Bridge to Life-
Mechanical Circulatory Support

Mechanical Circulatory Support
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Mechanical Circulatory Support (MCS) @ UCSF

VAD / ECMO Alphabet Soup
- VAD LVAD BTT DT BTR ECMO ECLS INTERMACS RVAD CHF RHF MCS MCSD
- BTC NHLBI CMS VT VF

HELP!!!!
Introduction of the Heart Lung machine more than 50 years ago proved in principle heart and lung function can be replaced, albeit for short periods.

Neither approach is well suited to providing full cardiac replacement—even temporarily.

Full cardiopulmonary support outside of the operating room became available with extracorporeal membrane oxygenation, first used successfully in 1972.

More than 16 million people currently diagnosed with heart failure in Europe and US, where its prevalence averages 2.5% of the population. (*)

Disease affects men and women equally, but differences in prevalence between races.

Incidence HF increases significantly after age 65, and the population in this age group will double in the next 20 years.

Heart Failure

- Estimated 0.2% of persons over 45 years of age in the US, or nearly 200,000 people, may have severe HF and reach a stage at which medical therapy is insufficient to sustain acceptable level of heart function.
- Investigators and medical-device industry have been pursuing development of mechanical support for more than 4 decades.

Significant advances in the treatment of Heart Failure, especially pharmacological therapy, but the mortality with either systolic or diastolic heart failure has increased to an average of 60% at 5 years after diagnosis and may be as high as 80% at one year in the most advanced forms.


Why MCS Devices?

- An increasing number of patients become unresponsive to optimal medical therapy.
- Severe shortage of donor hearts limits the use of transplantation as a solution to the expanding number of patients.

General Definition of MCS

- Providing advanced therapies (Ventricular Assist Devices - VADs or extracorporeal life support (ECLS) to assist failing hearts (or lungs).
- Mechanical Circulatory Support (MCS) Devices are defined as mechanical pumps assisting or replacing the left, right, or both ventricles of the heart to pump blood.
- While the term Left Ventricular Assist Device (LVAD) indicates left ventricular support, the broader term MCS has been adopted to include LV, RV, and biventricular devices as well as complete heart replacement devices.
Construction

- Progress has been intermittent but has accelerated in the past 10 years, with Mechanical circulatory support devices (MCS) reaching an impressive degree of sophistication and complexity owing to the contributions from clinicians, engineers, scientists, industrialists, and others.

MCS Milestones

*Evolved significantly in past 25 years*

**Three major milestones to date:**
1. Conversion from external to internal placement of the devices
2. Conversion from pneumatic to electrical power
3. Transition from pulsatile to continuous flow devices.

Materials and Labor

- Types of devices
- Indications (BTT, BTC, DT)

Specific Forms

- Over the past two decades, MCS devices have been developed at a rapid pace with the goal of supporting patients with advanced heart failure as a bridge to cardiac transplantation (BTT), a bridge to recovery (BTR), and an alternative to transplantation (destination therapy or DT).
- Current generation of devices provides a differentiated spectrum of circulatory support, ranging from short to intermediate and long term duration.
- On a technical level, the device positions range from paracorporeal pumps to completely implantable systems.
Cardiac Blood Pump Technology Uses

Mechanical Circulatory Support Devices

Acute/Short-Term (days/weeks)
Mid-Term – Long Term (months – years)

Bridge to Recovery
Bridge to Transplant
Permanent DT Therapy

Blood Pump Technology Landscape

Acute/Short-Term (days/weeks)
Mid-Term – Long Term (months – years)

Pulsatile
Continuous

Pulsatile
Continuous

Pulsatile
Continuous

Blood Pump Technology Landscape

Clinical Factors Involved in the Selection of a Ventricular Assist Device.

Clinical Factors Involved in the Selection of a Ventricular Assist Device

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‡The HeartMate XVE is the only device approved by the Food and Drug Administration for destination therapy. However, approval of other devices for this indication is anticipated.

