Advanced Heart Failure

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Section of Heart Failure and Cardiac Transplantation
Disclosures

• No personal disclosures or relationships
• Recognize the indications for advanced therapies in heart failure (HF).
• Review the risks and benefits of cardiac transplantation and mechanical circulatory support (MCS).
• Review the management of patients following cardiac transplantation.
• Assess the role of other surgical options for the management of chronic HF.
Epidemiology-Stage D Heart Failure

• ~3.0-3.5 million people in the United States who have systolic HF, there are 150,000-250,000 patients ages <75 years who have advanced HF with NYHA class IIIb and IV symptoms

• Among patients with Stage C HFrEF, 4.5% progress to Stage D HF each year, with earlier progression among black and nonischemic patients (Kalogeropoulos, JACC HF 2017)
• in a cohort from Olmsted County, Minnesota, the prevalence of stage D HF (defined as a functional capacity able to perform <2 METS) was only 0.2%

• Difficult to accurately estimate the incidence and prevalence as this is heterogeneous class, with high morbidity/mortality, often underdiagnosed.
Definition

• Advanced or stage D HF describes the progression of the HF syndrome into a condition characterized by severe symptoms despite optimal medical, surgical, and device therapy.

• Stage D HF includes patients with HFrEF and also with HFpEF who have become refractory.

• Stage D HF is usually a chronic condition that with time becomes refractory to optimal therapies, but it also involves patients who present with acutely refractory HF.
In the REMATCH trial, stage D patients had 75% mortality at 1 year and virtually no survival at 2 years.

In the INTREPID trial (NOVACOR VAD) had survival rates of 22% at 6 months and 11% at 1 year.

In a population-based sample from Olmstead County, stage D heart failure was associated with only 20% 5-year survival.
Definition of Stage D Heart Failure

1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA class III or IV)
2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or reduced cardiac output at rest (peripheral hypoperfusion)
3. Objective evidence of severe cardiac dysfunction shown by at least 1 of the following:
   a. LVEF <30%
   b. Pseudonormal or restrictive mitral inflow pattern
   c. Mean PCWP >16 mm Hg and/or RAP >12 mm Hg by PA catheterization
   d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes
4. Severe impairment of functional capacity shown by 1 of the following:
   a. Inability to exercise
   b. 6-Minute walk distance ≤300 m
   c. Peak $V_\text{O}_2$ <12 to 14 mL/kg/min
5. History of ≥1 HF hospitalization in past 6 mo
6. Presence of all the previous features despite “attempts to optimize” therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated
Determining prognosis: Cardiopulmonary exercise testing

Class I:
1. A maximal cardiopulmonary exercise (CPX) test is defined as one with a respiratory exchange ratio (RER) >1.05 and achievement of an anaerobic threshold on optimal pharmacologic therapy (Level of Evidence: B).
2. In patients intolerant of a beta-blocker, a cutoff for peak VO₂ of ≤14 ml/kg/min should be used to guide listing (Level of Evidence: B).
3. In the presence of a beta-blocker, a cutoff for peak VO₂ of ≤12 ml/kg/min should be used to guide listing (Level of Evidence: B).

Class IIa:
1. In young patients (<50 years) and women, it is reasonable to consider using alternate standards in conjunction with peak VO₂ to guide listing, including percent predicted (≤50%) peak VO₂ (Level of Evidence: B).

Class IIb:
1. In the presence of a submaximal CPX test (RER <1.05), use of the ventilation equivalent of carbon dioxide (VE/VO₂) slope of >35 may be considered to guide listing (Level of Evidence: C).
2. In obese (body mass index >30 kg/m²) patients, adjusting peak VO₂ to lean body mass may be considered. A lean body mass-adjusted peak VO₂ of <19 ml/kg/min can serve as an optimal threshold to guide prognosis (Level of Evidence: B).

