CHF (HFrEF) 1st Care Roadmap 2016

Non-Invasive Disease-Modifying Rx
- ACE/ARB
- Hydralazine/ISDN
- Beta-Blocker
- Ivabradine
- Aldosterone Antagonist
- Valsartan/Sacubitril

Sx-Modifying Rx
- Diuretics
- Digoxin

Common Modifiable Comorbidities
- Anemia, HTN, T-4, Thiamine, Alcohol, COPD, CAD

Lifestyle & Immunizations
- Na+/H2O, Weight, Exercise, FluVax, PneumoVax

HFrEF Disease-Modifying Interventions
- ACE
- ARB
- Beta Blocker
- Aldosterone Antagonist
- Hydralazine/Isosorbide
- Ivabradine
- ARB/Sacubitril
- Cardiac Rehab
- Exercise
- ICD
- CRT
- Home Visits
- Frequent Visits
- Phone Support
CHF Vocabulary

<table>
<thead>
<tr>
<th>Old Terminology</th>
<th>Current Terminology</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>Heart Failure (HF)</td>
</tr>
<tr>
<td>Systolic Dysfunction</td>
<td>HF with Reduced Ejection Fraction</td>
</tr>
<tr>
<td>EF &lt;40%</td>
<td>HFrEF ('Heff-Ref')</td>
</tr>
<tr>
<td>Diastolic Dysfunction</td>
<td>HF with Preserved Ejection Fraction</td>
</tr>
<tr>
<td>EF &gt;50%</td>
<td>HFpEF ('Heff-Peff')</td>
</tr>
</tbody>
</table>

**HF: Functional Definition**

A clinical syndrome that occurs when cardiac output is inadequate for tissue metabolic requirements

**HF: Pathophysiologic Definition**

- Clinical syndrome resulting from structural or functional impairment of ventricular filling or ejection of blood.
  - Exercise Intolerance (dyspnea & fatigue)
  - Fluid Retention (NOT everyone; #CHF)
- Cardiac output(CO) ≠ tissue metabolic requirement
  - Sustained Sympathetic Nervous Sys (SNS) Activation
  - Sustained RAAS activation

NYHA Functional Classification (HF & Angina)

- **CLASS I**: No undue symptoms on ordinary activity; No limitation of physical activity
- **CLASS II**: Slight to moderate limitation of activity (IIa-IIIm); patient comfortable at rest
- **CLASS III**: Marked limitation of activity; patient comfortable at rest
- **CLASS IV**: Discomfort with any physical activity; symptoms may exist even at rest

NYHA Functional Classification (SOMA)

- **CLASS I**: Strenuous activity → Sx
- **CLASS II**: Ordinary ADL → Sx
- **CLASS III**: Minimal activity → Sx
- **CLASS IV**: Any activity/at rest → Sx

NYHA Classification Stage of HF

<table>
<thead>
<tr>
<th>ACCF/AHA Stages of HF</th>
<th>NYHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>At high risk <em>but</em> Asymptomatic + NO structural heart disease</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>I</td>
</tr>
<tr>
<td>Structural heart dz <em>but</em> Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>I-IV</td>
</tr>
<tr>
<td>Structural heart dz with current or prior symptoms</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>IV</td>
</tr>
<tr>
<td>Refractory HF</td>
<td></td>
</tr>
</tbody>
</table>

*From Clyde W. Yancy et al. / Circulation. 2013;128:1810-1852*
Are We Too Complacent About the Dx?

“The prognosis of affected individuals is dismal, as fewer than 50% of these people survive 5 years from the time of initial Dx.”

Mulrow C. JAMA 1987;259(23):3422-3425

Heart Failure
The Hemodynamic Malignancy

“Mortality from CHF is high, averaging 30% within the 1st year, 50% by 3-4 years, and 80% by 6-10 years”

Anderson J. Modern Medicine 1987;55(May)
Heart Failure: The Hemodynamic Malignancy

A Prospective Cohort Study (n=558)

- Total mortality at 5 years
  - Systolic Dysfunction = 42%
  - Diastolic Dysfunction = 25%


PATHOPHYSIOLOGY

...once upon a time, a young man was walking his elephant....
When along came an adversary….

OUCH!!

Lots & lots of blood

RAAS To The RESCUE!!
- A-II: Selective Vasoconstriction
- NE: Vascular Tone, Heart Rate, Contractility
- Aldosterone: Salt, Water retention, Thirst

Silent. I’m hiding

Agape! Foiled again!

