Tradition
Just because you've always done it that way doesn't mean it's not incredibly stupid.
Heart Failure

• HF is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood

• Cardinal manifestations of HF are dyspnea, fatigue, limited exercise tolerance, and fluid retention

• HF is not defined by EF or BNP level
Growing Epidemic of Heart Failure

Prevalence of HF

- **2010**: 5,000,000
- **2020**: 7,000,000
- **2030**: 9,000,000

- **Age > 65**
- **Age < 65**

Adapted from Heidenreich et al. Circ Heart Failure 2013
One Size Does Not Fit All

- HF treatment must be individualized:
  - Pathophysiology
  - Comorbidities
  - Goals of treatment
Spectrum of Heart Failure

Chronic Stable HF

HF with Preserved EF
- Diastolic HF
- HFpEF
- EF ≥ 50%

Systolic + Diastolic

EF 40-50%

HF with Reduced EF
- Systolic HF
- HFrEF
- EF ≤ 40%

Advanced HF

Acute Decompensated HF
Survival Difference

Adjusted HR 0.68 (0.64, 0.71)

Number at risk:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
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<tbody>
<tr>
<td>HF-REF</td>
<td>28803</td>
<td>21012</td>
<td>16510</td>
<td>12247</td>
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<tr>
<td>HF-PEF</td>
<td>9518</td>
<td>6725</td>
<td>5728</td>
<td>4346</td>
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</tbody>
</table>

EF cut off 50%

MAGGIC Investigators  Eur Heart J 2012
HF is a Progressive Disease

Clinical Course

Onset of CHF  Sudden Death  Decompensations  Pump Failure

Intensity of Care

Traditional Care
Including disease-modifying therapies

Palliative Care
Including symptom management

Quality of Life
Heart Failure is Cardiac Cancer

Mortality from Time of Diagnosis

- 30 day: 10%
- 1 year: 22%
- 1 year: 18%
- 1 year: 16%
- 5 years: 50%
- 5 years: 35%
- 5 years: 44%

Chart showing mortality rates for Heart Failure, All Cancers, and Colon Cancer.
HF Discharged to SNF

Mortality form Time of Diagnosis

- 30 day:
  - Heart Failure: 10%
  - HF in SNF: 15%
- 1 year:
  - Heart Failure: 50%
  - HF in SNF: 51%
  - Esophageal Cancer: 22%

AHA Heart Disease & Stroke Statistics 2013    Allen et al J Cardiac Fail 2011    National Cancer Institute 2010
Systolic Heart Failure - HFrEF

Treatment Strategy

• Reverse remodeling with RAAS and SNS blockade
• Sudden death protection
• Disease management
• LVAD or transplant when appropriate
Benefits of Therapy for HFrEF

1991-2013

Relative Risk Reduction

- ACEI/ARB
  - Mortality: -17%
  - Hospitalization: -31%

- Beta Blockers
  - Mortality: -35%
  - Hospitalization: -41%

- Aldosterone Antagonists
  - Mortality: -30%
  - Hospitalization: -35%

- ICD
  - Mortality: -31%

- ICD+CRT
  - Mortality: -31%
  - Hospitalization: -30%
Effect of HFrEF Therapies are Additive

Heart Failure Therapies

<table>
<thead>
<tr>
<th>Therapies</th>
<th>24-Month Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blocker</td>
<td>-39% (-26% to -45%)</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB</td>
<td>-63% (-54% to -71%)</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD</td>
<td>-76% (-68% to -81%)</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD + HF education</td>
<td>-81% (-75% to -86%)</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD + HF education + antiocoagulation for AF</td>
<td>-83% (-77% to -88%)</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD + HF education + antiocoagulation for AF + CRT</td>
<td>-81% (-72% to -87%)</td>
</tr>
</tbody>
</table>

Fonarow et al J Am Heart Assoc 2012
IMPROVE HF Registry
Response to Reverse Remodeling Treatment
Change in Forward Stroke Volume
Clinical Pearls in Ambulatory HF Care

• Drugs to avoid in HF:
  – NSAIDs
  – CCB with negative inotropic properties
    • Verapamil
    • Diltiazem
  – TZDs
    • Avandia
    • Actos

• Sleep disordered breathing common
  – Prevalence in HF is 50%
  – Cheyne Stokes breathing is most common
  – Snoring is an insensitive marker of SDB in HF
Recognizing Congestion

• Dominant symptom in heart failure

• Reflects elevated filling pressures

• High left sided filling pressures
  • Orthopnea
  • Bendopnea
  • Immediate dyspnea with minimal activity
  • Elevated JVP, positive HJR

• High right sided filling pressures
  • Early satiety, abdominal fullness
  • Anorexia
  • Edema, Ascites
Bendopnea