Class III:
1. Listing patients based solely on the criterion of peak oxygen consumption (VO₂) measurement should not be performed (Level of Evidence: C).
Indicators of Stage D HF to trigger evaluation for Advanced Therapies

- Need for IV inotropic therapy for symptomatic relief or maintain end-organ function
- Peak VO₂ <14 ml/kg/min or <50% of predicted
- 6-minute walk distance <300 meters
- ≥2 HF admissions in 12 months
- >2 unscheduled visits (e.g., ED or clinic) in 12 months
- Worsening right HF and secondary pulmonary hypertension
- Diuretic refractoriness associated with worsening renal function
- Circulatory-renal limitation to RAAS Inhibition or beta-blocker therapy
- Progressive/persistent NYHA functional class III – IV symptoms
- Increased 1-year mortality (e.g., 20 - 25%) predicted by HF survival models (e.g., SHFM, HFSS)
- Progressive renal or hepatic end-organ dysfunction
- Persistent hyponatremia (serum sodium <134 mEq/L)
- Recurrent refractory ventricular tachyarrhythmias; frequent ICD shocks
- Cardiac cachexia
- Inability to perform ADL
### INTERMACS Classification

<table>
<thead>
<tr>
<th>ADULT PROFILES</th>
<th>Current CMS - DT Functional Indication</th>
<th>IV INO*</th>
<th>Official Shorthand</th>
<th>NYHA CLASS Assumed</th>
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* Intravenous inotropic therapy only approved for refractory Class IV symptoms

Mortality and symptomatic benefit from VADs
How to estimate prognosis in Stage C HF?

**Calculation of Heart Failure Survival Score**

<table>
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<tr>
<th>Clinical Characteristic</th>
<th>Value (X)</th>
<th>Coefficient (β)</th>
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<td>Serum sodium (mg/dL)</td>
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- **HFSS and SHFM should be used in outpatients**
- **They underestimate risk**
Listing criteria for Heart transplantation

- Cardiopulmonary exercise testing: VO2 max <14ml/kg/min if patients intolerant to BB; <12ml/kg/min in the presence of BB; or <50% of predicted VO2 in young patients (50yrs) and women.
- BMI <35
- PVR <3, TPG <15
- Age <70
- Diabetes well controlled
- Absence on neoplasm
- Psychosocial support
Contraindications

ISHLT guidelines recommend a vasodilator challenge when the (PASP) is ≥50 mm Hg, the TPG is ≥ 15mm Hg, or pulmonary vascular resistance (PVR) is ≥3 Wood units

- Noncompliance with medical regimen
- Active substance abuse
- Severe symptomatic cerebrovascular disease
- Severe organ dysfunction (lung, kidney, liver, coagulopathy)
- Active infection
- Active mental illness
- Inadequate social support
- Fixed, severe pulmonary hypertension
- Morbid obesity (BMI > 35 kg/m2)
- Age > 70 years
- Recent or uncured malignancy
Transplant Listing

• Each US transplant center is part of the nationwide United Network of Organ Sharing (UNOS), which is divided into eleven regions, each with specific local organ procurement organizations (OPO).
• Patients are listed by OPO, transplant center, and ABO blood type, and prioritized by medical urgency (UNOS Status).
Transplant Listing

<table>
<thead>
<tr>
<th>Status</th>
<th>Current Criteria</th>
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| 1A     | I. Mechanical Circulatory Support  
|        | 1. 30 day elective ventricular assist device (VAD) time  
|        | 2. Total artificial heart  
|        | 3. Intra-aortic balloon pump  
|        | 4. Extracorporeal membrane oxygenation  
|        | II. VAD with complications  
|        | III. Mechanical ventilation  
|        | IV. Pulmonary artery catheter with 1 high dose or multiple lower dose inotropes  
|        | V. Exception granted by regional review board |
| 1B     | I. Mechanical circulatory support beyond 30 day interval  
|        | II. Continuous intravenous inotropic support  
|        | III. Exception granted by regional review board |
| 2      | I. Those who do not meet criteria for status 1A or 1B |

