Treat the Numbers and Not the Patients – The Revolution of Pulmonary Artery Pressure Guided Medical Therapy in Heart Failure

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Heart Failure Is Associated with High Hospitalization and Readmission Rates

- In 2010, there were 1 million hospitalizations in the US with HF as the principal diagnosis\(^1\)
  - Hospitalization rate did not change significantly from 2000\(^1\)
- Average length of hospital stay
  - Approximately 5 days (US)\(^2\)
  - 11 days (Europe)\(^3\)
- HF is also associated with high readmission rates:
  - ~25% all-cause readmission within 30 days and ~50% within 6 months\(^5\)
  - A mortality rate is 12% at 1 month and 33% at 1 year f/u.

1. CDC NCHS National Hospital Discharge Survey, 2000-2010
Economic Risks of HF Readmissions in the US

Medicare’s Hospital Readmissions Reduction program penalizes hospitals that have above average all-cause readmissions within 30 days following HF discharge.

Percent withholding of all inpatient Medicare payments will increase to up to 3% by 2015 and beyond.

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>2013</th>
<th>2014</th>
<th>2015+</th>
</tr>
</thead>
<tbody>
<tr>
<td>% payment withholding</td>
<td>up to 1%</td>
<td>up to 2%</td>
<td>up to 3%</td>
</tr>
</tbody>
</table>

3. CMS Hospitals Readmissions Reductions Program of the Patient Protection and Affordable Care Act (PPACA), 2010.
Increases in pressure start the cycle of worsening heart failure. Adapted from Jaski BE, “Basics of Heart Failure A Problem Solving Approach.”
I DIDN'T SIGN UP FOR THIS!!!
Acute Exacerbations May Contribute to the Progression of the Disease

With each event, hemodynamic alterations contribute to progressive ventricular dysfunction.

Outpatient Monitoring of Congestion

- Signs and symptoms
- Daily weights
- Natriuretic peptides (BNP and NT-pro BNP)
- Implanted impedance monitors
- Implanted hemodynamic sensors
Absence of Specific Signs, Symptoms and CXR Findings Doesn’t Exclude High PCWP

- Ability to predict PCWP > 18-20 mmHg in pts. with severe heart failure

<table>
<thead>
<tr>
<th>Sign</th>
<th>Sens.</th>
<th>Spec.</th>
<th>PPV</th>
<th>NPV</th>
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</thead>
<tbody>
<tr>
<td>Dyspnea on exertion</td>
<td>66</td>
<td>52</td>
<td>45</td>
<td>27</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>66</td>
<td>47</td>
<td>61</td>
<td>37</td>
</tr>
<tr>
<td>Edema</td>
<td>46</td>
<td>73</td>
<td>79</td>
<td>46</td>
</tr>
<tr>
<td>JVD</td>
<td>70</td>
<td>79</td>
<td>85</td>
<td>62</td>
</tr>
<tr>
<td>S3</td>
<td>73</td>
<td>42</td>
<td>66</td>
<td>44</td>
</tr>
<tr>
<td>CXR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>97</td>
<td>10</td>
<td>61</td>
<td>---</td>
</tr>
<tr>
<td>Redistribution</td>
<td>60</td>
<td>68</td>
<td>75</td>
<td>52</td>
</tr>
<tr>
<td>Interstitial edema</td>
<td>60</td>
<td>73</td>
<td>78</td>
<td>53</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>43</td>
<td>79</td>
<td>76</td>
<td>47</td>
</tr>
</tbody>
</table>

Adapted from Butman SM. Et al. J Am Coll Cardiol. 1993; 22: 968
BNP Levels and Clinical Class in Heart Failure

21% had BNP < 100 pg/mL

2 Tang W et al. J Card Fail. 2002; 8: S83
Residential Tele Home Health
(Telemonitoring failed in large trials)

- Patient weight
- Systolic/diastolic (mean) blood pressure
- Pulse
- Oxygen saturation
- Monitoring volume status, metabolic panel
- Follow up by phone and visit with RN
Telemonitoring did not reduce HF readmissions or mortality at 6-21 mo f/u.

