

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Research grant (Medtronic)
HF Advisory Board (Abiomed)
Research Grant (Actelion)
The Burden of Congestive Heart Failure

- Nearly 6.5 million Americans w/ HF ~ 8 million by 2030
- > 960,000 new cases/yr
- $32 billion expenditures
- ~ $70 billion 2030
- #1 DRG > 1 million hosp
- 50% readmitted within 6 mos
- 50% dead within 5 years
- 90% 1 yr mortality for Stage D

Class I 1.79 M (35%)
Class II 1.79 M (35%)
Class III 1.28 M (25%)
Class IV 255 K (5%)
Mechanical Circulatory Support: Indications

• Cardiogenic Shock (post-MI, dilated, valvular)
• Post-cardiotomy syndrome (failure to wean off CPB)
• Hemodynamic instability/deterioration despite OMM
• Long anticipated wait for suitable donor (big O)
• Inotrope / IABP / ECMO dependence
• Recurrent ventricular tachycardia / VT storm
• Viral myocarditis / PP CMY w/ CS (BTR vs BTT)
• Frequent admissions for ADHF
• Cardio-renal syndrome / intolerance to HF therapies
• S/P cardiac arrest; support until candidacy det. (BTD)
Contraindications to MCS

• **Absolute contraindications**
  – Irreversible hepatic disease (cirrhosis)
  – Irreversible renal dz/chronic HD (unless kid tx candidate)
  – Irreversible neurologic dz
  – Severe lung dz or systemic illness limiting survival
  – Severe psycho-social limitations (no caregiver) non-compl.

• **Relative contraindications**
  – Obesity (BMI > 35) cachexia (< 18)
  – Neuromuscular disorder impairing rehab / survival
  – Active sepsis / recent CVA/ICH or vent dependence
  – Untreated malignancy / active GIB / coagulopathy / +HIT
  – Severe PVD / Diabetes w/ mod end organ involvement
  – Active substance abuse / psychiatric disorder / cognitive impair.
MCS: General Considerations

• Importance of selecting critically ill patients to justify risk of surgical intervention (risk stratification)
• Need to avoid patients who are too ill for any reasonable chance for successful outcome (IM 0/MSOF/adv age)
• Selecting the correct MCS device
  – Temporary vs durable device
  – Left, right or biventricular support
  – Need for short term MCS/RHC to optimize
  – Estimated waiting period for donor
• Expeditious intervention once decision made to proceed
• Cost and insurance considerations
Patient Selection for MCS: Risk Assessment
Defining the Population with Advanced Heart Failure

AHA/ACC classification

NYHA classifications

INTERMACS Profiles

Range of DT Approval and CMS Coverage

INTERMACS 4: Resting symptoms on oral therapy

INTERMACS 5: Exertion intolerant

INTERMACS 6: Exertion limited

INTERMACS 1-3: Inotrope-Dependent

ROADMAP

Patients with advanced cardiogenic shock
1. s/p card arrest
2. Active CPR
3. MSOF
4. IABP/Vent/TCS
5. Profound acidosis

*IM 1 surv w/ LVAD ~ 50%

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Slide Concept: David Farrar, PhD
Natural History of Heart Failure and Timing of MCS

NYHA CLASS

Adapted from Bristow, MR Management of Heart Failure, Heart Disease: A Textbook of Cardiovascular Medicine, 6th edition, ed. Braunwald et al.

Adapted from Mark Slaughter, MD

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Keys to Successful MCS Outcome

- **Appropriate Patient Selection**
- **Timing of implantation**
  - INTERMACS profile 3-4 ideal
  - IM profile 1-2 higher risk (may need TAH, ECMO as short term bridge to decision or BTB)
  - IM 5-6 if long anticipated wait
- **Device selection**
- **Early referral to tertiary center!**
Device Selection
Strategies for MCS

Cardiogenic Shock

Recovery 5-10%

Decision or Long term Device

ECMO/pVAD BTD

Long-term / durable MCS

Heart Transplant

Inotropes / IABP

Destination

BTR

BTT

Short-term / temporary MCS

53x59
ECMO
Short-term bridge to decision (BTD) or (BTB)
VA ECMO
Indications*

• Cardiogenic shock refractory to medical management
• Witnessed cardiac arrest
• INTERMACS 0-1 profiles cardiogenic shock pts with potential for OHT/durable devices (BTD/BTB)
• Acute or fulminant myocarditis
• Post-partum cardiomyopathy with shock
• Acute massive MI with pulmonary edema
• Acute refractory transplant rejection
• Cardiotoxic poisoning / overdose
• Post-cardiotomy syndrome
• VA ECMO does not unload the LV
ECMO
Contraindications