<table>
<thead>
<tr>
<th>Status</th>
<th>Criteria</th>
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</table>
| 1      | I. ECMO (up to 14 days of support)  
|        | II. Non-dischargeable BIVAD or RVAD  
|        | III. Mechanical circulatory support with life-threatening ventricular arrhythmia |
| 2      | I. Intra-aortic balloon pump (up to 14 days of support)  
|        | II. Acute percutaneous endovascular circulatory support device (up to 14 days of support)  
|        | III. Ventricular tachycardia/ventricular fibrillation, mechanical support not required  
|        | IV. Mechanical circulatory support with device malfunction/mechanical failure  
|        | V. Total artificial heart  
|        | VI. Dischargeable BIVAD or RVAD |
| 3      | I. LVAD for up to 30 days  
|        | II. Multiple inotropes or single high-dose inotropes with continuous hemodynamic monitoring (up to 14 days of support)  
|        | III. Mechanical circulatory support with device-related complications such as infection, hemolysis or thromboembolism  
|        | IV. Mechanical circulatory support with device infection  
|        | V. Mechanical circulatory support with thromboembolism |
| 4      | I. Diagnosis of congenital heart disease (CHD)  
|        | II. Diagnosis of ischemic heart disease with intractable angina  
|        | III. Diagnosis of hypertrophic cardiomyopathy  
|        | IV. Diagnosis of restrictive cardiomyopathy  
|        | V. Stable LVAD candidates after 30 days  
|        | VI. Inotropes without hemodynamic monitoring  
|        | VII. Diagnosis of amyloidosis  
|        | VIII. Retransplant |
| 5      | Combined organ transplants |
Survival post Transplant

Year of transplant:  
- 1982-1991 (N=21,478)  
- 1992-2001 (N=40,077)  
- 2002-2008 (N=26,039)  
- 2009-6/2015 (N=26,164)  

Median survival (years):  
- 1982-1991: 8.6  
- 2002-2008: 12.2  
- 2009-2015: NA  

All pair-wise comparisons significant at p < 0.05
Survival according to MCS type

Survival (%)

Years after transplant

Type of support at transplant:
- Pulsatile flow LVAD (N=1,217)
- Continuous flow LVAD (N=5,753)
- ECMO (N=164)
- No Inotropes/No LVAD (N=6,970)
- Inotropes/No LVAD (N=7,679)

p < 0.05:
- all comparisons with ECMO
- inotropes/No LVAD vs. Pulsatile flow LVAD
Survival according to Donor age

Donor age:
- 0-10 yrs (N=297)
- 11-39 yrs (N=69,330)
- 40-59 yrs (N=34,101)
- 60+ yrs (N=1,855)

Median Survival (years):
- 0-10 yrs: 10.6
- 11-39 yrs: 11.5
- 40-59 yrs: 9.7
- 60+ yrs: 7.4

All pair-wise comparisons significant at p < 0.05 except
0-10 vs. 11-39 and 0-10 vs. 40-59
Heart Transplant surgery

There are three basic surgical implantation techniques:

1) biaatrial orthotopic,
2) bicaval orthotopic
3) the rarely used heterotopic

• The key to a successful transplant is the donor ischemic time, defined as the time from aortic cross-clamping in the donor to the release of aortic cross-clamping in the recipient.

• The ideal ischemic time is the shortest time possible, with the desirable upper limit to be <4 hours.

• Concerns about the loss of normal atrial anatomy using the biaatrial technique has led to more frequent use of the bicaval technique.

• The bicaval technique may result in a longer donor heart ischemic time, but is associated with lower right atrial pressure, lower incidence of atrial tachyarrhythmias, and less tricuspid valve incompetence
Post Transplant Care

Induction Immunosuppression (used in >50% of centers): lymphocyte-depleting antibodies (antithymocyte globulin, thymoglobulin), and lymphocyte-activation inhibiting antibodies (basiliximab, daclizumab).→ **myelosuppression**

Maintenance Immunosuppression

1. Calcineurin Inhibitor (CNI)
   - Tacrolimus (*Prograf*)
   - Cyclosporine (*CyA*)

2. Antiproliferative Agent/Antimetabolite
   - Mycophenolate mofetil (MMF); *Cellcept*
   - Azathiaprine (AZA)*Imuran*)

3. mTOR antagonists (**can replace CNI or AM to prevent CAV, CMV, nephrotoxicity, skin cancer**)
   - Sirolimus
   - Everolimus