Selective vasoconstriction: stopped bleeding
Flow maintained to muscles, heart, brain
4 quarts low: ↑ heart rate, contractility
Insensitive fluid losses stemmed (saliva, sweat, urine)
Thirsty
...and they all LIVED happily ever after.

ISCHEMIA
HYPERTENSION
MYOPATHY

A-II
CATECHOLS
ADH
REMODELING

Tissue Injury

Compensation

HF: Back to Basics

Consequence

CO
SYSTOLIC DYSF
DIASTOLIC DYFS
COMBINED DYSF

RAAS ↔ HF

Angiotensinogen

RENIN

Angiotensin I

ACE

Angiotensin II

Aldosterone

AFTERLOAD

PRELOAD

Vasoconstriction/↑SVR

Na+ retention/↑IVV
Myocardial Collagen Balance

Clastic Cardiac Fibroblast

Collagen Degradation (Collagenase)

Collagen Proliferation

Blastic Cardiac Fibroblast

RAAS HYPERACTIVATION

XS Collagen

DIAGNOSIS
BNP

- BNP = brain natriuretic peptide
- Originally: brain natriuretic peptide (first isolated in porcine brain)
- synthesized (but not stored) in ventricular myocytes
- Ventricular stress → ↑ BNP


BNP: Potential Clinical Roles

- Dx ASx CHF
- Prognostic Indicator
- Monitor CHF progress
- Differentiate CHF look-alikes

"Indeed, plasma BNP proves...to be as good or better than any other non-invasive measure in the assessment of heart function & prognosis after MI."


BNP: Diagnostic Clinical Role

- STUDY: Unselected dyspnea pts presenting to VA (n=250)
- METHOD: compare BNP (rapid bedside test) with cardiologist assessment of Dx

BNP Levels in Patients With Dyspnea Secondary to CHF or COPD

- COPD N = 36
- CHF N = 94
- BNP Concentration (pg/ml)
  - COPD: 86 ± 39
  - CHF: 1076 ± 138

BNP: Degree of CHF Severity

- Mild N = 27
- Moderate N = 34
- Severe N = 36
- BNP Concentration (pg/ml)
  - Mild: 186 ± 22
  - Moderate: 791 ± 165
  - Severe: 2013 ± 266

BNP to Guide CHF Rx

- STUDY: Pts with systolic dysfunction in Cardiology HF clinic, NYHA II-IV, EF <40% (n=60)
- GOAL: BNP <200 vs clinical heart failure score <2
- METHOD: ‘Standard’ clinical assessment vs BNP Q 3 months X 1 year

HEART-FAILURE SCORING SYSTEM

<table>
<thead>
<tr>
<th>Condition</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopnea</td>
<td>0.5</td>
</tr>
<tr>
<td>PND</td>
<td>1.0</td>
</tr>
<tr>
<td>↓Exercise tolerance</td>
<td>0.5</td>
</tr>
<tr>
<td>Resting Sinus tachycardia</td>
<td>0.5</td>
</tr>
<tr>
<td>JVP &gt;4cm</td>
<td>0.5</td>
</tr>
<tr>
<td>Hepatojugular reflex +</td>
<td>1.0</td>
</tr>
<tr>
<td>S-3 Heart Sound</td>
<td>1.0</td>
</tr>
<tr>
<td>Basal crackles</td>
<td>1.0</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>0.5</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>0.5</td>
</tr>
</tbody>
</table>


BNP vs Clinical Evaluation to Guide CHF Rx: Results

- Total CV events (death, hospital admission, or worse HF): 19 vs 54 (p=0.02)
- At 6 months 27% BNP vs 53% traditional had experienced a first CV event
- LV function, QOL, Renal Fx, adverse events ≤


BNP to Guide CHF Rx: Interpretation

“N-BNP guided Rx of heart failure reduced total CV events, and delayed time to first event compared with intensive clinically guided Rx.”

