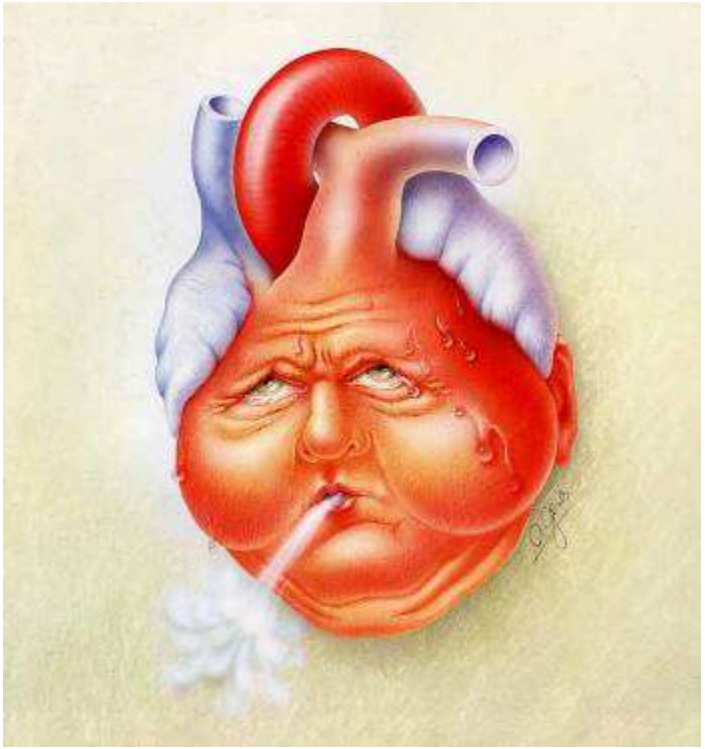
Heart Failure Management



Philip Formica, MD FACC

Southcoast Physicians Group

Financial Disclosures

None

Outline

- Definition and classification of heart failure
- Pathophysiology of CHF
- Approach to the management of CHF
  - Drug therapy
  - Monitoring and Guiding Therapy
- New Developments

ACCF/AHA Practice Guideline

2013 ACCF/AHA Guideline for the Management of Heart Failure

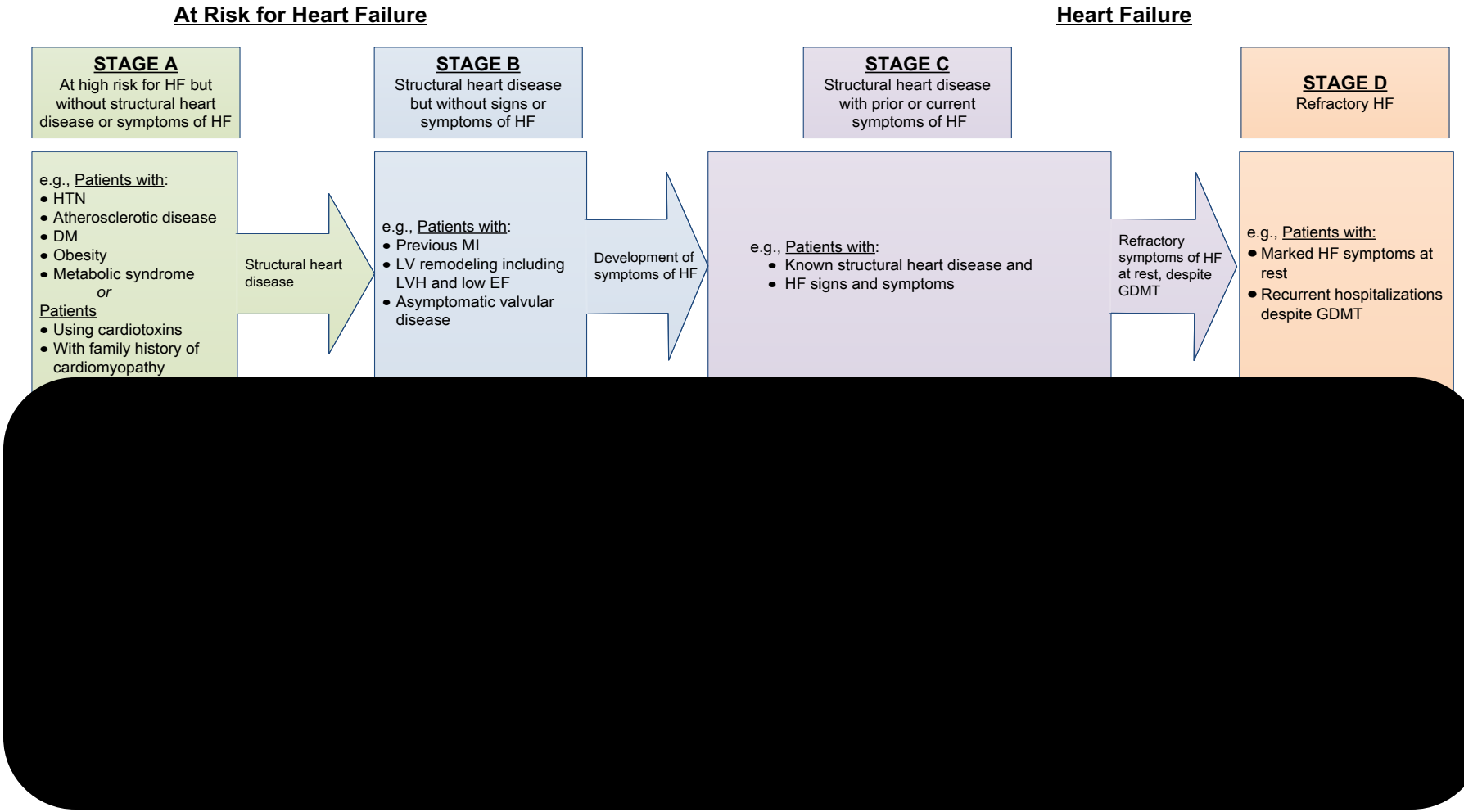
A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Types of Heart Failure

Classification	EF (%)	Description
I. Heart failure with reduced ejection fraction (HF*r*EF)	≤40	Also referred to as systolic HF. Randomized controlled 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 patients 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.

2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240-e327

Stages of Heart Failure



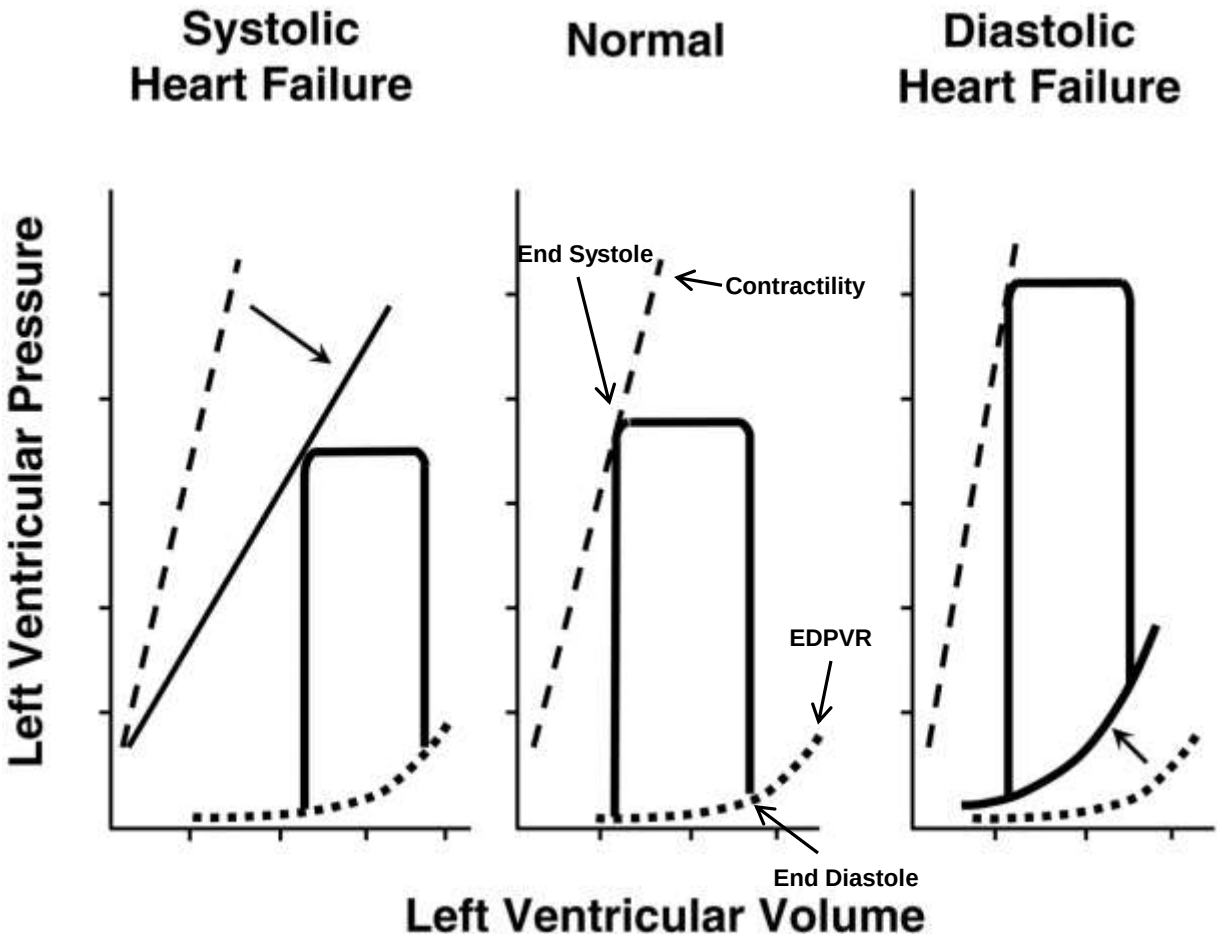
2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240-e327

Comparison Between ACC/AHA HF Stage and NYHA Functional Class

ACC/AHA HF Stage[1]	NYHA Functional Class[2]
A At high risk for heart failure but without structural heart disease or symptoms of heart failure (eg, patients with hypertension or coronary artery disease)	
B Structural heart disease but without symptoms of heart failure	I Asymptomatic
C Structural heart disease with prior or current symptoms of heart failure	II Symptomatic with moderate exertion
	III Symptomatic with minimal exertion
D Refractory heart failure requiring specialized interventions	IV Symptomatic at rest

[1]Hunt SA et al. *J Am Coll Cardiol.* 2001;38:2101–2113.
[2]New York Heart Association/Little Brown and Company, 1964.
Adapted from: Farrell MH et al. *JAMA.* 2002;287:890–897.

