Implementing the CardioMEMS™ HF System into the Management of Heart Failure Patients

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Director, Heart Failure
Disclosures

- Robert W. Hull MD FACC
  - No disclosures

The content in this presentation represents the beliefs of the speaker and does not necessarily represent the views of St. Jude Medical.
Objectives

- Brief overview of heart failure therapies
- Overview CardioMEMS™ HF System
- Champion Trial
- Case presentations
Heart Failure: Impact on U.S. Health Care

- Overall 2.1% prevalence: 5.1M heart failure patients in 2010
- 825,000 people ≥ 45 years of age are newly diagnosed each year with HF
- Projected increase of 46% by 2030 to > 8 million pts

Heidenreich PA et al. Circ Heart Failure 2013.
Shift from Acute to Chronic Disease Management

Coronary Deaths

Coronary deaths are down by half...

Heart Failure Hospitalizations

But heart failure has almost tripled

Source: National Hospital Discharge Survey, CDC/NCHS and NHLBI.
Economic Burden Of HF Through 2030

- Based on current practices, AHA estimates total medical costs for CHF projected to increase to $70B by 2030 → a 2-fold increase from 2013

- 50% of costs attributed to hospitalization

Current Management Strategies: Heart Failure Preserved Ejection Fraction

- 11.2 Exclude ischemic heart disease (Strength of evidence C)
- 11.3 Blood pressure monitoring (Strength of evidence C)
- 11.4 Counseling on low sodium diet (Strength of evidence C)
- 11.5 Diuretic therapy (Strength of evidence C)
- 11.6 ACE-inhibitors and ARB’s may be considered (Strength of evidence C)
- 11.8 Beta Blockers recommended in setting hypertension (Strength of evidence B)
- 11.9 Calcium channel blockers should be considered in setting of hypertension (Strength of evidence C)

NO GUIDELINE THERAPIES

Heart Failure Society of America 2010 Comprehensive Heart Failure Practice Guidelines
Current Management Strategies: Heart Failure Reduced Ejection Fraction

- Study-proven ACE-inhibitor or ARB
- Study-proven B-blocker
- Study-proven aldosterone-antagonists
- Study-proven hydralazine/nitrates in African-Americans
- Study-proven cardiac resynchronization therapy
- Study-proven implantable defibrillator
- Digoxin
- Volume management: loop diuretics +/- thiazide diuretic
### Established Benefits Of Guideline-recommended HF Therapies

<table>
<thead>
<tr>
<th>Guideline Recommended Therapy</th>
<th>Relative Risk Reduction in Mortality</th>
<th>Number Needed to Treat for Mortality</th>
<th>NNT for Mortality (standardized to 36 months)</th>
<th>Relative Risk Reduction in HF Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI/ARB</td>
<td>17%</td>
<td>22 over 42 months</td>
<td>26</td>
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<td>Beta-blocker</td>
<td>34%</td>
<td>28 over 12 months</td>
<td>9</td>
<td>41%</td>
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<td>30%</td>
<td>9 over 24 months</td>
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<td>Hydralazine/Nitrate</td>
<td>43%</td>
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<td>7</td>
<td>33%</td>
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<tr>
<td>CRT</td>
<td>36%</td>
<td>12 over 24 months</td>
<td>8</td>
<td>52%</td>
</tr>
<tr>
<td>ICD</td>
<td>23%</td>
<td>14 over 60 months</td>
<td>23</td>
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</tr>
</tbody>
</table>

Established Benefits Of Guideline-recommended HF Therapies

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Current HF Management Inadequate in Managing Congestion Leading to Decompensation

- 90% of HF hospitalizations present with symptoms of pulmonary congestion
- Post hoc analysis of 463 acute decompensated HF patients from DOSE-HF and CARRESS-HF trials showed:
  - 40% of patients are discharged with moderate to severe congestion
  - Of patients decongested at discharge, 41% had severe or partial re-congestion by 60 days

Krum H and Abraham WT. Lancet 2009
Lala A, et al. JCF 2013
Causes Of Hospital Readmissions For Heart Failure

- Diet Noncompliance: 24%
- Inappropriate Rx: 16%
- Rx Noncompliance: 24%
- Failure to Seek Care: 19%
- Other: 17%

Over 2/3 of HF Hospitalizations Preventable

Annals of Internal Medicine 122:415-21, 1995
Physiologic Monitoring: Commonly Employed Parameters

- Symptoms
- Weight
- Blood pressure
- Physical exam
Meta-analysis of Remote Heart Failure Monitoring

![Bar chart showing parameters monitored in RCTs and cohort studies](image)

**Figure 2** Parameters Monitored in RCTs and Cohort Studies

- ECG = electrocardiogram; RCT = randomized controlled trial; RV = right ventricular.