A

Right atrial pressure

- Bendopnea
- No Bendopnea

B

Pulmonary capillary wedge pressure

- Bendopnea
- No Bendopnea

Thibodeau et al. JACC Heart Failure 2014
Diastolic Heart Failure

- Difficult diagnosis to make
- HTN extremely common
- Comorbidities include:
  - DM
  - CAD
  - Obesity
  - Afib highly prevalent
Pathophysiology of Diastolic HF

- Slowed LV relaxation
- Enhanced LV stiffness
- Impaired diastolic suction
- Abnormal ventricular-arterial coupling
Exercise Physiology in HFPpEF

- HFPpEF patients have markedly reduced diastolic reserve
- With exercise, they can not increase LV suction and keep LA pressure normal
- Increased blood flow with exercise comes at the price of elevated LA pressure
Ventricular-Arterial Coupling

- Increased vascular stiffness leading to abnormal ventricular-arterial coupling is a prominent feature in HFpEF
- This abnormal VA coupling is most exacerbated during exercise
Treatment Failures in Diastolic HF

**PEP-CHF**
- Patients at risk:
  - Perindopril: 424
  - Placebo: 426
- Time (y):
  - 0, 1, 2, 3
- Proportion having an event (%):
  - Placebo: 10, 20, 30, 40
  - Perindopril: 20, 30, 40, 50

**CHARM-Preserved**
- Number at risk:
  - Candesartan: 1514, 1458, 1377, 833, 182
  - Placebo: 1509, 1441, 1359, 824, 195
- Time (years):
  - 0, 1, 2, 3, 4, 5
- Proportion with cardiovascular death or hospital admission for HF (%):
  - Candesartan: 0, 5, 10, 15
  - Placebo: 0, 5, 10, 15

**I-PRESERVE**
- Cumulative incidence of primary outcome (%):
  - Placebo: 0, 10, 20, 30
  - Irbesartan: 0, 10, 20, 30
- Months since randomization:
  - 0, 6, 12, 18, 24, 30, 36, 42, 48, 54, 60

**TOPCAT**
- Number at risk:
  - Spironolactone: 1723, 1502, 1452, 1108, 870, 614, 330, 53
  - Placebo: 1723, 1462, 1140, 824, 581, 331, 53
- Probability:
  - Spironolactone: 0.00, 0.05, 0.10, 0.15, 0.20, 0.25, 0.30
  - Placebo: 0.00, 0.05, 0.10, 0.15, 0.20, 0.25, 0.30
- HR = 0.89 (0.77 – 1.04)
- p = 0.138
PH-HFpEF

15 15 65/15 65/30 (42) 25 25 25 160/25

TPG = 17

IVC RA RV PA (mean) PCWP PV LA LV

TPG = 8

5 5 47/5 47/26 (33) 25 25 25 160/25

HFpEF

Prognostic Impact of PASP in HFpEF

PASP <48 mm Hg

PASP ≥48 mm Hg

P=0.002

Number remaining
PASP <48 mm Hg 98 86 80 44
PASP ≥48 mm Hg 105 78 67 38

Unadjusted HR=1.28 per 10 mm Hg; P<0.001
Age-adjusted HR=1.22 per 10 mm Hg; P=0.005

Lam C et al: JACC 2009
BNP Levels in Normal Subjects

![Graph showing BNP levels by age and gender](image-url)

- **Biosite BNP assay**
- **Women**
- **Men**
BNP Level in Heart Failure

• BNP < 100
  – Heart failure highly unlikely
  – Negative predictive value = 90%

• BNP > 500
  – Heart failure highly likely
  – Positive predictive value = 90%

• BNP 100 – 500
  – Grey zone
  – Consider other diagnoses
  – Baseline BNP level is helpful

• A 40% change in BNP level is clinically meaningful
BNP Caveats

• Wide clinical variation

• A Fib patients have a higher baseline BNP
  – Normal likely < 200 if afib present

• Obesity lowers BNP by 50 - 70%

• Not all symptomatic HF patients have elevated BNP and not all HF patients with elevated BNP have symptoms

• Non-HF conditions can raise BNP
  – Pulmonary hypertension
  – Sepsis
  – Valve disease
  – Renal failure
## BNP and Renal Function

<table>
<thead>
<tr>
<th>GFR</th>
<th>HF Absent</th>
<th>HF Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90</td>
<td>&lt;100</td>
<td>&gt;500</td>
</tr>
<tr>
<td>60 - 90</td>
<td>&lt;150</td>
<td>&gt;650</td>
</tr>
<tr>
<td>30 - 60</td>
<td>&lt;300</td>
<td>&gt;750</td>
</tr>
<tr>
<td>15 – 30</td>
<td>&lt;300</td>
<td>&gt;850</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Adapted from McCullough et al. *Am J Kidney Disease* 2003

Breathing Not Properly Study
- HABIT Trial
  N=187
  recently symptomatic HF
- Home BNP testing
- Wide daily BNP fluctuations more common in HFP EF than HFr EF