Breathing Not Properly (BNP) Study: Dx and Prognosis

- Prospective Obs. study; n=1,586 w/ Ac. SOB
- 2 Dx Methods compared to Cardiologist Dx
  1. NHANES and Framingham criteria for Dx CHF
  2. BNP

OUTCOME:
- Single BNP more accurate than criteria scores for Dx of CHF
- pts whose 30d BNP level was > discharge BNP level were at highest risk for decompensation/readmission


Causes for ↑ Natriuretic Peptide Levels

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Noncardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure, including RV</td>
<td>Advancing age</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>Anemia</td>
</tr>
<tr>
<td>Heart muscle dz (LVH)</td>
<td>Renal failure</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>Pulm: OSA; PNA, Pulm HTN</td>
</tr>
<tr>
<td>Pericardial disease</td>
<td>Critical illness</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Bacterial sepsis</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>Severe burns</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>Toxic-metabolic insults (eg chemotherapy, envenomation)</td>
</tr>
<tr>
<td>Cardioversion</td>
<td></td>
</tr>
</tbody>
</table>

*Clinical Practice Guidelines for Heart Failure* (2006)


BNP Study: Obesity and BNP Levels

No Acute CHF  Acute CHF

<table>
<thead>
<tr>
<th>BMI &lt; 25</th>
<th>25≤ BMI &lt; 35</th>
<th>BMI ≥ 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>462</td>
<td>247</td>
</tr>
<tr>
<td>35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P<0.05

“The benefits observed from aggressive monitoring strategies (eg, brain BNP guided therapy) suggest that treatment beyond clinical congestion may improve outcomes.”

Colucci SW "Overview of the therapy of heart failure due to systolic dysfunction" UpToDate Accessed 4/23/2013

Rx

HFrEF Disease-Modifying Interventions
ACE
ARB
Beta Blocker
Aldosterone Antagonist
Hydralazine/Isosorbide
Ivabradine
ARB/Sacubitril
Cardiac Rehab
Exercise
ICD
CRT
Home Visits
Frequent Visits
Phone Support
BP Control

- Long-term tx of both systolic and diastolic HTN reduces risk of HF by ~50%
  - 2013 ACCF/AHA HF Guidelines

- SPRINT Trial (n=9,361)
  - Non DM pts with HTN were ~40% less likely to develop HF if treated to a goal SBP <120 compared to a SBP goal <140

Sodium Restriction?

- **Obs. study**: 902 pts NYHA II-III; Systolic or Diastolic HF

- **METHOD**: Na+ intake assessed over 36 months using a food freq. questionnaire; pts classified as either Na+ Restricted (<2500mg/d) or Unrestricted (≥2500 mg/d).

- **OUTCOME**: composite of death or HF hospitalization


- Na+ Restriction → **Higher Risk of HF hospitalization or death** (42% v 26%; HR 1.85; p=0.004)

- Highest risk increase in those not taking ACE/ARB (HR 5.78; P=0.002) and NYHA II (HR 2.36; P=0.003)

- ACCF/AHA SOR for Na+ restriction downgraded — Class I (recommended) → Class IIa (reasonable)

CLINICAL BENEFITS OF ACE-I in HF

- ↓ HF Sx
- Prevents Progression
- Improves QOL
- ↓ Hospitalizations
- ↓ Mortality

HF Sx
Prevents Progression
Improves QOL
↓ Hospitalizations
↓ Mortality

ACE Inhibitor (Fosinopril): ETT

\[ \text{P} = 0.047 \]


ACE Inhibitor (Fosinopril): NYHA Classification

\[ \text{Fosinopril (n=114)} \]

\[ \text{Placebo (n=119)} \]

ACE Inhibitor (Fosinopril): Individual CHF Sx (p<0.05)

- Placebo
- Fosinopril


Fatigue

PND

% Improved

% Worse

Dyspnea

Fatigue

PND

SOLVD: Death or Hospitalization

- Placebo
- Enalapril

P < 0.001


SAVE Trial: CHF, CV, or MI Death

- Placebo
- Captopril

Risk reduction = 24%

p < 0.001

ACE Inhibitors & CHF

- Meta-analysis 32 trials (n = 7,105)
- Most pts severe CHF (EF < 35-40%) Rx ≥ 8 weeks

RESULTS

<table>
<thead>
<tr>
<th></th>
<th>ACE</th>
<th>PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>15.8%</td>
<td>21.9%</td>
</tr>
<tr>
<td>Hospitalization or death</td>
<td>22.4%</td>
<td>32.6%</td>
</tr>
</tbody>
</table>

- NO APPRECIABLE DIFFERENCE AMONG STUDY DRUGS (ALL ACE = EFFICACY)

JAMA 1995; 273:1450

2013 ACCF/AHF HF Guidelines:

ARBs

“ARBs are recommended in pts w/ HFrEF w/ current or prior Sx who are ACEI intolerant, to reduce morbidity and mortality.” (Class I Rec; LOE: A)


ARBS in Patients Not Taking ACE Inhibitors: Val-HeFT & CHARM-Alternative

![Graph showing survival and CV death or hospitalization rates for Val-HeFT and CHARM-Alternative](image-url)
2013 ACCF/AHA HF Guidelines: Beta-Blockers (BB)

“1 of the 3 BBs proven to reduce mortality (bisoprolol, carvedilol, metoprolol succinate) is recommended for ALL pts w/ current or prior symptoms of HF/EF to reduce morbidity and mortality.”

