Is It Time to Treat Heart Failure Like Cancer

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Baylor Scott & White, Temple TX
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Disclosures

• Speakers Bureau: Boehringer Ingelheim, CareDx
Objectives

- To understand the high mortality rate associated with a heart failure diagnosis
- To be able to explain the pathophysiologic mechanisms that contribute to the mortality rate associated with heart failure with reduced ejection fraction (HFrEF)
- After hearing the presentation the participant should be able to apply referral guidelines for Advanced Heart Cardiology to their practice

Case

35 y/o woman is admitted for observation to the hospital with progressively worsening right chest tenderness. On exam she is noted to have a palpable mass on the R breast. CT chest and mammogram reveal a 3 x 3 cm lesion concerning for malignancy.

What is the next step?
- A. Send her home and tell her to follow up with her PCP
- B. Refer her to a PCP that sees a lot of patients with cancer
- C. Treat Conservatively, do not refer to a specialist
- D. Consult Oncologist immediately to determine diagnostic (FNA, resection, LN biopsy) and Treatment course (Mastectomy, chemotherapy, radiation, lumpectomy, LN biopsy, etc)
Cancer

- According to the NIH National Cancer Institute Cancer Trends Progress Report the death rate for all cancers combined in 2016 was 155.7/100,000

- There are therapies (most curative) for cancer if caught early enough

- Most cancers are treated by an Oncologist

- Oncology consultations tend to be triggered by radiology once lesions are discovered and do not wait for primary physician to refer

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Treat Heart Failure Like Cancer
So is Heart Failure as Deadly as Cancer?

<table>
<thead>
<tr>
<th>US Heart Failure (HF) Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>6.5 million</strong> Adults in the US have heart failure</td>
</tr>
<tr>
<td>• HF was a contributing cause of <strong>1 in 8 deaths</strong> in 2017</td>
</tr>
<tr>
<td>• Approximately <strong>HALF</strong> of people who develop HF <strong>Die w/i 5 yrs of initial diagnosis</strong></td>
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<tr>
<td>• <strong>NYHA Class IV</strong> patients have an annual <strong>Mortality rate of &gt; 50%</strong></td>
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<tr>
<td>• <strong>HF Goal Directed Medical Therapy (GDMT) only Reduces Mortality in HFrEF</strong></td>
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<tr>
<td>• <strong>Highest Mortality Rates in African American Men</strong></td>
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</table>


### US Heart Failure Statistics

- **US adults 65 years and older increased 22.9% from 41.4 million to 50.9 million between 1/1/2011 – 12/31/2017**
  - Population of adults younger than 65 years increased by only 1.7%

- **Age-adjusted Mortality rates**
  - Decreased 5.0% for Heart Disease (HD)
  - Decreased 14.9% for Coronary Heart Disease (CHD) while increasing
  - **INCREASED 20.7% for HEART FAILURE**

- **The number of Heart Failure Deaths INCREASED by 38 %**
  - A total of 80% of HD deaths occurred in the group of adults aged 65 years and older

Heart Failure Hospitalizations Increase Mortality

Mortality Associated w/ HF Hospitalization

- 30-day mortality 10.4%
- 1-year mortality 22.0%
- 5-year mortality 42.3%
Heart Failure Hospitalizations Increase Mortality

14,374 Patients Hospitalized w/ New Dx of Heart Failure in British Colombia, Canada 2000 – 2004

- 7401 patients died during the follow up period
- The 30-day all-cause mortality after the first HF hospitalization was 12%, and the 1-year mortality was 34%
- The median survival (50% mortality) was 2.4 years
- Significant increase in all-cause mortality with advanced age

Heart Failure Hospitalizations Increase Mortality

Mortality Significantly ↑ After Each Additional HF Hospitalization

- Median survival times after each HF hospitalization
  - First                  2.4 years (95% CI 2.3-2.5)
  - Second                 1.4 years (95% CI 1.2-1.5)
  - Third                  1.0 years (95% CI 0.9-1.1)
  - Fourth                 0.6 years (95% CI 0.5-0.9)

- Most patients were alive 2 years after the first HF hospitalization, but approximately half were dead by 1 year after 3 hospitalizations


Why Is Heart Failure So Deadly

Review of Heart Failure Pathophysiology
HFrEF Hemodynamics

Activation Neurohormonal Cascade

- Sympathetic nervous system (SNS)
- Renin-angiotensin-aldosterone system (RAAS)
- Arginine-vasopressin (AVP) and endothelin (ET) axis

