COMPLICATIONS OF VAD THERAPY

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CENTRIMAG MAGLEV PUMP

• Elimination of seals and bearings

• Elimination of friction and heat generation in the blood path reducing the risk for thrombus formation and hemolysis

• Uniform washing of the rotor surface minimizes areas of blood stagnation and turbulence in the pump

CENTRIMAG® SYSTEM COMPONENTS
CENRIMAG PUMP

- Max. pump speed: 5500 RPM
- Max. flow: 9.9 LM
- Rotor has magnetic core

CENRIMAG PUMP & MOTOR

BEARINGLESS PUMP & MOTOR

- No bearing and seals
- Disposable pump head
- 31 cc priming volume
- Max. pump speed: 5500 RPM
- Max. flow: 9.9 LM
- Rotor has magnetic core
GOOD NEWS AND BAD NEWS

• Good News: Outcomes are better
• Survival for V-A ECMO up to 65%
WHAT’S BEHIND THE GOOD NEWS?

- Streamlined circuitry
- Electromagnetically-suspended impellar (CentriMag) and cutting-edge centrifugal pumps (Cardiohelp) instead of roller pumps and standard centrifugal pumps
- More efficient membrane oxygenators have replaced silicone membrane oxygenators
- Overall much less hemolysis since current devices are less damaging to cells and anticoagulation management is easier

GOOD NEWS AND BAD NEWS

- Bad News:
  - There are still complications
  - There are still complications
  - There are still complications

NOW FOR THE COMPLICATIONS……..

- LV Distension – can we avoid it?
  - Echo monitoring
  - Consider an indwelling miniature TEE probe (the size of an NGT) that can give you images when you need them for up to 72 hours at a time
  - IABP, if needed for LV unloading, is a good place to start; another option is Impella 4.0
MINIATURE HTEE PROBE (IMACOR)

• Same diameter as NGT
• Quick learning curve – used by intensivists, residents at bedside)
• Can remain in place for 72 hours at a time
• Good imaging quality
• 24/7 capability to assess contractility, chamber size, tamponade

COMPLICATIONS OF ECMO FOR TREATMENT OF CARDIOGENIC SHOCK AND CARDIAC ARREST: A META-ANALYSIS OF 1,866 ADULT PATIENTS

• Complication rate in this population of patients is not well-understood, partly due to small study sizes
• Analyzed adults only, in reports that included over 10 patients (range: 17-517 patients)
• Survival ranged from 21-65%


LOWER EXTREMITY COMPLICATIONS

• Lower extremity ischemia: 16.9%
  • Range: 12.5 – 22.6%
• Fasciotomy or compartment syndrome: 10.3%
  • Range: 7.3 – 14.5%
• Lower extremity amputation: 4.7%
  • Range: 4.2 – 8.3%
OTHER COMPLICATIONS...

- Stroke: 5.9%
  - Range: 4.2 – 8.3%
- Other neurologic complications: 13.3%
  - Range: 9.9 – 17.7%
- Acute kidney injury: 55.6%
  - Range: 35.5 – 74%

MORE COMPLICATIONS.....

- Major/significant bleeding: 40.8%
  - Range: 26.8 – 56.6%
- Significant infection: 30.4%
  - Range: 19.5 – 44%

TAKE HOME MESSAGES....

- ECMO is relatively simple to initiate in a dying patient and outcomes are significantly better
- It is not a “free ride” – serious complications still occur
  - Kidney injury in over 50%
  - Serious bleeding in 41%
  - Significant infection in 30%
SET THE BENCHMARKS

- Use the data to set the benchmarks to help determine what morbidities need to be reduced
- V-A ECMO is an important treatment modality for cardiogenic shock – we must continue to use it, but need to continue to increase its safety profile

ECMO: RAPID COMPLETE SUPPORT FOR HEMODYNAMIC COLLAPSE

- Tremendous improvements in ECMO technology have resulted in better outcomes
- Newer generation oxygenators are much smaller and less likely to cause hemolysis
- Cannulation of femoral artery and vein are easiest, but other approaches possible
- Reperfusion catheter in femoral artery to avoid limb ischemia

![Graph showing survival rates and mean age, EF, and percentage on inotropes](image-url)
Inflow Cannula
Inserted into the apex of the left ventricle
Outflow Graft
Anastomosed to the ascending aorta
Preload Dependent
Volume is important for VAD patients
Afterload Sensitive
Maintain blood pressure
MAP 70 – 80 mmHg

