Taking the FAILURE out of CHF

Denzil Moraes, MD, FACC
Our Lady of the Lake Heart & Vascular Institute
CHAIR – Heart Failure Committee
The Burden of Heart Failure

Prevalence of Heart Failure

~ Currently 5.7 Million
~ By 2030 8 Million

Hospital Discharges

~ One Million Annually
~ Within 6 months 50% Readmitted
~ Essentially unchanged over the last Decade

Cost

~ $21 Billion Dollars Annually
~ By 2030 $53 Billion Dollars Annually
CALL TO ACTION

How Can We Better Manage Heart Failure?
Physician Inertia
~ Systematic approach – Optimize Electronic Health Record Use
~ Engage in Prevention
~ Understand basis for contemporary treatment

Use the Hospitalization as a Sentinel Event
~ Scrutinize patient “Ask Why?”
~ Multidisciplinary approach
~ Novel forms of monitoring / Out-patient Follow-up
Contemporary Treatment
Pharmacologic Treatment for Stage C HFrEF

HFrEF Stage C
NYHA Class I – IV
Treatment:

Class I, LOE A
ACEI or ARB AND
Beta Blocker

For all volume overload, NYHA class II-IV patients
Add

Class I, LOE C
Loop Diuretics

For persistently symptomatic African Americans, NYHA class III-IV
Add

Class I, LOE A
Hydral-Nitrates

For NYHA class II-IV patients. Provided estimated creatinine >30 mL/min and K^+ <5.0 mEq/dL
Add

Class I, LOE A
Aldosterone Antagonist
Stages of Heart Failure and Treatment Options for Systolic Heart Failure

Stage A
High risk with no symptoms

Stage B
Structural heart disease, no symptoms

Stage C
Structural disease, previous or current symptoms

Stage D
Refractory symptoms requiring special intervention

Hospice
VAD, transplantation
Inotropes
Aldosterone antagonist, nesiritide
Consider multidisciplinary team
Revascularization, mitral-valve surgery
Cardiac resynchronization if bundle branch present
Dietary sodium restriction, diuretics, digoxin
ACEIs or ARBs and beta blockers in all patients
ACEIs or ARBs in all patients; beta blockers in selected patients
Treat HTN, diabetes, dyslipidemia; ACEIs or ARBs in some patients
Risk-factor reduction, patient and family education

Physician Inertia

“Better Understanding of Pathophysiology…”
Primary myocardial injury

Secondary myocardial effects
- LV remodelling
- Contractility
- Hypertrophy
- Apoptosis
- Cytokines
- Fibrosis
- NOS/ROS
- Electrophysiology

Neurohormones
- ↑SNS activity
- ↑RAS
- ↑Endothelin
- ↑ANP/BNP
- ↑Cytokines

Endothelium
- Vasoconstriction
- NOS/ROS
- Structural change
- Cytokines

CHF outcomes: sudden death, progressive pump failure, symptoms
Altered Phenotypes in the Failing Heart

“The failing heart is not simply an enlarged version of the normal heart”

Louis N. Katz, 1966

Changes in:

- Architectural Phenotype
- Cellular Phenotype
- Molecular Phenotype
Architectural Phenotypes

- Concentric hypertrophy
- Normal
- Eccentric hypertrophy
The Heart with Hypertrophy reverts to the Fetal phenotype

1. Low ATPase myosin (β myosin heavy chain)
   ↓ myocardial contractility

2. Less sarcoplasmic reticulum
   ↓ intracellular Ca stores
     ↓ myocardial contractility
   ↑ dependence on extracellular Ca
   ↑ arrhythmias
Hypothesis: β-Blockade improves myocardial function and reverses remodeling by altering cardiac myocyte gene expression

- Study subjects: 53 patients with dilated cardiomyopathy
- Randomized to metoprolol, carvedilol, or placebo for 6 months

Myocardial gene expression in dilated cardiomyopathy in response to β-blocker therapy

Metoprolol or carvedilol for 6 mo

*Change in gene mRNA expression*

- **β₁-receptor**
- **β₂-receptor**
- Atrial natriuretic peptide
- Sarcoplasmic reticulum calcium ATPase
- α-myosin heavy chain
- β-myosin heavy chain

*Response (n = 26)*
*No response (n = 6)*

(↑ LVEF)

*Molecules mRNA × 10⁻⁵ μg total RNA*

Hypothetical mechanism of \( \beta \)-blocker induced improvement in myocardial function and reversal of remodeling