• Unrecoverable cardiac function in non-Tx/durable MCS pts
• MSOF
• Prolonged CPR w/o adequate tissue perfusion
• Unwitnessed cardiac arrest (neurologic)
• Terminal illness (end-stage COPD, malignancy, CVA etc)
• Massive septic shock*
• Non-medical contraindications
  – cognitive limitations
  – psychiatric limitations
  – social limitations
  – advanced age / size

Mortality inc exponentially > 7 days support
Temporary Mechanical Circulatory Support

Role of Percutaneous LVADs (or pVADs)
The Impella Catheters

**Impella 2.5**
- Percutaneous access – 12F
- Actively unloads the LV
- Provides up to 2.5 liters/min of flow
- Rapid insertion in cath lab or CVOR

**Impella CP**
- Femoral / axillary artery percutaneous access
- Actively unloads the LV
- Provides up to 4.3 liters/min of flow
- Rapid insertion in cath lab or CVOR

**Impella 5.0**
- Femoral / Axillary cut-down using vascular graft (9 F catheter)
- Surgically placed (21 F pump)
- Provides up to 5.0 liters/min of flow
- Preferred pVAD for cardiogenic shock esp large BSA

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Impella Position in LV
CXR/fluoro & Echo
Percutaneous VADs
Indications & Advantages

• Short-term management of cardiogenic shock
• FDA approved for left heart failure (Impella 5.0/CP 6/4d)
• Impella 5.0 requires vascular access/graft; CP percut.
• Easy to place (subclavian/femoral) rapidly deployed
• Hemodynamically superior to IABP (flow 3-5 l/min)
• Potential for short term bridge to heart transplant
• Subclavian approach allows ambulation
• Works best with dilated LV - unloads LV; reduces MR
• Contra: severe PAD, LVT, severe AS/AI, VT storm; VSD, severe RHF (use w/ TandemHeart RVAD = “Tandella”)

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Potential Complications of pVADS

- Vascular injury / occlusion / dissection
- Bleeding (transfusion requirements)
- Hemolysis
- Infection
- CVA
- Ventricular arrhythmias (VT)
- Mitral insufficiency (chordal rupture)
- Tricuspid insufficiency (TandemHeart RVAD)
- Device thrombosis / failure
Impella 5.0 Outcomes (2017)

37/49 = 75% successful outcome
Right, Left or BiVentricular MCS?
## Evaluating RV function

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Favor LVAD alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVP on OMM</td>
<td>&lt; 10 mm Hg (OMM)</td>
</tr>
<tr>
<td>RVSWI (MPA – RA x SV/BSA)</td>
<td>&gt; 300 mm Hg ml/m2</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>minimal to moderate</td>
</tr>
<tr>
<td>PVR (PAPi)</td>
<td>&lt; 4 WU ( &gt; 1)</td>
</tr>
<tr>
<td>Transpulmonary gradient</td>
<td>&lt; 15 mm Hg</td>
</tr>
<tr>
<td>RV size / RVEF</td>
<td></td>
</tr>
<tr>
<td>– RVEDV</td>
<td>&lt; 200 ml</td>
</tr>
<tr>
<td>– RVESV</td>
<td>&lt; 177 ml</td>
</tr>
<tr>
<td>– RVEF</td>
<td>&gt; 30%</td>
</tr>
<tr>
<td>Need for pre-op vent. support</td>
<td>none</td>
</tr>
</tbody>
</table>

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RV failure post-LVAD implant inc mortality 19 to 49%
## Which Device?

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Favors LVAD</th>
<th>Favors BiVAD/TAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echo RV dysfunction</td>
<td>None-mild (mod)</td>
<td>severe</td>
</tr>
<tr>
<td>TAPSE/PAPI</td>
<td>&gt; 1 cm / &gt; 1.5</td>
<td>&lt; 1 cm / &lt; 1.4</td>
</tr>
<tr>
<td>TR / MR</td>
<td>Mild-mod / severe</td>
<td>Severe / severe</td>
</tr>
<tr>
<td>Hemodyn: RAP</td>
<td>&lt; 10 mmHg OMM</td>
<td>&gt; 15 mmHg</td>
</tr>
<tr>
<td>RVSWI</td>
<td>High (&gt;200)</td>
<td>Low (&lt;100)</td>
</tr>
<tr>
<td>INTERMACS Profile</td>
<td>3-6 (2)</td>
<td>1-2</td>
</tr>
<tr>
<td>Etiology</td>
<td>Dilated/ischemic</td>
<td>Restrictive/anatomic</td>
</tr>
<tr>
<td>Arrhythmia (refract VT)</td>
<td>----</td>
<td>TAH/BiVAD preferred</td>
</tr>
<tr>
<td>End-organ dysfx/TCS</td>
<td>----</td>
<td>TAH/BiVAD preferred</td>
</tr>
</tbody>
</table>
MCS - Temporary RV support