HeartMate II Design Features

INTERMACS PROFILE

VAD COMPLICATIONS

- Right ventricular (RV) failure
- Aortic insufficiency
- GI bleed
- Pump thrombosis and hemolysis
- Drive – line infections (very rare in our institution) = 0.06% (compared to the 20% in INTERMACS data)
VAD COMPLICATIONS

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RV FAILURE

The RV and LV even though they are genetically separate entities -> they cannot be analyzed as separate entities because their fibers are a continuum within the superficial and deep layers -> the RV and LV interact functionally

SUCKDOWN AND RV FAILURE

- Left ventricular collapse or "suckdown" -> right-heart failure
- When LV is sucked dry, the septum gets -> septal dysfunction -> RV dilates -> RV failure
- Suck-down™ phenomenon -> septal displacement -> TV leaflets tethering -> dilation of TA -> worsening TR -> RVVO -> RVF

LVEDD< 6.4 cm -> RF for chronic RVF
PREDICTORS OF RV FAILURE

- Echocardiography: pre-LVAD implant
  - TAPSE
  - RV short/long D > 0.6 (spherical shape of the RV)
  - Severe TR
  - RV/LV EDD (TEE) > 0.75
  - LVEDD > 7.4cm
  - LAD/LVEDD > 0.66
  - RV peak GLS > -9.6

Multiple risk scores (clinical/ biochemical/ echocardiographic/ hemodynamic) are used to predict RVI - no single variable adequately discriminates or is reliable for patient selection.
3/1/2017

TAPSE = 2.5 cm
Abnormal TAPSE and S wave

S wave = 11 cm/sec

TAPSE = 1.5 cm

Average Longitudinal Strain = -6.7
Average Longitudinal Strain = -1.7

33%
89%
MANAGING RVF

<table>
<thead>
<tr>
<th>Pre-operative</th>
<th>Operative</th>
<th>Post-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical assessment</td>
<td>Monitor RV function</td>
<td>Consider correction of RV failure</td>
</tr>
<tr>
<td>Right heart catheterization</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aggressive use of inotropes</td>
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<tr>
<td></td>
<td></td>
<td>Ventricular assist device</td>
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</tbody>
</table>

TR repair controversial: TV procedures in moderate to severe TR failed to reduce early mortality or need for early RVAD and was associated with more post op renal failure and prolong ICU and hospital length of stay.

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AI IN CF-LVAD PATIENTS

- Pre-existing AI = mild → progression to moderate-severe/ severe AR during CF-LVAD support
- De-Novo AI = development of AI during CF-LVAD support in patients without AI at baseline and without AV surgery
  - Prevalence of AI = no of cases of AI that are present in the LVAD population at a given period of time = At 1 year of CF-LVAD support: 25-50%
  - Cumulative incidence = measures the disease (at least moderate AI) frequency during a period of time = 30% at 3 years
- Patients on longer duration of CF-LVAD support → worse AI than those on shorter duration
- The AI development is:
  - time dependent
  - progressive with longer CF-LVAD support duration

ETIOLOGY OF AI

- CF-LVAD support → pressure generation during IVCT ≤ ≤ pressure in the Ao → AoV closed → AoV fusion due to fibrinous degeneration of the aortic cusps on the root side
- CF-LVAD support → pressure generation during IVCT ≤ ≤ pressure in the Ao → AoV closed → "disuse theory" → thrombus formation on the LVOT/Aor root → leaflet fusion

- Proximal Ao cannulation → high velocity retrograde flow → hitting the root side of the aortic valve → high shear stress → AV damage → Ao sinus dilation (SMC apoptosis)
- Proximal Ao cannulation → high retrograde pressure → valve malcoaptation during both S/D
Recirculation with AI
LV → LVAD → Aorta (systemic circulation) → LV →
Regurgitant Flow → Systemic Flow
Asymptomatic mild to moderate AI → asymptomatic
moderate to severe AI → ↑LVd at fixed pump
speed → ↑LVEDP → left-sided HF symptoms →
reactive PHT → right-sided HF symptoms
THERAPY OF AR

Table 2: Pros and Cons of Preventive and Treatment Strategies for Bi- Valve AI

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Decrease pump speed to permit at least intermediate Ao opening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Diathermic therapy to maintain occluder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Increase pump speed with concomitant diagnosis right heart catheterization if refractory does not fit above measures</td>
<td>Can fail pump speed setting to pump speed associated with PMV reduction</td>
<td></td>
</tr>
<tr>
<td>Associated with reduction in HF symptoms and signs</td>
<td>Hemodynamic deterioration, high heart rate, or high cardiac output</td>
<td></td>
</tr>
</tbody>
</table>