Reductions In Heart Failure Admissions

# Sensitivity of Intrathoracic Impedance

<table>
<thead>
<tr>
<th>Study</th>
<th>FP/pt/yr</th>
<th>PPV %</th>
<th>Sensitivity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSE-HF</td>
<td>1</td>
<td>4.7</td>
<td>20.7-42.1</td>
</tr>
<tr>
<td>DEFEAT-PE Nominal</td>
<td>0.96</td>
<td>16.07</td>
<td>26.6%</td>
</tr>
<tr>
<td>DEFEAT-PE Programmable</td>
<td>0.92</td>
<td>18.18</td>
<td>29.1%</td>
</tr>
</tbody>
</table>

Physiologic Markers Of Acute Decompensation

* Graph adapted from Adamson PB, et al. Curr Heart Fail Reports, 2009

* Time Preceding Hospitalization (Days)

- Hemodynamically Stable
- Presymptomatic Congestion
- Decompensation

- Filling Pressure Increase
- Autonomic Adaptation
- Intrathoracic Impedance Changes

- Symptoms
- Weight Change

- Hospitalization
Average 30-day Readmission Rates for Heart Failure
Objectives

- Brief overview of heart failure therapies
- Overview CardioMEMS™ HF System
- Champion Trial
- Case presentations
Design Features of the HF Pressure Sensor

Sensor:
- No Battery
- No Leads
- Small Size (3.5 x 2 x 15mm)

Sensor Wire Loops:
- Function: Maintain Sensor Position in Vessel
- Wire Material: Nitinol
- Wire Diameter: 0.006”
- Loop Diameter/Width: 10 mm

[Diagram of the HF Pressure Sensor with labeled parts: Pressure Sensitive Capacitor, Fused Silica Housing with Silicone Coating, Inductor Coil]
Patient Electronics
Target pressure ranges:
- PA Pressure systolic 15–35 mmHg
- PA Pressure diastolic 8–20 mmHg
- PA Pressure mean 10–25 mmHg

Objectives

- Brief overview of heart failure therapies
- Overview CardioMEMS™ HF System
- Champion Trial
- Case presentations
Champion Trial: Prospective, Randomized, Single-blind Trial

Major Inclusion Criteria

- NYHA Class III heart failure
- HFrEF patients receiving proven therapies- ACE/ARB, Beta Blocker and CRT if indicated
- HF hospitalization within past 12 months
- PA branch diameter 7-15 mm and distance from target vessel to back < 10 cm
Major Exclusion Criteria

- Recurrent PE or DVT
- GFR < 25 ml/min and non-responsive to diuretic therapy or on dialysis
- Major cardiovascular event within 2 months
- Known coagulation disorder
- Hypersensitivity to aspirin +/or clopidogrel
Management Trends Based on PA Pressures

**PA Pressure Ranges**

- **PA Systolic:** 15-35 mmHg
- **PA Diastolic:** 8-20 mmHg
- **PA Mean:** 10-25 mmHg

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**Low PA Pressure (Hypo-volemic)**

*PA Mean Pressure trending* below the normal hemodynamic range

- Poor perfusion *in the absence of S&S of congestion*
- **Lower or discontinue diuretic**
  - if on thiazide and loop diuretic, lower or D/C the thiazide diuretic
  - if only on loop diuretic, lower the dose or discontinue
  - consider liberalization of oral fluid or salt restriction
- **Lower or hold vasodilators**
  if postural hypotension present
- **Re-evaluate PA pressures**
  2-3 days per week until PA pressures stabilize
- **Lower or hold ACE/ARB dose**
  if worsening renal function present with hypotension