Maisel et al  J Am Coll Cardiol  2013
Inflection Points in HF Care

• HF hospitalizations

• High dose or escalating diuretic requirements

• Worsening renal function

• Need to reduce HF medication doses

• New or worsening hyponatremia
Hospitalization for Heart Failure

Hospital Discharges for HF

- 1979: 580,000
- 2010: 1,100,000

AHA Heart & Stroke Facts 2013
Hospitalization for HF & Prognosis

**Median Survival Decreases Progressively after Each Hospitalization**

2 or more HF hospitalizations in 1 year should prompt consideration for entry in to HF disease management program
High dose or escalating diuretic dose requirement should prompt consideration for entry in to HF disease management program.

Mielniczuk et al. J Cardiac Failure 2007
Persistent worsening renal function should prompt consideration for entry into HF disease management program.
Worsening hyponatremia should prompt consideration for entry into HF disease management program.
Advanced Heart Failure

- EF typically below 30%
- Conventional therapies no longer effective or tolerated
- Continued decline with ≥ 2 HF decompensations / year
- Require high dose or escalating doses of diuretics
- Worsening renal function or hyponatremia
- Poor functional capacity despite optimal medical rx
- 1 year mortality approaches 50%

Allen et al. Circulation 2012
Treatment Options for Advanced HF

- Continued medical therapy
- Palliative Care & Hospice
- Home inotrope infusion
- Heart transplantation
- Mechanical circulatory support (LVAD)
Medical Therapy for Advanced HF

Survival

Months

0% 25% 50% 75% 100%

0 6 12 18 24

REMATCH Trial  NEJM  2001
Palliative Care & Hospice

Diagnosis on Entry to Hospice or Palliative Care

- Cancer: 37%
- Dementia: 13%
- Heart Failure: 11%
- Other: 39%

N = 1,500,000

NHPCO Facts & Figures 2013
Number of donor hearts available annually has not changed since 1990
Mechanical Circulatory Support - LVAD
LVAD & Continuous Flow
LVAD Survival Advantage

LVAD Destination Therapy (HMII Trial)

Medical Management (REMATCH, NEJM 2001)
Rise of the Machines
Disease Management

Munson HF Clinic

HF Cardiologist
Mid Level Provider
Advanced Practice RN
Pharmacist
Social Worker
Exercise Specialist
Psychologist
Palliative Care
Home Care

All members function at the top of their credential.
Munson HF Clinic

Established 2012
Follow 203 patients
Average EF = 22%
IP referrals seen average of 8 days after discharge
Average predicted 30 day readmission risk 27%
Average predicted 5 yr survival 47%
21 pts on home inotropes

As of 10.1.14
MMC HF Clinic Experience

30 day Readmission Rate

- State of MI Overall: 24%
- MMC Overall: 19%
- MMC HF Clinic: 10%
- HFC Readmits for HF: 5%
HF Decompensations Develop Slowly

Heart failure low EF

Heart failure preserved EF

21 days

Time (days)

Zile et al
COMPASS Investigators
Circulation 2008
Paradigm-HF Trial

- Angiotensin receptor-neprilysin inhibitor (ARNI)
  LCZ696 = sacubitril + valsartan

- Symptomatic HF and EF<40%

- Randomized 8,000 pts to enalapril or LCZ696

- Composite endpoint of all cause mortality and HF hospitalization

McMurray et al  NEJM 2014
### Paradigm-HF

#### A Primary End Point
- **Hazard ratio, 0.80 (95% CI, 0.73–0.87)**
- **P<0.001**

<table>
<thead>
<tr>
<th>Days since Randomization</th>
<th>Cumulative Probability</th>
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<tbody>
<tr>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>180</td>
<td>0.2</td>
</tr>
<tr>
<td>360</td>
<td>0.3</td>
</tr>
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- **No. at Risk**
  - LCZ696: 4187, 3922, 3663, 3018, 2257, 1544, 896, 249
  - Enalapril: 4212, 3883, 3579, 2922, 2123, 1488, 853, 236

#### B Death from Cardiovascular Causes
- **Hazard ratio, 0.80 (95% CI, 0.71–0.89)**
- **P<0.001**

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- **No. at Risk**
  - LCZ696: 4187, 4056, 3891, 3282, 2478, 1716, 1005, 280
  - Enalapril: 4212, 4051, 3860, 3231, 2410, 1726, 994, 279

#### C Hospitalization for Heart Failure
- **Hazard ratio, 0.79 (95% CI, 0.71–0.89)**
- **P<0.001**

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  - Enalapril: 4212, 3883, 3579, 2922, 2123, 1488, 853, 236

#### D Death from Any Cause
- **Hazard ratio, 0.84 (95% CI, 0.76–0.93)**
- **P<0.001**

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*McMurray et al, NEJM 2014*