

Heart Failure Guideline Updates 2019

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Disclosures

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Summary

- Background of Heart Failure
- 2017 Heart Failure Guidelines Update
- Initiation, Continuation, Switching and Withdrawal of Heart Failure Medical Therapies During Hospitalization
- Device Based Solutions

Heart Failure Terminology

- **Heart failure** is a global term for the physiological state in which cardiac output is insufficient for the body's needs. Heart Failure is a condition in which a problem with the structure or function of the heart impairs its ability to supply sufficient blood flow to meet the body's needs.

Heart Failure Pathophysiology

Heart failure is caused by any condition which reduces the efficiency of the myocardium leading to overload on the myocardium. Over time the increased workload will produce changes to the heart:

- Reduced contractility, or force of contraction, due to overloading of the ventricle.
- A reduced stroke volume, as a result of a failure of systole, diastole or both.
- Increased heart rate, stimulated by increased sympathetic activity in order to maintain cardiac output.
- Hypertrophy of the myocardium, caused by the terminally differentiated heart muscle fibers increasing in size in an attempt to improve contractility.
- Enlargement of the ventricles, contributing to the enlargement and spherical shape of the failing heart.

Heart Failure Statistics

Prevalence

- Heart failure (HF) affects an estimated 5.1 million Americans \geq 20 years of age.
- 400,000 new cases of heart failure are diagnosed in the United States annually.

Incidence

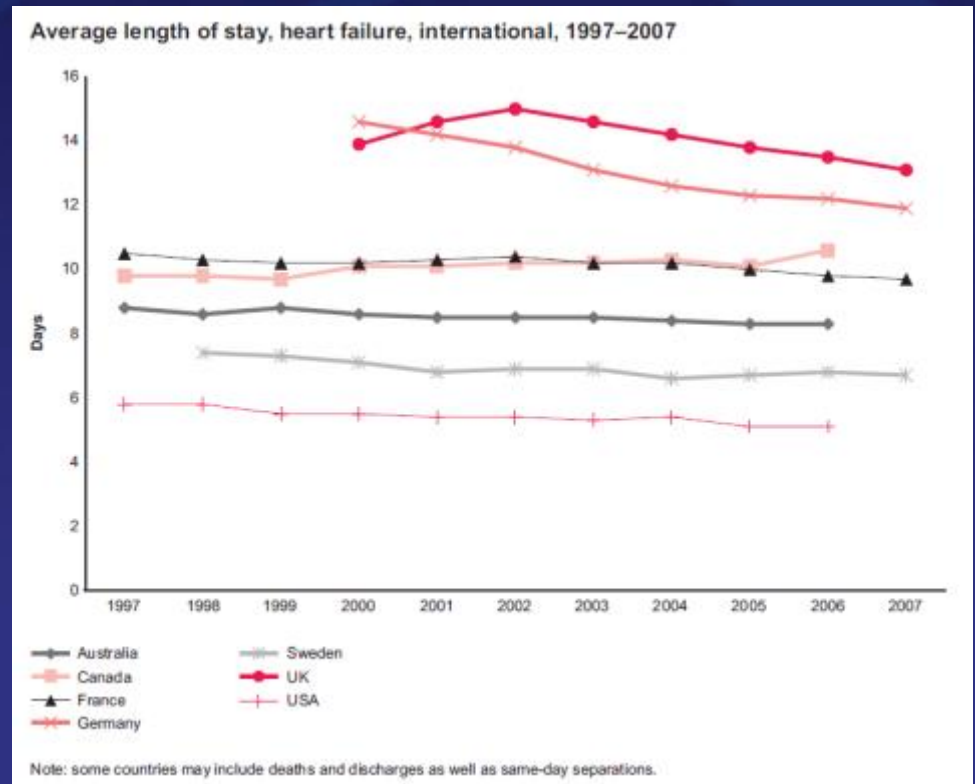
- One-percent of adults 50 to 60 years of age.
- Seventy-five percent of HF cases have antecedent hypertension.
- Ten-percent of adults 80 years of age or older.

Mortality and Morbidity

- The lifetime risk for people with BP $>$ 160/90 mmHg is double that of those persons with BP $<$ 140/90 mmHg
- At 40 years of age, the lifetime risk of developing HF for both men and women is 1 in 5; at 80 years of age, the lifetime risk of developing new HF is 20%.
- Most frequent cause of hospitalizations in the elderly and is responsible for 7 to 12 percent of all hospital admissions.
- Contributes to approximately 275,000 deaths every year.