Chronic Neurohormonal Activation

Laplace’s Law: Wall stress ~ P*r/2h

Normal Heart

Heart Failure With Reduced Ejection Fraction

†wall stress, †O₂ demand
↓pump efficiency, †mitral insufficiency, dyssynchrony

Courtesy of Dr. Barry Borlaug of the Mayo Clinic CV Board Review 2014
Systolic Dysfunction Stage Progression

LV Volume

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Systolic Dysfunction Stage Progression

Normal Stage B HF (ASLVD) Stage C HF NYHA II-III

LVP SV SV SV

SBP

LV Volume

Systolic Dysfunction Stage Progression

Normal Stage B HF (ASLVD) Stage C HF NYHA II-III Stage D HF NYHA IV

LVP SV SV SV LVEDP

SBP SV SV

LV Volume

Courtesy of Dr. Barry Borlaug of the Mayo Clinic CV Board Review 2014
Afterload Sensitivity of HFREF

Vasoconstriction
Vasodilation

LV Pressure

Normal
Systolic HF

LV Volume

Preload Sensitivity of HFREF

Normal
Systolic HF
Advanced HFREF

PCWP or LVDP

Diuretic

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Treat Heart Failure Like Cancer
Signs & Symptoms of Heart Failure

<table>
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<th>Congestion (Fluid)</th>
<th>History- Symptoms</th>
<th>Exam- Signs</th>
<th>Tests</th>
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<td>• Dyspnea On Exertion</td>
<td>• Elevated JVP</td>
<td>• ↑ Liver Enzymes</td>
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<td>• Bendorpnea</td>
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<td>• Echocardiogram</td>
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<td>• Pulsatile Liver</td>
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<td>• Abdominal distension</td>
<td>• Edema</td>
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Cardiogenic Shock

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<th>Exam- Signs</th>
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<td>• Short of Breath at Rest</td>
<td>• Low BP</td>
<td>• ↑ Creatinine</td>
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<tr>
<td>• Fatigue</td>
<td>• Fast HR</td>
<td>• ↑ Liver Enzymes</td>
</tr>
<tr>
<td>• Nausea/Dry Heaving</td>
<td>• Cool Extremities</td>
<td>• Lactic Acid</td>
</tr>
<tr>
<td>• Poor Appetite</td>
<td>• Low Urination</td>
<td>• Echocardiogram</td>
</tr>
<tr>
<td>• Confusion</td>
<td></td>
<td>• Right Heart Catheterization</td>
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<td>• Weight Loss</td>
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Classification of Heart Failure

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<th>ACCF/AHA Stages of HF</th>
<th>NYHA Functional Classification</th>
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<tr>
<td>A</td>
<td>At high risk for HF but without structural heart disease or symptoms of HF</td>
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<tr>
<td>B</td>
<td>Structural heart disease but without signs or symptoms of HF</td>
</tr>
<tr>
<td>C</td>
<td>Structural heart disease with prior or current symptoms of HF</td>
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<tr>
<td></td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>III</td>
</tr>
<tr>
<td>D</td>
<td>Refractory HF requiring specialized interventions</td>
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ACC/AHA Heart Failure Stages

Stage A
High risk without structural disease

Stage B
Structural disease without symptoms

Stage C
Structural disease with symptoms

Stage D
Refractory, end-stage heart failure

Main goals:
Relieve symptoms, prevent progression, reduce mortality


Survival By ACC/AHA Stage of HF

OPTIME Study

No survival benefit with Milrinone in Stage D HF

<table>
<thead>
<tr>
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<th>Placebo</th>
<th>Milrinone</th>
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<tr>
<td>Death or readmit</td>
<td>35.3%</td>
<td>35.0%</td>
</tr>
<tr>
<td>within 60 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean # days of hosp</td>
<td>13.5</td>
<td>13.4</td>
</tr>
<tr>
<td>within 60 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death within 60 days</td>
<td>8.9%</td>
<td>10.3%</td>
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JAMA 2002;287:1541

REMATCH

Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure

- Randomized clinical trial of Optimal Medical Therapy vs. Pulsatile flow LVAD
  - Non-transplant candidates (n=129)
    - EF ≤ 25%
    - peak VO2 < 12 ml/kg/min
    - or continuous infusion inotropes
  - 25% One Year Survival in Medical Therapy Cohort
  - FDA approval for XVE as destination therapy

