9:45 – 10:45 am

Heart Failure: State of the Art 2015

SPEAKER
Gregg Fonarow, MD, FACC, FAHA

Presenter Disclosure Information

The following relationships exist related to this presentation:

- Gregg C. Fonarow, MD, FACC, FACP, FAHA: Consultant for Amgen, Inc.; Johnson & Johnson; Medtronic, Inc.; and Novartis Pharmaceuticals Corporation. Grant support from NIH/AHRQ.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives

- Outline the prevalence, risk factors for, diagnosis and prognosis with heart failure
- Describe current evidence-based guideline recommendations for heart failure therapy
- Describe the impact of medical therapies on heart failure patient outcomes
- Highlight the benefits of device therapy and disease management for heart failure

Heart Failure Background

Population Group	Prevalence	Incidence	Mortality	Hospital Discharges	Cost
Total population	5,700,000	870,000	50% at 5 years	1,023,000	$30.7 billion

- 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

American Heart Association. *2015 Heart and Stroke Statistical Update.* Dallas, Tex: American Heart Association; 2015

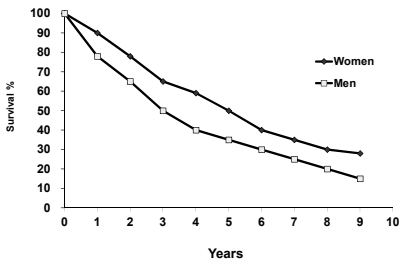
Prognosis with Heart Failure

Overall
5-year mortality 50%

Hospitalized Patients
1-year mortality:

Mild to Moderate Symptoms
10-20%

Severe Symptoms
40-60%



Survival after the onset of congestive heart failure in Framingham Heart Study subjects
AHA. 1998 Heart and Statistical Update
Ho Circulation. 1993;88:107-115 Statistics

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

Fonarow GC et al. *J Card Failure.* 2003;9:S79
Jong P et al. *Arch Intern Med.* 2002;162:1689

Approach to the Classification of Heart Failure

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

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

Classification of Heart Failure

ACCF/AHA Stages of HF		NYHA Functional Classification	
A	At high risk for HF but without structural heart disease or symptoms of HF.	None	
B	Structural heart disease but without signs or symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
C	Structural heart disease with prior or current symptoms of HF.	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.
D	Refractory HF requiring specialized interventions.		

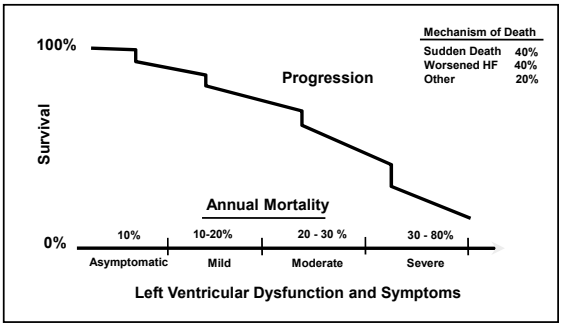
Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

Definition of Heart Failure

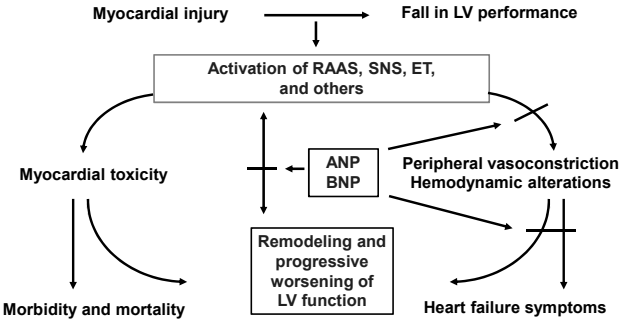
Classification	Ejection Fraction	Description
I. Heart Failure with Reduced Ejection Fraction (HF*r*EF)	≤40%	Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HF*r*EF and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart Failure with Preserved Ejection Fraction (HF*p*EF)	≥50%	Also referred to as diastolic HF. Several different criteria have been used to further define HF*p*EF. The diagnosis of HF*p*EF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.
a. HF*p*EF, Borderline	41% to 49%	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HF*p*EF.
b. HF*p*EF, Improved	>40%	It has been recognized that a subset of patients with HF*p*EF previously had HF*r*EF. 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.

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

Natural History of Heart Failure



Heart Failure Pathophysiology



Fonarow GC. *Rev Cardiovasc Med*..2001;2:7–12.

