Management of Heart Failure: Role of the Advanced Heart Failure Clinic

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Disclosures

• PI: Cardiomems post-approval study (St. Jude)
• Consultant:
  - Novartis
  - Abbott
• Director: Compassionate Care Hospice
Objectives

1. Define heart failure, review epidemiology and outcomes associated with diagnosis

2. Describe the role of a heart failure clinic and associated advanced heart failure program

3. Identify available therapies for patients with advanced heart failure
Heart Failure: Definition

• Heart failure is a *clinical syndrome* caused by various cardiac pathologies

• It is characterized by *specific symptoms of impaired cardiac output, venous congestion, and fluid retention*

• It results from any structural or functional disorder that impairs the ability of the ventricle to *fill with or eject blood*

• *Can be due to HFrEF, HFpEF, infiltrative cardiomyopathy or other cardiac conditions*
Stages of Heart Failure

A: No structural heart disease
   - At risk population: HTN, DM, Anthracycline

B: Minimal structural heart disease
   - No symptoms or signs of HF

C: Moderately severe structural heart disease
   - Previous or current symptoms

D: Severe structural heart disease
   - Refractory symptoms requiring special RX
Hospital Discharges for Heart Failure

Number of discharges

Year


600,000  700,000  800,000  900,000  1,000,000  1,100,000  1,200,000

701,000  701,000  701,000  701,000  701,000  701,000  701,000  701,000  701,000  701,000  701,000  701,000  701,000  1,092,000

Projected US Heart Failure Prevalence and Direct Cost

Projected US Prevalence of Heart Failure (%)

Projected US Direct Costs for Heart Failure (billions 2008$)

Adapted from Heidenreich PA et al. Circulation. 2011;123:933-944
AHA Statement: Forecasting the future of CV disease in US
Left ventricular modeling post MI

POST-MI REMODELING

- Acute Infarction
- Infarct Zone Thinning & Elongation
- Spherical Ventricular Dilation

- Increased Interstitial Collagen
- Fibrous Scar
- Myocyte Hypertrophy
Role of the Heart Failure Clinic

1. Assist patients with heart failure symptoms to arrive at the correct diagnosis
All Heart Failure is Not the Same

Dilated Cardiomyopathy

Restrictive Cardiomyopathy

Hypertrophic Cardiomyopathy

Amyloid Cardiomyopathy
Role of the Heart Failure Clinic

1. Assist patients with heart failure symptoms to arrive at the correct diagnosis

2. Treat patients with heart failure, titrating evidence based therapies
Goal of Therapies: Reverse Remodeling

- Left Ventricle Pressure vs. Left Ventricle Volume
  - ESPVR: Normal
  - EDPVR: CHF
  - Reverse Remodeling
Drugs for Long-term Therapy for Heart Failure with Reduced LVEF

Clinical Trial Benefit

✓ ACE inhibitors or Angiotensin receptor blockers
✓ Beta-blockers
✓ Aldosterone blockers
✓ Nitrate/Hydralazine
✓ Digoxin*
Life Saving Therapy

Drugs that inhibit the renin-angiotensin system have modest effects on survival.

Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF
Improvement of Systolic Function is Related to Beta Blocker Dose

Heart Failure Cocktail: Effect of Adding Therapies
Device Therapy

ICD therapy is recommended for primary prevention of SCD in selected patients with HF/EF at least 40 d post-MI with LVEF ≤35% and NYHA class II or III symptoms on chronic GDMT, who are expected to live >1 y.

CRT is indicated for patients who have LVEF ≤35%, sinus rhythm, and LBBB with a QRS ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT.

ICD therapy is recommended for primary prevention of SCD in selected patients with HF/EF at least 40 d post-MI with LVEF ≤30% and NYHA class I symptoms while receiving GDMT, who are expected to live >1 y.

CRT can be useful for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with a QRS ≥150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT.

CRT can be useful for patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT.

CRT can be useful in patients with AF and LVEF ≤35% on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or rate control allows near 100% ventricular pacing with CRT.

CRT can be useful for patients on GDMT who have LVEF ≤35% and are undergoing new or replacement device implantation with anticipated ventricular pacing (>40%).

An ICD is of uncertain benefit to prolong meaningful survival in patients with a high risk of nonsudden death such as frequent hospitalizations, frailty, or severe comorbidities.

CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT.

CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with a QRS ≥150 ms, and NYHA class II symptoms on GDMT.

CRT may be considered for patients who have LVEF ≤30%, ischemic etiology of HF, sinus rhythm, LBBB with QRS ≥150 ms, and NYHA class I symptoms on GDMT.

CRT is not recommended for patients with NYHA class I or II symptoms and a non-LBBB pattern with QRS <150 ms.

CRT is not indicated for patients whose comorbidities and/or frailty limit survival to <1 y.
New Therapies?
LCZ696: Angiotensin Receptor Neprilysin Inhibition

Entresto™ (sacubitril/valsartan) tablets
24/26mg • 49/51mg • 97/103mg

Angiotensin receptor blocker + Inhibition of neprilysin

McMurray J, Packer M et al. NEJM 2014;371: Sept 11
Neprilysin Inhibition Potentiates Actions of Endogenous Vasoactive Peptides That Counter Maladaptive Mechanisms in Heart Failure

Endogenous vasoactive peptides
(natriuretic peptides, adrenomedullin, bradykinin, substance P, calcitonin gene-related peptide)

Neprilysin
Inactive metabolites

Neprilysin inhibition

Neurohormonal activation
Vascular tone
Cardiac fibrosis, hypertrophy
Sodium retention
<table>
<thead>
<tr>
<th></th>
<th>LCZ696 (n=4187)</th>
<th>Enalapril (n=4212)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>914 (21.8%)</td>
<td>1117 (26.5%)</td>
<td>0.80 (0.73-0.87)</td>
<td>0.0000002</td>
</tr>
<tr>
<td><strong>Cardiovascular death</strong></td>
<td>558 (13.3%)</td>
<td>693 (16.5%)</td>
<td>0.80 (0.71-0.89)</td>
<td>0.00004</td>
</tr>
<tr>
<td><strong>Hospitalization for heart failure</strong></td>
<td>537 (12.8%)</td>
<td>658 (15.6%)</td>
<td>0.79 (0.71-0.89)</td>
<td>0.00004</td>
</tr>
</tbody>
</table>

McMurray J, Packer M et al. NEJM 2014:371; Sept 11
<table>
<thead>
<tr>
<th>Table: PARADIGM-HF: Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prospectively identified adverse events</strong></td>
</tr>
<tr>
<td>Symptomatic hypotension</td>
</tr>
<tr>
<td>Serum potassium &gt; 6.0 mmol/l</td>
</tr>
<tr>
<td>Serum creatinine ≥ 2.5 mg/dl</td>
</tr>
<tr>
<td>Cough</td>
</tr>
<tr>
<td><strong>Discontinuation for adverse event</strong></td>
</tr>
<tr>
<td>Discontinuation for hypotension</td>
</tr>
<tr>
<td>Discontinuation for hyperkalemia</td>
</tr>
<tr>
<td>Discontinuation for renal impairment</td>
</tr>
<tr>
<td>Angioedema (adjudicated)</td>
</tr>
<tr>
<td>Medications, no hospitalization</td>
</tr>
<tr>
<td>Hospitalized; no airway compromise</td>
</tr>
<tr>
<td>Airway compromise</td>
</tr>
</tbody>
</table>

McMurray J, Packer M et al. NEJM 2014;371:993-1004
Drugs for Long-term Therapy for Heart Failure with Reduced LVEF

Clinical Trial Benefit

- ACE inhibitors or Angiotensin receptor blockers
- Beta-blockers
- Aldosterone blockers
- Nitrate/Hydralazine
- Digoxin

Sacubitril/Valsartan (ENTRESTO)
Learning to Live with Heart Failure

Heart Failure with Reduced Ejection Fraction (HFrEF or "systolic" heart failure)

This occurs when the heart is weak and enlarged and is unable to pump as much blood as it should. The EF is 50% or less.

Foods to Avoid

Weigh Yourself Daily!
Stay on top of any major changes in your weight.