Variety of Devices-3 Classifications

- Centrifugal
- Volume-displacement
- Axial flow

Mechanisms of Action of Cardiac-Support Devices.


**Centrifugal Pumps**

- Typically consist of cone-shaped rotor contained within a plastic or metal housing.
- Blood flows into pump at the cone’s apex and exits at the edge of the base.
- Spinning of the rotor creates a centrifugal force that is imparted to the blood—creating a constant, nonpulsatile flow.
- Biomedicus (Medtronic)—one of the earliest
- CentriMag (Levitronics)

**Volume-displacement Pumps**

- Consists of a chamber or sac that fills either passively or by suction applied during chamber expansion.
- Sac is compressed by externally applied pressure, causing ejection of blood.
- These pumps mimic the cyclic systole and diastole of the heart and generate pulsatile blood flow.
- They include an inflow valve (bioprosthetic or mechanical), which allows unidirectional flow into the device and prevents regurgitation during mechanical systole,
- and an outflow valve to prevent regurgitation during mechanical relaxation.
- Examples include: HeartMate, XVE, Thoratec PVAD and IVAD, Abiomed AB5000.

**Volume-displacement Pumps (continued)**

- The Total Artificial Heart is another form of Volume-displacement device.
- TAH generate pulsatile flow through the filling and compression of an internal chamber.
- During implantation, the patient’s own left and right ventricles are removed and the device is inserted orthotopically.
- Examples are the CardioWest (Syncardia) and Abiocor (Abiomed)
Axial-Flow Pumps

- These devices contain an impeller: a rotor with helical blades that curve around a central shaft.
- The spinning of the impeller draws blood from the inflow cannula through the device to the outflow cannula.
- Examples: Jarvik 2000 (Jarvik Heart), MicroMed DeBakey (MicroMed), HeartMate II (Thoratec).

Percutaneous Devices

- Most MCS devices require cardiac surgery.
- Some percutaneous devices can be placed in the cath lab.
- Examples: Impella pump (Abiomed)- an axial flow pump located on the distal end of a catheter.
- Inserted in the femoral artery and advanced retrograde into left ventricle.
- Another percutaneous device: TandemHeart (Cardiac Assist), extracorporeal centrifugal pump whose inflow catheter is placed percutaneously in the left atrium through a transeptal approach and whose cannula is placed in the femoral artery.

3 Distinct Clinical Indications

- Bridge to Transplant
- Destination Therapy
- Bridge to Decision/ Candidacy (Temporary Support)

Surgical Intervention: VADs

- Post-Cardiotomy Recovery
  - Mechanical support for patients who are unable to be weaned from the cardio/pulmonary by-pass pump.
- Bridge-to-Transplantation
  - Mechanical support of the heart for patients awaiting transplant.
  - Improve post-transplant outcomes.
- Bridge-to-Recovery
  - Mechanical support allowing patients to recover sufficient myocardial function to allow device explantation.
- Destination Therapy
  - Mechanical support for patients who are ineligible for cardiac transplantation due to age, malignancy or co-morbidities.
Acute / Short Term Devices Available

Indications: BTR or Bridge to Decision

- ECMO (BioMedicus)
- Tandem Heart
- Abiomed BVS 5000i / AB5000
- CentriMag
- Impella 2.5 and 5.0

Reasonable Evidence to Justify Bridge-to-Decision concept

- Patients in refractory cardiogenic shock with contraindications for permanent VAD can be:
  1. Supported safely with temporary support
  2. Be bridged to a permanent VAD once contraindications for permanent VAD no longer exist
  3. Suitability for bridge to transplant ascertained while on initial temporary support

Background

- High mortality for acute cardiogenic shock refractory to inotropes / IABP / revascularization
- Use of permanent VADs an option
- Difficulties with permanent VADs –
  1. Major surgery in unstable setting
  2. Expensive option with often futile results
  3. Often need for biventricular support

Which ‘Acute’ Pump to Use?

