Telemonitoring in Heart Failure

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Director, Division of Cardiovascular Medicine
Background

- Despite current therapies and disease management approaches, the rate of heart failure hospitalization remains unacceptably high
  - > 1.1 million heart failure hospitalizations annually
  - > 25% readmission rate at 1 month; 50% at 6 months
  - > $18 billion in annual direct costs

- Current methods for monitoring heart failure patients have not adequately addressed this issue
Key Therapeutic Goal in Heart Failure:
Maintain Optimal Volume/Pressure Status

Hypervolemia/Elevated Intra-cardiac and Pulmonary Artery Pressures:
*Increased symptoms, increased risk of hospitalization, increased risk of arrhythmias, increased mortality*

Euvolemia/Normal Intra-cardiac and Pulmonary Artery Pressures:
*Low risk*

Hypovolemia/Low Intra-cardiac and Pulmonary Artery Pressures:
*Symptomatic hypotension, syncope, pre-renal azotemia*
What Do We Really Need To Monitor?

- What do we really want to know?
  - Pulmonary congestion / left ventricular filling pressure (LVFP)

- How do we currently assess these in patients with chronic heart failure?
  - Symptoms
  - Daily weights
  - Physical examination
  - Biomarkers

- How well do these assessments perform?
  - Not very well
Limitations of Available Monitoring Systems

- **Weight and Symptoms** – Recent large, landmark clinical studies (Tele-HF, TIM-HF) investigating the effectiveness of telemonitoring demonstrated no benefit in reducing HF hospitalizations.

- **BNP - PRIMA** and other studies guided identification of patients at risk for HF events, but showed no significant reduction in HF-related admissions.

- **Device-Based Diagnostics** - May be useful for identifying patients that may be at higher risk for a HF hospitalization (PARTNERS-HF Study), but have not demonstrated a reduction in HF-related hospitalizations.

*Tele-HF: Yale Heart Failure Telemonitoring Study; NEJM, 2010*
*TIM-HF: Telemonitoring Intervention in Heart Failure, Eur J. Heart Failure, 2010*
*PRIMA: Can Pro-BNP guided heart failure therapy improve morbidity and mortality? J Am Coll Card, 2010*
*PARTNERS-HF: Combined Heart Failure Device Diagnostics Identify Patients at Higher Risk of Subsequent Heart Failure Hospitalizations. J Am Coll Card, 2010*
Premise of Physiological Heart Failure Monitoring (1)
Premise of Physiological Heart Failure Monitoring (2)

-21 -14 - 7 Days

Proactive

Medical Intervention

Hemodynamic Changes

Averted Heart Failure Event

Days

Proactive
Implantable Hemodynamic Monitors

- LV Pressure Sensor
- RV Pressure Sensors
- LA Pressure Sensor
- PA Pressure Sensors
The Pulmonary Artery Pressure Measurement System*

Catheter-based delivery system

MEMS-based pressure sensor

Home electronics

PA Measurement database

*CardioMEMS Inc., Atlanta, Georgia, USA
Primary Results of the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) Trial

Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynn Warner Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group*

Summary

Background Results of previous studies support the hypothesis that implantable haemodynamic monitoring systems might reduce rates of hospital admission in patients with heart failure. We undertook a single-blind trial to assess this approach.

Methods Patients with New York Heart Association (NYHA) class III heart failure, irrespective of the ejection fraction, and a previous hospital admission for heart failure were enrolled in 64 centres in the USA. They were randomly assigned by use of a centralised electronic system and assigned to management with a wireless implantable...
CHAMPION Study Design

- Prospective, multi-center, randomized (1:1), controlled single-blind clinical trial
  - Treatment group received traditional HF management guided by hemodynamic information from the sensor
  - Control group received traditional HF disease management

- 550 subjects enrolled at 63 sites in the U.S. between October 2007 and September 2009

- All subjects followed in their randomized single-blind study assignment until the last patient reached 6 months of follow-up
Cumulative HF Hospitalizations Over Entire Randomized Follow-Up Period

$p < 0.001$, based on Negative Binomial Regression
No Adverse Impact on Non-HF Hospitalizations

Hemodynamic monitoring reduced heart failure related hospitalizations without increasing non-heart failure hospitalizations

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cause Hospitalizations</td>
<td>229</td>
<td>263</td>
</tr>
<tr>
<td>- HFR</td>
<td>83</td>
<td>120</td>
</tr>
<tr>
<td>Non-HF Hospitalizations</td>
<td>146</td>
<td>143</td>
</tr>
<tr>
<td>All Days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cause Hospitalizations</td>
<td>484</td>
<td>590</td>
</tr>
<tr>
<td>- HFR</td>
<td>153</td>
<td>253</td>
</tr>
<tr>
<td>Non-HF Hospitalizations</td>
<td>331</td>
<td>337</td>
</tr>
</tbody>
</table>
## Secondary Efficacy Results