<table>
<thead>
<tr>
<th>Nutrition Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serving Size</strong> 1 cup (226 g)</td>
</tr>
<tr>
<td><strong>Serving per Container</strong> about 2</td>
</tr>
<tr>
<td><strong>Amount per Serving</strong></td>
</tr>
<tr>
<td><strong>Calories</strong> 250 Calories from Fat 110</td>
</tr>
<tr>
<td><strong>Total Fat</strong> 12g (18%)</td>
</tr>
<tr>
<td><strong>Saturated Fat</strong> 3g (15%)</td>
</tr>
<tr>
<td><strong>Trans Fat</strong> 0g</td>
</tr>
<tr>
<td><strong>Cholesterol</strong> 30 mg</td>
</tr>
<tr>
<td><strong>Sodium</strong> 470 mg (20%)</td>
</tr>
<tr>
<td><strong>Total Carbohydrate</strong> 31g (10%)</td>
</tr>
<tr>
<td><strong>Dietary Fiber</strong> 0g</td>
</tr>
<tr>
<td><strong>Sugars</strong> 5g</td>
</tr>
<tr>
<td><strong>Proteins</strong> 5g</td>
</tr>
</tbody>
</table>

**Step 1. Look at the Serving Size**
- The information on the label for sodium is for one serving
- 1 serving = 1 cup

**Step 2. Find Amount of Sodium**
- Look at the sodium per serving
- 1 serving = 470 mg

**Step 3. Calculate the Total Amount of Sodium**
- If you eat more or less than the listed serving size, you will get more or less sodium

<table>
<thead>
<tr>
<th>How much sodium in a cup?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 cups = 2 servings</td>
</tr>
<tr>
<td>2 x 470 mg per serving = 940 mg</td>
</tr>
</tbody>
</table>

**Medication Class**

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Live Longer</th>
<th>Feel Better</th>
<th>Stay Out of Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitor</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>ARB</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Diuretic</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Aldosterone Blocker</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Hydralazine &amp; Isosorbide</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Digoxin</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>
Role of the Heart Failure Clinic

1. Assist patients with heart failure symptoms to arrive at the correct diagnosis

2. Treat patients with heart failure, titrating evidence based therapies

3. Act as an acute care clinic, managing patients with decompensated heart failure to avoid hospitalization
Heart Failure Hospitalization is Ominous

Setoguchi. Am Heart J. 2007
High risk patients for readmission

- Initial discharge
- Median Time from hospital discharge
- Palliation and Priorities
- Transition Phase
- Plateau Phase
Diuretic Resistance

• Inadequate dose
• Poor absorption, consider torsemide
• Reinforce salt restriction
• Add thiazide
• Add MRA
• Stop NSAIDS
• Consider low output heart failure
IV Diuretic in Clinic
HF Hospitalization Starts **Weeks** Before Admission!

**Time Course of Decompensation**

- **Physiologic Markers of Acute Decompensation**
  - Filling Pressure Increase
  - Autonomic Adaptation
  - Intrathoracic Impedance Changes

**Time Preceding Hospitalization (Days)**

- Hemodynamically Stable
- Presymptomatic Congestion
- Decompensation

*Graph adapted from Adamson PB, et al. Curr Heart Fail Reports, 2009.*
Wireless Pulmonary Hemodynamic Monitoring
Patient Management Database

Trend Data
- Easy-to-read
- Physician alerts
- Home transmission
- Secure, encrypted web-based access

Discrete Data

<table>
<thead>
<tr>
<th>Reading</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>24</td>
</tr>
<tr>
<td>Mean</td>
<td>19</td>
</tr>
<tr>
<td>Diastolic</td>
<td>16</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>81</td>
</tr>
</tbody>
</table>
Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

- ≤ 6 Months: 28% RRR (p < 0.0002)
- > 6 Months: 45% RRR (p < 0.0001)

Study Duration: 37% RRR (p < 0.0001)

Cumulative Number of HF Hospitalizations

- Control: 254 HF Hospitalizations
- Treatment: 158 HF Hospitalizations

Hazard ratio 0.63 (95% CI 0.52-0.77) (p < 0.0001)

<table>
<thead>
<tr>
<th>HR for HF Hsp at 6 Mo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFpEF 0.48</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HFrEF 0.76</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Role of the Heart Failure Clinic

1. Assist patients with heart failure symptoms to arrive at the correct diagnosis

2. Treat patients with heart failure, titrating evidence based therapies

3. Act as an acute care clinic, managing patients with decompenated heart failure to avoid hospitalization

4. Manage patients with end-stage heart failure: advance therapies (transplant or LVAD) or palliative (inotropes)
Transplant Is Not a Viable Option for Many Patients

