Heart Failure: State of the Art

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Learning Objectives

1. To convey the prevalence, risk factors for, diagnosis, and prognosis with heart failure
2. Describe current evidence-based guideline recommendations for heart failure therapy
3. To describe the impact of medical therapies on heart failure patient outcome
4. To highlight the benefits of device therapy and disease management for heart failure

Heart Failure Background

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Prevalence</th>
<th>Incidence</th>
<th>Mortality</th>
<th>Hospital Discharges</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>5,100,000</td>
<td>825,000</td>
<td>50% at 5 years</td>
<td>1,023,000</td>
<td>$30.7 billion</td>
</tr>
</tbody>
</table>

- Heart failure (HF) is a major public health problem resulting in substantial morbidity, mortality, and healthcare expenditures
- Major cost-driver of HF is high incidence of hospitalizations
- Despite treatment advances large number of eligible patients are not receiving one or more evidence-based HF therapies

Prognosis with Heart Failure

Survival after the onset of congestive heart failure in Framingham Heart Study subjects

Overall 5-year mortality 50%
Hospitalized Patients 1-year mortality:
- Mild to Moderate Symptoms 10-20%
- Severe Symptoms 40-60%
Outcomes During and After HF Hospitalization

- **In-hospital**
  - Length of stay (mean) 6.2 days
  - Mortality rate 4.1%
- **Hospital readmissions**
  - 20% at 30 days
  - 50% at 6 months
- **Longer-term mortality**
  - 11.6% at 30 days
  - 33.1% at 12 months


Approach to the Classification of Heart Failure

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patient Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High risk for developing heart failure (HF)</td>
</tr>
<tr>
<td></td>
<td>Hypertension, CAD, Diabetes mellitus, Family history of cardiomyopathy</td>
</tr>
<tr>
<td>B</td>
<td>Asymptomatic HF</td>
</tr>
<tr>
<td></td>
<td>Previous MI, LV systolic dysfunction, Asymptomatic valvular disease</td>
</tr>
<tr>
<td>C</td>
<td>Symptomatic HF</td>
</tr>
<tr>
<td></td>
<td>Known structural heart disease, Shortness of breath and fatigue, Reduced exercise tolerance</td>
</tr>
<tr>
<td>D</td>
<td>Refractory end-stage HF</td>
</tr>
<tr>
<td></td>
<td>Marked symptoms at rest despite maximal medical therapy (eg, those who are repeatedly hospitalized or cannot be safely discharged from the hospital without specialized interventions)</td>
</tr>
</tbody>
</table>

Definition of Heart Failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart Failure with Reduced Ejection Fraction (HFrEF)</td>
<td>&lt;40%</td>
<td>Heart failure with reduced LV ejection fraction (HFrEF). This group includes patients with overt heart failure and reduced LV systolic function.</td>
</tr>
<tr>
<td>II. Heart Failure with Preserved Ejection Fraction (HFpEF)</td>
<td>&gt;40%</td>
<td>Heart failure with preserved LV ejection fraction (HFpEF). This group includes patients with subtle or mild symptoms and normal or near-normal LV systolic function.</td>
</tr>
<tr>
<td>a. HFpEF, Borderline</td>
<td>41% to 49%</td>
<td>These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HFpEF.</td>
</tr>
<tr>
<td>b. HFpEF, Improved</td>
<td>&gt;50%</td>
<td>It has been recognized that a subset of patients with HFpEF previously had HFpEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.</td>
</tr>
</tbody>
</table>

Natural History of Heart Failure

- **Survival**
  - <10%
  - 10-20%
  - 20-30%
  - 30-60%
  - 60-80%

- **Mechanism of Death**
  - Sudden Death 40%
  - Worsened HF 40%
  - Other 20%

- **Left Ventricular Dysfunction and Symptoms**

Heart Failure Pathophysiology

- **Myocardial injury**
- **Activation of RAAS, SNS, ET, and others**
- **Myocardial toxicity**
- **Peripheral vasoconstriction**
- **Remodeling and progressive worsening of LV function**
- **Heart failure symptoms**