- Impella-RP
- Protekduo catheter
- TandemHeart
- CentriMag
TandemHeart RVAD + Impella LVAD = “Tandella”
“Tandella”
Percutaneous BiVentricular Temp MCS

June 18, 2018
Devices by INTERMACS Profiles

TAH

LVAD

P1 P2 P3 P4 P5 P6 P7

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Durable MCS Options for ESHD

370,000 Class IIIb/IV

~70,000 potential VAD candidates for DT

~100,000 Heart Tx candidates

~200,000 Non-Tx/VAD

2,300 Heart transplants/yr

~97,000 waiting medical Rx

~3-4,000 MCS*
  2,800 LVADs
  200 TAHs

Palliative Care

~2,800 LVADs
~200 TAHs

~97,000 waiting medical Rx

~3-4,000 MCS*

* MCS: Mechanical Circulatory Support
HeartMate II LVAD

- Axial continuous flow
- Silent; 3-8 liters/min flow
- Single moving part
- 2 industrial ruby bearings
- Valveless
- Durable (5-10 yrs)
- > 20,000 implanted
- Electrically powered percutaneous driveline
- FDA approved for BTT, DT

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The HeartWare Ventricular Assist System

- HVAD™ smallest implantable pump
  - Up to 10 liters of flow
  - Centrifugal pump (vs axial)
  - Hybrid magnetic / hydrodynamic suspension (bearingless system)
  - No pump pocket
  - > 14,000 implanted WW / CE mark

- ADVANCE Trial (BTT)
  - FDA approved for BTT

- ENDURANCE (DT) Supplement Trial: CEDARS-SINAI ongoing

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HeartMate III LVAD

- Centrifugal pump – full maglev technology: no bearings
- Flow: 2.5 – 10 l/min
- Enhanced AE profile
  - Larger channels
  - Built in pulsatility
- Ease of implant-no pocket
- Durable- single moving part
- Enhanced longevity-no contact/valves
- MOMENTUM: lowest pump thrombosis rate

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Cedars-Sinai MCS Program
Durable MCS Implants (2007-2018)

As of Dec 31, 2018
<table>
<thead>
<tr>
<th>Year</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCS/Tx</td>
<td>18/89</td>
<td>24/95</td>
<td>31/119</td>
<td>29/122</td>
<td>32/132</td>
<td>47/122</td>
<td>28/103</td>
<td>42/103*</td>
</tr>
<tr>
<td>% Tx Pts bridged by MCS</td>
<td>20.2%</td>
<td>25.3%</td>
<td>26.1%</td>
<td>23.8%</td>
<td>23.5%</td>
<td>38.5%</td>
<td>27.8%</td>
<td>40.8%*</td>
</tr>
</tbody>
</table>

* 14 pts bridged to Tx w/ Impella 5.0
Continuous Flow LVAD/BiVAD Implants: 2008 – 2016, n=17633

<table>
<thead>
<tr>
<th>Months</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95%</td>
</tr>
<tr>
<td>12</td>
<td>81%</td>
</tr>
<tr>
<td>24</td>
<td>70%</td>
</tr>
<tr>
<td>36</td>
<td>59%</td>
</tr>
<tr>
<td>48</td>
<td>49%</td>
</tr>
</tbody>
</table>

n=17633, Deaths=5398
Implants: June 2006 – December 2016, n=18987

BTT: Listed CFLVADs implants 2015-2016, n=1375

- Tx/Ongo/Rec @ 1 yr=88%
- 53% Alive (device in place)
- 34% Transplanted
- 12% Dead
- 1% Recovery

Months after Implant

Proportion of Patients

[Graph showing implant outcomes over time]
Continuous Flow LVAD/BiVAD Implants: 2008 – 2016, n=17633

Instantaneous Death Rate (Hazard) for selected causes

Cause of Death
Infection
RHF
Neurological
Device Malfunction
MSOF

Deaths/Month

0.010
0.009
0.008
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0.000

Months post implant

0  6  12  18  24  30  36  42  48

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The Journal of Heart and Lung Transplantation 2017 36, 1080-1086DOI: (10.1016/j.healun.2017.07.005)
RC with HM II LVAD
Syncardia t-TAH