\( \beta_1 \)-Adrenergic blockade \( \rightarrow \) De-induction of cardiac myocyte fetal gene program \( \rightarrow \) Reverse remodeling \( \rightarrow \) ↑ Systolic function

Aldosterone and Heart Rate
HF hospitalization or CV death vs All cause mortality

EMPHASIS

HF hospitalization or CV death

All cause mortality

NEJM 2011; 364: 11-21
EMPHASIS

All cause Hospitalization vs HF Hospitalization

- In patients receiving placebo, the risk of all-cause hospitalization was 29.9% compared to 35.8% in the eplerenone group (p<0.001).
- The risk of HF hospitalization was 12% in the placebo group and 18.4% in the eplerenone group (p<0.001).

Graphs showing the cumulative incidence of hospitalization over time for both groups, indicating a statistically significant reduction in hospitalization for both all-cause and HF hospitalization with eplerenone treatment.

NEJM 2011; 364: 11-21
Aldosterone Antagonists
Ivabradine - SHIFT

Heart Rate during study

Lancet 2010; 376. 875-85
Ivabradine - SHIFT

Cardiovascular death or Heart Failure Hospitalization

Lancet 2010; 376. 875-85
Ivabradine - SHIFT

First HF Hospitalization

Cardiovascular death

Lancet 2010; 376. 875-85
African Americans
A-HeFT: African American Heart Failure Trial

- NYHA class III or IV HF with decreased EF
- Patients self-identified as African American
- Added isosorbide dinitrate plus hydralazine (ID+H) or placebo to standard HF therapy (ACEI)
- ID+H significantly increased survival and decreased mortality
  - Mortality 39% RR
  - (ID+H=6.2% Placebo=10.2%)

Neprilysin Inhibition
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
LCZ696: Angiotensin Receptor Neprilysin Inhibition

LCZ696

Angiotensin receptor blocker + Inhibitor of neprilysin
PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

Kaplan-Meier Estimate of Cumulative Rates (%)

Enalapril (n=4212)
LCZ696 (n=4187)

HR = 0.80 (0.73-0.87)
P = 0.0000002
Number needed to treat = 21
PARADIGM-HF: Cardiovascular Death

HR = 0.80 (0.71-0.89)  
P = 0.00004  
Number need to treat = 32

Enalapril  
(n=4212)  
693  
558

LCZ696  
(n=4187)  

Patients at Risk  
<table>
<thead>
<tr>
<th></th>
<th>LCZ696</th>
<th>Enalapril</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4187</td>
<td>4212</td>
</tr>
<tr>
<td>180</td>
<td>4056</td>
<td>4051</td>
</tr>
<tr>
<td>360</td>
<td>3891</td>
<td>3860</td>
</tr>
<tr>
<td>540</td>
<td>3282</td>
<td>3231</td>
</tr>
<tr>
<td>720</td>
<td>2478</td>
<td>2410</td>
</tr>
<tr>
<td>900</td>
<td>1716</td>
<td>1726</td>
</tr>
<tr>
<td>1080</td>
<td>1005</td>
<td>994</td>
</tr>
<tr>
<td>1260</td>
<td>280</td>
<td>279</td>
</tr>
</tbody>
</table>
Devices and Telemedicine
ICD only (N=620)  CRT–ICD (N=746)

Change in Volume (ml)

- LVEDV: 15 ml vs. 52 ml decrease from baseline
- LVESV: 18 ml vs. 57 ml decrease from baseline

Change in Ejection Fraction

- LVEF: 0.03 vs. 0.11 increase from baseline

P < 0.001 for all comparisons.
Thoracic Impedance

Daily change of weight prior to hospitalization (n=268)

Adamson, P. B. et al. J Am Coll Cardiol 2003;41:565-571
CHAMPION TRIAL

Hemodynamic Information
Treatment Guideline & Support

Significantly Improved Clinical Outcomes
CardioMEMS *Champion* HF Monitoring System

**Pressure Sensor on Catheter-based Delivery System**

- Pressure sensor
- Catheter-based delivery system
- Dimensions: 4.5cm and 120cm

**Home Electronics**

**PA Monitoring Database**

- Proprietary database for secure storage of patient data
Telemanagemen: Clinical Management Without Hemodynamics

  - 1,653 patients randomized to telemonitoring or usual care
  - No reduction in risk of readmission or death
  - No reduction in risk of HF hospitalization

  - 710 patients randomized to remote telemedical management or usual care
  - No reduction in risk of all cause death
  - No reduction in CV death and HF Hospitalization