Pathophysiologic Effects of Angiotensin II and Epinephrine/Norepinephrine

Cardiac Myocyte
- Hypertrophy
- Apoptosis
- Cell Sliding
- Increased Wall Stress
- Increased O2 Consumption
- Impaired Relaxation

Fibroblast
- Hyperplasia
- Collagen Synthesis
- Fibrosis

Peripheral Artery
- Vasoconstriction
- Endothelial Dysfunction
- Hypertrophy
- Decreased Compliance

Coronary Artery
- Vasoconstriction
- Endothelial Dysfunction
- Atherosclerosis
- Restenosis
- Thrombosis

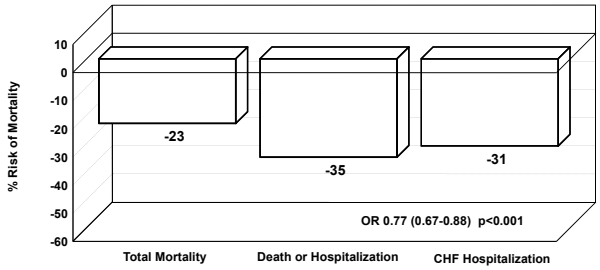
ACC/AHA HF Guidelines: Management of Heart Failure (Stage C)

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

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

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



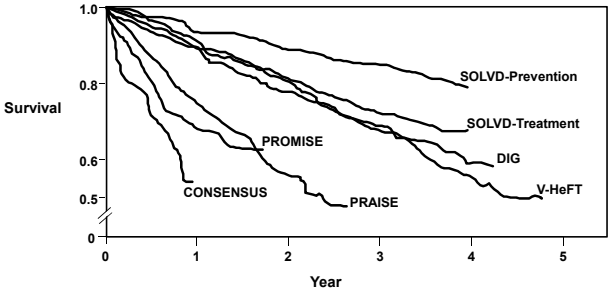
32 Trials of ACEI in Heart Failure ACEI (n = 3870) Placebo (n = 3235)
Collaborative Group on ACE Inhibitor Trails JAMA 1995;273:1450-1456

High vs Low Dose ACEI Therapy for Heart Failure

	Low Dose	High Dose	OR	
Death or Hospitalization	1339/1596 83.9%	1251/1568 79.8%	0.88 (0.82-0.95)	p=0.002
Death	717/1596 44.9%	666/1568 42.5%	0.92 (0.81-1.03)	p=0.128

3164 patients with Class II-IV CHF ave f/u 46 months
Lisinopril Low Dose 2.5 to 5.0 mg/d High Dose 32.5 to 35.0 mg/d
Packer Circulation 1999;100:1-7

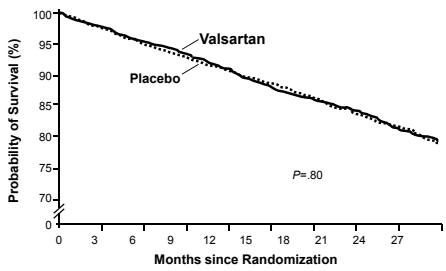
Survival Rates in Patients Receiving ACE Inhibitors Across NYHA Classes



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

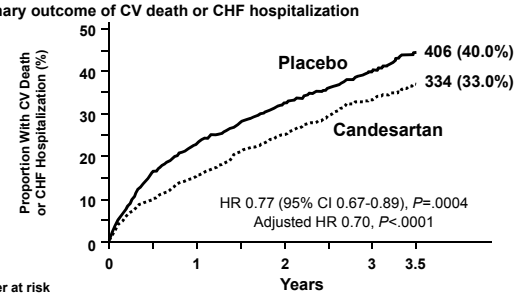
Mortality



Cohn J et al. *N Engl J Med.* 2001;345:1667–1675.

CHARM-Alternative

Primary outcome of CV death or CHF hospitalization



Number at risk					
Candesartan	1,013	929	831	434	122
Placebo	1,015	887	798	427	126

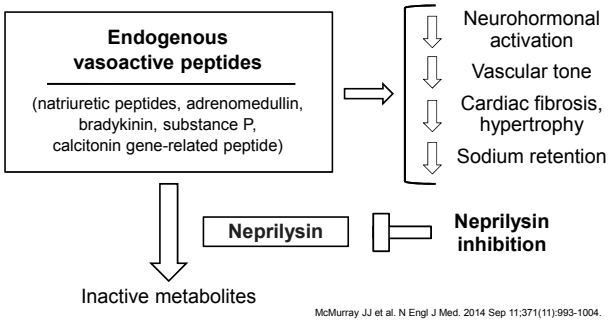
Granger CB, et al. *Lancet.* 2003;362:772-776.

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.