No study to date → impact on short/long-term survival → with echo-guided device management → to promote AoV opening

THERAPY OF AR

DE-NOVO AI – AFTER CF-LVAD IMPLANT

NEW PERCUTANEOUS-BASED VALVE REPLACEMENT

A

Surgical Aortic Valve

B

Amplatzer™ Occluder
THERAPY OF AR
DE-NOVO AI – AFTER CF-LVAD IMPLANT
NEW PERCUTANEOUS-BASED VALVE REPLACEMENT

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~25% incidence of GIB reported in patients with HMII (vs. > than for pulsatile pumps)
Algorithm for evaluating and managing suspected gastrointestinal bleeding in continuous-flow ventricular assist device patients.

Adjunct medical therapy (? Not really proven): octreotide/primarin/danazol/doxycycline (inhibits ADAMTS 13 – levels > 10x than the usual AB use)

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PUMP THROMBOSIS

Pump thrombosis is a dreaded complication of long-term implantable ventricular assist devices
PUMP THROMBOSIS

- Pump thrombosis:
  - 6-12% - for HMII
  - 8% - for HVAD
  - 0% - for HMIII (at 3 and 6 months)

VAD THROMBOSIS

What can trigger the thoughts for VAD thrombosis?

1) Clinical data:
   - CHF/ SOB/ Cardiogenic shock
2) LVAD parameters:
   - Interplay between Pulsatility Index (PI) and Power (P)
2) Laboratory results:
   - LDH/ haptoglobin/ free plasma Hb (FP Hb)
3) Echo data:
   - Ramp study
VAD Thrombosis
Interplay between Pulsatility Index (PI) ↓ and Power (P) ↓
Outflow cannula obstruction

VAD Thrombosis
Interplay between Pulsatility Index (PI) ↓ and Power (P) ↓
Outflow cannula obstruction

VAD THROMBOSIS
INTERPLAY BETWEEN PULSATILITY INDEX (PI) ↓ AND POWER (P) ↑
INFLOW CANNULA/

"young clot" → acute pump failure → seen around the inlet and outlet stators → serum proteins (+) fibrin (+) RBC breakdown products
- cellular

"chronic clot" → partial pump obstruction → seen mostly in the rotor → fibrin (+) RBC breakdown products (+) platelet aggregates
- few cellular infiltrates → mostly macrophages
Unexplained abrupt increase in left ventricular assist device thrombosis

Occurrence of confirmed pump thrombosis increased steeply from: March 2011 from 2.2% at 3 months after implantation to 8.4% by January 2013 (almost 4x) — Similar pattern at all 3 institutions

837 pts → 895 LVADs from 2004 to 2013 → 72 pump thrombosis in 66 pts

Before 3/1/2011 — median time from implant to thrombosis was ~ 18.6 mths

After 3/1/2011 — median time from implant to thrombosis was ~ 2.7 mths

High LDH levels doubled within the week before LVAD thrombosis

OHT: 11 pts (1 died)
Pump exchange (21) (1 died)
Medical therapy: 40 pts (19 died)

WHY SUDDEN INCREASED IN PUMP THROMBOSIS?

• No bridge with heparin post implant – coumadin started in POD# 2-3

• Patient factors not included:
  - pro-coagulant genetic factors
  - sepsis
  - other RF for pro-coagulant state

• Is this a real trend towards increased pump thrombosis?
Hemolysis = the destruction of red blood cells before their normal life span is up

- Pump bearing forces → destruction of RBCs → liberation of Hb in plasma → free plasma Hb (FP Hb) (> 0.04) → FP Hb binds haptoglobin (protein produced in the liver) → the rate of haptoglobin production < than elimination → ↓ haptoglobin (<b>)

- RBC destruction → liberation of LDH in plasma → ↑ LDH (> 600) (but is nonspecific)

- Obs. LDH is a “screening test” for hemolysis - we MUST HAVE confirmatory tests for pump thrombosis

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VAD Thrombosis

LDH/ haptoglobin/ free plasma Hb (FP Hb)

VAD Thrombosis

Ramp study

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Nonnormal loading conditions due to AI or elevated MAP may result in false positive ramp tests
UPDATE ON PUMP THROMBOSIS 2015
ANALYSIS OF ~ 10,000 HMII IMPLANTS SINCE 2008
INTERMACS 7TH

- The small but progressive increase in the incidence of pump thrombosis observed between 2010 and 2013 with the HMII has reversed in the first half of 2014, returning to the levels seen in 2011, but not to the low levels observed in 2008 to 2010

- Survival with HMII: > 80% at 1 year and > 70% at 2 year
PUMP THROMBOSIS

Pump thrombosis is a dreaded complication of long-term implantable ventricular assist devices.