Pathophysiologic Effects of Angiotensin II and Epinephrine/Norepinephrine

- **Cardiac Myocyte**
  - Hypertrophy
  - Apoptosis
  - Cell Sclerosis
- **Fibroblast**
  - Hypertrophy
  - Collagen Synthesis
  - Fibrosis
- **Peripheral Artery**
  - Vasocostriction
  - Endothelial Dysfunction
  - Atherosclerosis
  - Thrombosis
- **Coronary Artery**
  - Vasocostriction
  - Endothelial Dysfunction
  - Atherosclerosis
  - Restenosis
ACC/AHA HF Guidelines:
Management of Heart Failure (Stage C)

Life Prolonging Medical Therapy

- ACE inhibitors or ARB (Class I, evidence A) all patients without contraindications or intolerance
- β-Blockers (Class I, evidence A) all patients without contraindications or intolerance
- Aldosterone antagonists (Class I, evidence A) all patients with Class II-IV HF without contraindications or intolerance, when close monitoring can be assured


Effect of ACE Inhibitors on Mortality and Hospitalizations in Patients with HF

Total Mortality Death or Hospitalization CHF Hospitalization

32 Trials of ACEI in Heart Failure  ACEI (n = 3870) Placebo (n = 3235)
Collaborative Group on ACE Inhibitor Trials  JAMA 1995;273:1450-1456

OR 0.77 (0.67-0.88)  p<0.001

High vs Low Dose ACEI Therapy for Heart Failure

<table>
<thead>
<tr>
<th>Low Dose</th>
<th>High Dose</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1339/1596</td>
<td>1251/1596</td>
<td>0.88</td>
</tr>
<tr>
<td>Death or Hospitalization</td>
<td>83.9%</td>
<td>79.8%</td>
</tr>
<tr>
<td>Death</td>
<td>717/1596</td>
<td>666/1596</td>
</tr>
<tr>
<td>44.9%</td>
<td>42.5%</td>
<td>(0.81-1.03)</td>
</tr>
</tbody>
</table>

ATLAS: 8% reduction in death and 14% reduction in death and HF hospitalization
SOLVD: 14% reduction in death and 26% reduction in death and HF hospitalization

Survival Rates in Patients Receiving ACE Inhibitors Across NYHA Classes

ACE inhibitor arms of CONSENSUS, V-HeFT, and SOLVD trials. Placebo arms of PRAISE, PROMISE, and DIG trials all receiving ACE inhibitors.

ValHeFT: ARB added to Standard HF Care Including ACEI

Mortality

<table>
<thead>
<tr>
<th>Probability of Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsartan</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>90</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>70</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>10</td>
</tr>
</tbody>
</table>

Months since Randomization

P=80

Primary outcome of CV death or CHF hospitalization

Placebo 334 (33.0%)  Candesartan 406 (40.0%)

HR 0.77 (95% CI 0.67-0.89), P<.0004
Adjusted HR 0.70, P<.0001

Number at risk
Candesartan 1,013 929 831 434 122
Placebo 1,015 887 798 427 126
ACEI/ARB in Heart Failure

- Indicated for all patients with asymptomatic LV dysfunction and for Class I to IV heart failure. (Contraindications: hyperkalemia, angioedema, pregnancy)
- Titrate to target doses (example enalapril 10 mg bid, lisinopril 20 qd, ramipril 10 mg qd, benazepril 40 qd, valsartan 160 mg bid, candesartan 32 mg qd)
- Monitor serum potassium and renal function. Advise checking chemistry panel 1-2 weeks after first dose.
- Use of ACE inhibitor together with ARB reserved as a consideration only in patients not candidates for aldosterone antagonist.

RALES: Aldosterone Antagonist Reduces All-Cause Mortality in Chronic HF

*Ejection fraction ≤35% Class III or IV symptoms at some point in prior 2 months.


Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms: EMPHASIS HF

Primary Endpoint: CV Mortality and HF Hospitalization

HR = 0.63 (0.54-0.74), p <0.001

Placebo

Eplerenone 249 (18.3%)

0123

50

40

30

20

10

0

Primary Endpoint: Cumulative K-M Rate (%)

Years from Randomization
No. at Risk

Placebo

Eplerenone

1373

848

1364

925

848

512

925

562

199

232


Aldosterone Antagonists in Heart Failure

- Indicated for patients with mild, moderate, or severe HF due to LVD (LVEF < 0.40). (Contraindications: hyperkalemia, Cr > 2.5 in men and > 2.0 in women)
- Spironolactone 12.5 mg PO qd starting dose (or 6.25 mg in higher risk patients) or Eplerenone 25 mg qd (or 12.5 mg in higher risk patients). Decrease potassium supplementation and loop diuretic dose at time of initiation.
- Critical to very closely monitor serum potassium and renal function. Advise checking chemistry panel at 72 hours, 1 week, and 4 weeks.
- Advance Spironolactone dose at 4 weeks to 25 mg PO qd or Eplerenone 50 mg which is the target dose. Avoid higher doses due to risk of hyperkalemia.

The Use of Beta Adrenergic Blocking Agents in Heart Failure

Initial hemodynamic deterioration followed by reverse remodeling (decrease in EDV and ESV) with improved ventricular function over time (increased LVEF)
Major Trials of β-Blockade in Heart Failure

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patients (n)</th>
<th>Follow-up (yrs)</th>
<th>NYHA Class</th>
<th>LVEF (%)</th>
<th>Effects on Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIBIS-4</td>
<td>2647</td>
<td>1.3</td>
<td>II-III</td>
<td>≤ 35</td>
<td>All-cause mortality: 34% (P=0.001)</td>
</tr>
<tr>
<td>MDC</td>
<td>383</td>
<td>1</td>
<td>II-III</td>
<td>≤ 40</td>
<td>Death or need for transplant: 35%, P=0.05</td>
</tr>
<tr>
<td>MERIT-HF</td>
<td>3991</td>
<td>1</td>
<td>II-III</td>
<td>≤ 40</td>
<td>All-cause mortality: 34% (P=0.001)</td>
</tr>
<tr>
<td>US Carvedilol Trials</td>
<td>1094</td>
<td>7.5</td>
<td>II-III</td>
<td>≤ 35</td>
<td>All-cause mortality: 65% (P=0.001)</td>
</tr>
<tr>
<td>COPERNICUS</td>
<td>2289</td>
<td>10.5</td>
<td>IV</td>
<td>≤ 25</td>
<td></td>
</tr>
</tbody>
</table>

Early Benefits and Early Safety of Carvedilol in Severe HF: COPERNICUS

<table>
<thead>
<tr>
<th>Early Mortality Reduction</th>
<th>Lower Risk for Worsening CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Carvedilol</td>
</tr>
<tr>
<td>6.4</td>
<td>5.1</td>
</tr>
<tr>
<td>(n=1,133)</td>
<td>(n=1,156)</td>
</tr>
<tr>
<td>11.6</td>
<td>11.4</td>
</tr>
<tr>
<td>(n=316)</td>
<td>(n=308)</td>
</tr>
</tbody>
</table>

Beta-Blockers Differ in Their Long-Term Effects on Mortality in HF

- Bisoprolol: Beneficial
- Bucindolol: No effect
- Carvedilol: Beneficial
- Metoprolol trandate: Not well studied
- Metoprolol succinate: Beneficial
- Nebivolol: No effect
- Xamoterol: Harmful

# References
COMET: Effect Carvedilol vs Metoprolol Tartrate on Mortality in HF


Time (years)

Mortality (%)

Carvedilol

Metoprolol Tartrate

Extrapolation from the survival curves suggested that carvedilol extended median survival by 1.4 years as compared with metoprolol tartrate.

Mortality rates: metoprolol 40%; Carvedilol 34%.

Metoprolol tartrate mean dose: 85 mg OD; Carvedilol mean dose: 42 mg OD.

COMET did not evaluate metoprolol succinate, the agent used in the MERIT-HF Trial.

Extrapolation from the survival curves suggested that carvedilol extended median survival by 1.4 years as compared with metoprolol tartrate.