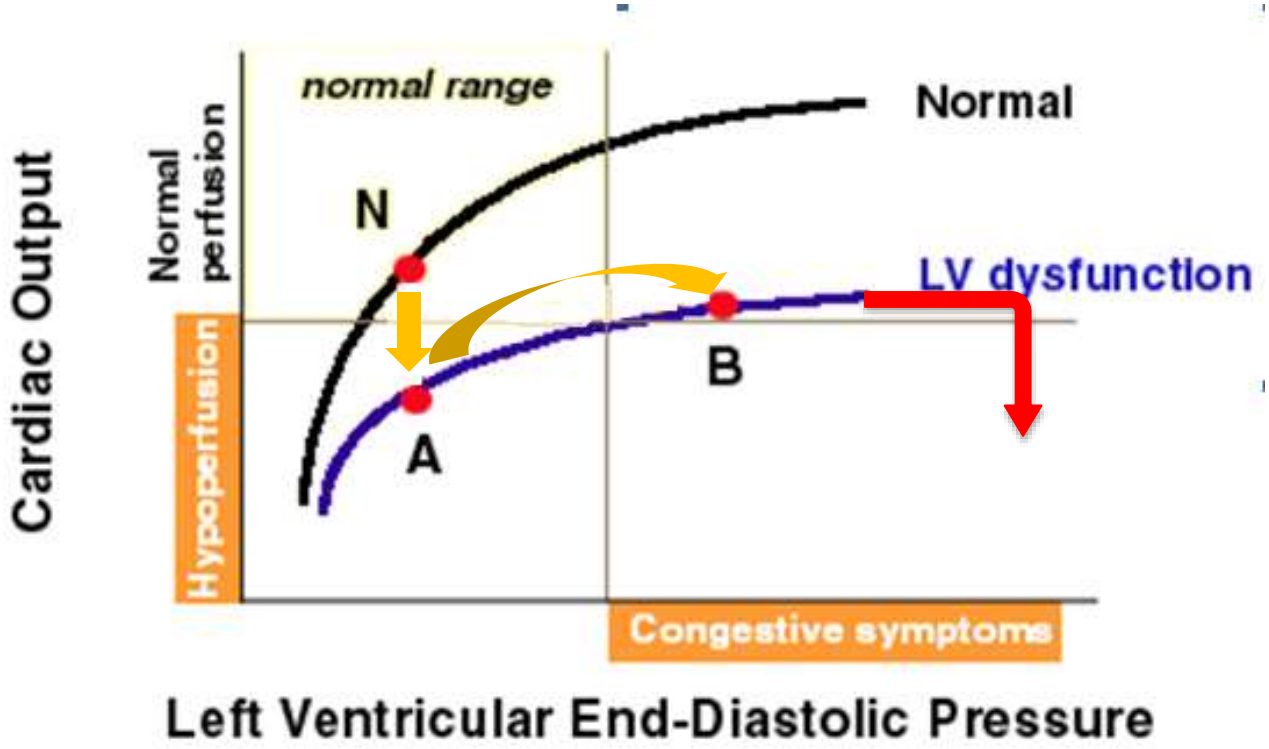
Pressure Volume Loops



In systolic HF, there is decreased contractility and subsequent increase in LV volume/LVEDP, shifting the loop **DOWN** and to the **RIGHT**

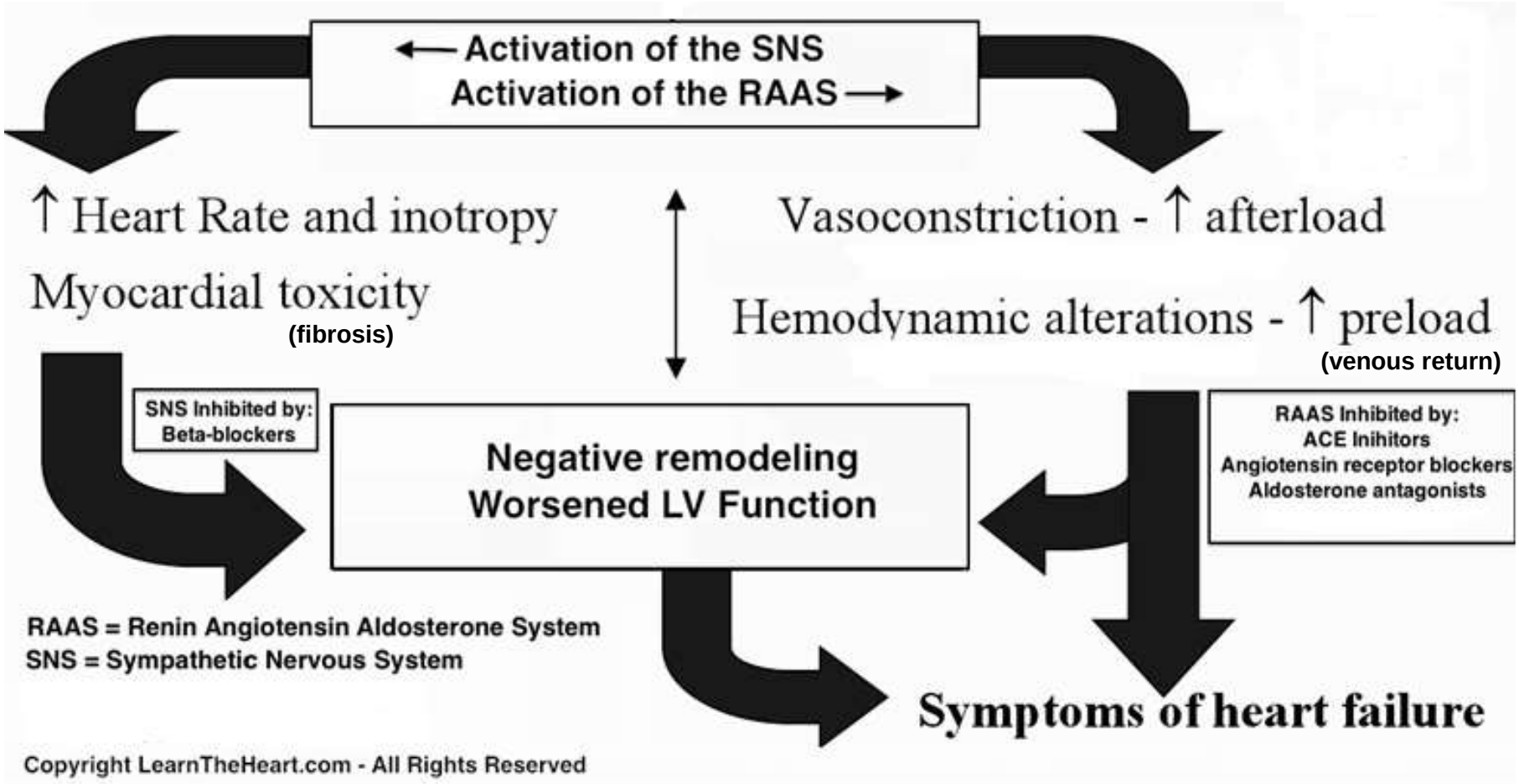
In diastolic HF, there is an increase in LVEDP due to increased stiffness with minimal effect on contractility, shifting the loop **UP** and to the **LEFT**

Pathologic Progression of systolic CHF



Line N to A represents the initial reduction in cardiac output

Line A to B represents the mechanism of compensation; an increase in LVEDP needed to maintain cardiac output


Activation of the SNS
Activation of the RAAS
↑ Heart Rate and inotropy
Myocardial toxicity
(fibrosis)
Vasoconstriction - ↑ afterload
Hemodynamic alterations - ↑ preload
(venous return)
SNS Inhibited by:
Beta-blockers
Negative remodeling
Worsened LV Function
RAAS Inhibited by:
ACE Inihitors
Angiotensin receptor blockers
Aldosterone antagonists
RAAS = Renin Angiotensin Aldosterone System
SNS = Sympathetic Nervous System
Symptoms of heart failure
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Recommendations for Treatment

Stage A

Class I

1. **Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF.**[27,94,311–314] ***(Level of Evidence: A)***
2. **Other conditions that may lead to or contribute to HF, such as obesity, diabetes mellitus, tobacco use, and known cardiotoxic agents, should be controlled or avoided.** ***(Level of Evidence: C)***

Stage B

Recommendations	COR	LOE
In patients with a history of MI and reduced EF, ACE inhibitors or ARBs should be used to prevent HF	I	A
In patients with MI and reduced EF, evidence-based beta blockers should be used to prevent HF	I	B
In patients with MI, statins should be used to prevent HF	I	A
Blood pressure should be controlled to prevent symptomatic HF	I	A
ACE inhibitors should be used in all patients with a reduced EF to prevent HF	I	A
Beta blockers should be used in all patients with a reduced EF to prevent HF	I	C
An ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 d post-MI, have an LVEF ≤30%, and on GDMT	IIa	B
Nondihydropyridine calcium channel blockers may be harmful in patients with low LVEF	III: Harm	C