VENTRICULAR DEVICE INNOVATION DRAMATICALLY IMPROVES OUTCOMES FOR PATIENTS WITH ADVANCED HEART FAILURE

HeartMate XVE
FDA Approved 2008

HeartMate II
FDA Approved 2001

HeartMate 3
Investigational

Inflow Conduit
Inserted into the apex of the left ventricle

Outflow Graft
Anastomosed to the ascending aorta

Preload Dependent
Volume is important for VAD patients

Afterload Sensitive
Maintain blood pressure < 90 mmHg

HeartMate 3 Design Features
- Inflow Conduit
- Outflow Graft
- Driveline
- Blood Pump

Diagrams showing the placement of inflow and outflow conduits, indicative of an implantable ventricular assist device.
Three important feature design:
1) True magnetic levitation
2) Artificial pulse
3) Internal sintering with textured titanium microsphere to allow for a biocompatible surface

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1) True magnetic levitation
2) Artificial pulse
3) Internal sintering with textured titanium microsphere to allow for a biocompatible surface

Augmenting the pulsatility – might benefit in AI/bleeding/thrombogenesis
FULLY MAGNETICALLY LEVITATED
LEFT VENTRICULAR ASSIST SYSTEM FOR
TREATING ADVANCED HF
A Multicenter Study

Jean Reimbold, MD, FACC; Florence Beaulieu, MD, Fibrin; Tony Sun, MD, Fibrin; David Jones, MD; Daniel Johnson, MD; Nicholas Soper, MD, Fibrin; Liza Caruthers, MD, Fibrin; Arthur Price, MD, Fibrin; and Michael Montague, MD; Nicholas Soper, MD, Fibrin; Liza Caruthers, MD, Fibrin; Arthur Price, MD, Fibrin; and Michael Montague, MD, Fibrin;

ABSTRACT

BACKGROUND: The HeartWare left ventricular assist system (LVAS) is intended to provide long-term support to patients with advanced heart failure. The centrifugal flow pump is designed for enhanced hemocompatibility by incorporating a magnetically isolated rotor with wide blood flow paths and an artificial pulse.

OBJECTIVES: The aim of this single-arm, prospective, multicenter study was to evaluate the performance and safety of this LVAS.

METHODS: The primary endpoint was 3-month survival compared with INTERMACS Registry data for mechanically assisted circulatory support (Macs). Patients were adults with ejection fraction < 20%, cardiac index < 2.2 L/min/m², without inotropic or vasoconstrictor-dependent on optimal medical management, or listed for transplant.

RESULTS: Fifty patients were enrolled at 10 centers. The indicators for LVAS support were bridge to transplantation in 14% or destination therapy in 86%. At 6 months, 96% of patients continued on support, 4% received a transplant, and 4% died. Thirty-day mortality was 2% and 3-month survival was 83%, which exceeded the 88% performance goal. Support with the fully magnetically levitated LVAS significantly reduced mortality risk by 86% compared with the Seattle Heart Failure Model-predicted survival of 36% (p = 0.0099). Key adverse events included separation for bleeding (4%), aortic stenosis (10%), gastrointestinal bleeding (9%), and delirium (modified delirium score: 10% of patients). There were no pump exchanges, pump malfunctions, pump thrombosis, or hemolysis events. New Heart Association classification, 6-min walk test, and quality-of-life scores showed progressive and sustained improvement.

CONCLUSIONS: The results show that the fully magnetically levitated centrifugal flow chronic LVAS is safe, with high 30-day and 3-month survival rates, favorable adverse event profile, and improved quality of life and functional status. (HeartWare P3 Clinical Investigation Plan [HVI-012] M21110210; NCT02171323) (J Am Coll Cardiol 2015;65:2029-89) © 2015 by the American College of Cardiology Foundation.
The MOMENTUM 3 U.S. IDE Clinical Trial is a prospective, multi-center, unblinded randomized study comparing the HeartMate 3 LVAS to the HeartMate II LVAS in advanced stage heart failure patients (class III/IV) as a non-inferiority trial.

**Primary Endpoint**

- Composite of survival to transplant/ recovery/ 6/ 24-months of LVAD support free of debilitating stroke or reoperation to replace the pump.