---

**Elevated PA Pressure (Hyper-volemic)**

*PA Mean Pressure trending* above the normal hemodynamic range

- **Add or increase diuretic**
  - increase/add loop diuretic
  - change loop diuretic
  - add thiazide diuretic
  - IV loop diuretic
- **Add or increase vasodilators**
  - add or increase nitrate
- **Re-evaluate PA pressures**
  2-3 days per week until PA pressures stabilize
- **Evaluate other etiologies**
  if PA pressures remain elevated i.e. dietary indiscretion, sleep apnea, etc.
Device/System Related Complications

<table>
<thead>
<tr>
<th>Adjudication</th>
<th>Complication</th>
<th>Days after Implant</th>
<th>Description and Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely</td>
<td>Sensor did not fully deploy</td>
<td>During Implant</td>
<td>Sensor remained attached to delivery catheter. Therapy: sensor removed with snare during same procedure. Patient discharged next day</td>
<td>Recovered without sequela</td>
</tr>
<tr>
<td>Definitely*</td>
<td>In-situ thrombus</td>
<td>14</td>
<td>CTA revealed a small thrombus in a non-sensor PA branch secondary to over-inflation of the Swan-Ganz balloon. Thrombus not associated with sensor. Therapy: adjusted anticoagulation</td>
<td>Recovered without sequela</td>
</tr>
<tr>
<td>Possibly*</td>
<td>Hemothysis</td>
<td>During Implant</td>
<td>Chronic cough exacerbated during implant. Bronchoscopy revealed well formed thrombus, in non-implant lung, positive for Klebsiella. Therapy: irrigation, suction, antibiotics</td>
<td>Recovered without sequela</td>
</tr>
<tr>
<td>Possibly</td>
<td>Atypical Chest Pain</td>
<td>1</td>
<td>ECG normal and isoenzymes negative. Therapy: nitrates and analgesics</td>
<td>Recovered without sequela</td>
</tr>
<tr>
<td>Possibly</td>
<td>TIA</td>
<td>8</td>
<td>History of Afib, INR subtherapeutic. Therapy: warfarin adjusted to obtain therapeutic INR</td>
<td>Recovered without sequela</td>
</tr>
<tr>
<td>Possibly</td>
<td>Arterial embolism</td>
<td>10</td>
<td>History of A-Fib, INR was subtherapeutic; Right arm arterial thrombus. Therapy: thrombectomy and adjusted anticoagulation</td>
<td>Recovered without sequela</td>
</tr>
<tr>
<td>Possibly</td>
<td>Sepsis</td>
<td>1</td>
<td>HIV, Hep C, worsening respiratory distress, hemodynamic instability, sepsis. Therapy: antibiotics, inotropes, nebulizers</td>
<td>DNR; care withdrawn</td>
</tr>
<tr>
<td>Possibly</td>
<td>Atrial Dysrhythmia</td>
<td>1</td>
<td>Arrhythmia lead to worsening cardiopulmonary status. Therapy: amiodarone, diuretics, dopamine</td>
<td>DNR; care withdrawn</td>
</tr>
</tbody>
</table>

*reported by Investigator as SADE
CHAMPION Clinical Trial: Reasons For Medication Changes

Cumulative HF Hospitalizations

- ≤ 6 Months: 28% RRR, p = 0.0002
- > 6 Months: 45% RRR, p < 0.0001

Study Duration: 37% RRR, p < 0.0001

<table>
<thead>
<tr>
<th>Days from Implant</th>
<th>Treatment (158 HF Hospitalizations)</th>
<th>Control (254 HF Hospitalizations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>180</td>
<td>180</td>
<td>180</td>
</tr>
<tr>
<td>270</td>
<td>270</td>
<td>270</td>
</tr>
<tr>
<td>360</td>
<td>360</td>
<td>360</td>
</tr>
<tr>
<td>450</td>
<td>450</td>
<td>450</td>
</tr>
<tr>
<td>540</td>
<td>540</td>
<td>540</td>
</tr>
<tr>
<td>630</td>
<td>630</td>
<td>630</td>
</tr>
<tr>
<td>720</td>
<td>720</td>
<td>720</td>
</tr>
<tr>
<td>810</td>
<td>810</td>
<td>810</td>
</tr>
<tr>
<td>900</td>
<td>900</td>
<td>900</td>
</tr>
</tbody>
</table>