**REMATCH**

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- **25% One Year Survival in Medical Therapy Cohort**

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**Survival Rates for LVADs versus Medical Therapy**

![Survival Rates Graph](image_url)

- Fang JC. NEJM 2009;361:31-32

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Treat Heart Failure Like Cancer
Strategies of Heart Failure Treatment

• Determine the Ejection Fraction
• Monitor for heart failure medication intolerance
• Look for easily reversible causes
  – Coronary Disease (Stress test, Calcium Score)
  – Metabolic (TSH, Ferritin, etc)
  – Drug (Amphetamine/cocaine) or ETOH abuse
  – Arrhythmia (ECG)
• If LVEF ≤ 40% Refer to HF Cardiologist or General Cardiologist
Timing of Referral to Heart Failure Cardiologist

• Earlier is better
• Prevents chance of multiorgan damage
• Patient has a better opportunity to become a Transplant recipient

2013 ACCF/AHA Guideline For Management of Heart Failure
Clinical Events & Findings Useful for Identifying Pts w AHF

• Repeated (≥2) hospitalizations or ED visits for HF in the past year
• Progressive Renal Dysfunction
• Cardiac Cachexia
• Intolerance to ACE inhibitors
• Intolerance to BB
• Frequent SBP <90 mm Hg
2013 ACCF/AHA Guideline For Management of Heart Failure
Clinical Events & Findings Useful for Identifying Pts w AHF

- Persistent dyspnea with dressing or bathing requiring rest
- Inability to walk 1 block on the level ground due to dyspnea or fatigue
- Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose >160 mg/d and/or use of supplemental metolazone therapy
- Progressive decline in serum sodium, usually to <133 mEq/L
- Frequent ICD shocks

Clinical Characteristics of HF Pts Who Should be Referred for Advanced Heart Failure Therapy


- Evidence of End Organ Failure
- Arrhythmias
- Cardiopulmonary Stress Testing
- Six Minute Walk Test
- Heart Failure Risk Model
- Low Cardiac Index
- Quality of Life Indices
## Clinical Characteristics of HF Pts Who Should be Referred for Advanced Heart Failure Therapy

### Evidence of End Organ Failure

- Arrhythmias
- Cardiopulmonary Stress Testing
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### Renal Failure

- Despite adequate diuretic dosing
- With GDMT (ACE-I, Spiro, Diuretics)

### Hepatic Dysfunction

- Elevated LFTs, INR, Bilirubin
- Ascites, Portal HTN

### GI Tract

- Reduced gut motility
- Bowel Ischemia

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## Clinical Characteristics of HF Pts Who Should be Referred for Advanced Heart Failure Therapy

- Evidence of End Organ Failure

**Arrhythmias**

- Cardiopulmonary Stress Testing
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### Increased Wall Stress

- Dilated LV Chamber Sizes ($\uparrow$LVEDD)
- Elevated Filling Pressures ($\uparrow$LVEDP)
- Thin Myocardium ($\downarrow$IVS, $\downarrow$LVPWT)

### Worsening Myocardial Oxygen Demand

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## Clinical Characteristics of HF Pts Who Should be Referred for Advanced Heart Failure Therapy

- **Evidence of End Organ Failure**
- **Arrhythmias**
  
  **Cardiopulmonary Stress Testing**
  - Six Minute Walk Test
  - Heart Failure Risk Model
  - Low Cardiac Index
  - Quality of Life Indices

- Peak VO₂ = The maximum capacity of the body to transport and use O₂ during exercise
  - Peak VO₂ > 14 ml/kg/min (4 METS) 1 & 2 yr Survival of 94% and 84% (Mancini et al. Circ. 1991)
  - Peak VO₂ ≤ 14 ml/kg/min 1 yr survival of 70% (Mancini et al. Circ. 1991)
  - In the Modern Era CRT-D and B-Blockers a Peak VO₂ > 12 ml/kg/min was associated with a survival benefit after heart transplant (Peterson et al. J Heart Lung Transplant. 2003)

- VE/VCO₂ Slope = The rate of increasing ventilation per unit of CO₂ production
  - Correlates with heart failure prognosis (Poggio et al. Am Heart J. 2010)

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