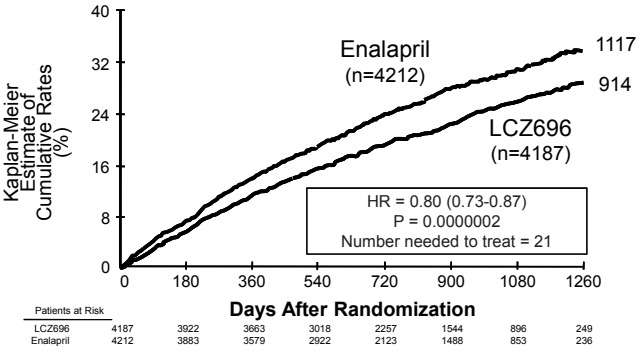
Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

Neprilysin Inhibition Potentiates Actions of Endogenous Vasoactive Peptides That Counter Maladaptive Mechanisms in Heart Failure



McMurray JJ et al. N Engl J Med. 2014 Sep 11;371(11):993-1004.

PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)



PARADIGM-HF: Summary of Findings

In heart failure with reduced ejection fraction, when compared with recommended doses of enalapril:

LCZ696 was *more effective* than enalapril in . . .

- Reducing the risk of CV death and HF hospitalization
- Reducing the risk of CV death by *incremental* 20%
- Reducing the risk of HF hospitalization by *incremental* 21%
- Reducing all-cause mortality by *incremental* 16%
- *Incrementally* improving symptoms and physical limitations

LCZ696 was *better tolerated* than enalapril . . .

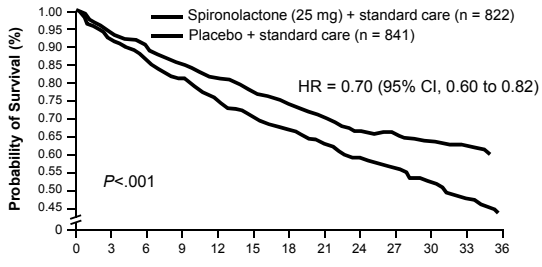
- Less likely to cause cough, hyperkalemia or renal impairment
- Less likely to be discontinued due to an adverse event
- More hypotension, but no increase in discontinuations
- Not more likely to cause serious angioedema

McMurray JJ et al. N Engl J Med. 2014 Sep 11;371(11):993-1004.

Sacubitril/Valsartan for Heart Failure

- The fixed-dose combination of the neprilysin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan is indicated to reduce the risk of cardiovascular death and heart failure hospitalization in patients with heart failure with reduced ejection fraction.
- Recommended starting dosage is 49/51 mg twice daily. The dose should be doubled after 2-4 weeks as tolerated to reach the target maintenance dosage of 97/103 mg twice daily. For patients not currently taking an ACEI or ARB, or for those with severe renal impairment (eGFR <30 mL/min/1.73 m2) or moderate hepatic impairment, the starting dosage of is 24/26 mg twice daily.
- ACE inhibitor treatment should be stopped for 36 hours before starting treatment.
- Contraindications: hyperkalemia, pregnancy, symptomatic hypotension or shock, concurrent use with ACEI.
- Side effects: Hypotension and hyperkalemia. Angioedema occurred in 0.5% of patients compared to 0.2% with ACEI.

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



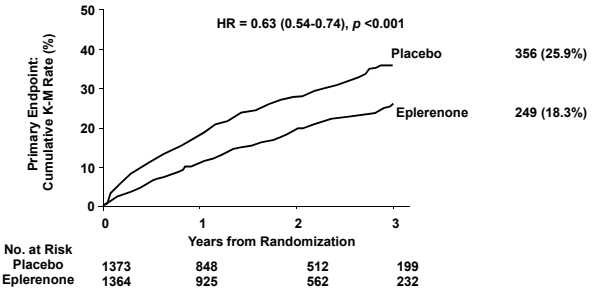
HR = hazard ratio; RR = risk reduction.

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

Pitt B et al. *N Engl J Med*. 1999;341:709-717.

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

Primary Endpoint: CV Mortality and HF Hospitalization



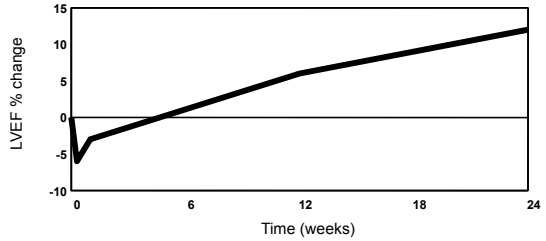
Zannad F. New Engl J Med. 2011;364:11-21.

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.