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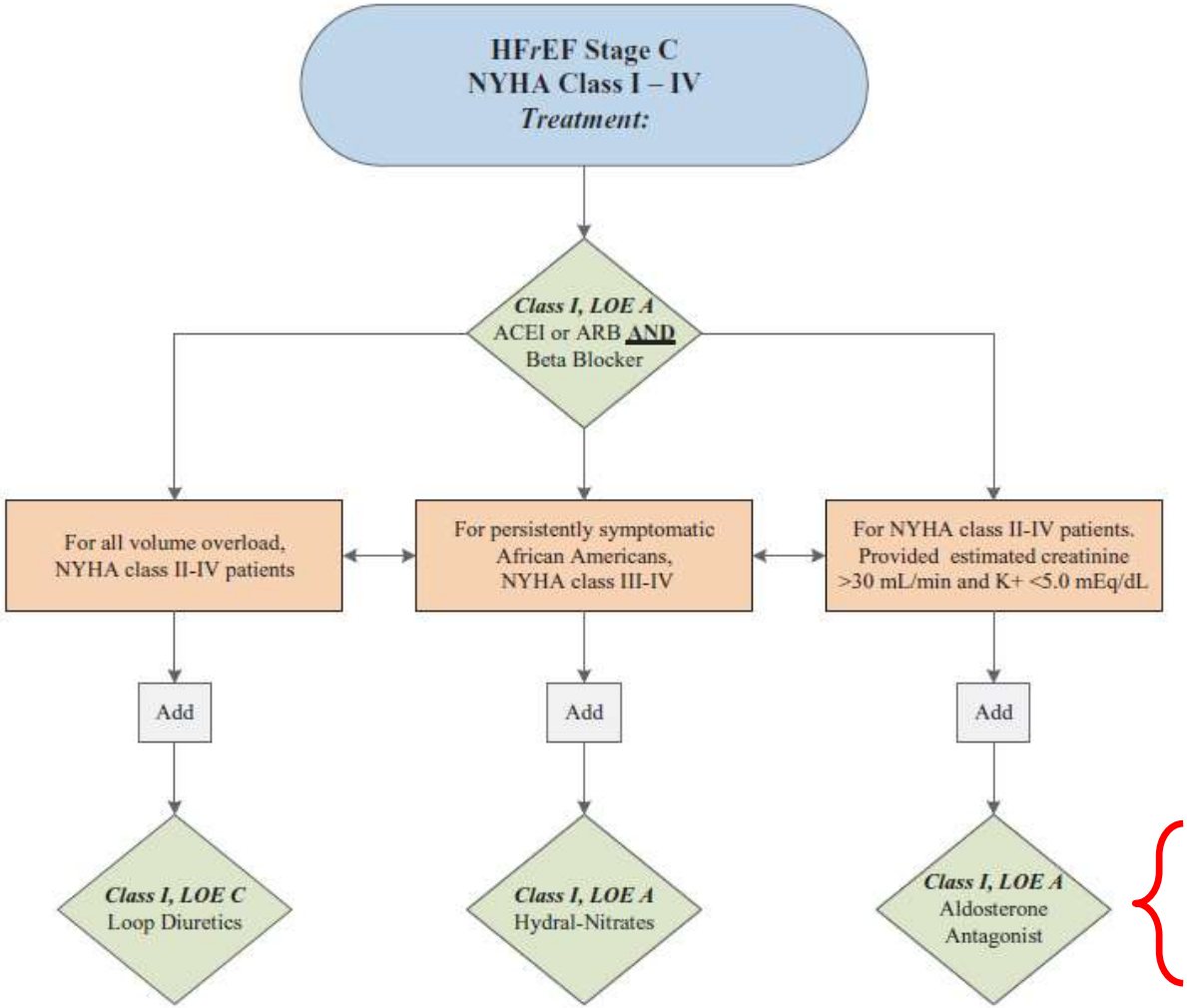


NYHA class II-IV and EF ≤ 35%
OR
EF ≤ 40% after an acute MI
and either has sx's of CHF or DM

2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240-e327

Drug	Initial Daily Dose(s)	Maximum Dose(s)	Mean Doses Achieved in Clinical Trials
ACE inhibitors			
Captopril	6.25 mg 3 times	50 mg 3 times	122.7 mg/d[422]
Enalapril	2.5 mg twice	10 to 20 mg twice	16.6 mg/d[413]
Fosinopril	5 to 10 mg once	40 mg once	N/A
Lisinopril	2.5 to 5 mg once	20 to 40 mg once	32.5 to 35.0 mg/d[445]
Perindopril	2 mg once	8 to 16 mg once	N/A
Quinapril	5 mg twice	20 mg twice	N/A
Ramipril	1.25 to 2.5 mg once	10 mg once	N/A
Trandolapril	1 mg once	4 mg once	N/A
ARBs			
Candesartan	4 to 8 mg once	32 mg once	24 mg/d[420]
Losartan	25 to 50 mg once	50 to 150 mg once	129 mg/d[421]
Valsartan	20 to 40 mg twice	160 mg twice	254 mg/d[108]
Aldosterone antagonists			
Spironolactone	12.5 to 25.0 mg once	25 mg once or twice	26 mg/d[425]
Eplerenone	25 mg once	50 mg once	42.6 mg/d[446]
Beta blockers			
Bisoprolol	1.25 mg once	10 mg once	8.6 mg/d[117]
Carvedilol	3.125 mg twice	50 mg twice	37 mg/d[447]
Carvedilol CR	10 mg once	80 mg once	N/A
Metoprolol succinate extended release (metoprolol CR/XL)	12.5 to 25 mg once	200 mg once	159 mg/d[448]
Hydralazine and isosorbide dinitrate			
Fixed-dose combination[424]	37.5 mg hydralazine/20 mg isosorbide dinitrate 3 times daily	75 mg hydralazine/40 mg isosorbide dinitrate 3 times daily	~175 mg hydralazine/90 mg isosorbide dinitrate daily
Hydralazine and isosorbide dinitrate[449]	Hydralazine: 25 to 50 mg, 3 or 4 times daily and isosorbide dinitrate: 20 to 30 mg 3 or 4 times daily	Hydralazine: 300 mg daily in divided doses and isosorbide dinitrate: 120 mg daily in divided doses	N/A

ACE indicates angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CR, controlled release; CR/XL, controlled release/extended release; HF/EF, heart failure with reduced ejection fraction; and N/A, not applicable.

2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240-e327

Treatment for Stage C: HFpEF

Recommendations	COR	LOE
Systolic and diastolic blood pressure should be controlled according to published clinical practice guidelines	I	B[27,91]
Diuretics should be used for relief of symptoms due to volume overload.	I	C
Coronary revascularization for patients with CAD in whom angina or demonstrable myocardial ischemia is present despite GDMT	IIa	C
Management of AF according to published clinical practice guidelines for HF*p*EF to improve symptomatic HF	IIa	C
Use of beta-blocking agents, ACE inhibitors, and ARBs for hypertension in HF*p*EF	IIa	C
ARBs might be considered to decrease hospitalizations in HF*p*EF	IIb	B[589]
Nutritional supplementation is not recommended in HF*p*EF	III: No Benefit	C

Stage D/Advanced HF

INTERMACS (The Interagency Registry for Mechanically Assisted Circulatory Support)

Profile*	Profile Description	Features
1	Critical cardiogenic shock ("Crash and burn")	Life-threatening hypotension and rapidly escalating inotropic/pressor support, with critical organ hypoperfusion often confirmed by worsening acidosis and lactate levels.
2	Progressive decline ("Sliding fast" on inotropes)	"Dependent" on inotropic support but nonetheless shows signs of continuing deterioration in nutrition, renal function, fluid retention, or other major status indicator. Can also apply to a patient with refractory volume overload, perhaps with evidence of impaired perfusion, in whom inotropic infusions *cannot be maintained* due to tachyarrhythmias, clinical ischemia, or other intolerance.
3	Stable but inotrope dependent	Clinically stable on mild-moderate doses of intravenous inotropes (or has a temporary circulatory support device) after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal).
4	Resting symptoms on oral therapy at home	Patient who is at home on oral therapy but frequently has symptoms of congestion at rest or with activities of daily living (dressing or bathing). He or she may have orthopnea, shortness of breath during dressing or bathing, gastrointestinal symptoms (abdominal discomfort, nausea, poor appetite), disabling ascites, or severe lower-extremity edema.
5	Exertion intolerant ("housebound")	Patient who is comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound.
6	Exertion limited ("walking wounded")	Patient who is comfortable at rest without evidence of fluid overload but who is able to do some mild activity. Activities of daily living are comfortable and minor activities outside the home such as visiting friends or going to a restaurant can be performed, but fatigue results within a few minutes or with any meaningful physical exertion.
7	Advanced NYHA class III	Patient who is clinically stable with a reasonable level of comfortable activity, despite a history of previous decompensation that is not recent. This patient is usually able to walk more than a block. Any decompensation requiring intravenous diuretics or hospitalization within the previous month should make this person a Patient Profile 6 or lower.

Treatment

Consists of 2 parts

- Support (ie- inotropes) until definitive therapy implemented
- Definitive therapy
  - medications/procedures (ie- revascularization, valve surgery)
  - MCS/Transplant
  - palliative care