- What was the pre-op status of the heart?
- Do you need uni-VAD or BiVad?
- Likely plan on recovery, and quickly?
- AB Ventricle
- Pulsatile better than continuous?
- Abiomed BVS
- CentriMag
- Do I think there is a ‘smaller’ chance at recovery?
- Is patient a ‘potential’ transplant candidate?
- Ambulation
- Longer term support?
- Potential for home discharge
- Consider
- PVAD / IVAD
Treatment Options

1. Insert IABP and continue aggressive medical management
2. Take patient immediately to OR
   - Temporary mechanical support (Biomedicus / CentriMag, Abiomed BVS, ECMO, Impella)
3. Take patient to Cath lab – percutaneous VAD support
4. Do nothing and allow patient to die.

Increased Role for Temporary Support

1. What is the ideal device?
2. Surgical or percutaneous implantation
3. Uni- or biventricular support?
4. When to institute temporary support?
5. For how long?
6. When to transition to a permanent VAD?

Treatment Classifications

- Bridge to Transplant
- Destination Therapy
- Bridge to Recovery

Mid to Long Term Cardiac Devices (months-years)

Pulsatile vs Continuous Flow

- Thoratec PVAD
- Thoratec IVAD
- HeartMate XVE
- HeartMate II
- AB5000
What are the ‘Approved’ Pumps Approved For?

- **PVAD / IVAD**
  - Post-cardiotomy
  - Bridge-to-transplant

- **Destination / Post-Transplant**
  - Support for recovery / short-term use
  - Clinical use up to 6 hours
  - RVAD support up to 30 days (CentriMag only)

- **Destination B**
  - Bridge-to-transplant
  - Destination Therapy

- **Bridge**
  - Bridge to transplant
  - Destination therapy

- **Abiomed BVS/ AB Ventricle**
  - Support for recovery / short-term use

- **CentriMag / Impella 2.5 / Tandem Heart**
  - Clinical use up to 6 hours
  - RVAD support up to 30 days (CentriMag only)
  - Hemodynamic parameters that might include:
    - Cardiac index (CI) of < 2.0 L/min/m2
    - Left atrial pressure (LAP) or pulmonary capillary wedge pressure (PCWP) > 20mmHg (if 15-20 patient still with severe effort intolerance)
    - Systolic blood pressure of 90 mmHg or less
    - MVO2 < 12

- **Heartmate II**
  - Bridge to transplant
  - Destination Therapy

- **Heartmate XVE**
  - Bridge to transplant
  - Destination therapy

- **Syncardia Cardiowest**
  - Bridge to transplant

Why can’t I use it ‘off-label’?

- Hospital may not get reimbursed without appropriate prior authorization

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Bridge to Transplant Patient Selection

- Irreversible ventricular failure with reversible end organ dysfunction with compromised hemodynamic parameters that might include:

  - Cardiac index (CI) of < 2.0 L/min/m2
  - Left atrial pressure (LAP) or pulmonary capillary wedge pressure (PCWP) > 20mmHg (if 15-20 patient still with severe effort intolerance)
  - Systolic blood pressure of 90 mmHg or less
  - MVO2 < 12

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BTT Patient Selection

- Must be approved cardiac transplant candidate.
- Compromised hemodynamic parameters despite maximal pharmacological support. Receiving significant inotropic and/or intra-aortic balloon pump support.
- On maximum attempted medical therapy as deemed by team of advanced heart failure physicians (failure to tolerate ACE-inhibitors due to systemic blood pressure constraints, significant worsening of renal function; failure to tolerate beta-blockade at survival enhancing doses when B-B started at reasonable hemodynamic profile)

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BTT Patient Selection

- BSA of at least 1.3m2
- Recent LVEF < 25 %
- Pulmonary hypertension that is not prohibitive to heart transplant unless bridged with VAD. (need to determine if patient will tolerate LVAD only in terms of RV failure. Trial on IABP with monitoring, echocardiographic RV function, trial with inotropic and vasodilator support.
- Post myocardial infarction with all possible pharmacological, IABP and/or inotropic support sufficient to sustain life.
### Destination Therapy Criteria