Beta Blocker Therapy in Heart Failure

- Indicated for all patients with asymptomatic LVD dysfunction and for Class I to IV Heart Failure with LVEF ≤ 0.40
- Contraindications: cardiogenic shock, severe reactive airway disease, 2/3rd degree HB
- Use one of the 3 evidence-based beta blockers in HF: eg carvedilol, metoprolol succinate, bisoprolol
- Start at very low HF doses and up-titrate to target doses at two week intervals, or highest dose short of target dose that is well tolerated
- Monitor HR and BP

Neurohormonal Activation as the Therapeutic Target in Heart Failure

Therapies with Demonstrated Benefit in Clinical Trials

Sympathetic Nervous System
Beta Adrenergic Blockers
Renin Angiotensin Aldosterone System
Angiotensin Converting Enzyme Inhibitors
Angiotensin II Receptor Antagonists
Aldosterone Antagonists

GISSI HF: All-cause Mortality

Adjusted HR (95% CI) 0.91 (0.833 – 0.998) p value 0.041

NNT = 56 ARR = 1.8%

Patients at risk
Omega 3 FA 3,494
Placebo 3,481

Probability of death

Months since randomization

Ivabradine and Outcomes in Chronic Heart Failure (SHIFT)

SHFT: Hazard ratios for primary and individual outcomes, Ivabradine vs placebo groups

Outcomes in SHFT

Ivabradine, n=3241 (%) Placebo, n=3264 (%) HR (95% CI) p

CV death or HF hospitalization 24 29 0.82 (0.75-0.90) <0.0001

Death from heart failure 3 5 0.74 (0.58-0.94) 0.014

HF hospitalization 16 21 0.74 (0.66-0.83) <0.0001

CV death, HF hospitalization, or admission for nonfatal MI 25 30 0.82 (0.74-0.89) <0.0001

The benefit of ivabradine appeared to go up with increasing heart rate (HR>77 HR 0.93; HR 0.77 HR 0.75)

6558 patients with LVEF ≤35%, Sinus rhythm ≥70 bpm

Swedberg et al. Lancet 2010
Effect of Digoxin on Mortality in Heart Failure: The Digitalis Investigation Group

DIG (Digitalis Investigation Group): 6,800 patients with LVEF < 45% randomized to digoxin (n=3,403) or placebo (n=3,397) in addition to therapy with diuretics and ACEI followed for 37 months.


Digoxin Placebo

Relative Risk 0.99
95% CI 0.91–1.07
P = .80

All-cause mortality rates: Placebo 35.1%; Digoxin 34.8%

Mortality From Any Cause (%)

CV Mortality 1%
HF Hospitalizations ↓ 28%
Total Hospitalizations ↓ 6%

Number of patients at risk:
Placebo 3,403 3,239 3,105 2,976 2,868 2,758 2,652 2,551 2,205 1,881 1,506 1,168 734 339
Digoxin 3,397 3,269 3,144 3,019 2,882 2,759 2,644 2,531 2,184 1,840 1,475 1,156 737 335

CV Mortality
HF Hospitalizations
Total Hospitalizations

Diuretic Therapy in Chronic Heart Failure

- Loop diuretics are mainstay of therapy for CHF (Given to > 85% of patients)
- Beneficial effects of diuretic therapy:
  - ↓ Dyspnea and other congestive symptoms
  - ↓ Volume overload
  - Facilitate successful initiation and titration of ACE inhibitors, β-blockers, vasodilators

No outcome studies of diuretic therapy in chronic HF and effects on morbidity and mortality unknown

Pharmacological Therapy for Management of Stage C HFREF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other Drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutritional supplements as treatment for HF are not recommended in HFREF</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
<tr>
<td>Hormonal therapies other than to replete deficiencies are not recommended in HFREF</td>
<td>II-B: No Benefit</td>
<td>C</td>
</tr>
<tr>
<td>Drugs known to adversely affect the clinical status of patients with HFREF are potentially harmful and should be avoided or withdrawn</td>
<td>II: Harm</td>
<td>B</td>
</tr>
<tr>
<td>Long-term use of an infusion of a positive inotropic drug is not recommended and may be harmful except as palliation</td>
<td>II: Harm</td>
<td>C</td>
</tr>
<tr>
<td>Calcium Channel Blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel blocking drugs are not recommended as routine in HFREF</td>
<td>III: No Benefit</td>
<td>A</td>
</tr>
</tbody>
</table>