- **TELE-HF Trial**

- **TIM-HF Trial**

- **Beat HF Trial**
  - presented on November 8, 2015 – AHA 2015 - Orlando
Percutaneous device therapy

- Poor clinical outcomes of HF patients
- High healthcare-related costs
- Urgent need to adopt aggressive strategies to favorably alter the course of HF condition
- Outpatient hemodynamic monitoring to reduce LV filling pressures and improve end organ perfusion in advanced HF patients
Devices to monitor hemodynamics

- Implantable device to measure impedance
  - Optivol system with pacemaker or ICD devices (MiD-HeFT and FAST Trials)

- Implantable pressure sensors
  - LA pressure: HeartPOD (Homeostasis, Laptop)
  - RV pressures: Medtronic Chronicle ICD sensor (Compass HF Trial)
  - PA pressures: CardioMems sensor (Champion HF Trial)
OPTIVOL Software

Pulmonary Vascular Congestion

→

Decrease in Intrathoracic Impedance

Medtronic Impedance Diagnostics in Heart Failure Patients Trial*

MIDHeFT Study
FAST
Fluid Accumulation Status Trial

- A detection rate of HF decompensation events:
  - 62% in Optivol intrathoracic impedance group
  - 8% in weight monitoring group

- Sensitivity to detect congestion
  - 71.4% in Optivol fluid index (impedance group)
  - 22.5% in weight monitoring group

- False alarm rate was 0.9 per 1 year of follow-up

*Presented at Heart Failure Society of America Meeting in Boston 2009*
Congestion Precedes Hospitalization

Adamson PB et al. J Am Coll Cardiol. 2003; 41: 565
COMPASS Trial: Hemodynamic Data

- Prospective, multicenter randomized, single-blind trial of 274 class III/IV HF patients
- Increases in RV Pressures – Not Body Weight – Precede HF Hospitalization

**Trial design:** Severe heart failure patients were randomized to therapy directed by the implantable Chronicle device (n = 134) or continued medical management (n = 140).

**Results**
- Freedom from device complications: 92%
- Freedom from hospitalizations, emergency department, or heart failure clinic visits: 44 Chronicle patients and 60 control (p = 0.33)

**Conclusions**
- The implantable Chronicle device was not superior to continued medical management in severe heart failure
- The Chronicle device did not reduce freedom from hospitalizations, emergency department, or heart failure clinic visits

Bourge RC, et al. JACC 2008;51:1073-9
HeartPOD device in HOMEOSTASIS Trial

* Sensor tip anchors in the left atrium

* Requires transeptal approach

Circulation. 2010 Mar 9;121(9):1086-95.
Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

William T Abraham MD, Philip B Adamson MD, Robert C Bourge MD, Mark F Aaron MD, Maria Rosa Costanzo MD, Lynne W Stevenson MD, Warren Strickland MD, Suresh Neelagaru MD, Nirav Raval MD, Steven Krueger MD, Stanislav Weiner MD, David Shavelle MD, Bradley Jeffries MD, Jay S Yadav MD,

for the CHAMPION Trial Study Group.

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

Pulmonary Artery Pressure Sensor

RHC with selective pulmonary angiogram

target implant site
Pulmonary Artery Pressure Sensor
Measurement System*
CHAMPION HF versus Other Trials

- No LVEF requirement (systolic or diastolic HF allowed)
- No QRS width requirement
- Pacemaker / ICD were not required
- Battery was not required (no need for procedure to replace software or battery)
- Wireless system
- No need for trans-septal puncture
**Cumulative HF Hospitalizations Over Entire Randomized Follow-up Period**

<table>
<thead>
<tr>
<th>Primary Efficacy Endpoint*</th>
<th>Treatment group (n=270)</th>
<th>Control group (n=280)</th>
<th>Relative Risk Reduction</th>
<th>P value</th>
<th>NNT = number needed to treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint: HF related admissions at 6 months*</td>
<td>83 patients (31%)</td>
<td>120 patients (44%)</td>
<td><strong>30%</strong></td>
<td>&lt;0.0001</td>
<td><strong>8</strong></td>
</tr>
<tr>
<td>Ancillary analysis: HF related admissions at 15 months</td>
<td>153</td>
<td>253</td>
<td><strong>39%</strong></td>
<td>&lt;0.0001</td>
<td><strong>4</strong></td>
</tr>
</tbody>
</table>