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

The Use of Beta Adrenergic Blocking Agents in Heart Failure

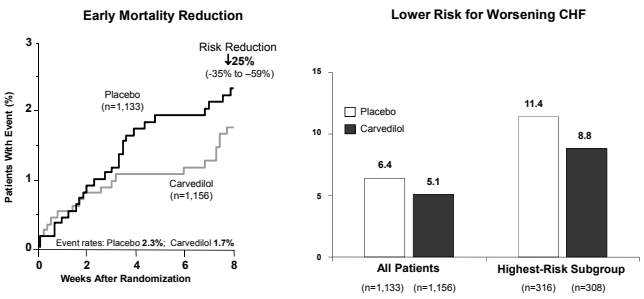


Initial hemodynamic deterioration followed by reverse remodeling (decrease in EDV and ESV) with improved ventricular function over time (increased LVEF)

Major Trials of β-Blockade in Heart Failure

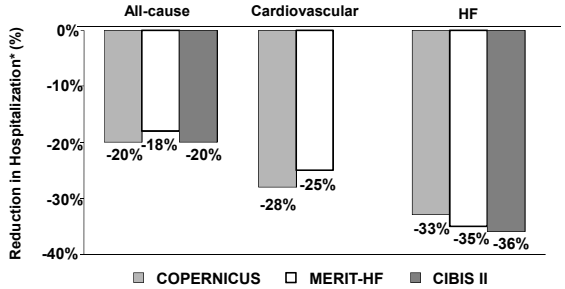
	Patients (n)	Follow-up (yrs)	NYHA Class	LVEF (%)	Effects on Outcomes
CIBIS	641	1.9	II-III	≤ 35	All-cause mortality: ↓ 22% NS
CIBIS-II	2647	1.3	II-III	≤ 35	All-cause mortality: ↓ 34% (*P*<.0001)
MDC	383	1	II-III	≤ 40	Death or need for transplant: ↓ 30%, P<0.05
MERIT-HF	3991	1	II-III	≤ 40	All-cause mortality: ↓ 34% (*P*=.0062)
US Carvedilol Trials	1094	7.5 months	II-III	≤ 35	All-cause mortality*: ↓ 65% (*P*=.0001)
COPERNICUS	2289	10.5 months	IV	≤ 25	

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



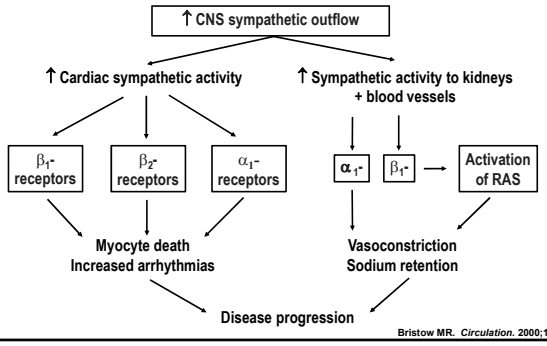
Packer M. *N Engl J Med.* 2001;344:1651–1658. Krum H. *JAMA.* 2003;289:712–718.

Effect of β-Blockade on Hospitalizations



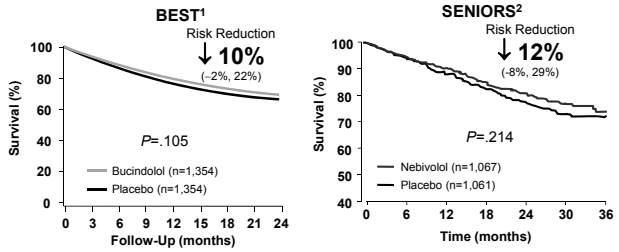
Only carvedilol and metoprolol CR/XL are FDA approved for HF therapy in the U.S.
[1]Packer M et al. *N Engl J Med.* 2001;344:1651–1658. [2]Hjalmarson A et al. *JAMA.* 2000;283:1295–1302.
[3]CIBIS II Investigators. *Lancet.* 1999;353:9–13.

Effects of Sympathetic Activation in Heart Failure



Bristow MR. *Circulation.* 2000;101:558-569.

Not All β-Blockers Reduce Mortality in HF



2,708 patients (CHF Class III–IV, average age 60, LVEF .23) randomized to placebo or bucindolol (3 mg titrated to 50 mg po BID). Number of events: bucindolol 411 (30%); placebo 449 (33%).

2,128 patients (CHF Class II–III, average age 76, average LVEF .36 with approximately 65% of patients with LVEF ≤.35) randomized to Placebo or nebivolol (1.25 mg titrated to 10 mg po QD). All-cause mortality was a secondary endpoint. Number of events: nebivolol 169 (15.8%); placebo 192 (18.1%).

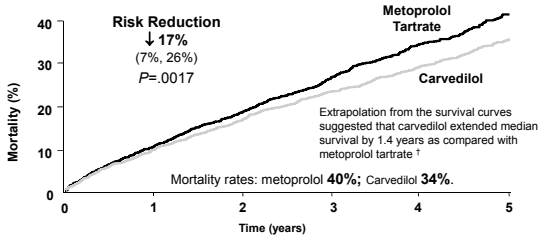
[1]BEST Investigators. *N Engl J Med.* 2001;344:1659-1667. [2]Flather, M et al. *Eur Heart J.* 2005;26:215-225.