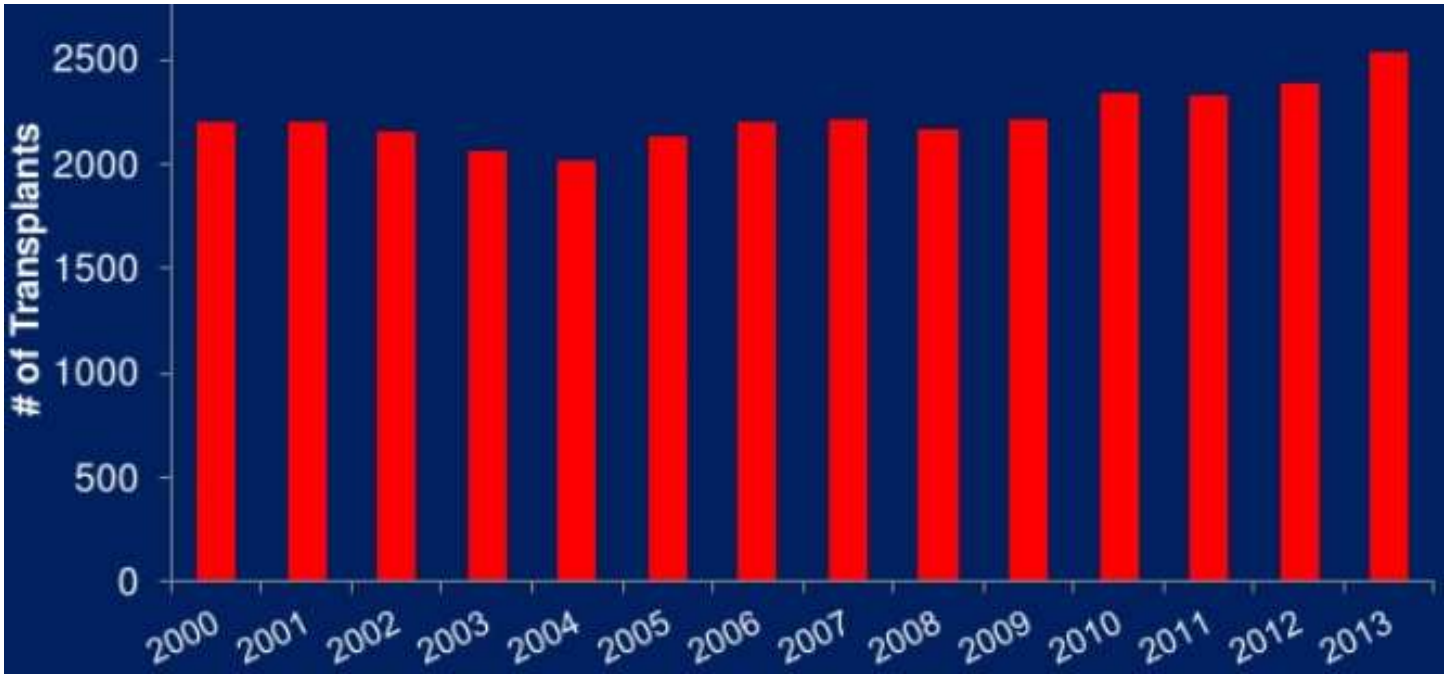
Inotropic Agent	Dose (mcg/kg) Bolus	Infusion (/min)	Drug Kinetics and Metabolism	Effects CO	HR	SVR	PVR	Adverse Effects	Special Considerations
Adrenergic agonists									
Dopamine	N/A	5 to 10	$t_{1/2}$: 2 to 20 min R,H,P	↑	↑	↔	↔	T, HA, N, tissue necrosis	Caution: MAO-I
	N/A	10 to 15		↑	↑	↑	↔		
Dobutamine	N/A	2.5 to 5	$t_{1/2}$: 2 to 3 min H	↑	↑	↓	↔	↑/↓BP, HA, T, N, F, hypersensitivity	Caution: MAO-I; CI: sulfite allergy
	N/A	5 to 20		↑	↑	↔	↔		
PDE inhibitor									
Milrinone	N/R	0.125 to 0.75	$t_{1/2}$: 2.5 h H	↑	↑	↓	↓	T, ↓BP	Renal dosing, monitor LFTs

T= tachyarrhythmia's

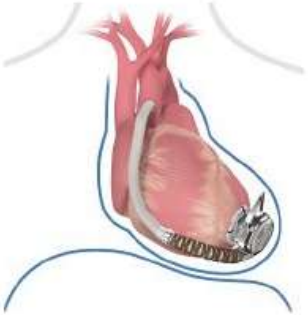
"OK, the old one's in my right hand, the donor's in my left. Right?"

- An estimated 5.7 million Americans ≥20 years of age have HF
- Projections show that the prevalence of HF will increase 46% from 2012 to 2030, resulting in >8 million people ≥18 years of age with HF

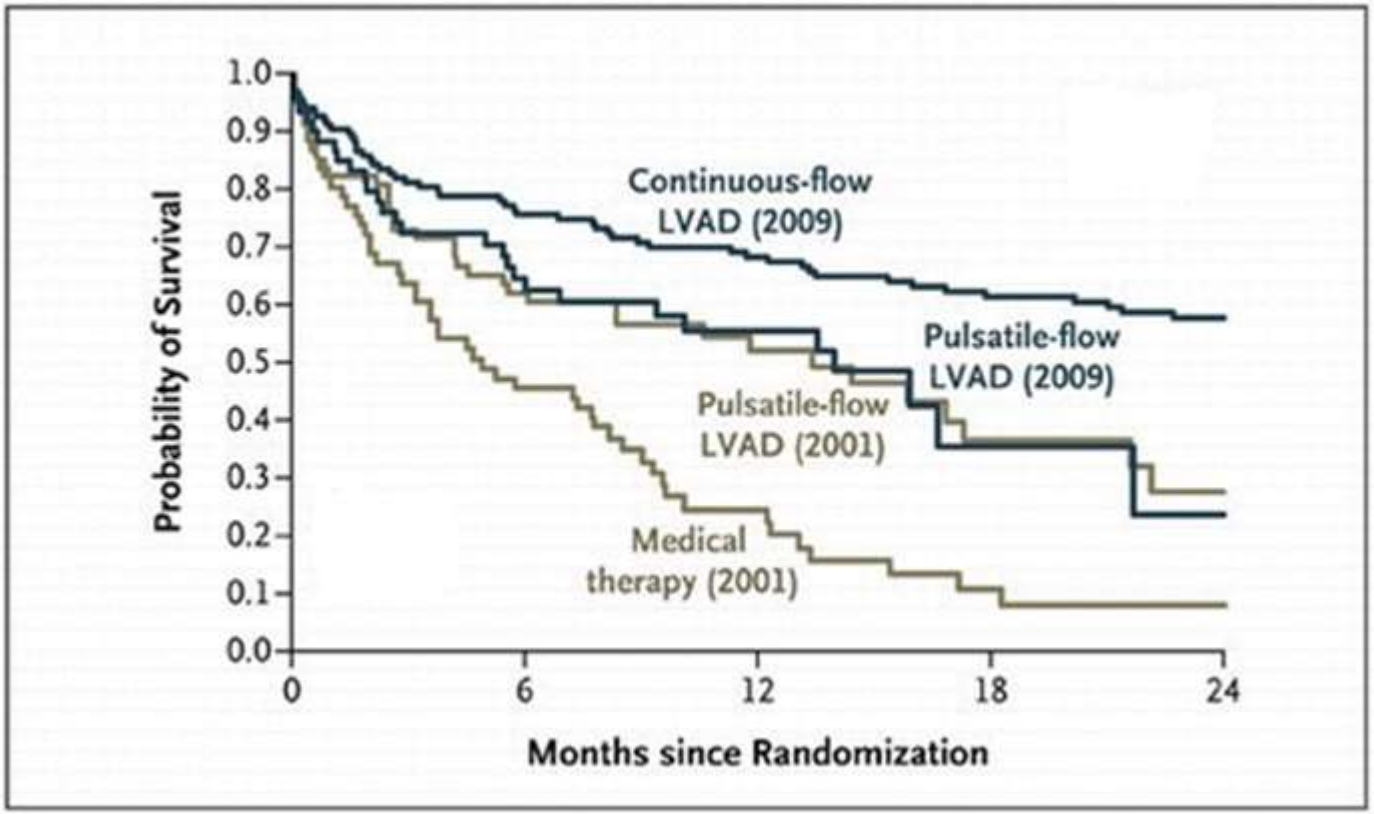
Heart Disease and Stroke Statistics—2015 Update A Report From the American Heart Association. *Circulation. 2015;131:e29-e322.*



OPTN Data, Duke Heart Center



LVAD for Destination Therapy



Fang et al. N Engl J Med 2009; 361:2282-2285

Summary of LVAD trials demonstrating ongoing survival improvements

Author, reference	Year	Device	Number of patients	1 year survival (%)
Rose *et al.* (5)	2001	Pulsatile Heartmate	68	52
Miller *et al.* (11)	2007	Heartmate II	133	68
Pagani *et al.* (12)	2009	Heartmate II	281	73
Slaughter *et al.* (15)	2009	Heartmate II	134	68
John *et al.* (14)	2011	Heartmate II	1,496	85
Starling *et al.* (13)	2011	Heartmate II	169	85
Aaronson *et al.* (17)	2012	Heartware HVAD	140	86
Slaughter *et al.* (31)	2013	Heartware HVAD	332	84
Strueber *et al.* (16)	2014	Heartware HVAD	254	85
1 year transplant survival rate				**87.8%**

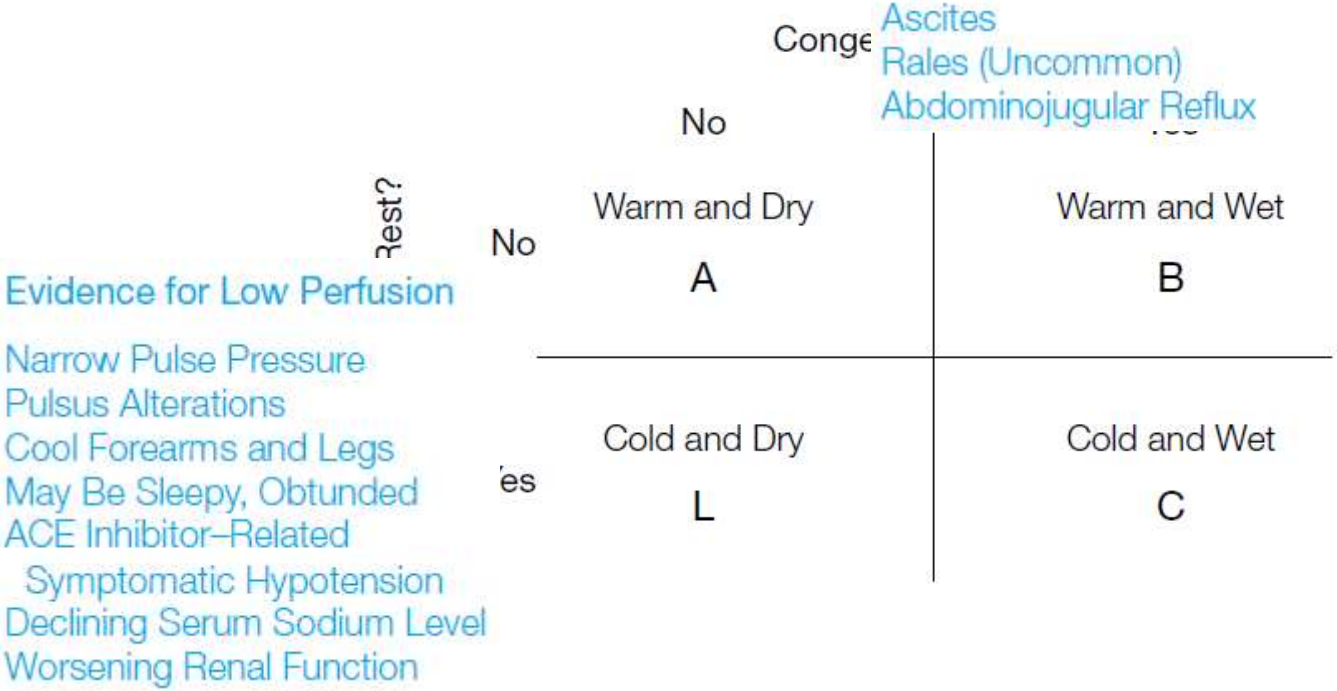
Holley et al. J Thorac Dis. 2014 Aug; 6(8): 1110–1119.