Cardiac Resynchronization Therapy for Heart Failure

- In patients with heart failure 27 to 53% of patients have IVCds (RBBB, LBBB, IVCD)
- Abnormal conduction contributes to abnormal ventricular activation/contraction and subsequent dysynchrony between the RV and LV
  - Reduced systolic performance
  - Mechanical inefficiency
  - Worsened prognosis


Cardiac Resynchronization Therapy: Weight of Evidence

- >8,000 patients evaluated in randomized controlled trials
- Consistent improvement in quality of life, functional status, and exercise capacity
- Strong evidence of reverse remodeling
  - ↓ LV volumes and dimensions
  - ↑ LVEF
  - ↓ Mitral regurgitation
- Reduction in HF and all-cause morbidity and mortality


CARE-HF: Effect of CRT Without an ICD on All-Cause Mortality

HR: 0.64 (95% CI: 0.48-0.85)
P = .0019

## CARE-HF: Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>OMT (n=404)</th>
<th>CRT + OMT (n=409)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death + CV Hospitalization</td>
<td>225 (55%)</td>
<td>159 (39%)</td>
<td>.63 (0.51 to 0.77)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CV Hospitalization</td>
<td>184 (46%)</td>
<td>125 (31%)</td>
<td>0.61 (.49 to .77)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HF Hospitalization</td>
<td>133 (33%)</td>
<td>72 (18%)</td>
<td>0.48 (.36 to .64)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>All-Cause Death</td>
<td>120 (30%)</td>
<td>62 (20%)</td>
<td>0.64 (.48 to .85)</td>
<td>&lt;.002</td>
</tr>
</tbody>
</table>

OMT = optimal medical therapy


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## Important Comorbidities in Heart Failure

- **Cardiovascular**
  - Hypertension
  - Coronary artery disease
  - Peripheral vascular disease
  - Cerebral vascular disease
  - Hyperlipidemia
  - Atrial fibrillation

- **Non-Cardiovascular**
  - Obesity
  - Diabetes
  - Anemia
  - Chronic kidney disease
  - Thyroid disease
  - COPD / Asthma
  - Smoking
  - Sleep disordered breathing
  - Liver disease
  - Arthritis
  - Cancer
  - Depression


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## Patient Education is Essential in HF

**Patient Instructions**
- Monitor daily weights
- Salt restricted diet (e.g. 2-3 gm sodium diet)
- Medications, need for adherence
- Activity Rx
- Smoking Cessation Advice/Counseling
- What to do if HF symptoms worsen
- Close follow-up and monitoring


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## Heart Failure with Preserved Ejection Fraction

Treatment of patients with predominantly diastolic dysfunction heart failure has not been well studied

- Control hypertension
- Diuretics should be used cautiously, at low dose initially, recognizing that the stiff heart is highly dependent on adequate preload
- Rate control for atrial fibrillation
- ACE inhibitors, calcium channel blockers, and beta blockers have favorable effects upon hemodynamics but their impact on longer term outcome is not known


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## ARB in HF with Preserved EF

**I-PRESERVE: Primary Endpoint Death or CV hospitalization**

- Primary Endpoint: Death or CV hospitalization
- HR (95% CI) = 0.95 (0.86-1.05)
- Log-rank p=.35

Clinical Effectiveness of Beta-Blockers in Heart Failure: CMS Matched Cohort

HF with LVEF < 40%

n = 3001

Adjusted HR 0.77 (95% CI 0.68-0.87)

HF with LVEF ≥ 40%

n = 4153

Adjusted HR 0.94 (95% CI 0.84-1.07)

7194 patients hospitalized with HF, eligible for beta-blockers, and previously not treated. 3421 (49%) were newly initiated on beta-blocker therapy.