4. Corticosteroids
   - Prednisone
   - Methylprednisolone (Solu-medrol)
   - Prednisolone

**Prophylactic antimicrobials** (antibacterial PCP/Tox, antifungal, antiCMV)

Agents to treat post-transplant complications and comorbidities

**Side effects:** nephrotoxicity, hypertension, hyperlipidemia, tremors, paresthesias, headache, seizures, diabetes (tacro), cancer. Hypertrichosis and gingival hyperplasia are more common with cyclosporine, but not with tacrolimus

**Side effects:** myelosuppression and gastrointestinal intolerance (nausea, abdominal pain, diarrhea)

**Side effects:** myelosuppression, hyperlipidemia, noninfectious pneumonitis, and poor wound healing
## Post Transplant Care

### Follow-Up Schedule of the Post Adult Cardiac Patient

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<th>M7</th>
<th>M8</th>
<th>M9</th>
<th>M12</th>
<th>M15-16</th>
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<th>Y2.5</th>
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</tr>
<tr>
<td>Provider/Coordinator</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Every 6-12 M: Every 6-12 months
Yearly: Every year
Rejection

• Acute cellular rejection
• Antibody mediated rejection
• Cardiac allograft vasculopathy
# Staging of Cellular Rejection

<table>
<thead>
<tr>
<th>2004</th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 0 R</strong></td>
<td><strong>No rejection</strong></td>
</tr>
<tr>
<td><strong>Grade 1 R, mild</strong></td>
<td>Interstitial and/or perivascular infiltrate with up to 1 focus of myocyte damage</td>
</tr>
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<tr>
<td><strong>Grade 2 R, moderate</strong></td>
<td>Two or more foci of infiltrate with associated myocyte damage</td>
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<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grade 3 R, severe</strong></td>
<td>Diffuse infiltrate with multifocal myocyte damage ± edema, ± hemorrhage ± vasculitis</td>
</tr>
</tbody>
</table>

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## Staging of AM Rejection

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pAMR 0</strong></td>
<td>Negative for pathologic antibody-mediated rejection (AMR); histologic and Immunopathologic studies are both negative.</td>
</tr>
<tr>
<td><strong>pAMR 1</strong></td>
<td>Suspicious for pathologic AMR; histologic findings positive, immunopathologic findings negative (pAMR 1-h), or immunopathologic findings positive, histologic findings negative (pAMR 1-l).</td>
</tr>
<tr>
<td><strong>pAMR 2</strong></td>
<td>Positive pathologic AMR; histologic <em>and</em> immunopathologic findings are present.</td>
</tr>
<tr>
<td><strong>pAMR 3</strong></td>
<td>Severe pathologic AMR; interstitial hemorrhage, capillary fragmentation, mixed inflammatory infiltrates, endothelial cell pyknosis, and/or karyorrhexis, and marked edema.</td>
</tr>
</tbody>
</table>
Treatment of Rejection

ACR:

• intravenous corticosteroids.
• In the presence of hemodynamic compromise, cytolytic therapy with antithymocyte antibodies
• Maintenance immunotherapy can be modified to improve compliance, increase baseline doses, and add or change immunosuppressants
Treatment of AMR

Class IIA:
1. These treatments can be used to disrupt the immune-mediated injury of the heart allograft in AMR: 1) high-dose IV cyclosporine, and 2) cytolytic immunosuppressive therapy. (Level of Evidence: C)

2. These treatments may be used to remove circulating anti-HLA antibodies or decrease their reactivity: 1) plasmapheresis, 2) immune apheresis (immunoadsorption), and 3) IV immunoglobulin. (Level of Evidence: C)

3. The following treatments are used to maintain adequate cardiac output and systemic blood pressure: 1) IV inotropes and vaspressors, and 2) MCS. (Level of Evidence: C)

4. When AMR is suspected, EMB examination should be expanded to include immunohistochemistry stains for complement split products and possibly antibody. (Level of Evidence: C)

5. Recipient serum should be screened for presence, quantity, and specificity of anti-donor (HLA) antibodies. (Level of Evidence: C)