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

Bisoprolol[1]	Beneficial
Bucindolol[2]	No effect
Carvedilol[3-5]	Beneficial
Metoprolol tartrate[6]	Not well studied
Metoprolol succinate[7]	Beneficial
Nebivolol[8]	No effect
Xamoterol[9]	Harmful

[1]CIBIS II Investigators and Committees. *Lancet.* 1999;353:9-13. [2]The BEST Investigators. *N Engl J Med* 2001; 344:1659-1667. [3]Colucci WS, et al. *Circulation* 1996;94:2800-2806. [4]Packer M, et al. *N Engl J Med* 2001;344:1651-1658. [5]The CAPRICORN Investigators. *Lancet.* 2001;357:1385-1390. [6]Waagstein F, et al. *Lancet.* 1993;342:1441-1446. [7]MERIT-HF Study Group. *Lancet.* 1999;353:2001-2007. [8]SENIORS Study Group. *Eur Heart J.* 2005; 26:215-225. [9]The Xamoterol in Severe heart Failure Study Group. *Lancet.* 1990;336:1-6.

COMET: Effect Carvedilol vs Metoprolol Tartrate on Mortality in HF



Metoprolol tartrate mean dose: 85 mg QD; Carvedilol mean dose: 42 mg QD.
COMET did not evaluate metoprolol succinate, the agent used in the MERIT-HF Trial

Poole-Wilson PA, et al. *Lancet.* 2003;362:7-13.

Beta Blocker Therapy in Heart Failure

- Indicated for all patients with asymptomatic LVD dysfunction and for Class I to IV Heart Failure with LVEF $\leq$ 0.40
- Contraindications: cardiogenic shock, severe reactive airway disease, 2/3rd degree HB
- Use one the 3 evidence-based beta blockers in HF: eg carvedilol, metroprolol 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

Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

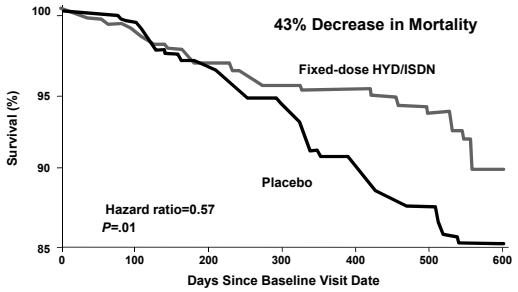
Neurohormonal Activation as the Therapeutic Target in Heart Failure

Therapies with Demonstrated Benefit in Clinical Trials

Sympathetic Nervous System
Beta Adrenergic Blockers

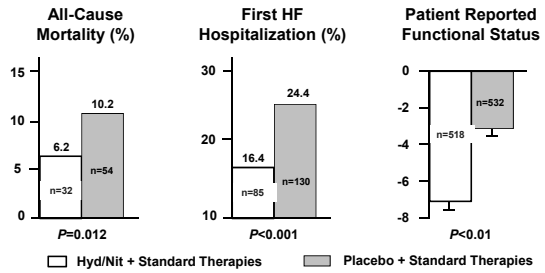
Renin Angiotensin Aldosterone System
Angiotensin Converting Enzyme Inhibitors
(Angiotensin II Receptor Antagonists)
Aldosterone Antagonists

AHeFT: Trial Summary



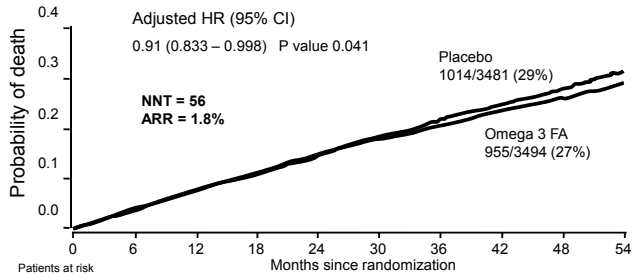
1050 African Americans with Class III to IV HF, LVEF 24%, on ACEI, BB, AA
Adapted from Taylor AL, et al. *N Engl J Med*. 2004;351:2052.

AHeFT: Trial Summary



1050 African Americans with Class III to IV HF, LVEF 24%, on ACEI, BB, AA
Adapted from Taylor AL, et al. *N Engl J Med*. 2004;351:2052.