- No. at Risk:
  - Treatment: 270, 262, 244, 240, 169, 131, 108, 82, 28, 5, 1
  - Control: 280, 267, 252, 215, 179, 137, 105, 67, 25, 10, 0
# Heart Failure Hospitalization and 30-day Readmission Rates

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Treatment (n=120)</th>
<th>Control (n=125)</th>
<th>Relative Risk Reduction</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause 30-Day Readmissions N (events/patient year)</td>
<td>13 (0.07)</td>
<td>31 (0.18)</td>
<td>58%</td>
<td>0.42</td>
<td>p=0.0062</td>
</tr>
<tr>
<td>HF 30-Day Readmissions N (events/patient year)</td>
<td>4 (0.02)</td>
<td>18 (0.10)</td>
<td>78%</td>
<td>0.22</td>
<td>p=0.0027</td>
</tr>
<tr>
<td>HF hospitalizations N (events/patient year)</td>
<td>60 (0.34)</td>
<td>117 (0.67)</td>
<td>49%</td>
<td>0.51</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

Adamson et al., Impact of Wireless Pulmonary Artery Pressure Monitoring on Heart Failure Hospitalizations and 30-Day Readmissions in Medicare-Eligible Patients with NYHA Class III Heart Failure: Results from the CHAMPION Trial AHA 2014, Chicago. Abstract 16744.
### CHAMPION Clinical Trial: The Number Needed To Treat (NNT) To Prevent One Hf-related Hospitalization Is Lower Vs. Other Therapies

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Trial</th>
<th>Mean Duration of Randomized Follow-Up</th>
<th>Annualized Reduction in HF Hospitalization Rates</th>
<th>NNT per year to Prevent 1 HF Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blocker</td>
<td>COPERNICUS</td>
<td>10 months</td>
<td>33%</td>
<td>7</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>RALES</td>
<td>24 months</td>
<td>36%</td>
<td>7</td>
</tr>
<tr>
<td>CRT</td>
<td>CARE-HF</td>
<td>29 months</td>
<td>52%</td>
<td>7</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>MERIT-HF</td>
<td>12 months</td>
<td>29%</td>
<td>15</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>SOLVD</td>
<td>41 months</td>
<td>30%</td>
<td>15</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>EMPHASIS-HF</td>
<td>21 months</td>
<td>38%</td>
<td>16</td>
</tr>
<tr>
<td>Digoxin</td>
<td>DIG</td>
<td>37 months</td>
<td>24%</td>
<td>17</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>Val-HeFT</td>
<td>23 months</td>
<td>23%</td>
<td>18</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>CHARM</td>
<td>40 months</td>
<td>27%</td>
<td>19</td>
</tr>
<tr>
<td>PA pressure monitoring</td>
<td>CHAMPION</td>
<td>17 months</td>
<td>33%</td>
<td>4</td>
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Impact On 30 Day Readmissions In Medicare Eligible Patients

<table>
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<tr>
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<th>Control (Standard of Care)</th>
<th>Treatment (PA pressure monitoring)</th>
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Pre-specified Subgroup Analysis: HF Hospitalization by Baseline EF

- **Reduced (EF<40%)**
  - Treatment: 0.36
  - Control: 0.47
  - N = 208
  - p = 0.0085
  - RRR = 24%

- **Preserved (EF≥40%)**
  - Treatment: 0.18
  - Control: 0.33
  - N = 62
  - N = 57
  - p = 0.0001
  - RRR = 46%

*p-value from two-group t-test*
Champion Clinical Trial: Substantial Reduction In Hospitalizations And Mortality In Patients On GDMT

- Post-hoc analysis HFrEF patients Champion Trial on guideline-directed medical therapy (ACE inhibitor/ARB and Beta Blocker)
- 456 patients analyzed: 163 treatment group managed with PA pressure and 174 control group managed with Standard of Care (SOC). Follow-up averaged 17 mos.
- Patients on GDMT managed with PA pressure had a 43% reduction in HF hospitalizations and 57% reduction in mortality
- Neurohormonal control combined with hemodynamic optimization through PAP management lead to substantial incremental clinical benefit