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.
Home Inotropic Therapy
Improved Outcomes in Stage D with Advanced Therapies for Heart Failure
Left Ventricular Assist Device
Improving Outcomes with LVAD

- HM XVE
- HeartMate II
- HeartWare

% Survival vs Months Post Op

- 2008
- 2005
- 1997

Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. Frazier OH, Rose EA, Oz MC et al. J Thor Cardiovasc Surg 2001:122

Survival at 2 years in the LT cohort

Kaplan-Meier estimates of all-cause survival

No. at Risk:
- HeartMate 3™ LVAD
- HeartMate II™ LVAD

Survival is 83% for HeartMate 3™ LVAD survival is comparable to transplant survival at 2 years²*.

## Adverse Events
### HeartMate II Destination Therapy Trial

<table>
<thead>
<tr>
<th></th>
<th>CF LVAD (n=133)</th>
<th>PF LVAD (n=59)</th>
<th>Risk Ratio [95% Confidence Interval]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[211 pt-years]</td>
<td>[41 pt-years]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pump Replacements</strong></td>
<td>0.06</td>
<td>0.51</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>0.13</td>
<td>0.22</td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>Ischemic</td>
<td>0.06</td>
<td>0.10</td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>0.07</td>
<td>0.12</td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Device-related infection</strong></td>
<td>0.48</td>
<td>0.90</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Local non-device infection</strong></td>
<td>0.76</td>
<td>1.33</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
<td>0.39</td>
<td>1.11</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bleeding requiring PRBC</strong></td>
<td>1.66</td>
<td>2.45</td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Bleeding requiring surgery</strong></td>
<td>0.24</td>
<td>0.29</td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td><strong>Other Neurological</strong></td>
<td>0.17</td>
<td>0.29</td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Right Heart Failure</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Extended Inotropes</strong></td>
<td>0.14</td>
<td>0.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RVAD</strong></td>
<td>0.02</td>
<td>0.07</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Cardiac Arrhythmias</strong></td>
<td>0.69</td>
<td>1.31</td>
<td></td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Respiratory Failure</strong></td>
<td>0.10</td>
<td>0.34</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Renal Failure</strong></td>
<td>0.01</td>
<td>0.00</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hepatic Dysfunction</strong></td>
<td>0.01</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Device Thrombosis</strong></td>
<td>0.02</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Re-hospitalizations</strong></td>
<td>2.64</td>
<td>4.25</td>
<td></td>
<td>0.02</td>
</tr>
</tbody>
</table>

---

**Key Events**
- **Stroke**
- **Infection**
- **Bleeding**
- **Right Heart Failure**
- **Pump Thrombosis**
VAD Complications

- Rehospitalization
- Bleeding
- Arrhythmia
- Local Infection
- Respiratory Failure
- Sepsis
- VAD Infection
- Right Heart Failure
- Other Neurologic
- Stroke
- Pump Replacement
Improved Quality of Life
Palliative Care: Not just for Stage D
A 56 y/o man with ischemic cardiomyopathy comes into clinic. He has been hospitalized four times this year for heart failure. He is extremely fatigued and had to stop twice on the way into clinic. His BP is 82/60 and he is not able to tolerate any medicines for heart failure. You should,

A. Start him on very low dose metoprolol
B. Increase his diuretics
C. Refer him to heart failure clinic for advanced therapies
You see a 59 y/o man in clinic with new onset heart failure, LVEF 20%. His BP is 97/60 and HR is 72. You are nervous about starting medications because of his low blood pressure but then you remember that if you start him on a beta blocker you could potentially reduce his mortality by:

A. 5%
B. 10%
C. 35%
Question #3

You see a 74 y/o M in clinic with end stage heart failure. He asks about the “new heart pump”. You tell him that left ventricular assist devices (LVAD) have been shown to:

A. Reduce heart failure mortality
B. Improve quality of life
C. Both
Additional Resources

PAR Heart Failure Clinic!
706-475-1700

www.hfsa.org/heart-failure-guidelines

www.hfsa.org/accakahahfsa-guideline-management-heart-failure-update/
Thank you

catherine.marti@piedmont.org