CHF Management

The Acute Setting

Evidence for Congestion
(Elevated Filling Pressure)

Orthopnea
High Jugular Venous Pressure
Increasing S_3
Loud P_2
Edema
Ascites
Rales (Uncommon)
Abdominojugular Reflux



Evidence for Low Perfusion

Narrow Pulse Pressure
Pulsus Alterations
Cool Forearms and Legs
May Be Sleepy, Obtunded
ACE Inhibitor–Related
Symptomatic Hypotension
Declining Serum Sodium Level
Worsening Renal Function

A: Management to prevent disease progression
B: Diuretics and vasodilators/afterload reduction (ie- HDLZ/NTG, ACEi)
C: Inotropic agents (ie- Dobutamine/milrinone) and diuretics
L: ?adjust outpatient meds, inotropes

Medical Management of Advanced Heart Failure. JAMA. 2002;287:628-640

Diuretic therapy

- Dose Equivalents

Furosemide	Torsemide	Bumetanide
40 mg	20 mg	1 mg

- Bolus vs Infusion, ideal dose for acute CHF?

  DOSE Trial…

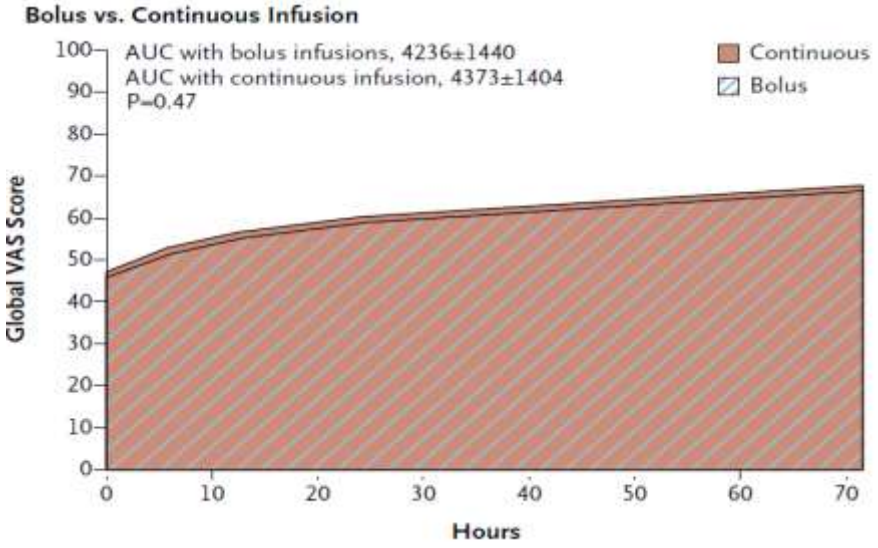
ESTABLISHED IN 1812 MARCH 3, 2011 VOL. 364 NO. 9

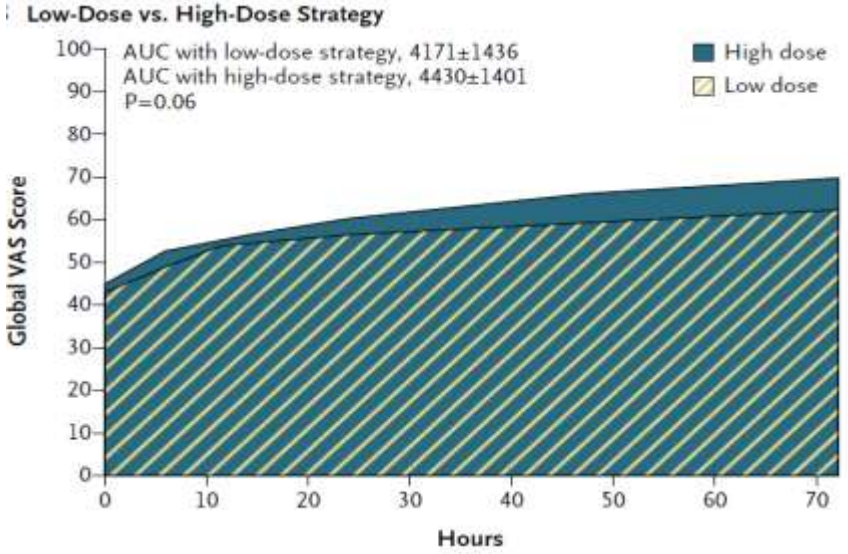
Diuretic Strategies in Patients with Acute Decompensated Heart Failure

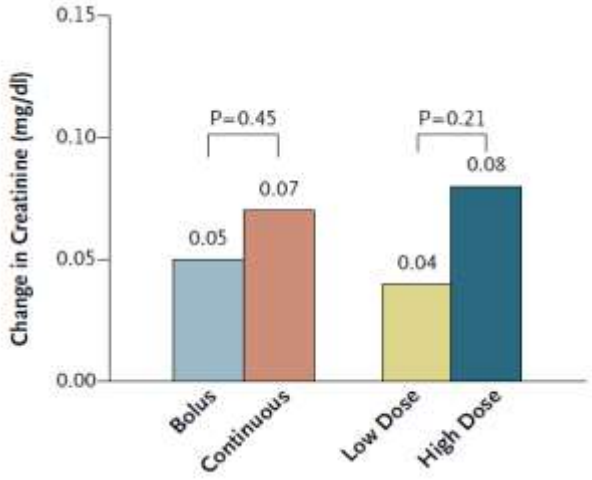
G. Michael Felker, M.D., M.H.S., Kerry L. Lee, Ph.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Lynne W. Stevenson, M.D., Steven R. Goldsmith, M.D., Martin M. LeWinter, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Elizabeth O. Ofili, M.D., M.P.H., Kevin J. Anstrom, Ph.D., Adrian F. Hernandez, M.D., Steven E. McNulty, M.S., Eric J. Velazquez, M.D., Abdallah G. Kfoury, M.D., Horng H. Chen, M.B., B.Ch., Michael M. Givertz, M.D., Marc J. Semigran, M.D., Bradley A. Bart, M.D., Alice M. Mascette, M.D., Eugene Braunwald, M.D., and Christopher M. O'Connor, M.D., for the NHLBI Heart Failure Clinical Research Network*

- prospective, double-blind, randomized trial
- 308 patients with acute decompensated heart failure to receive furosemide IV either as a bolus every 12 hours or continuous infusion **AND** at either a low dose (equivalent to the patient's previous oral dose) or a high dose (2.5 times the previous oral dose)
- 2 coprimary end points after 72hrs: patient's global assessment of symptoms (VAS), change in Cr

N Engl J Med 2011;364:797-805.


Bolus vs. Continuous Infusion
AUC with bolus infusions, 4236±1440
AUC with continuous infusion, 4373±1404
P=0.47
Continuous
Bolus
Global VAS Score
Hours


Low-Dose vs. High-Dose Strategy
AUC with low-dose strategy, 4171±1436
AUC with high-dose strategy, 4430±1401
P=0.06
High dose
Low dose
Global VAS Score
Hours


Change in Creatinine (mg/dl)
P=0.45
P=0.21
0.05
0.07
0.04
0.08
Bolus
Continuous
Low Dose
High Dose

Secondary Endpoints

Bolus vs. Continuous

Low-dose vs. High-dose

No congestion at 72 hours
14% vs. 15% (P=0.78)
11% vs. 18% (P=0.09)

Weight change at 72 hours
-6.8 vs. -8.1 lbs (P=0.20)
-6.1 vs. -8.7 lbs (P=0.01)

Net fluids at 72 hours
-4,237 vs. -4,249 mL (P=0.89)
-3,575 vs. -4,899 mL (P=0.01)

Persistent or worsening HF
25% vs. 23% (P=0.78)
26% vs. 22% (P=0.40)

Hospital stay
5 vs. 5 days (P=0.97)
6 vs. 5 days (P=0.55)

All-cause mortality, rehospitalization, or ED visit
HR for continuous infusion 1.15 (95% CI 0.83-1.60; P=0.41)
HR for high-dose 0.83 (95% CI 0.60-1.16; P=0.28)

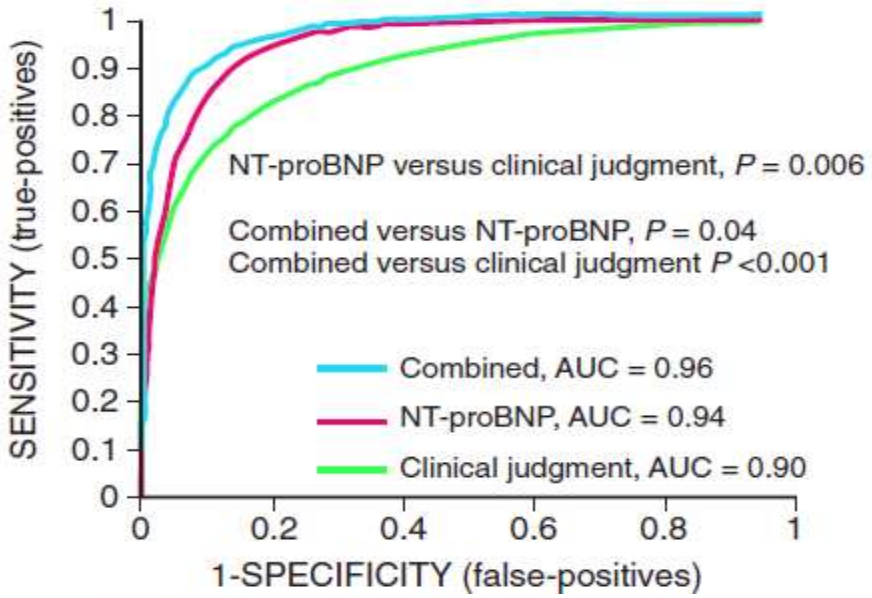
Monitoring and Guiding Therapy

One of the Best Devices for Monitoring Heart Failure

NP Guided Therapy

BIOMARKERS		CLASS OF RECOMMENDATION	LEVEL OF EVIDENCE
BNP or NT-proBNP	Diagnosis	I	A
	Prognosis	I	A
	Guided-therapy (chronic HF)	IIa	B
	Guided-therapy (acute HF)	IIb	C