Heart Failure Is Associated with High Hospitalization and Readmission Rates

- In 2010, there were 1 million hospitalizations in the US with HF as the principal diagnosis¹
 - Hospitalization rate did not change significantly from 2000¹
- Average length of hospital stay
 - Approximately 5 days (US)²
 - 11 days (Europe)³
- HF is also associated with high readmission rates:
 - ~25% all-cause readmission within 30 days and ~50% within 6 months⁵



Graph from www.health.org.uk. Bridging the gap: Heart Failure, 2010.
Data from Organization for Economic Cooperation and Development, 2009.

1. CDC NCHS National Hospital Discharge Survey, 2000-2010
2. Yancy et al. JACC, 2006.
3. Cleland et al. EuroHeart, 2003.
4. Krumholz HM, et al. Circ Cardiovas Qual Outcomes 2009.
5. Wexler DJ, et al. Am Heart J 2001.

Categorization of Heart Failure

There are many different ways to categorize heart failure, including:

- Which side of the heart involved (left heart failure versus right heart failure)
- Whether the abnormality is due to contraction (systolic dysfunction) or relaxation of the heart (diastolic)
- Degree of functional impairment conferred by the abnormality (as in the NYHA functional classification)
- Whether the problem is primarily increased venous back pressure (behind) the heart, or failure to supply adequate arterial perfusion (in front of) the heart (backward vs. forward failure)
- Whether the abnormality is due to low cardiac output with high systemic vascular resistance or high cardiac output with low vascular resistance (low-output heart failure vs. high-output heart failure)