Cumulative HF Hospitalizations

only standard of care HF management

6 months

15 months

using PA sensor measurements

**Lancet. 2011 Feb 19;377(9766):658-66.**
Freedom From Death or First HF Hospitalization using PA sensor measurements only standard of care HF management

Hazard Ratio 0.71 (95% CI 0.55-0.92) p=0.0086

Lancet 2011
Rate of HF Hospitalizations by Baseline Ejection Fraction

Reduced (EF<40%)
- Treatment: 0.36, n=208
- Control: 0.47, n=220
- RRR=24%, p=0.0085

Preserved (EF≥40%)
- Treatment: 0.18, n=6
- Control: 0.33, n=5
- RRR=46%, P=0.0001

22% pts had preserved LVEF


6 months f/u
A. Cumulative heart failure hospitalizations in patients with preserved LVEF. 

B. Cumulative heart failure hospitalizations in patients with reduced LVEF.

17.6-month follow-up

Adamson PB, et al. Circ Heart Failure 2014
CHAMPION Clinical Trial: HF Medication Changes

CHAMPION Clinical Trial: Accurate Titrations of Medical Therapy Resulted In Fewer HF Hospitalizations In Treatment Group

Impact of Diastolic Pulmonary Artery Pressure on Diuretic Changes


Diuretic Changes (Average / Patient)

Baseline PA Diastolic (mmHg)

PA Pressure Guided HF Management (Treatment Group)
Standard of Care HF Management Only (Control Group)

CardioMEMs

2.8X

Control

2.8X
Impact of Diastolic Pulmonary Artery Pressure on Vasodilator Changes


CardioMems

Control

3X
No Change in Renal Function
All cohort


<table>
<thead>
<tr>
<th></th>
<th>Active Monitoring Group (N = 270)</th>
<th>Blind Therapy Group (N = 280)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline creatinine</td>
<td>1.40 ± 0.47 (270)</td>
<td>1.35 ± 0.42 (280)</td>
<td>0.56</td>
</tr>
<tr>
<td>Creatinine change from</td>
<td>0.10 ± 0.45 (230)</td>
<td>0.07 ± 0.38 (235)</td>
<td>0.28</td>
</tr>
<tr>
<td>baseline to 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline GFR</td>
<td>60.4 ± 22.5 (270)</td>
<td>61.8 ± 23.2 (280)</td>
<td>0.56</td>
</tr>
<tr>
<td>GFR change from baseline</td>
<td>-3.1 ± 7.0 (230)</td>
<td>-1.0 ± 6.4 (235)</td>
<td>0.20</td>
</tr>
<tr>
<td>to 6 months</td>
<td></td>
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</table>
“Wireless Swan” - Example

extra diuretic dose effect

↑diuretic dose

vasodilator

VACATION
Torsemide and Isosorbide doses increased. Metolazone added.
Heart failure management using CardioMems pulmonary artery pressure monitoring resulted in a significant reduction in HF hospitalizations.

- 30% reduction in HF hospitalizations at 6 months.
- 38% reduction in annualized HF hospitalization rate for the entire randomized follow-up.
- Hospitalization reductions were significant and even greater in diastolic HF patients with preserved LVEF with sensor hemodynamic-guided care with benefit maintained at 17.6 month follow-up.
- Improvements in PAPs, proportion of patients hospitalized, days out of the hospital, and quality of life.

The accurate titration of heart failure medications (diuretics and vasodilators) according to sensor hemodynamic data led to reduced rate of HF hospitalizations as compared to standard of care HF management.

The CardioMems sensor monitoring system represents a significant improvement if HF management for NYHA Class III HF patients.

Fight Congestion in Heart Failure: Conclusions

- Congestion is an important predictor of mortality and morbidity.
- Congestion is the primary cause of heart failure hospital admissions and predicts readmissions.
- Congestion is often difficult to recognize, delaying appropriate interventions.
- Clinical congestion often lags behind rising filling pressures.
- Congestion contributes to progression of heart failure.
- Improved methods to monitor congestion by knowledge of PA pressures may improve clinical management and outcomes.