6. Follow-up EMB should be performed 1-4 weeks after initiation of therapy and include immunohistochemistry examination. (Level of Evidence: C)

7. Adjustment of maintenance immunosuppressive therapy may be considered. This can include increase in the dose of current immunosuppressive agent(s), addition of new agent(s), or conversion to different agent(s). (Level of Evidence: C)

Class IIIB:
1. Systemic anticoagulation may decrease intravascular thrombosis in the heart allograft. (Level of Evidence: C)

2. Emergent retransplantation may be considered if the above measures do not restore acceptable heart allograft function, but outcomes in this situation are unfavorable. (Level of Evidence: C)
Cardiac Allograft Vasculopathy

- Rapidly progressive form of atherosclerosis, characterized by silent development
- Diffuse intimal hyperplastic lesions of the vascular tree, leading to vessel narrowing and eventually to allograft ischemia
- Standard coronary imaging is less insensitive
- Because of the cardiac denervation, no chest pain
- 1st presentation can be HF, VT, SCD
Angiographic presentation

Discrete, tubular or multiple stenoses.

Abrupt onset with distal diffuse concentric narrowing and obliterated vessels.

Gradual, concentric tapering with distal portion having sonic residual lumen.

Distal pruning.

Gao S et al. JACC 1988
CAV vs. CAD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cardiac allograft vasculopathy</th>
<th>Coronary artery disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel involvement</td>
<td>All vessel types within the allograft</td>
<td>Mostly intramyocardial vessels</td>
</tr>
<tr>
<td>Plaque pattern</td>
<td>Diffuse and concentric</td>
<td>Focal and eccentric</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Yes</td>
<td>Rarely</td>
</tr>
<tr>
<td>Internal elastic lamina</td>
<td>Intact</td>
<td>Disrupted</td>
</tr>
<tr>
<td>Calcium deposition</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Typical nontransplant atherosclerosis:
- Lumen diameter: Variable
- Plaque: Heterogeneous
- Lumen location: Eccentric
- Remodeling: Present
- Adventitial fibrosis: Absent

Typical transplant vascular disease:
- Lumen diameter: Similar
- Plaque: Homogeneous
- Lumen location: Central
- Remodeling: Absent
- Adventitial fibrosis: Present
Marked concentric intimal hyperplasia and proliferation associated along with a predominance of lymphocytes and foam cells.

Fibrotic plaque with a paucity of lymphocytes, eccentric proliferation of the intima, in contrast to the concentric intimal hyperplasia.

Pollack A, et al. JACC Imaging 2013
Angiography

Multiple sequential lesions, diffuse narrowing of the coronary arteries, and prominent pruning of the distal vasculature

CAV can also appear similar to typical atherosclerotic coronary artery disease in a native heart
Infections

- Bacteria and viruses account for >80% of infections after transplantation.
- The most common bacterial infections early after transplantation are nosocomial, due to infected intravascular catheters or lines, and gram-negative pneumonias.
- The most common viral infections are caused by the herpes viruses, cytomegalovirus, herpes zoster, and herpes simplex.
- In the past, cytomegalovirus infection was associated with significant morbidity and mortality, but the use of ganciclovir and pre-emptive viral monitoring has significantly improved the prognosis.
- 1/3 of patients will have an infection in the first year.
Cancer

- Malignancy is identified in 3-18% of the recipients, with an estimated risk of 1-2% per year.
- After the third year post-transplant, malignancy overcomes CAV as the leading cause of death.
- Cutaneous malignancy is the most common type, seen in up to 17% of patients, with a predominance of squamous cell carcinoma.
- Post-transplant lymphoproliferative disease is a recognized complication of solid organ transplantation. The incidence is approximately 5% after heart transplantation in some centers.
- PTLD: It is more frequent early, looks like lymphoma, CHECK EBV, reduce immunosuppression, treat with Rituximab.
Mechanical Circulatory Support

- Temporary MCS
- MCS with left ventricular assist device (LVAD) is a treatment option.
  - Bridge to transplant (BTT)
  - Destination therapy (DT)
  - Bridge to decision (BTD)
  - Bridge to recovery
- Improves Survival and QOL
- It is a rapidly evolving field
Implants: June 2006 – December 2016, n=18987