Diagnosis For HF

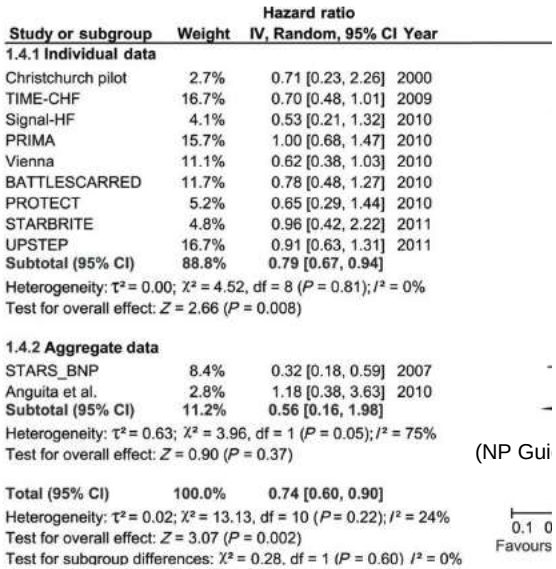


Heart Failure: A Companion to Braunwald's Heart Disease. 3rd Edition. Mann and Felker

Meta-An Evaluating
NI rapy

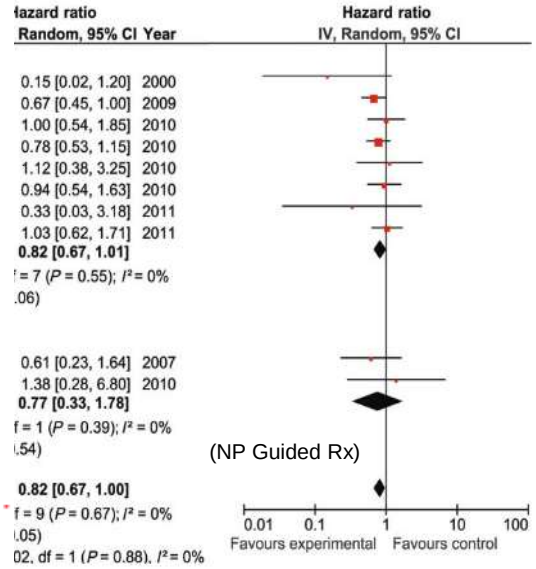
	Peptide target
Christchurch Pilot[5]	NT-proBNP <1700 pg/mL
TIME-CHF[6]	NT-proBNP <400[a]; NT-proBNP <800[b]
Vienna[7]	NT-proBNP <2200 pg/mL
PRIMA[8]	Individual: lowest NT-proBNP at discharge or at 2-week follow-up
SIGNAL-HF[9]	NT-proBNP reduction >50% from baseline
BATTLESCARRED[10]	NT-proBNP <1300 pg/mL
STARBRITE[11]	Individual BNP at discharge
UPSTEP[12]	BNP <150 ng/L[a]; BNP <300 ng/L[b]
PROTECT[c][13]	NT-proBNP <1000 pg/mL
Studies providing aggregate data	
STARS-BNP[14]	BNP < 100 pg/mL
Anguita *et al*[15]	BNP < 100 pg/mL

All Cause Mortali



(NP Gui

Hospitalization

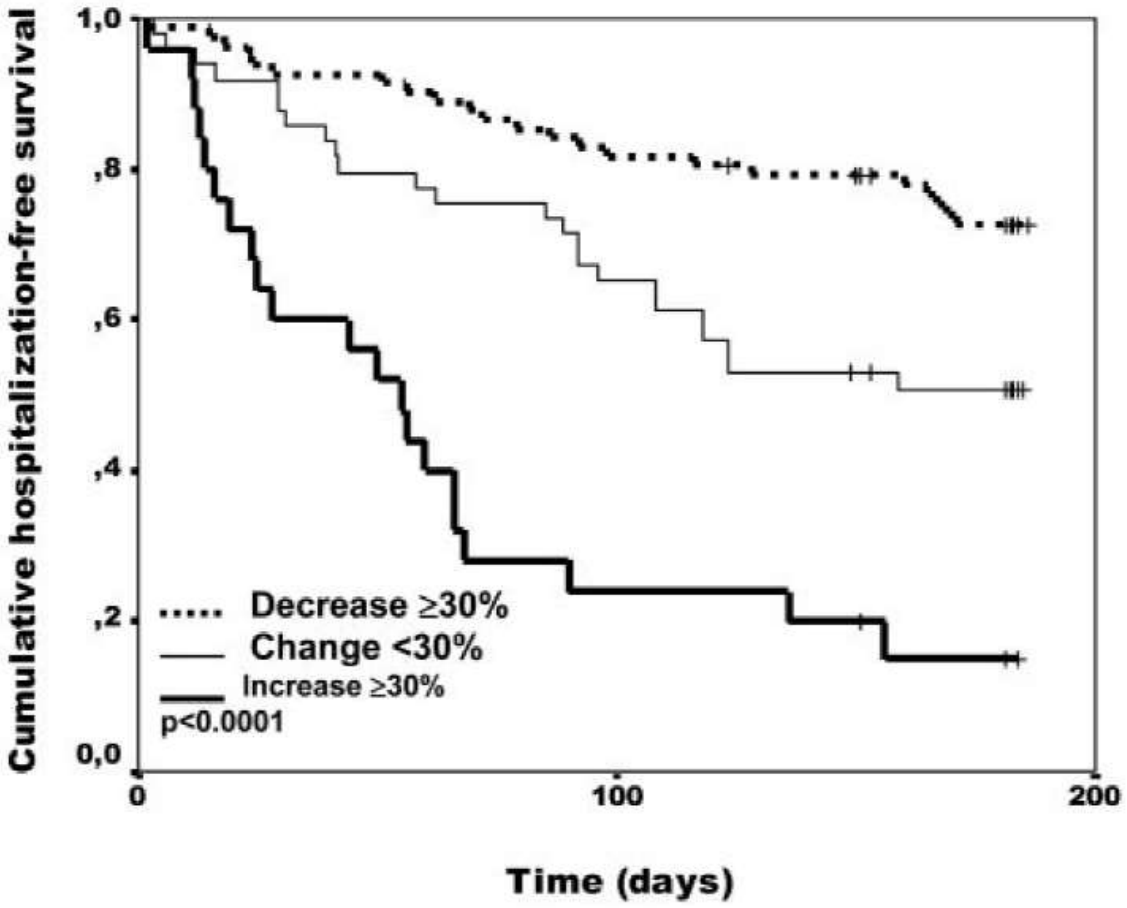


(NP Guided Rx)

RW Troughton, et al. Effect of B-type natriuretic peptide-guided treatment of chronic heart failure on total mortality and hospitalization: an individual patient meta-analysis. European Heart Journal. Mar 2014

N-Terminal–Pro-Brain Natriuretic Peptide Predicts Outcome After Hospital Discharge in Heart Failure Patients

Paulo Bettencourt, PhD; Ana Azevedo, MD; Joana Pimenta, MD; Fernando Friões, MD;
Susana Ferreira, MD; António Ferreira, PhD



Circulation. 2004;110:2168-2174

Competing Risk of Cardiac Status and Renal Function During Hospitalization for Acute Decompensated Heart Failure

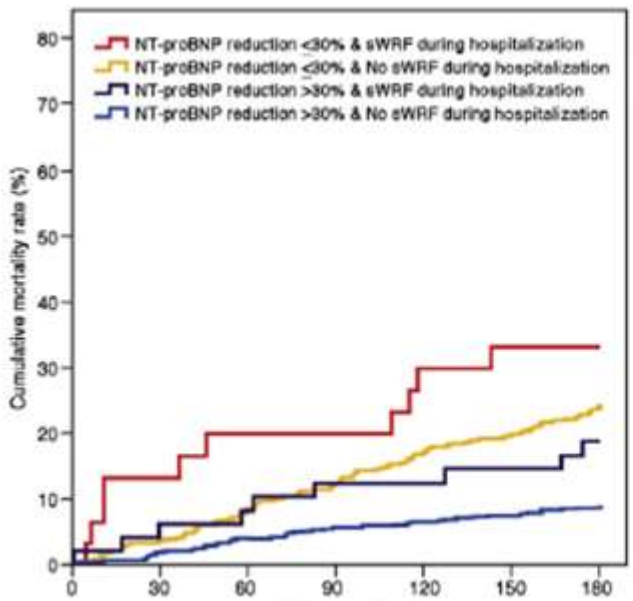
Khibar Salah, MD,* Wouter E. Kok, MD, PhD,* Luc W. Eurlings, MD,† Paulo Bettencourt, MD, PhD,‡ Joana M. Pimenta, MD, PhD,‡ Marco Metra, MD, PhD,§ Valerio Verdiani, MD, PhD,‖ Jan G. Tijssen, PhD,* Yigal M. Pinto, MD, PhD*

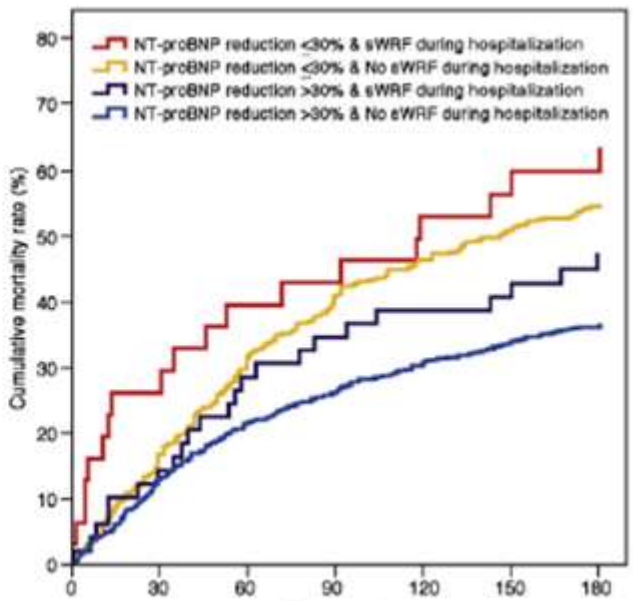
- Evaluate dynamic changes in renal function (sWRF: absolute increase in serum Cr level of >0.5 mg/dl in combination with >25% increase in serum Cr level) compared to dyanmic changes in Pro-BNP