  - 426 patients randomized to remote telemedical management or usual care
  - No reduction in days dead or hospitalized
  - No reduction in the number of hospitalizations and mortality
CHAMPION

Hemodynamic Information + Treatment Guidelines & Support

Significantly Improved Clinical Outcomes
Pressure Based Medical Management Workflow
Cumulative HF Hospitalizations Reduced
At 6 Months and Full Duration

≤ 6 Months
28% RRR, p = 0.0002

> 6 Months
45% RRR, p < 0.0001

Study Duration
37% RRR, p < 0.0001

Days from Implant

Cumulative Number of HF Hospitalizations

No. at Risk
Treatment 270 262 244 210 169 131 108 82 29 5 1
Control 280 267 252 215 179 137 105 67 25 10 0
Increase use of outpatient to Diuresis
Increase dietary counseling
Sleep Apnea Treatment
Discontinue NSAIDS, Type2DM
Exercise
Cardiovascular death and HF Hospitalization

Years from Randomization

Event Rate

HR 0.87 (95% CI: 0.75, 1.00), \( P = 0.06 \)
HR 0.85 (95% CI: 0.74, 0.99), \( P = 0.03 \)
All Cause Mortality or Hospitalization

Event Rate vs. Years from Randomization

- Usual Care
  - HR 0.93 (95% CI: 0.84, 1.02), $P = 0.13$

- Exercise
  - HR 0.89 (95% CI: 0.81, 0.99), $P = 0.03$
Distinguishing Systolic Heart Failure from Preserved Left Ventricular Ejection Fraction Heart Failure

Patient with probable HF*

Measure LVEF: <40%?

NO

Likely diastolic dysfunction

YES

SYSTOLIC HF
Classify by symptoms and treat

*Some signs and symptoms of HF:
- Pulmonary rales
- Fluid overload
- Dyspnea on exertion or at rest
- PND
- Inability to sleep with daytime fatigue
- Loss of appetite
- Difficulty concentrating, reading, calculating

HF, heart failure; LVEF, left ventricular ejection fraction; PND, paroxysmal nocturnal dyspnea.
**1° Outcome**
(CV Death, HF Hosp, or Resuscitated Cardiac Arrest)

Spironolactone

Placebo

HR = 0.89 (0.77 – 1.04)

p = 0.138

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Spiro</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1722</td>
<td>1723</td>
</tr>
<tr>
<td>12</td>
<td>1502</td>
<td>1462</td>
</tr>
<tr>
<td>24</td>
<td>1168</td>
<td>1145</td>
</tr>
<tr>
<td>36</td>
<td>870</td>
<td>834</td>
</tr>
<tr>
<td>48</td>
<td>614</td>
<td>581</td>
</tr>
<tr>
<td>60</td>
<td>330</td>
<td>331</td>
</tr>
<tr>
<td>72</td>
<td>53</td>
<td>53</td>
</tr>
</tbody>
</table>

351/1723 (20.4%)

320/1722 (18.6%)
**Total HF Hosp**
- **Spiro**: 394
- **Placebo**: 475

**P<0.01***

**HR = 0.83 (0.69 – 0.99)**

**p=0.042**

*poisson regression*
Exploratory (post-hoc): Placebo vs. Spiro by region

US, Canada, Argentina, Brazil
HR=0.82 (0.69-0.98)

Placebo: 280/881 (31.8%)

Russia, Rep Georgia
HR=1.10 (0.79-1.51)

Placebo: 71/842 (8.4%)

Interaction p=0.122
Sleep Breathing Disorders
Overview of Sleep Apnea

- Sleep-Disordered Breathing (SDB) describes a number of nocturnal breathing disorders
- Sleep apnea is the dominant type of SDB
  - Obstructive sleep apnea (OSA)
  - Central sleep apnea (CSA)
- OSA and CSA are highly prevalent in patients with cardiovascular disease
VPAP Adapt SV™ for Heart Failure Patients

A highly evolved bilevel device designed for the specific purpose of treating central sleep apnea (CSA) in all its forms

• Adaptive-servo ventilation suppresses CSA and improves sleep quality more than CPAP, bilevel or oxygen therapy,

• Adaptive-servo ventilation may reduce BNP in heart failure patients with Cheyne-Stokes respiration (CSR)