- **Continuous Flow Intracorporeal LVAD Pump**
  - Axial
  - Centrifugal
- **Pulsatile Flow Intracorporeal TAH**
- **Pulsatile Flow Intracorporeal LVAD Pump**
- **Pulsatile Flow Paracorporeal LVAD Pump**

**Implants per year**

<table>
<thead>
<tr>
<th>Year</th>
<th>CF Intra Pump/Axial</th>
<th>CF Intra Pump/Centrif</th>
<th>PF Intra TAH</th>
<th>PF Intra Pump</th>
<th>FF Para Pump</th>
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<td>0</td>
<td>0</td>
<td>1</td>
<td>76</td>
<td>18</td>
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<tr>
<td>2007</td>
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<td>22</td>
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<td>2008</td>
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<td>20</td>
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<tr>
<td>2012</td>
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<td>24</td>
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<tr>
<td>2013</td>
<td>0</td>
<td>0</td>
<td>71</td>
<td>1</td>
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<td>2016</td>
<td>0</td>
<td>0</td>
<td>1</td>
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</table>
Ventricular Assist Devices (VADs) as Destination Therapy

- The device has received FDA approval for a destination therapy indication, and only for patients with New York Heart Association (NYHA) Class IV end-stage ventricular heart failure who are not candidates for heart transplant, and

- Who meet all of the following conditions:
  - Have failed to respond to optimal medical management (including beta-blockers, and Angiotensin-Converting Enzyme (ACE) inhibitors if tolerated) for at least 45 of the last 60 days, or have been balloon pump-dependent for 7 days, or IV inotrope-dependent for 14 days;
  - Have a Left Ventricular Ejection Fraction (LVEF) < 25%; and,
  - Have demonstrated functional limitation with a peak oxygen consumption of \( \leq 14 \text{ ml/kg/min} \) unless balloon pump or inotrope dependent or physically unable to perform the test.

*<2 years of life expectancy
*>50% 1 year predicted mortality
Exclusion Criteria

• Active systemic infection
• Uncorrectable aortic insufficiency
• Renal insufficiency that may require dialysis in the near future
• History of cardiac transplant
• Any condition, other than heart failure, which is expected to limit survival to less than 2 years
Types of MCS

• Left ventricular assist device (LVAD)
• Biventricular support (BiVAD)
• Total artificial heart (TAH)
Types of LVADs

- First generation pumps
  - Pulsatile pumps

- Second generation pumps
  - Continuous axial flow pumps

- Third generation pumps
  - Magnetically levitated pump rotor
Improved Survival with MCS
HM 3 LVAD Trial

- Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) ongoing trial.

*Same survival, but lower stroke, pump thrombosis and need for device replacement with HM3

Mehra, M.R. et al. 2019
Adverse events

• The adverse events have decreased significantly in the last years, mainly from the introduction of second- and third-generation LVADs and by the growing clinical experience required to take care of these patients.

• Bleeding requiring transfusion (54%), arrhythmias (37%), device infection (19%), Aortic regurgitation (25%), RV failure (18%), ischemic stroke (4%), hemorrhagic stroke (7.7%), and pump thrombosis (3.6%)
**RV failure**

**Diagnostic Criteria for RV Failure:**
Symptoms and signs persistent right ventricular dysfunction, CVP >18 mm Hg with a CI <2.0 L/min/m²; In the absence of elevated left atrial/pulmonary capillary wedge pressure >18 mm Hg, tamponade, ventricular arrhythmias or pneumothorax; Requiring RVAD implantation; or requiring inhaled nitric oxide or inotropic therapy for duration of more than one week at any time after LVAD implantation.

**Severity Scale:**
- **Severe**: RVAD implantation;
- **Moderate**: inotropes or use of IV or inhaled pulmonary vasodilator (INO or prostaglandin E);
- **Mild**: 2 of the 4 following criteria:
  - CVP >18 mm Hg or mean RA pressure >18 mm Hg;
  - CI <2.3 L/min/m² (using a pulmonary artery catheter);
  - Ascites or evidence of moderate to worse peripheral oedema;
  - Evidence of elevated CVP by echocardiogram (dilated inferior vena cava without collapse), and in physical exam (signs of increased jugular venous pressure).