- 1,232 pts hospitalized for ADHF (74% HFrEF, 26% HFpEF)

- Endpoints were all-cause mortality and the composite of all-cause mortality and/or readmission for a cardiovascular reason within 180 days after discharge

J Am Coll Cardiol HF 2015;3:751–61





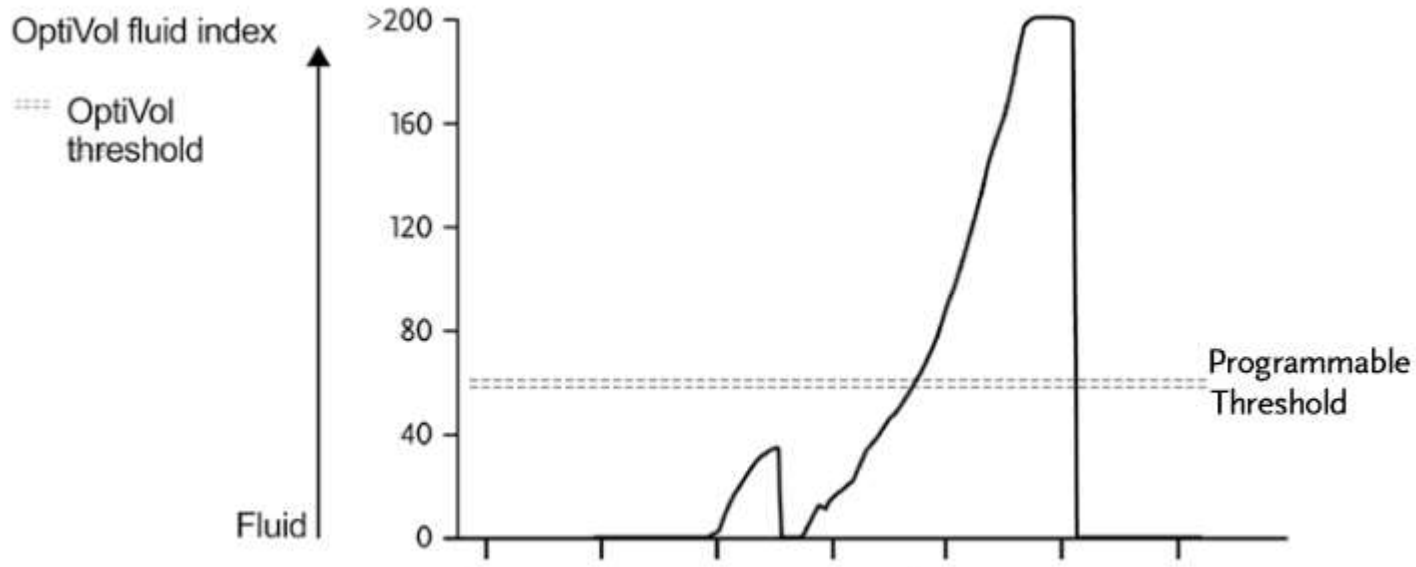
alization.

Key objective in CHF treatment: relieve congestion and achieve euvolemia

≥ 30% BNP reduction ~ ↓ 15% in 180 mortality

…BNP is stronger predictor of outcomes vs renal fnc

OptiVol in Patients with CRT/ICD Devices



- Measures intrathoracic impedance, which is inversely related to PCWP
- The OptiVol fluid index will rise as intrathoracic fluid level increases

Upon Discharge

Clinical Status Goals

Achievement of dry weight
Definition of optimal blood pressure range
Walking without dyspnea or dizziness

Stability Goals

Twenty-four hours without changes in oral heart failure regimen
At least 48 hours off intravenous inotropic agents, if used
Fluid balance even on oral diuretics
Renal function stable or improving

Home Maintenance Plan

Patient and family education about
- Sodium restriction
- Fluid limitation
- Medication schedule
- Medication effects
- Exercise prescription

Flexible diuretic plan
Scheduled call to patient within 3 days
Indications for when to call nurse, physician, or 911
Clinic appointment within 5 to 10 days

Medical Management of Advanced Heart Failure. JAMA. 2002;287:628-640

New Developments

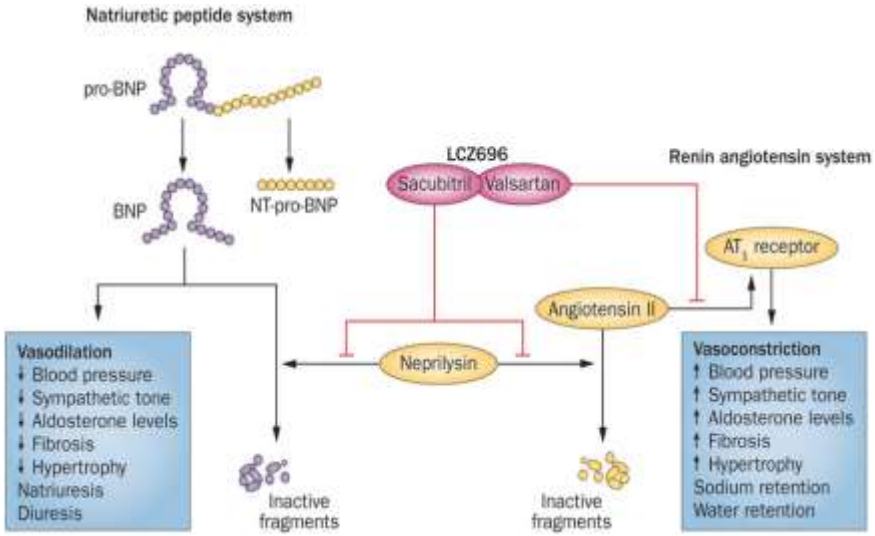
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 11, 2014 VOL. 371 NO. 11

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

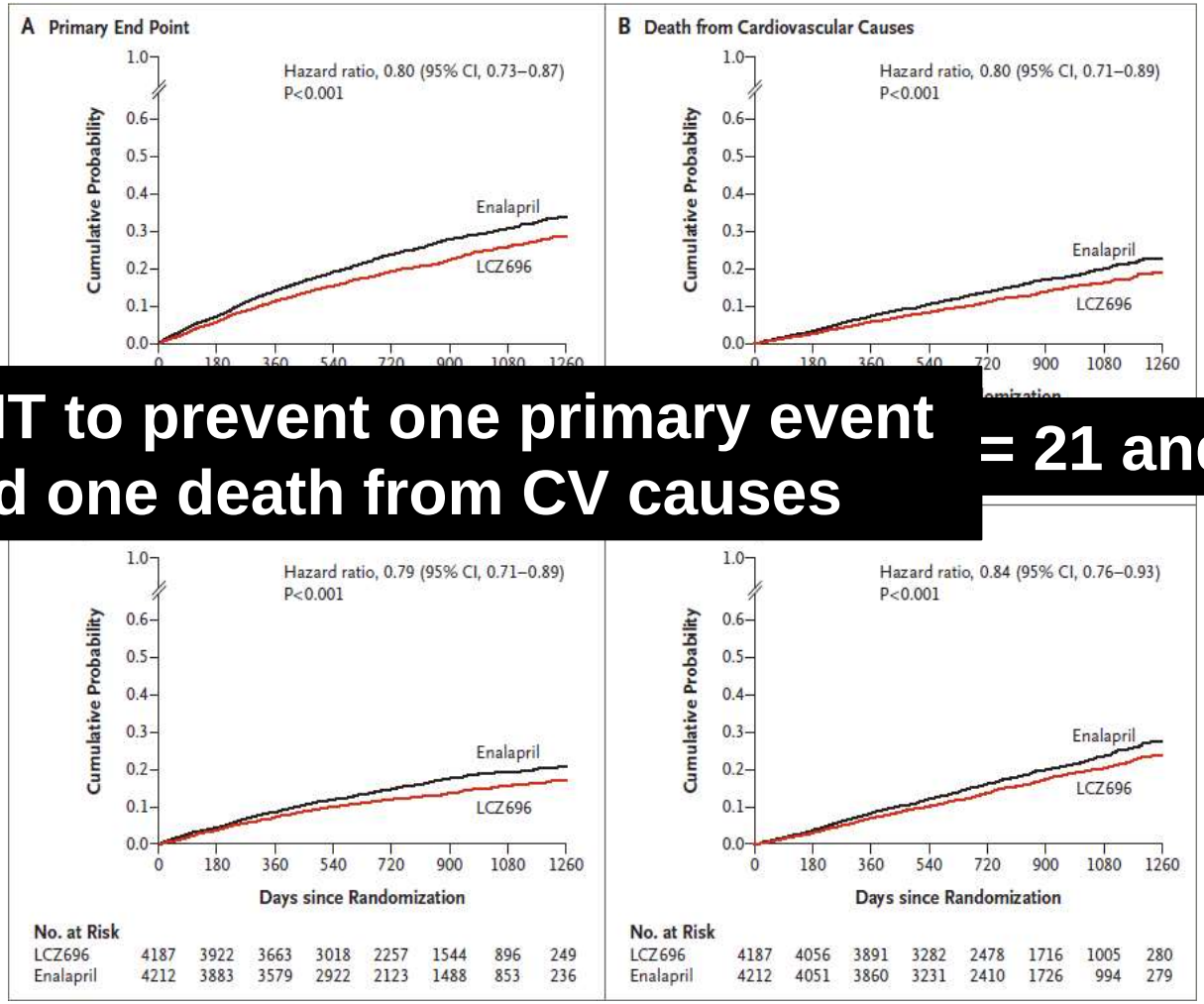
John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

- Prospective, randomized double blind trial
- 8442 pts with EF ≤ 40%, NYHA II-IV
- LCZ696 (ARB valsartan + neprilysin inhibitor) vs. enalapril (mean dose 18.9mg)
- Primary Endpoint: Death from cardiovascular causes or hospitalization for heart failure