GISSI HF: *All-cause Mortality*



Patients at risk

Omega 3FA	3,494	3,336	3,215	3,080	2,947	2,844	2,680	2,164	1,588	844
Placebo	3,481	3,344	3,209	3,083	2,941	2,805	2,631	2,122	1,558	816

β-Blocker Dose and Heart Rate Reduction in Patients with Chronic Heart Failure

Results of univariable meta-regressions evaluating the effect of individual covariates on the potential mortality benefits of β-blockers in heart failure

Potential Modifier	# Trials	# Subjects	Ratio of Relative Risks (95% CI)	*P* Value
Heart rate reduction	17	17,831	0.82 (0.71-0.94) per 5 bpm	0.006
β-blocker dose	17	17,660	1.02 (0.93-1.10) per increment	0.69
Baseline heart rate	19	17,981	1.07 (0.88-1.32) per 5 bpm	0.47

Meta-analysis of 17 randomized trials in subjects with heart failure to examine whether the β-blocker dose or the magnitude of heart rate reduction could account for differences in treatment effects among heart failure β-blocker trials, 1966-2008.

McAlister FA, et al. *Ann Intern Med*. 2009;150:784-794.

Ivabradine and Outcomes in Chronic Heart Failure (SHIFT)

SHIFT: Hazard ratios for primary and individual outcomes, ivabradine vs placebo groups

Outcomes in SHIFT	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

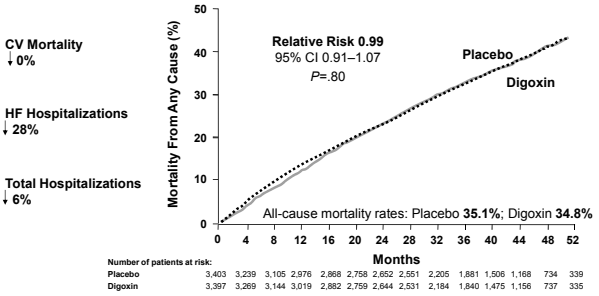
The benefit of ivabradine appeared to go up with increasing heart rate (HR<77 HR 0.93; HR≥77 HR 0.75)

6558 patients with LVEF ≤35%, Sinus rhythm ≥70 bpm
Swedberg et al. Lancet 2010

Ivabradine for Heart Failure

- Indicated to reduce the risk of hospitalization for worsening HF in patients with stable, symptomatic chronic HF with LVEF ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.
- Starting dose is 5 mg twice daily. After 2 weeks of treatment, adjust dose based on heart rate. The maximum dose is 7.5 mg twice daily. In patients with conduction defects or in whom bradycardia could lead to hemodynamic compromise, initiate dosing at 2.5 mg twice daily.
- Contraindications: acute decompensated HF, BP < 90/50 mmHg, SSS or 3rd degree AV block, unless a functioning demand pacemaker is present, resting heart rate less than 60 bpm prior to treatment, severe hepatic impairment.
- Most common adverse reactions occurring in ≥ 1% of patients are bradycardia, hypertension, atrial fibrillation and luminous phenomena (phosphenes).

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.

The DIGITALIS Investigation Group. *N Engl J Med*. 1997;336:525–532.

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 HF*r*EF

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

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

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

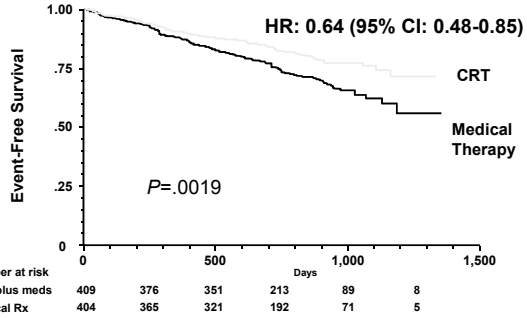
Abraham WT et al. *Circulation*. 2003;108:2596-2603.

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

Updated from Abraham WT. et al *Circulation*. 2003;108:2596-2603.

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



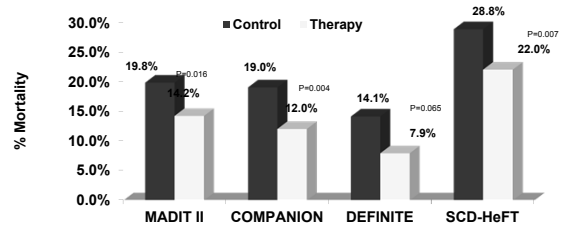
Cleland JG, et al. *N Engl J Med*. 2005;352;1539-1549.

CARE-HF: Clinical Outcomes

	OMT (n=404)	CRT + OMT (n=409)	Hazard Ratio (95% CI)	*P* Value
Death + CV Hospitalization	225 (55%)	159 (39%)	.63 (.51 to .77)	<.001
CV Hospitalization	184 (46%)	125 (31%)	0.61 (.49 to .77)	<.001
HF Hospitalization	133 (33%)	72 (18%)	0.48 (.36 to .64)	<.001
All-Cause Death	120 (30%)	82 (20%)	0.64 (.48 to .85)	<.002

OMT=optimal medical therapy.
Cleland JG et al. *N Engl J Med*. 2005;352:1539-1549.