### Hemodynamic Parameters Associated With RV Function

<table>
<thead>
<tr>
<th>Variable</th>
<th>Calculation</th>
<th>Thresholds Associated With Clinical Events in Specific Populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP</td>
<td>RAP (or CVP)</td>
<td>&gt;15 mm Hg (RHF after LVAD)</td>
</tr>
<tr>
<td>Right-to-left discordance of filling pressures</td>
<td>RAP:PCWP</td>
<td>&gt;0.63 (RHF after LVAD); &gt;0.86 (RHF in acute MI)</td>
</tr>
<tr>
<td>PA pulsatility index</td>
<td>(PAS−PADP)/RAP</td>
<td>&lt;1.0 (RHF in acute MI); &lt;1.85 (RHF after LVAD)</td>
</tr>
<tr>
<td>RV stroke work index</td>
<td>(MPAP−CVP)×SVI</td>
<td>&lt;0.25–0.30 mm Hg-L/m² (RHF after LVAD)</td>
</tr>
<tr>
<td>PVR</td>
<td>(MPAP−PCWP)/CO</td>
<td>&gt;3.6 WU (RHF after LVAD)</td>
</tr>
<tr>
<td>PA compliance</td>
<td>SV/(PAS−PADP)</td>
<td>&lt;2.5 mL/mm Hg (RHF in chronic HF, RV-PA coupling in PAH)</td>
</tr>
</tbody>
</table>
Revascularization

• The **STICH** (Surgical Treatment for Ischemic Heart Failure) trial enrolled 1,212 patients with EF ≤35% and coronary artery disease amenable to CABG and randomizing them to medical therapy or CABG.

• There was significant difference in the primary outcome of death from any cause at 10 years of follow-up (NNT = 14)

• Secondary endpoints of death from a cardiovascular cause and death from any cause or hospitalization for a cardiovascular cause favored the surgical arm of the study (NNT=11)
Revascularization

- A substudy of the STICH trial examined the value of viability testing in patients undergoing CABG, demonstrated that evidence of myocardial viability by SPECTor dobutamine echocardiography did not identify patients more likely to benefit from CABG.
- However, less than one-half of the STICH study population underwent viability assessment (n = 601).
- Patients with viable myocardium died less.
- Current evidence does not support surgical ventricular remodeling or mitral valve repair for most patients with severe systolic HF.
- Based on the results of the STICH trial, revascularization in severe ischemic LV dysfunction should generally be individualized.
Palliative and Hospice care

• The focus of palliative care is symptom relief, but does not preclude reasonable active treatment, unless the patient has transitioned to hospice.

• Patient preferences are a key component to decision making, and a multidisciplinary care approach (e.g., delivered by a palliative care team) is important and fully supportable.

• Medical therapy for HF should be continued unless it is not tolerated or upon patient/family request.
Palliative care

• Judicious use of oxygen, opioids, and diuretics should be used to control symptoms of anxiety, dyspnea, and pain.

• For patients who are not candidates for cardiac transplant or VAD therapy, chronic, continuous outpatient IV inotropic therapy can be used, but requires significant caregiver support.

• Inotropes may improve the patient’s symptoms and overall quality of life, but also may accelerate mortality. The goals of therapy should be discussed in detail with the patient and caregivers.
Palliative care

• It is reasonable to forgo generator change in a patient whose device has reached the end of battery life, but this decision requires review with the patient and family.

• Selective deactivation of an ICD should be discussed with the patient and family members when the patient enters the terminal phase of HF in order to prevent shocks in the dying patient.

• Unlike ICDs, CRT has been shown to improve quality of life. Therefore, it may be appropriate to continue biventricular pacing for patients even when the decision has been made to turn off ICDs.
Hospice care

• Hospice care is a specialized form of palliative care in which the patient has decided to forgo all life-prolonging treatment. Hospice patients usually have a life expectancy of less than 6 months.