**Inclusion Criteria:**

- **Inotrope dependent**  
- Failed weaning attempts
- Tolerating maximum medical therapy with  
  \[ \text{VO}_2 < 10 \ (\text{if not able to tolerate beta-blockers, then VO}_2 < 12) \]

**Exclusion Criteria:**
1. Renal dysfunction
   - a. Cr > 3.0
2. Hepatic failure
   - a. INR > 2.5
   - b. ALT, AST > 3x control
3. BMI < 18 and > 35, or BSA < 1.5 m²
4. FEV₁ < 1 without intrinsic lung disease
5. PVR > 8 wood units
6. Severe right ventricular dysfunction with expectation for RV mechanical support.
7. Previous neurological event
8. High surgical risks (i.e. ascending aorta calcification), > 2 cardiac surgeries.
9. Comorbidity with life expectancy of <2 years (i.e. malignancy)

### Device Selection

- **What devices do you have?**
- **What is the ‘expected realistic’ end-point of support?**
  - Recovery?
  - Transplant?
  - DT?
- **If the ‘expected realistic’ end-point is not achieved, what would the options be?**
  - No recovery – Transplant?
  - No recovery – DT?
  - Can one device address both of the above?

### Device Selection

**Issues to consider**

- Expected duration of support
- Type of support needed (R,L, BiV)
- Cost
- Device-related morbidity
- Patient-related issues (size)

### Timeliness is Critical

**Patient Referral Indicators**

- Ideal time for referral is when patient progresses from stable heart failure to advanced heart failure
- Clinical risk factors for mortality
  - Patients who are NYHA Classification III or IV, with more than one of the indicators below, should be considered for referral for a MCS/cardiac transplantation evaluation at a tertiary care center
    - Walk < 1 block (300m) without dyspnea
    - Serum sodium < 136 mmol/L
    - BUN > 40 mg/dL or Serum Creatinine > 1.8 mg/DL
    - Intolerant or refractory to ACE/ARB/BB
    - Diuretic dose > 1.5 mg/kg/d
    - One heart failure-related hospital admission in the past six months
    - QRS > 140 ms without or refractory to CRT therapy
    - Hematocrit < 35%

When Should the MCS Discussion Begin?

The Right Time for VAD Implantation

Key to Survival

Operative Risk Death

Successful Implants

Futile Implants

1-Year Survival 19%

1-Year Survival 69%

Worsening of nutritional state, end-organ and RH function

The Right Time for VAD Implantation

Important to recognize the risk factors for increased mortality on medical therapy.

Important to refer a patient with multiple risk factors for evaluation and consideration of new therapies.

General Guidelines for Patient Selection

- Patients failing optimal medical and alternative surgical therapy.
- Prognostic Scoring Systems (pt. selection is driven by anticipated ratio of therapeutic risks vs potential benefits.)-Seattle Heart failure Model
- Age
- Size/Obesity/Nutrition
- Renal failure
- Hepatic failure
- Right heart failure
- Inotrope dependence

Treatment of Advanced HF

- Few therapeutic options for advanced HF (VADs, transplant, inotropes, and palliative care)

- Important to recognize the risk factors for increased mortality on medical therapy.

- Important to refer a patient with multiple risk factors for evaluation and consideration of new therapies.
**INTERMACS / Oversight**

- Interagency Registry for Mechanical Circulatory Support
- National Heart, Lung, and Blood Institute (NHLBI), FDA, Center for Medicaid & Medicare Services (CMS), and the advanced heart failure/MCS professional community, began prospective patient enrollment and data collection on June 23, 2006.

**INTERMACS**

- Ongoing evolution of both strategies for device application and the types of available devices has continued to refine the landscape of MCS.
- INTERMACS only collects data on devices that are FDA approved for clinical use.