2 Pepperell JC et al. Am J Respir Crit Care Med
Programs
IMPROVING PATIENT CARE

A Reengineered Hospital Discharge Program to Decrease Rehospitalization

A Randomized Trial

Brian W. Jack, MD; Veerappa K. Chetty, PhD; David Anthony, MD, MSc; Jeffrey L. Greenwald, MD; Gail M. Sanchez, PharmD, BCPS; Anna E. Johnson, RN; Shaula R. Forsythe, MA, MPH; Julie K. O'Donnell, MPH; Michael K. Paasche-Orlow, MD, MA, MPH; Christopher Manasseh, MD; Stephen Martin, MD, MEd; and Larry Culpepper, MD, MPH

3 February 2009 | Volume 150 Issue 3 | Pages 178-187
Study Characteristics

- Setting: General medical service at urban academic hospital (Boston)
- N=749 hospitalized adults (mean age 50) with a variety of Dx
- Outcome measures:
  - ER visits
  - Readmission within 30 days
Intervention

NURSE DISCHARGE ADVOCATE
Arranged f/u appointments
Did medication reconciliation
Provided patient education

CLINICAL PHARMACIST
Called pts 2-4 days after discharge to review meds
Cumulative hazard rate of hospital utilization for 30 days after index hospital discharge

NOTE: ONLY 30 DAY F/U

How to best transition care?

• Personal physician visits to home
• Visiting nurses trained in HF care
• Phone monitoring by a nurse/team
• Early/frequent visits to HF team
• Home monitoring (scale, phone systems, devices, internet based reporting)
• Let the patient decide when to call
Our Lady of the Lake Heart & Vascular Institute Experience
Our Lady of the Lake Heart & Vascular Institute
Heart Failure Readmissions (30 Day All Cause) IP
July 2014 - September 2015

- HF Navigation Process began August 2014
- HF Documentation Tool Implemented
- MEDS To BEDS Pilot Began
- Begin Transitional Care Clinic
- Increase Access with LSU/Ambulatory Appointments
Heart Failure Discharge Readiness Check List

Physician Component:
☐ Exacerbating factors addressed
☐ Ejection fraction documented
☐ Optimal volume status achieved with discharge weight ≤ admit weight (consider weight loss goal of at least 3 Kg)
☐ Discharge BNP level is less than admit BNP level (BNP decrease of at least 30%)
☐ CBC and Creatinine levels are trending down
☐ Oxygen saturation with activity ≥ 92% or at baseline documented
☐ Code status & Prognosis discussed (all patients) and palliative care referral if appropriate (considered for all patients with NYHA stage IV or stage III with recurrent admissions in spite of optimal treatment)

Physician, Pharmacy, and RN:
☐ Oral medication regimen stable for 24 hours
☐ No intravenous vasodilator or isotropic agent for 24 hours
☐ Near optimal pharmacologic therapy achieved
☐ ACE-I/ARB for patients with low EF ≥ 40% or
  ☐ No ACE-I/ARB because of ☐ EF > 40% ☐ Allergy/intolerance
☐ A reconciled list of medications that precisely matched those in the discharge summary
☐ Counseled on avoidance of tobacco products, and ongoing smoking cessation

RN:
☐ Patient and family education completed with documented teach-back
☐ Given written instructions for activity, salt restriction, and daily weight assessments
☐ Specific written recommendations to follow-up for ongoing management, and to address changes in weight or symptoms

RN with PT:
☐ Document ambulation & 02 Sats prior to discharge to assess functional capacity after therapy.
☐ Absence of orthostatic hypotension

Case Management:
☐ Scale present in home and is suitable for patient’s specific condition
☐ Barriers to obtain medications, home care, transportation, & family support identified and addressed
☐ TCC appointment for week after discharge on ______________
☐ Physician appointment for second week after discharge on ______________
☐ Referral appointment if necessary with __________________
☐ Nursing telephone follow-up no longer than 3 days after discharge

Admit wgt _______ Kg  Discharge wgt _______ Kg  Output balance ____________
Discharge B/P _______ Kg  Discharge HR _______ Rhythm ____________
HEART FAILURE: Future Directions

• Clarification of pathophysiology
  • Antimicrobial therapy analogy-new drugs
  • Acute decompensated heart failure
• Prevention
  • Vaccination analogy-prevent the problem in the first place
• Pharmacogenomics and tailored therapy
  • Diastolic dysfunction
• Non pharmacologic strategies
  • Mechanical circulatory support
  • Volume overload management
  • Cell therapies
• Increase in public awareness
  • Lipid, HTn, ASCVD, Diabesity epidemic education
“I have been on the end of defeat many times…. I will not make excuses, I assess it and come back STRONGER”

Conor McGregor
UFC Featherweight Champion