Hernandez A et al. J. Am. Coll. Cardiol. 2006;53;184-192

Evidence-Based, Guideline-Recommended Heart Failure Reduced Ejection Fraction Therapies

<table>
<thead>
<tr>
<th>Guideline Recommended Therapy</th>
<th>Relative Risk Reduction in Mortality</th>
<th>Number Needed to Treat for Mortality (standardized to 36 months)</th>
<th>NNT for Mortality Reduction in HF Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI/ARB</td>
<td>17%</td>
<td>22 over 43 months</td>
<td>26</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>34%</td>
<td>28 over 12 months</td>
<td>9</td>
</tr>
<tr>
<td>Aldosterone Antagonist</td>
<td>30%</td>
<td>9 over 24 months</td>
<td>6</td>
</tr>
<tr>
<td>Hydralazine/Nitrates</td>
<td>43%</td>
<td>25 over 10 months</td>
<td>7</td>
</tr>
<tr>
<td>CRT</td>
<td>34%</td>
<td>12 over 24 months</td>
<td>8</td>
</tr>
<tr>
<td>ICD</td>
<td>25%</td>
<td>14 over 60 months</td>
<td>NA</td>
</tr>
</tbody>
</table>


Potential Impact of Optimal Implementation of Evidence-Based HF Therapies on Mortality

<table>
<thead>
<tr>
<th>Guideline Recommended Therapy</th>
<th>HF Patient Population Eligible for Treatment, n²</th>
<th>Current HF Population Eligible and Untreated, n (%)</th>
<th>Potential Lives Saved per Year</th>
<th>Potential Lives Saved per Year (Sensitivity Range*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI/ARB</td>
<td>2,450,644</td>
<td>301,767 (20.4)</td>
<td>6916</td>
<td>(3026-71,260)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>2,512,560</td>
<td>381,805 (14.4)</td>
<td>12,922</td>
<td>(8610-22,329)</td>
</tr>
<tr>
<td>Aldosterone Antagonist</td>
<td>653,014</td>
<td>385,228 (58.3)</td>
<td>21,407</td>
<td>(10,800-36,581)</td>
</tr>
<tr>
<td>Hydralazine/Nitrates</td>
<td>150,754</td>
<td>130,749 (82.7)</td>
<td>6955</td>
<td>(3407-17,303)</td>
</tr>
<tr>
<td>CRT</td>
<td>328,131</td>
<td>199,004 (61.2)</td>
<td>837</td>
<td>(4528-14,372)</td>
</tr>
<tr>
<td>ICD</td>
<td>1,125,132</td>
<td>852,512 (46.9)</td>
<td>12,179</td>
<td>(6236-21,045)</td>
</tr>
<tr>
<td>Total</td>
<td>7,526,188</td>
<td>5,301,767 (70.4)</td>
<td>61,956</td>
<td>(34,813-117,497)</td>
</tr>
</tbody>
</table>


Cumulative Impact of Clinical Trial Evidence Based Heart Failure Therapies

<table>
<thead>
<tr>
<th>Relative-risk 2 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>ACE Inhibitor</td>
</tr>
<tr>
<td>Beta Blocker</td>
</tr>
<tr>
<td>Aldosterone Ant</td>
</tr>
<tr>
<td>CRT-D (EF&lt;35, QRS&gt;120)</td>
</tr>
<tr>
<td>Omega-3 FA</td>
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</tbody>
</table>

Absolute risk reduction: 28%, NNT = 4

Adapted from Fonarow GC. Rev Cardiovasc Med. 2006;7:S3-11

Heart Failure Prevention

Patients at risk for heart failure:
- Treat systolic and diastolic hypertension according to guidelines
- Treat diabetes according to guidelines
- Treat atherosclerosis according to guidelines
- Treat lipid disorders according to guidelines
- Encourage smoking cessation
- Encourage exercise
- Discourage heavy alcohol intake, illicit drug use
- Consider ACEI/ARB and beta blocker use in those at risk for HF


Advances in the Treatment of HF

- Increased attention to prevention
- ACEI / β-blocker / aldosterone antagonist combination established as the “cornerstone” of therapy
- Evidence that β-blockers’ effects are not homogeneous
- Downgrade in recommendation for use of digoxin
- Integration of CRT and ICD device therapy into the standard therapeutic regimen
- Recognition that “special populations” of HF patients may benefit from or require different approaches
- New strategies to improve utilization of evidence based therapies

The economic burden of HF continues to grow and HF is one of the single most expensive and deadly health care problems.

Medical therapies and nonpharmacologic measures for HF that can impact patients’ need for re-hospitalization, costs of care, and survival are underutilized in conventional practice settings.

Every effort should be made to implement evidence-based HF therapies when indicated and optimize care of HF.

Questions?