- **Class:** implantable pulsatile (pneumatic)

- **Indications:** (temp. biventricular replacement)
  - bridge to OHT (FDA approved)
  - severe irreversible biventricular failure

- **Limitations:**
  - Requires full anticoagulation
  - Size requirement BSA $\geq$ 1.6 m²

- "Freedom" portable driver available

- Only TAH approved by FDA/CMS BTT

- 79% successfully transplanted

- Nearly 1,600 implanted WW

- 70 cc DT Trial (Jan 2015); 50 cc TAH trial underway

*Copeland J, Arabia F et al; NEJM 351: 859-867 2004
Candidates for TAH

• Irreversible, severe biventricular failure
• Larger, critically ill patients in cardiogenic shock w/ significant end-organ dysfunction
• Unique anatomic issues
• (LV thrombus, VSD, massive MI, primary cardiac malign, complex CHD
• Hypertrophic, amyloid, restrictive CMY
• Heart tx w/ severe CAV or refractory rejection
• Incessant VT/VF

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Leading the Quest
TAH Competing Outcomes

Intermacs TAH Patients June 2006 through April 2017 (n=450)

- 52.8% Transplant
- 34.1% Death
- 13.1% Alive (device still in place)

1 yr success (Tx/ongoing) = 65.9%
TAH Competing Outcomes (N=94)

1 yr Success/Ongoing = 67%

incl 5/6 – 50 cc TAH
Range of pt size for 70 cc TAH

6' 7"

5' 2"

June 9, 2014
MR - S/p 50 cc TAH (POD #35)

August 16, 2018
# 1 yr Post-Tx Survival by Device

<table>
<thead>
<tr>
<th>Transplant Year - All Indications</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVAD</td>
<td>1/1</td>
<td>6/6</td>
<td>15/16</td>
<td>10/10</td>
<td>7/8</td>
<td>14/15</td>
<td>53/56</td>
</tr>
<tr>
<td>TAH</td>
<td>8/9</td>
<td>8/8</td>
<td>14/16</td>
<td>12/13</td>
<td></td>
<td></td>
<td>42/46</td>
</tr>
<tr>
<td>BIVAD</td>
<td>8/9</td>
<td>6/8</td>
<td>5/5</td>
<td>1/1</td>
<td>0/1</td>
<td></td>
<td>20/24</td>
</tr>
<tr>
<td>All</td>
<td>9/10</td>
<td>12/14</td>
<td>28/30</td>
<td>19/19</td>
<td>21/25</td>
<td>26/28</td>
<td>115/126</td>
</tr>
</tbody>
</table>
Destination Therapy

(DT)
Criteria for Destination Therapy

- LVEF ≤ 25%
- Peak VO2 < 14 ml/kg/min (or 50% pred.age/sex)
- And either
  - NYHA Class IV heart failure symptoms despite optimal medical therapy for at least 45 of prior 60 days or
  - Dependence on IV inotropes for at least 14 days, or
  - Dependence on an IABP for at least 7 days
- Not a candidate for transplantation
- No irreversible renal, pulmonary or hepatic dysfunction or active infection
- Devices approved by FDA for DT: HM II HeartWare HVAD
- DT Trials ongoing with HM III, TAH
Magnitude of survival benefit with LVAD DT therapy?
Device Algorithm by INTERMACS Profile

Potential Tx Candidate

IM profile 1 (or 2)
- TAH/BiVAD
- ECMO/TCS Bridge to decision

IM profile 2-6
- Durable LVAD

If stable on drips & high on list: pVAD Impella

Heart Transplant

DT LVAD Medical therapy palliative care

Stable for OR?
- Yes
  - Improved candidacy?
    - Yes
      - Heart Transplant
    - No
      - Palliative Care
  - No
    - No

Yes

No
CONCLUSIONS

• In Adv HF and cardiogenic shock, successful outcomes depend upon appropriate patient and device selection along with expeditious referral
• MCS candidates should be ill enough to justify risks of implantation but not so ill to be associated with poor outcome (prefer IM 2-5 vs IM I)
• Continuous flow LVADs w/ extended durability are MCS devices of choice; Implant early!
• IM 1 may do better w/ BiVAD/TAH
• Inc utilization of percutaneous temporary MCS (Impella/Tandem) as BTT/BTD/BTB/BTR
• Consider DT LVAD for non-Tx candidate w/ ESHD