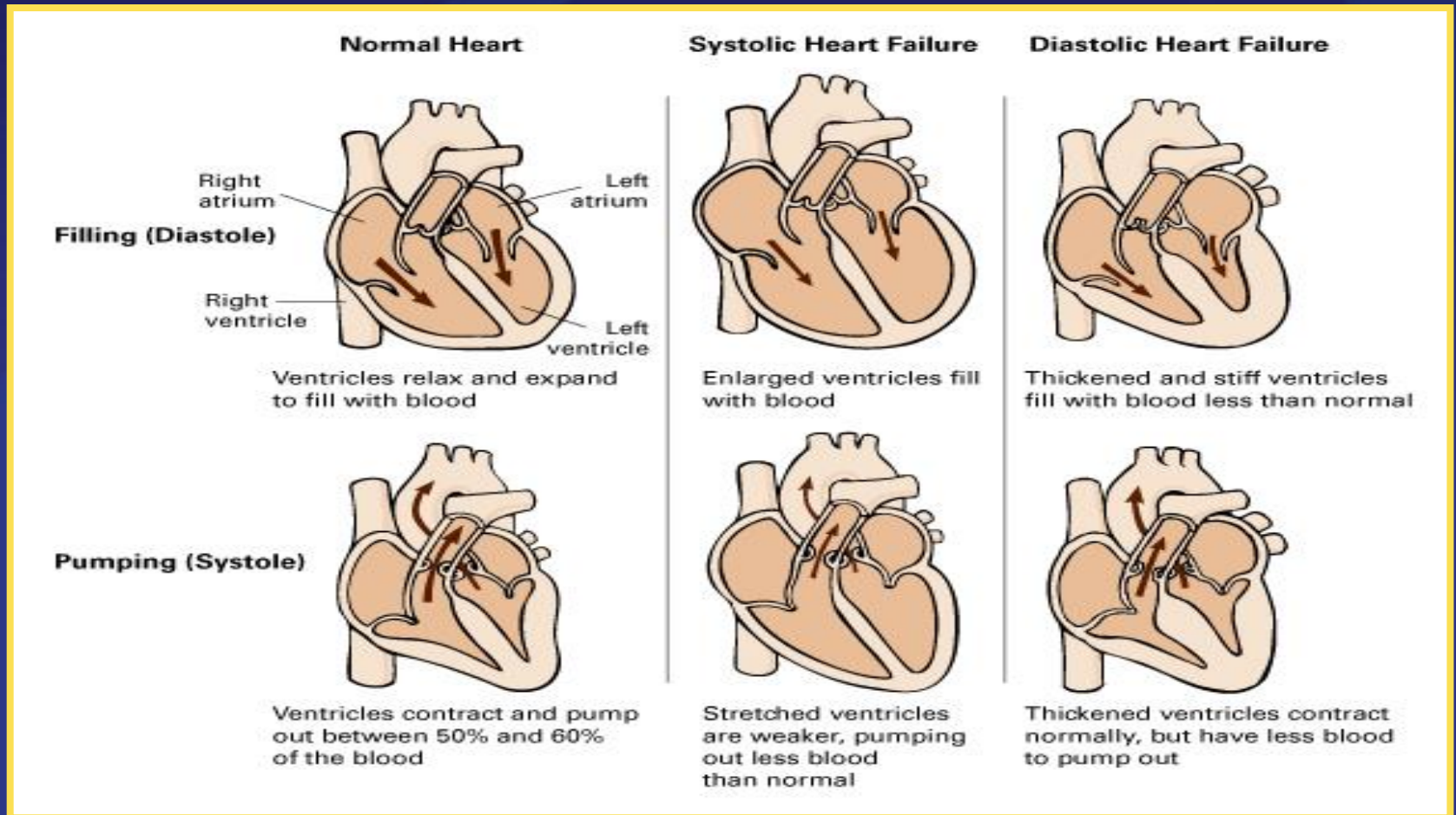
Types of Heart Failure

Classification of heart failure is based on which heart function or which side of the heart is most affected by the condition.

- ***Systolic heart failure (HFrEF)*** – failure of contraction to pump blood out of the chambers. This is measured by ejection fraction (EF) or the percentage of blood that is ejected out of the ventricle. Normal is 50% or higher.
- ***Diastolic heart failure (HFpEF)*** – failure of relaxation to fill the chambers with blood

HFrEF and HFpEF

Each beat of the heart consists of contraction in systole and relaxation in diastole. When the heart contracts, chambers of the heart (ventricles) pump out blood into the lungs and the rest of the body. When the heart relaxes and expands, the ventricles fill completely with blood.



Characteristics of HFpEF as Compared with Those of HFrEF

Table 1. Characteristics of Diastolic Heart Failure as Compared with Those of Systolic Heart Failure.*

Characteristic	Diastolic Heart Failure	Systolic Heart Failure
Clinical features		
Symptoms (e.g., dyspnea)	Yes	Yes
Congestive state (e.g., edema)	Yes	Yes
Neurohormonal activation (e.g., brain natriuretic peptide)	Yes	Yes
Left ventricular structure and function		
Ejection fraction	Normal	Decreased
Left ventricular mass	Increased	Increased
Relative wall thickness†	Increased	Decreased
End diastolic volume	Normal	Increased
End diastolic pressure	Increased	Increased
Left atrial size	Increased	Increased
Exercise		
Exercise capacity	Decreased	Decreased
Cardiac output augmentation	Decreased	Decreased
End diastolic pressure	Increased	Increased

* The clinical features of diastolic heart failure are similar to those of systolic heart failure, but left ventricular structure and function are distinctly different.

† The descriptor of left ventricular geometry is the relative wall thickness, defined as the ratio of left ventricular wall thickness to the radius of the left ventricular cavity.

Clues for Differentiating Between HFrEF and HFpEF in Patients with Heart Failure

Clues from the Evaluation	Systolic Dysfunction HFrEF	Diastolic Dysfunction HFpEF
History		
Hypertension	XX	XXX
Coronary Artery Disease*	XXX	XX
Diabetes mellitus	XXX	XX
Valvular heart disease*	XXX	—
Physical Examination		
Third heart sound (S3) gallop*	XXX	X
Fourth heart sound (S4) gallop	XX	XXX
Rales	XX	XX
Jugular venous distention	XX	X
Edema	XX	X
Displaced point of maximal impulse*	XX	—
Mitral regurgitation*	XXX	X

Clues for Differentiating Between HFrEF and HFpEF in Patients with Heart Failure

Clues from the evaluation	HFrEF	HFpEF
Chest Radiograph		
Cardiomegaly*	XXX	X
Pulmonary congestion	XXX	XXX
Electrocardiogram		
Q wave	XX	X
Left ventricular hypertrophy*	X	XXX
Echocardiogram		
Decreased ejection fraction*	XXX	—
Dilated left ventricle*	XX	—
Left ventricle hypertrophy*	X	XXX

X = suggestive, the number of Xs reflects the relative weight; — = not suggestive.* and — Particularly helpful in distinguishing systolic from diastolic dysfunction in heart failure.

NYHA Functional Classification

Class	Description
I (Mild)	No limitation of physical activity - ordinary physical activity doesn't cause tiredness, heart palpitations, or shortness of breath
II (Mild)	Slight limitation of physical activity, comfortable at rest, but ordinary physical activity results in tiredness, heart palpitations, or shortness of breath
III (Moderate)	Marked or noticeable limitations of physical activity, comfortable at rest, but less than ordinary physical activity causes tiredness, heart palpitations, or shortness of breath
IV (Severe)	Severe limitation of physical activity, unable to carry out any physical activity without discomfort. Symptoms also present at rest. If any physical activity is undertaken, discomfort increases.