Abraham, et al. ACC 2015
Outcomes in HFrEF Patients Already On GDMT

<table>
<thead>
<tr>
<th>GDMT Class</th>
<th>PAP Monitoring (Treatment Group) N=222</th>
<th>HF SOC (Control Group) N=234</th>
<th>Total Daily Dose</th>
<th>HF Hospitalizations</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor or ARB</td>
<td>173 (78%)</td>
<td>183 (78%)</td>
<td>19.6 mg</td>
<td>0.59 (0.46-0.75)</td>
<td>4</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>206 (93%)</td>
<td>220 (94%)</td>
<td>29.3 mg</td>
<td>0.66 (0.53-0.81)</td>
<td>5</td>
</tr>
<tr>
<td>ACE inhibitor or ARB &amp; Beta Blocker</td>
<td>163 (73%)</td>
<td>174 (74%)</td>
<td>19.8 mg</td>
<td>0.57 (0.45-0.74)</td>
<td>3</td>
</tr>
</tbody>
</table>

[1] ACE inhibitor or ARB doses are converted to enalapril equivalents. Beta blocker doses are converted to carvedilol equivalents.
[2] number needed to treat (NNT) to prevent one event per year
[3] hazard ratio, 95% Confidence Interval, and p-value from Andersen-Gill model
[4] hazard ratio and 95% Confidence Interval from Cox regression and p-value from logrank test

ACC 2015
The CardioMEMS™ HF System HRRP readmission ratio of 0.74 was lower than all hospital ratios in 2011. 0.74 - Readmission ratio for patients managed with CardioMEMS HF System.
Objectives

- Brief overview of heart failure therapies
- Overview CardioMEMS™ HF System
- Champion Trial
- Case presentations
Case Presentation

• 72 year old gentleman, ischemic cardiomyopathy, EF 20%
• 4 CHF admissions over past 12 months between VA and WV
• Frequent ER visits for CHF
• CRT-D
• NYHA class III
• Medications include:
  • digoxin 125 mcg qod
  • furosemide 20 mg qd
  • lisinospril 2.5 mg qd
  • metoprolol succinate 25 mg qd
  • amiodarone 200mg qd
  • warfarin as directed
Doubled diuretic
Traveled to VA, PRN diuretic
Reduced diuretic
Departed for cruise
Returned ill from cruise, PA mean dropped, stopped diuretic
Case Presentation

- 64 year old male with ischemic CM s/p remote CABG and EF 30-35%, NYHA Class III
- CHF admission June, re-admitted August
- DM, HTN, COPD, and PVD
- Referring cardiologist: “he only comes out of the woods to get admitted with HF.”
- Medications include:
  - metoprolol succinate 50 mg qd
  - hydralazine 25 mg tid
  - imdur 30 mg qd
  - furosemide 40 mg qd
Increased diuretic
Case Presentation

- 72 year old woman, non-communicative due to mental retardation, lives at group care facility
- HTN with LVH and diastolic dysfunction
- Admitted Aug with CHF and BNP 5670, re-admitted late Aug with decompensated CHF
- Medications include: furosemide 80 mg qd, losartan 50 mg qd and aldactone 25 mg qd
Case Presentation

- 70 year old gentleman with combined systolic and diastolic heart failure; EF 45%
- COPD with restrictive PFT’s, DM, HTN
- Estimated GFR 36 ml/min.
- 2 admissions for CHF 2014
- NYHA class III on carvedilol, furosemide, hydralazine, nitrates, and spironolactone
Implant PAS/PAD 76/25  PA 48  PCWP 32
Current HF Management Inadequate in Managing Congestion Leading to Decompensation

- 90% of HF hospitalizations present with symptoms of pulmonary congestion
- Post hoc analysis of 463 acute decompensated HF patients from DOSE-HF and CARRESS-HF trials showed:
  - 40% of patients are discharged with moderate to severe congestion
  - Of patients decongested at discharge, 41% had severe or partial re-congestion by 60 days

Krum H and Abraham WT. Lancet 2009
Lala A, et al. JCF 2013
Summary

Enables proactive and personalized HF management

May be used in risk stratification, but not actionable

Unreliable, late