SCD-HeFT and Other ICD Device Trials in HF



HF Etiology	**Ischemic: 100%**	**Ischemic:59% Non-ischemic:41%**	**Non-ischemic: 100%**	**Ischemic: 52% Non-ischemic:48%**
NYHA Class	**I/II/III (35%/35%/30%)**	**III/IV (87%/13%)**	**I/II/III (20%/60%/20%)**	**II/III (71%/29%)**
LVEF	**≤ 30%**	**≤ 35%**	**≤ 35%**	**≤ 35%**
No. Pts	**1232**	**1520**	**458**	**2521**
Follow-Up	**20 months**	**12 months**	**24 months**	**45 months**
Hazard Ratio	**0.69**	**0.64**	**0.66**	**0.77**

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

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**

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

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

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

Heart Failure with Preserved Ejection Faction

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

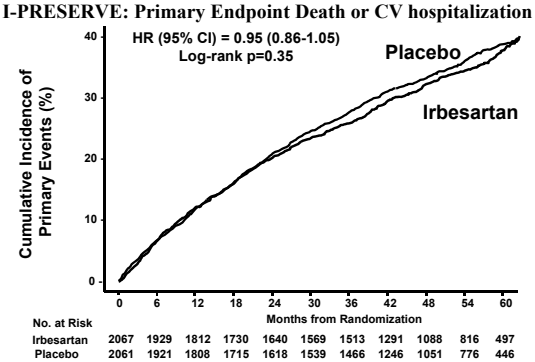
Rate control for atrial fibrillation

ACE inhibitors, calcium channel blockers, and beta blockers have favorable effects upon hemodynamics but their impact on longer term outcome is not known

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

ARB in HF with Preserved EF

I-PRESERVE: Primary Endpoint Death or CV hospitalization



No. at Risk											
Irbesartan	2067	1929	1812	1730	1640	1569	1513	1291	1088	816	497
Placebo	2061	1921	1808	1715	1618	1539	1466	1246	1051	776	446

Massie BM et al. NEJM 2008;359(23):2456-2467.

Implantable Wireless Heart Sensor

No batteries or internal power source, sensor is powered by RF- energy provided by an external electronics module.

Coil and a pressure sensitive capacitor encased in a hermetically sealed silica capsule covered by silicone. The device has no leads or batteries. Two nitinol loops at the ends of the capsule serve as anchors in the pulmonary artery. The coil and capacitor form an electrical circuit that resonates at a specific frequency, and pressure applied to the sensor causes deflections of the pressure-sensitive surface. An external antenna provides power to the device, continuously measuring its resonant frequency, which is then converted to a pressure waveform. The interrogating device has an atmospheric barometer which automatically subtracts the ambient pressure from that measured from the implanted sensor.

Wireless Pulmonary Artery Hemodynamic Monitoring in Chronic Heart Failure: CHAMPION

550 patients with NYHA Class III HF, irrespective of LVEF, and a previous HF hospital admission were enrolled in 64 centers the US

Randomly assigned to management with a wireless implantable hemodynamic monitoring (W-IHM) system (treatment group) or to a control group for at least 6 months

Clinicians used daily measurement of pulmonary artery pressures in addition to standard of care versus standard of care alone in the control group, with goal of keeping PAD pressures normal and specific recommendations provided

The primary efficacy endpoint was the rate of HF related hospitalizations at 6 months

Abraham WT, et al Lancet. 2011 Feb 19;377(9766):658-66.

Other Findings from CHAMPION

• Mean PAP fell substantially over 6 months in the sensor-guided-therapy group and rose in the control group (p=0.008).

• Quality of life at six months, as assessed by the MLWHFQ, was better in the PAP-guided therapy group (p=0.024).

• The length of stay for HF-related hospitalizations was significantly shorter in the treatment group than in the control group (2.2 days [SD 6.8] vs 3.8 days [11.1], p=0.02).

• Significant reduction in the rate of HF-related hospitalizations for preserved (0·16 vs 0·33, p<0·0001) and reduced systolic function (0·36 vs 0·47, p=0·007) patients during 6 months.

• Incremental cost-effectiveness ratio of integrating W-IHM into standard of care for management of the HF is estimated to be $13,979 per QALY gained.

Abraham WT, et al Lancet. 2011 Feb 19;377(9766):658-66.

HeartMate II LVAS

- A surgically implanted, rotary continuous-flow device in parallel with the native left ventricle
  - Left ventricle to ascending aorta
- Percutaneous driveline
- Electrically powered
  - Batteries & line power
- Fixed speed operating mode
- Home discharge

Mechanical Circulatory Support (MCS) Indications

- Failure to wean off CPB (post-cardiotomy syndrome)
- ESHD pt with inadequate organ perfusion despite optimal medical management (BT Tx)
- Acute myocarditis/post-partum CMY (BT Recovery)
- Acute, massive MI with shock
- Destination therapy (DT) for non-transplant candidates with end stage HD
- Incessant VT/cardiac arrest

CPB, cardiopulmonary bypass; ESHD, end-stage heart disease; BTT, bridge to transplant; CMY, cardiomyopathy; BTR, bridge to recovery; VT, ventricular tachycardia.