AHA/ACC 2009 - Staging System of Heart

Stage	Description	Examples
A	People at high risk for developing heart failure but without structural heart disease or symptoms of heart failure. Encompasses "pre heart failure" where intervention with management can avert Progression to symptoms	CAD (coronary artery disease), diabetes, hypertension, metabolic syndrome, obesity, using cardiotoxins or alcohol, family history of cardiomyopathy, cerebrovascular accident (CVA), personal history of rheumatic fever
B	People with structural heart disease but without signs and symptoms of heart failure NYHA Class I	Left ventricular hypertrophy (LVH) or reduced left ventricular ejection fraction (LVEF), asymptomatic valvular heart disease, previous MI
C	People with structural heart disease with prior or current symptoms of heart failure NYHA Class II and III	Known structural heart disease with dyspnea, fatigue, inability to exercise
D	People who have advanced heart failure and severe symptoms difficult to manage with standard treatment NYHA Class IV	Marked symptoms at rest despite maximal medical therapy, with recurrent hospitalizations

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

Classification of Recommendations and Levels of Evidence

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS I (STRONG) Benefit >>> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Is recommended ■ Is indicated/useful/effective/beneficial ■ Should be performed/administered/other ■ Comparative-Effectiveness Phrases†: <ul style="list-style-type: none"> ○ Treatment/strategy A is recommended/indicated in preference to treatment B ○ Treatment A should be chosen over treatment B 	LEVEL A <ul style="list-style-type: none"> ■ High-quality evidence‡ from more than 1 RCT ■ Meta-analyses of high-quality RCTs ■ One or more RCTs corroborated by high-quality registry studies
CLASS IIa (MODERATE) Benefit >> Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Is reasonable ■ Can be useful/effective/beneficial ■ Comparative-Effectiveness Phrases†: <ul style="list-style-type: none"> ○ Treatment/strategy A is probably recommended/indicated in preference to treatment B ○ It is reasonable to choose treatment A over treatment B 	LEVEL B-R (Randomized) <ul style="list-style-type: none"> ■ Moderate-quality evidence‡ from 1 or more RCTs ■ Meta-analyses of moderate-quality RCTs
CLASS IIb (WEAK) Benefit ≥ Risk Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ May/might be reasonable ■ May/might be considered ■ Usefulness/effectiveness is unknown/unclear/uncertain or not well established 	LEVEL B-NR (Nonrandomized) <ul style="list-style-type: none"> ■ Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies ■ Meta-analyses of such studies
CLASS III: No Benefit (MODERATE) Benefit = Risk <i>(Generally, LOE A or B use only)</i> Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Is not recommended ■ Is not indicated/useful/effective/beneficial ■ Should not be performed/administered/other 	LEVEL C-LD (Limited Data) <ul style="list-style-type: none"> ■ Randomized or nonrandomized observational or registry studies with limitations of design or execution ■ Meta-analyses of such studies ■ Physiological or mechanistic studies in human subjects
CLASS III: Harm (STRONG) Risk > Benefit Suggested phrases for writing recommendations: <ul style="list-style-type: none"> ■ Potentially harmful ■ Causes harm ■ Associated with excess morbidity/mortality ■ Should not be performed/administered/other 	LEVEL C-EO (Expert Opinion) Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Introduction