(Level of Evidence: A)


HFSA 2006 Practice Guideline (7.6)
Pharmacologic Therapy: Beta Blockers

CONCOMITANT DISEASE

Beta blocker therapy is recommended in the great majority of patients with LV systolic dysfunction—even if there is concomitant diabetes, chronic obstructive lung disease or peripheral vascular disease.

- Use with caution in patients with:
  - Diabetes with recurrent hypoglycemia
  - Asthma or resting limb ischemia.

- Use with considerable caution in patients with marked bradycardia (<55 bpm) or marked hypotension (SBP < 80 mmHg).

- Not recommended in patients with asthma with active bronchospasm. Strength of Evidence = C


The Additional Value of Beta Blockers Post-MI: CAPRICORN

Studied impact of beta blocker (carvedilol) on post-MI patients with LVEF ≤ 40% already receiving contemporary treatments, including revascularization, anticoagulants, ASA, and ACEI:

- All-cause mortality reduced (HR = 0.077; p = 0.03)
- Cardiovascular mortality reduced (HR = 0.75; p = .024)
- Recurrent non-fatal MIs reduced (HR = .59; p = .014)

SENIORS
Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalization in Seniors with heart failure

- 2128 patients with HF or LVEF ≤35%
- ≥70 years of age (mean, 76 years)
- Randomly assigned to
  - Nebivolol titrated to 10 mg QD over 4 months
  - Placebo (n = 1061)
- Primary outcome: Composite of all-cause mortality or CV hospital admission (time to first event)
- Follow-up: median 21 months


SENIORS: Primary and secondary outcomes

RALES: Spironolactone in Severe Heart Failure

- STUDY: NYHA III-IV CHF, EF <35% (n = 1663)
- INCLUSION: on ACE + loop diuretic with (+ dig or vasodilators OK), K+ < 5.0, Cr < 2.5
- Rx: spironolactone 25 mg QD vs placebo X 3 years

Spironolactone in Severe Heart Failure: Results


Blockade of aldosterone receptors by spironolactone, in addition to standard therapy, substantially reduces the risk of both morbidity and death among pts with severe heart failure.

Spironolactone in Severe Heart Failure

Hospitalizations
- Spironolactone: 260 pts
- Placebo: 336 pts

NYHA class ↑
- Spironolactone: 41%
- Placebo: 33%

NYHA class ↓
- Spironolactone: 38%
- Placebo: 48%

Hyperkalemia
- Spironolactone: 2% (NS)
- Placebo: 1%

Gynecomastia
- Spironolactone: 10%
- Placebo: 1%
EPHESUS
Eplerenone Post-Acute MI HF Efficacy and Survival Study

- Study: RDBPCT in Post-MI HF pts
- Rx: eplerenone 25-50 mg/d vs placebo X 16 months (n=6,632)
- Outcomes:
  - All-cause mortality
  - CV Death
  - CV Hospitalizations

Pitt B et al  NEJM 2003;348:1309-1321

EPHESUS: All Cause Mortality

Pitt B et al NEJM 2003;348:1309-1321

EPHESUS: CV Death or CV Hospitalization

Pitt B et al NEJM 2003;348:1309-1321
EMPHASIS: Eplerenone in Mild Patients Hospitalization & Survival Study

- Study: DBRPCT NYHA II CHF
- Rx: Eplerenone 25-50 mg/d vs placebo X 21 months
- Outcomes
  - CV Death
  - HF hospitalization
  - Hyperkalemia

Zannad F et al NEJM 2011;364:11-21

EMPHASIS: CV Death or HF Hospitalization

EMPHASIS: All Cause Mortality

Zannad F et al NEJM 2011;364:11-21
Aldosterone Antagonist in HFrEF

“Clinicians should strongly consider the addition of the aldosterone receptor antagonists spironolactone or eplerenone for all patients with HFrEF already on ACEI (or ARBs) and BBs.”