<table>
<thead>
<tr>
<th>Measure</th>
<th>Treatment (n=270)</th>
<th>Control (n=280)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change from Baseline in Mean Pulmonary Artery Pressure at 6 Months Mean AUC</td>
<td>-156</td>
<td>33</td>
<td>0.008</td>
</tr>
<tr>
<td>Subjects Hospitalized for Heart Failure at 6 Months # (%)</td>
<td>54 (20)</td>
<td>80 (29)</td>
<td>0.022</td>
</tr>
<tr>
<td>Days Alive Outside Hospital at 6 Months Mean</td>
<td>174.4</td>
<td>172.1</td>
<td>0.022</td>
</tr>
<tr>
<td>Minnesota Living with Heart Failure Questionnaire at 6 Months Mean</td>
<td>45</td>
<td>51</td>
<td>0.024</td>
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</table>
# Heart Failure Medication Changes at 6 Months

<table>
<thead>
<tr>
<th></th>
<th>baseline medications</th>
<th>medication changes up to 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Patients</td>
</tr>
<tr>
<td></td>
<td>Treatment (270)</td>
<td>Control (280)</td>
</tr>
<tr>
<td>ARB</td>
<td>42 (15.6%)</td>
<td>59 (21.1%)</td>
</tr>
<tr>
<td>Ace Inhibitors</td>
<td>170 (63.0%)</td>
<td>173 (61.8%)</td>
</tr>
<tr>
<td>Aldosterone Antagonist</td>
<td>117 (43.3%)</td>
<td>115 (41.1%)</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>243 (90.0%)</td>
<td>261 (93.2%)</td>
</tr>
<tr>
<td>Diuretic-Loop</td>
<td>250 (92.6%)</td>
<td>264 (94.3%)</td>
</tr>
<tr>
<td>Diuretic-Thiazide</td>
<td>48 (17.8%)</td>
<td>51 (18.2%)</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>36 (13.3%)</td>
<td>33 (11.8%)</td>
</tr>
<tr>
<td>Nitrate</td>
<td>66 (24.4%)</td>
<td>57 (20.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>280</td>
</tr>
</tbody>
</table>

**HF Medication Changes**

<table>
<thead>
<tr>
<th>Mean±StdDev (N)</th>
<th></th>
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<tbody>
<tr>
<td>9.2±7.5 (270)</td>
<td>3.8±4.5 (280)</td>
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</table>

**P < 0.0001**

**5.4 incremental medication changes**
CHAMPION: Putting It Altogether

- Pulmonary Artery Pressure
  - Medication Changes On Basis of Pulmonary Artery Pressure
    - Pulmonary Artery Pressure Reduction
      - Heart Failure Related Hospitalization Reduction
        - Quality of Life Improvement
          - P values for Treatment Vs Control Group

- P<0.0001
- P=0.008
- P=0.024
Left Atrial Pressure Monitor*

Sensor module features
- Hermetic Ti housing /sensing diaphragm
- Custom ASIC measures LAP, IEGM, Temp
- Folding nitinol septal fixation anchors
- Full digital waveform telemetry
- RF power, no implanted battery

*St. Jude Medical, Sylmar, CA
Handheld Patient Advisor Module

(s) carvedilol(25mg), 1 tab  
(s) lisinopril(20mg), 1 tab  
*(d) furosemide(40mg), 1 tab
DynamicRx Guided HF Therapy: How it works

LAP ≥28 ... Very High... furosemide 80mg, call MD
LAP 19-27 ... High......... 40mg
LAP 10-18 ... Optimal...... 20mg
LAP 6-9 ... Low............ 10mg
LAP ≤ 5 ... Very Low.... hold, increase fluid intake

Optimal LAP makes it easier to up-titrate β-Blockers and ACE-I/ARBs

Remote (patient’s home)
Direct USB (in-clinic)
RF Telemetry

Application Software
Trends, Waveforms, Prescriptions
PC or Web Based

PAM™
Physician-Directed Patient Self-Management of Left Atrial Pressure in Advanced Chronic Heart Failure
Circulation published online Feb 22, 2010;
HOMEOSTASIS I & II
Endpoints, Design, Subject Accounting

Open-label, registry

1º Endpoint (safety)
- Freedom from Major Adverse Cardiac and Neurological Events (MACNE) at 6 weeks

2º Endpoints (functionality)
- Calibration
- LAP vs. PCWP

3º Endpoints (Effectiveness surrogates)
- Control of LAP
- Hospitalization
- Clinical parameters
HF Event Rates
(ADHF and All-Cause Death)
Comparison of Periods with and without LAP-Guidance

<table>
<thead>
<tr>
<th>Period</th>
<th>Annualized Event Rate</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-mo period before enrollment</td>
<td>1.4 (1.1-1.9)</td>
<td>0.054</td>
</tr>
<tr>
<td>First 3 mo Observation Period</td>
<td>0.68 (0.33-1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>After mo 3 Titration/Stability Periods</td>
<td>0.28 (0.18-0.45)</td>
<td>0.041</td>
</tr>
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</table>
New Approach to the Non-Invasive Assessment of Lung Water

- Proprietary RF monitoring and imaging technology*
- As fluid replaces air, there is an increase in the dielectric coefficient
- Measurement is localized (lung-specific) as opposed to other modalities (e.g., bio-impedance)
- Enables non-invasive and continuous monitoring of lung fluid concentration
- Validated against “gold standard” (CT) in animals
- First human studies ongoing

*ReDS™ Technology, Sensible Medical Innovations, Netanya, Israel