Evidence-Based Heart Failure Therapies

Guideline Recommended Therapy	Relative Risk Reduction in Mortality	Number Needed to Treat for Mortality	NNT for Mortality (standardized to 36 months)	Relative Risk Reduction in HF Hospitalizations
ACEI/ARB	17%	22 over 42 months	26	31%
ARNI	16%	36 over 27 months	27	21%
Beta-blocker	34%	28 over 12 months	9	41%
Aldosterone Antagonist	30%	9 over 24 months	6	35%
Hydralazine/Nitrate	43%	25 over 10 months	7	33%
CRT	36%	12 over 24 months	8	52%
ICD	23%	14 over 60 months	23	NA

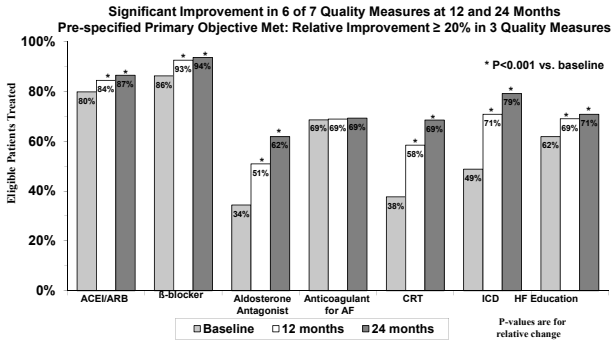
Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030.

ACC/AHA: Implementation of Guidelines

- Academic detailing or educational outreach visits are useful to facilitate the implementation of practice guidelines
- Chart audit and feedback of results can be effective to facilitate implementation of practice guidelines
- The use of reminder systems can be effective to facilitate implementation of practice guidelines
- The use of performance measures based on practice guidelines may be useful to improve quality of care

Hunt SA, et al. *ACC/AHA 2005 Practice Guidelines*. Available at http://www.acc.org.

IMPROVE HF Primary Results: Improvement in Quality Measures at 24 Months (Patient Level Analysis)



Fonarow GC, et al. Circulation. 2010;122:585-596.

Improved Adherence to HF Guidelines Translates to Improved Clinical Outcomes in Real World Patients

- Each 10% improvement in ACC/AHA heart failure guideline recommended composite care was associated with a 13% lower odds of 24-month mortality (adjusted OR 0.87; 95% CI, 0.84 to 0.90; *P<0.0001)*.

ACC/AHA Guideline Directed Therapy for Heart Failure Improves Outcomes

Fonarow GC, et al. *Circulation*. 2011;123:1601-1610.

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

Guideline Recommended Therapy	HF Patient Population Eligible for Treatment, n*	Current HF Population Eligible and Untreated, n (%)	Potential Lives Saved per Year	Potential Lives Saved per Year (Sensitivity Range*)
ACEI/ARB	2,459,644	501,767 (20.4)	6516	(3336-11,260)
Beta-blocker	2,512,560	361,809 (14.4)	12,922	(6616-22,329)
Aldosterone Antagonist	603,014	385,326 (63.9)	21,407	(10,960-36,991)
Hydralazine/Nitrate	150,754	139,749 (92.7)	6655	(3407-11,500)
CRT	326,151	199,604 (61.2)	8317	(4258-14,372)
ICD	1,725,732	852,512 (49.4)	12,179	(6236-21,045)
Total	-	-	67,996	(34,813-117,497)

Fonarow GC, et al. Am Heart J 2011;161:1024-1030.

Cumulative Impact of Clinical Trial Evidence Based Heart Failure Therapies

	Relative-risk	2 yr Mortality
None	- -	35%
ACEI or ARB	↓ 23%	27%
Beta Blocker	↓ 35%	18%
Aldosterone Ant	↓ 30%	13%
CRT-D (EF≤35, QRS≥120)	↓ 36%	8.3%
ARNI	↓ 16%	6.9%

Cumulative risk reduction if all evidence-based therapies are used: 80%
Absolute risk reduction: 28.1%, NNT = 3.6

Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196.

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 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**

Yancy CW et al. *J Am Coll Cardiol*. 2013;62:1495-1539.

Advances in the Treatment of HF

- Increased attention to prevention
- ACEI / β-blocker / aldosterone antagonist combination established as the “cornerstone” of therapy
- ARNI further reduce morbidity and mortality
- 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

Revised from Yancy CW et al. *J Am Coll Cardiol.* 2013;62:1495-1539.

The Approach to Heart Failure

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