-2013 ACC/AHA Guidelines
A-HeFT
(African American Heart Failure Trial)

Taylor AL, Ziesche S, Yancy C, et al
“Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure”

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A-HeFT

- **STUDY**: Black patients with CHF, NYHA III-IV (n=1050) followed 18 months
- **PREMISE**: Previous CHF trials → beneficial I/H effects in black subgroup
- **Rx**: isosorbide dinitrate/hydralazine 37.5mg/20 mg one t.i.d. → two t.i.d.

Taylor AL, Ziesche S, Yancy C, et al “Combination of ISDN and Hydralazine in Blacks with Heart Failure” N Engl J Med 2004;351:2049-57

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A-HeFT: Primary Endpoint

![Chart showing primary endpoint comparison between Placebo and I/H]

Taylor AL, Ziesche S, Yancy C, et al “Combination of ISDN and Hydralazine in Blacks with Heart Failure” N Engl J Med 2004;351:2049-57
A-HeFT Composite Score
Individual Components: Death


A-HeFT Composite Score
Individual Components: 1st HF Hospitalization


A-HeFT Composite Score
Individual Components: QOL Change

MLWHF Score

LOWER NUMBER INDICATES IMPROVEMENT

A-HeFT: Mortality

![Graph showing mortality rates over days since baseline visit.](image)


A-HeFT: Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>I/H</th>
<th>Placebo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache (all)</td>
<td>47.5%</td>
<td>19.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Headache (severe)</td>
<td>5.2%</td>
<td>0.9%</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>29.3%</td>
<td>12.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HF Exacerbation</td>
<td>8.7%</td>
<td>12.8%</td>
<td>0.04</td>
</tr>
<tr>
<td>HF Exacerbation (severe)</td>
<td>3.1%</td>
<td>7.0%</td>
<td>0.005</td>
</tr>
</tbody>
</table>


20113 ACCF/AHA Recommendation

“The combination of ISDN/H is recommended for pts self-described as AA w/ NYHA III-IV HFrEF receiving optimal tx w/ ACEI/B-binders.”

*(Level of Evidence: A)*

Ivabradine (Corlanor)

- Selective Inhibitor of the “funny channel (If)” which modulates SA pacemaker → ↓ Sinus Rate

- Does not effect atrial conduction, AV node, or ventricles → no effect on contractility
  - Difference from BB and CCB

- Reduces HR by ~ 10 bpm → ↓ cardiac workload

Colucci, WS. Use of beta blockers and ivabradine in heart failure with reduced ejection fraction. In: UpToDate, Gottlieb SS (Ed), Waltham, MA. (Accessed on March 31, 2016).

SHIFT Trial: Systolic Heart Failure tx with If Inhibitor Ivabradine Trial

- RCT; 6558 pts w/ HF Sx and LVEF ≤ 35%
  - HR ≥ 70bpm
  - HF Admission in previous year
  - On background GDMT (ACE/ARB, BB, Aldo Antagonist)

- 1º Outcome: CV Death or Hosp for worsening HF


SHIFT: CV Death or Hosp for Worsening HF

![Graph showing outcomes](https://example.com/graph)

**SHIFT Trial: Ivabradine in Chronic HF**

- No increase Serious AES
  - Increased Sx'tic Bradycardia (5% vs 1%)
  - Increased Visual side effects (3% vs 1%)

- Conclusion: HR reduction w/ Ivabradine ↓ CV Mortality and Hospitalizations for pts with persistent HF Sx, HF > 70bpm on background tx


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**Sacubitril-valsartan**

- Sacubitril = nepriysin inhibitor

- Neprilysin inhibition $\rightarrow$ ↑ vasoactive peptides $\rightarrow$ vasodilatation, natriuresis/diuresis, ↓ LV remodeling

- Indicated for NYHA II-IV HF/EF in place of ACE/ARB

- Increased risk of angioedema w/ concurrent ACEI

Colucci, WS and Pfeffer MA. Use of angiotensin II receptor blocker and neprilysin inhibitor in HF with reduced EF. UpToDate, Gottlieb SS (Ed), UpToDate, Waltham, MA. (Accessed on April 12, 2016).