• Palliative and hospice care improve patient-centered outcomes but not mortality and re-hospitalization.
A 44-year-old man has a 5-year history of NICM. He presents to your office following his third hospitalization in the past year for volume overload. He is short of breath with minimal exertion, but appears euvolemic on exam. His echocardiogram demonstrates LVEF 20%, the left ventricular cavity size is dilated, and there are no major valvular abnormalities. Prognosis in this patient is best determined by which of the following?

1. CPEX
2. RHC
3. TTE/CMR
4. SHFM
5. 6MWT
Question 2

A 62-year-old woman with chronic heart failure with reduced ejection fraction is transferred to the coronary care unit. She was started on milrinone when she was admitted to the floor 3 days ago where she was awaiting heart transplantation. A pulmonary artery catheter is placed.

The hemodynamics are (in mm Hg where appropriate):

- Right atrial pressure: 20
- Pulmonary capillary wedge pressure: 30
- Pulmonary artery pressure: 60/30/40
- Cardiac index: 1.5 L/min/m²
- Blood pressure: 80/50/65

Which of the following is the next most appropriate step?

1. LVAD
2. Sildenafil
3. Nitrates
4. Phenylephrine
Patient with evidence of stage D HF comes to the office for further evaluation. RHC shows:

- Right atrial pressure: 20 mm Hg
- Pulmonary artery pressure (PAP): 45/20 mm Hg with a mean PAP 32 mm Hg
- Pulmonary capillary wedge pressure: 25 mm Hg
- Cardiac output: 4 L/min
- Cardiac index: 1.8 L/min/m²

Which is the most appropriate:
1. Heart Transplant
2. Inotropes
3. Upgrade to CRT
4. LVAD
5. MV repair
Question 4

- 64 yo with ICM, severe MR, EF30%. Which approach is the most effective to decrease MR?

1. MVR
2. Surgical reconstruction
3. CRT
4. Carvedilol
5. Inotropes
Question 5

• Survival post transplant:
  1. 1 year=90%, 5 year 70%, >10 years 50%
  2. 1 year=60%, 5 year 30%, >10 years 20%
  3. 1 year=30%, 5 year 20%, >10 years 10%
  4. 1 year=90%, 5 year 90%, >10 years 80%
Question 6

1. Infection
2. Rejection
3. CAV
4. Malignancy
5. Primary graft failure
Question 7

- 62-year-old man presents to the hospital with 2 weeks of progressive mid-sternal chest pressure when walking at a normal pace on level ground. His vital signs are blood pressure 123/84 mm Hg and heart rate 88 bpm. His echocardiogram shows global left ventricular (LV) hypokinesis with an LV ejection fraction (LVEF) of 20%, LV diastolic diameter of 6 cm, and mild concentric LV hypertrophy. Coronary angiography demonstrates multivessel coronary disease with focal proximal stenoses of 70% in the circumflex, 70% in the left anterior descending artery, and 80% in the right coronary artery. He is on GDMT and has persistent angina

Which of the following is the next step in management of this patient?

1. CABG
2. LVAD
3. Heart Transplant
4. SPECT MPI
5. Cardiac MRI
Question 8

• Patient with an LVAD presents with power alarms, elevated LDH 600, SOB, DOE, leg edema.

   Diagnosis:

1. RV failure
2. Pump thrombosis
3. AI
4. Non compliance
Question 9

- Patient with LVAD presents with low flow alarms, LDH ~300, lower GI bleeding, anemia and VT.

What’s next:

1. Transfuse, stop the bleeding, decrease INR
2. Amiodarone, magnesium
3. VT ablation
4. RV support
Question 10

• Find correct combination of side effects:

1. Tacrolimus: hypertension, sirolimus: proteinuria, mycophenolate: diarrhea

2. Tacrolimus: hypotension, sirolimus: renal dysfunction, mycophenolate: diabetes

3. Tacrolimus: gingival hyperplasia, sirolimus: cancer, mycophenolate: hypertension
Conclusions

- Early recognition, evaluation and treatment of HF
- Non-invasive and invasive hemodynamic assessment
- Identify signs of stage D HF
- LVADs and Transplantation substantially improve QOL & survival
- Be aware of the main complications