**INTERMACS**

- Between June 2006 and March 31, 2009, 1,420 pt entered into INTERMACS database.
- Demographics (79% male, 21% female)
- Age at implant (mean 52, range 4.5-79.9)
- LVAD (1158); RVAD (18); BiVAD (193); TAH (51)
- Types of LVAD (Pulsatile 48%: intracorporeal 42%, paracorporeal 6.2%; Continuous flow 51.6%)

**INTERMACS level at Implant for 1092 primary LVAD**

1. Critical cardiogenic shock (30%)
2. Progressive decline (40%)
3. Stable but inotrope dependent (15.4%)
4. Recurrent advanced heart failure (9.7%)
5. Exertion intolerant (1.9%)
6. Exertion limited (1.1%)
7. Advanced NYHA III (1.8%)
**Timeframe for Definitive Interventions based on INTERMACS classifications**

- **AHA/ACC classification**
  - Stage C
  - Stage D

- **NYHA classifications**
  - Class III
  - Class IIIb/IV
  - Class IV

- **INTERMACS classifications**
  - 7
  - 6
  - 5
  - 4
  - 3
  - 2
  - 1

- **Brief descriptions**
  - Advanced NYHA Class III
  - Exertion limited/"walking wounded"
  - Exercise intolerant/"house-bound"
  - Recurrent decompensation/"frequent flyer"
  - Stable but inotropic-dependent/"dependent stability"
  - Progressive decline/"sliding on inotropes"
  - Critical cardiogenic shock/"crash and burn"

- **Timeline for definitive intervention**
  - Transplantation or circulatory support not currently indicated
  - Variable, depends upon nutrition, organ function, and activity
  - Elective over weeks to months as long as treatment of episodes restores stable baseline, including nutrition
  - Elective over a few weeks
  - Needed within a few days

- **Survival and Causes of Death**
  - Actuarial survival of the primary LVAD cohort: 83% at 6 months, 74% at 1 yr, 55% at 2 yrs.
  - **Causes of Death early:**
    - Cardiac failure 30.4% (RHF and VT/VF)
    - MSOF (15.9%)
    - CNS event (11.6%)
  - **Causes of death later 1 month:**
    - Cardiac failure 22%
    - Infection 16.2%
    - CNS event 14.1%

- **INTERMACS Summary**
  - Transitional period from pulsatile pumps to continuous flow pumps
  - Fluctuations in designation of device strategies as BTT, BT candidacy BTC, and DT.
  - Evolving indications, changing patient profiles, and refinement of device strategies in the developing landscape of MCS.

- **Conclusions**
  - MCS as a therapeutic option in heart failure as a bridge to decision, BTT, or DT.
  - MCS for “crash and burn” patients is not effective.
  - We’ve come a long way!
  - We have a long way to go!!!
The Future ???

Future Directions

- One of the greatest strengths of MCS is that it provides an ideal platform to apply adjunctive therapies directly targeting the causes of disease and potentially leading to myocardial regeneration and restoring heart function. *


Adjunctive Therapy

- Stem Cell Therapy.
- Gene therapy to manipulate critical genes differentially regulated in advanced heart failure.
- Cardiac tissue engineering

Conclusions

- Optimal timing for MCS implantation to increase survival and minimize morbidity remains unclear.
- Complicated by heterogeneous mix of patients’ characteristics, intent of therapy, and the different types of devices available.
- Medical therapy, transplantation, and other alternative surgical therapies continue to evolve as well.
- Currently, patients failing outpatient oral regimens should be considered for VAD implantation prior to the onset of end organ dysfunction.
Better Bridges

- Field of MCS Therapy is expanding.
- New generation of pumps. (outcomes and device durability).
- Development of validated risk stratification models will lead to improved patient selection and timing of device implant.
- Clinical trials are needed to demonstrate the potential of all these promising therapies.