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**PARADIGM-HF: Sacubitril-valsartan in HFrEF**

- 8442 HF NYHA II-IV and EF ≤ 40%
- Randomized to:
  - Sacubitril + Valsartan 200mg BID
  - Enalapril 10mg BID
- 27 months

- OUTCOMES:
  - 1° Outcome: Composite CV death or HF Hosp
  - 2° Outcomes: CV Death; All-Cause Death

**PARADIGM-HF: 1° Outcome**

(CV Death or HF Hospitalization; HR 0.80, p*)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>CV Death (HR 0.80; p*)</th>
<th>HF Hospitalization (HR 0.79; p*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril</td>
<td>26.5%</td>
<td>21.8%</td>
</tr>
<tr>
<td>Sacubitril/Valsartan</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


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**PARADIGM-HF: All-Cause Mortality**

Death from Any Cause

Hazard ratio, 0.84 (95% CI, 0.76–0.93)  
P<0.001

Days since Randomization


---

**PARADIGM-HF: Adverse Events**

<table>
<thead>
<tr>
<th>Event</th>
<th>LCZ696 (N=4125)</th>
<th>Enalapril (N=4122)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More Hypotension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic with systolic blood pressure &lt;90 mm Hg</td>
<td>358 14 (0.3)</td>
<td>388 9 (0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elevated serum creatinine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2.5 mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less Renal Impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2.5 mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated serum potassium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5.5 mEq/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less Hyperkalemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5.5 mEq/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6.0 mEq/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>181 (4.7)</td>
<td>236 (5.6)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>474 (11.3)</td>
<td>661 (14.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

PARADIGM-HF: Conclusion

Sacubitril-losartan was superior to enalapril in reducing risk of death and risk of HF hospitalization.

*No guideline recommendations


HF Guideline Recommendations:
ICD (Implantable Cardioverter-Defibrillator)

- 1° SCD prevention in pts > 40 days Post-MI, on GDMT and expected survival > 1 yr:
  - nonischemic DCM or ischemic heart disease w/ EF ≤ 35%, NYHA II-III Sx (LOE: A)
  - w/ EF ≤ 30%, NYHA I Sx (LOE: B)

- Refer to cardiology when EF ≤ 35%


MADIT-II: Multictr Automatic Defib Implantation Trial II

Prophylactic ICD compared w/ standard of care led to 31% RRR in all-cause mortality in post-MI pts w/ EF ≤ 30%

MADIT-CRT Trial

- CRT-ICD decreased risk of HF event in ASx’tic pts (NYHA I-II) w/ LVEF ≤30% and wide QRS (≥130ms)
  - 1 Outcome: All-cause death or Nonfatal HF event (ICD-CRT 17.2% vs ICD alone 25.3%; HR 0.66; p=0.001)


HF Guidelines: Cardiac Resynchronization Therapy (CRT)

- CRT is indicated for pts w/ EF ≤ 35%, NSR, LBBB, QRS ≥150ms, and NYHA class II-IV Sx on GDMT
  - May consider in non-LBBB pattern, QRS duration 120-149ms, Afib

- Refer to cardiology when EF ≤ 35%


Thiamine and CHF

- 30 CHF pts on Lasix ≥ 80 mg/d chronically
- Rx thiamine IV X 1 week + 200mg/ d PO X 6 weeks vs placebo
- Results of thiamine compared to placebo:
  - LV end diastolic function ↑ 22%
  - diuresis & Na+ excretion improved
  - NYHA class ↓ from 2.6-2.2

**Thiamine and CHF: Postulates**

- Subclinical thiamine deficiency (furosemide known to deplete thiamine)
- Diuretic effect of thiamine
- Direct cellular thiamine effect
- Commentary: Because the adverse effects were few, and the benefits potentially great, thiamine supplementation could be useful.


**CHF Alternative Medicine: Coenzyme Q₁₀**

- **Trial**: RPC trial (n=651) NYHA Class III-IV
- **Rx**: CoQ 2 mg/kg/d X 1 year
- **RESULTS**: ↓ hospitalizations, pulmonary edema; no ↓ mortality
- **ADVERSE EFFECTS**: Minimal (GI)


**CHF (HFrEF) 1ˢᵗ Care Roadmap 2016**

- Non-Invasive Disease-Modifying Rx
  - ACE/ARB
  - Beta-Blocker
  - Aldosterone Antagonist
  - Hydralazine/ISDN
  - Ivabradine
  - Valsartan/Sacubitril
- Sx-Modifying Rx
  - Diuretics
  - Digoxin
- Common Modifiable Comorbidities
  - Anemia, HTN, T-4, Thiamine, Alcohol, COPD, CAD
- Lifestyle & Immunizations
  - Na⁺/H₂O, Weight, Exercise, FluVax, PneumoVax