N Engl J Med 2014;371:993-1004

21.8% vs 26.5%



13.3% vs 16.5%

NNT to prevent one primary event and one death from CV causes

= 21 and 32

12.8% vs 15.6%

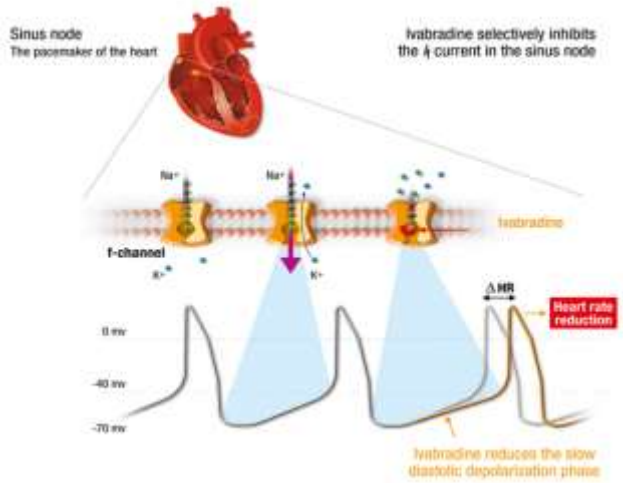
17% vs 19.8%

Articles

Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

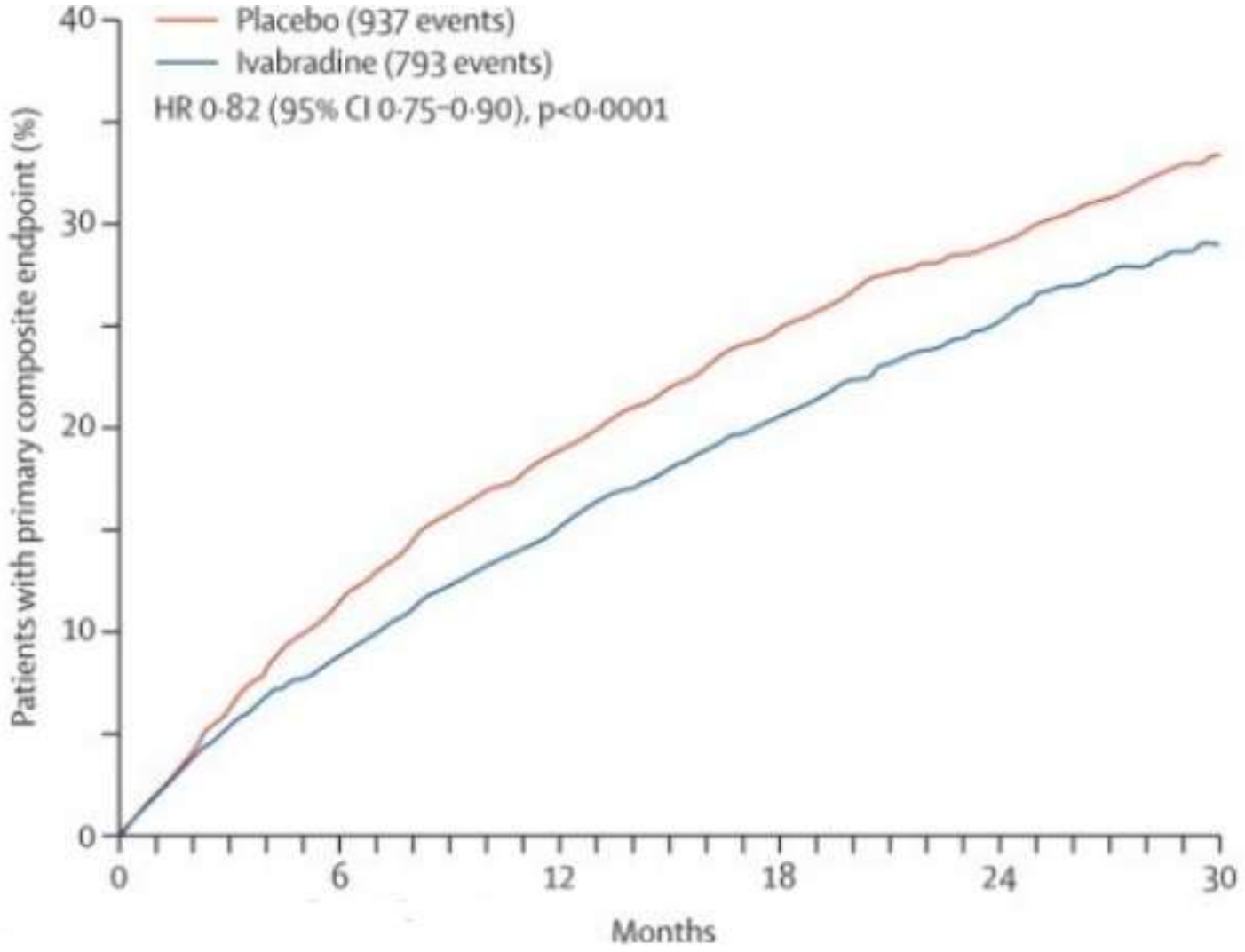
Prof Karl Swedberg, MD, Prof Michel Komajda, MD, Prof Michael Böhm, MD, Prof Jeffrey S Borer, MD, Prof Ian Ford, PhD, Ariane Dubost-Brama, MD, Guy Lerebours, MD, Prof Luigi Tavazzi, MD, on behalf of the SHIFT Investigators

- Double-blinded multi-center RCT
- Ivabradine vs placebo
- 6558 pts with EF ≤ 35% AND
  - Sinus rhythm
  - HR ≥ 70
  - Symptomatic, hosiptalized for CHF within past year
  - On stable chronic therapy, including BB



- Primary Endpoint: Composite of cardiovascular death or hospital admission for worsening heart failure

Lancet. 2010 ;376:875-85



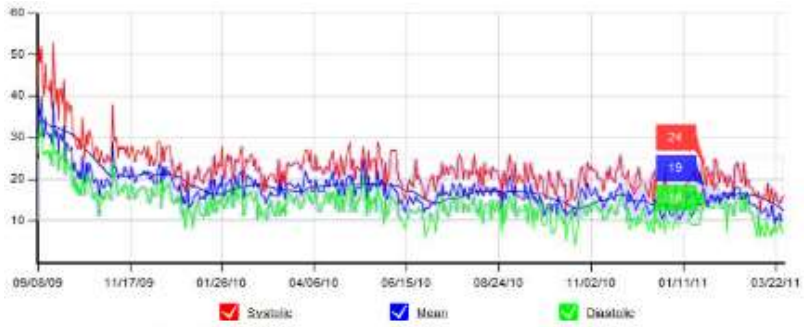
Mainly driven by reduction in HF hospitaliztions

CardioMEMS

Inserted via RHC

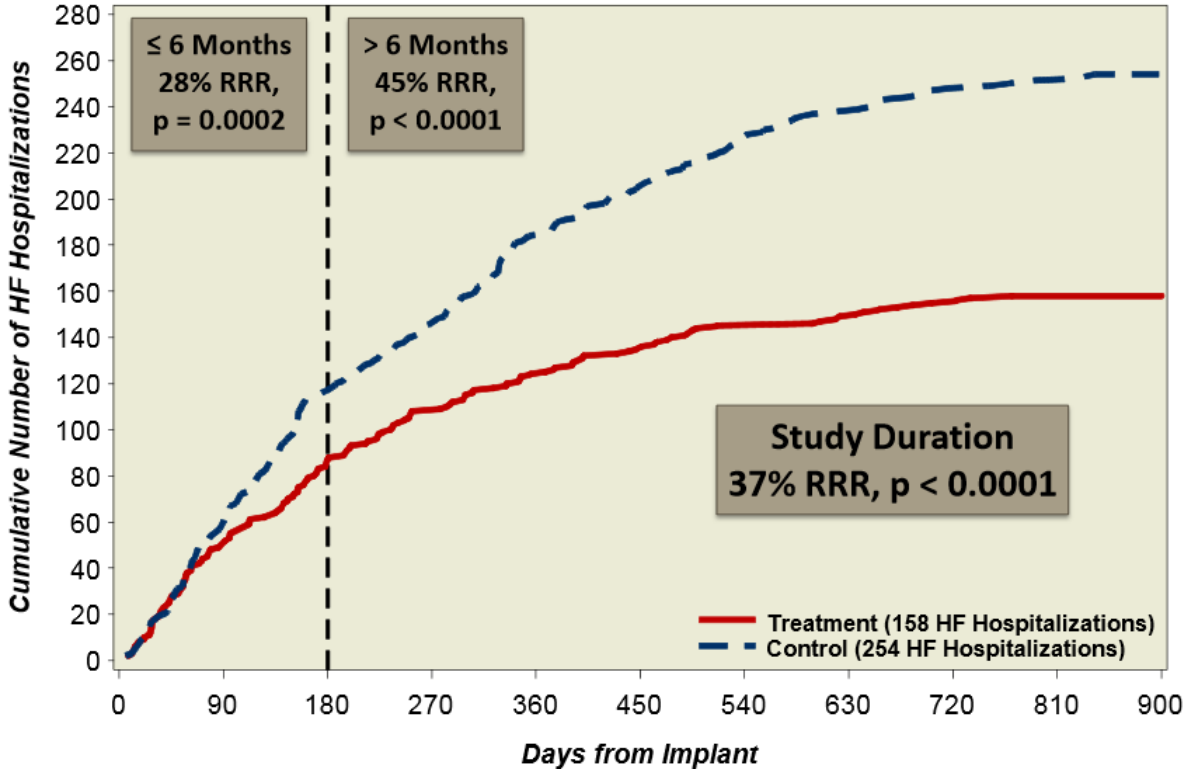
Placed in branch of PA

Measures PAP (PASP, PADP, mean)



Cumulative HF Hospitalizations Reduced

At 6 Months and Full Duration



Take Home Points

- Treatment based on Type/Stage of CHF
- Systolic (HFrEF) vs Diastolic (HFpEF) CHF: different pathophysiology
- Evaluation of CHF pt: congestion and perfusion
- Key is to relieve congestion

Thank You