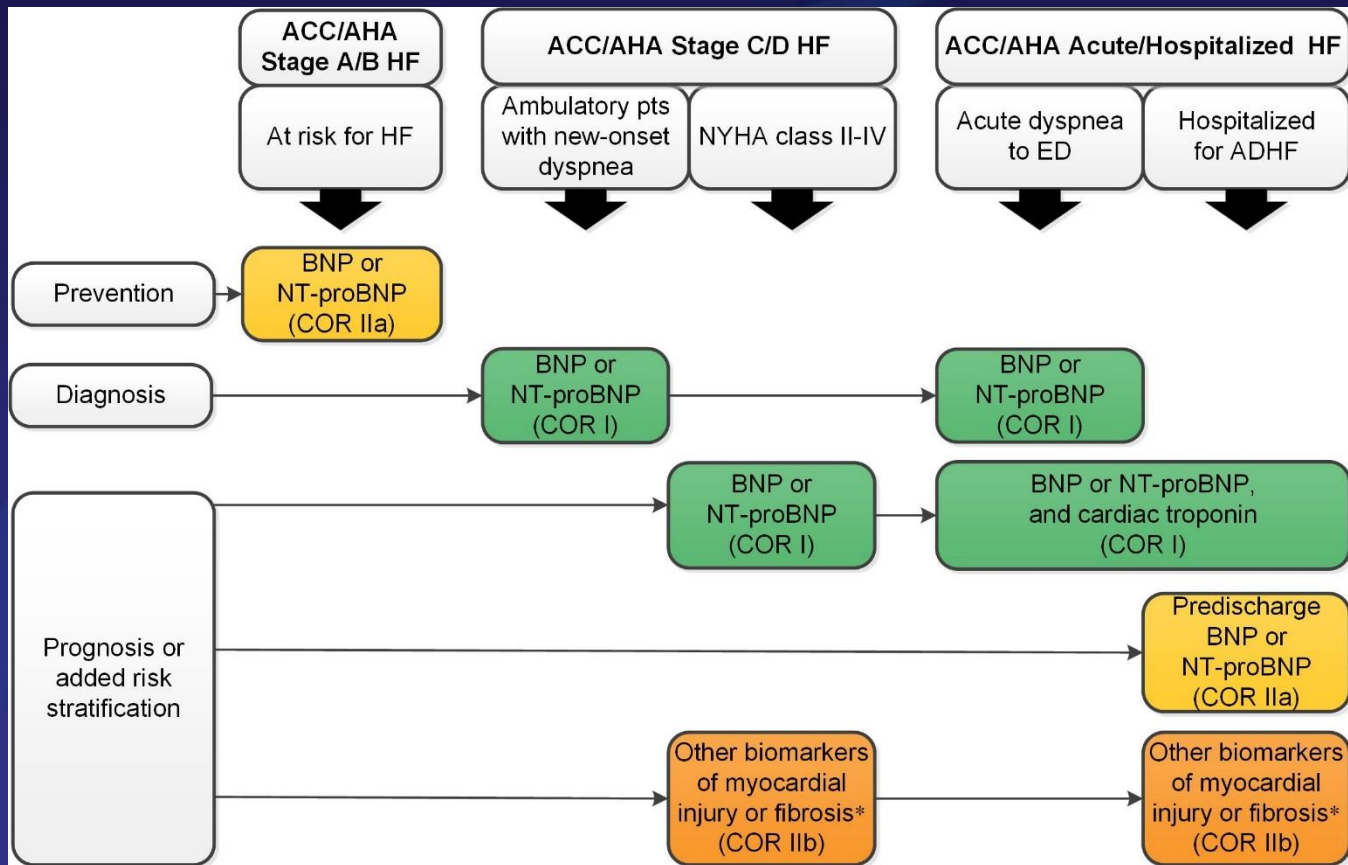
- The purpose of this focused update is to update the “2013 ACCF/AHA Guideline for the Management of Heart Failure” (2013 HF guideline) in areas where in which new evidence has emerged since its publication.
- The scope of the focused update includes revision to the sections on
 - Biomarkers
 - New therapies indicated for stage C HF with reduced ejection fraction (HF_rEF)
 - Updates on HF with preserved ejection fraction (HF_pEF)
 - New data on important comorbidities, including sleep apnea, anemia, and hypertension
 - And new insights regarding the prevention of HF

Initial and Serial Evaluation of Heart Failure

Initial and Serial Evaluation of Heart Failure

Biomarkers

Biomarkers Indications for Use



*Other biomarkers of injury or fibrosis include soluble ST2 receptor, galectin-3, and high-sensitivity troponin. ACC indicates American College of Cardiology; AHA, American Heart Association; ADHF, acute decompensated heart failure; BNP, B-type natriuretic peptide; COR, Class of Recommendation; ED, emergency department; HF, heart failure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; and pts, patients.

Biomarkers

Biomarkers Indications for Use

COR	LOE	Recommendation	Comment/ Rationale
IIa	B-R	For patients at risk of developing HF, natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF.	NEW: New data suggest that natriuretic peptide biomarker screening and early intervention may prevent HF.

Biomarkers

Biomarkers for Diagnosis

COR	LOE	Recommendation	Comment/ Rationale
I	A	In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF.	MODIFIED: 2013 acute and chronic recommendations have been combined into a diagnosis section.

Biomarkers

Biomarkers for Prognosis or Added Risk Stratification

COR	LOE	Recommendations	Comment/ Rationale
I	A	Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF.	2013 recommendation remains current.
I	A	Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF.	MODIFIED: Current recommendation emphasizes that it is admission levels of natriuretic peptide biomarkers that are useful.

Biomarkers

Biomarkers for Prognosis or Added Risk Stratification

COR	LOE	Recommendations	Comment/ Rationale
IIa	B-NR	During a hospitalization for HF, a predischage natriuretic peptide level can be useful to establish a postdischarge prognosis.	NEW: Current recommendation reflects new observational studies.
IIb	B-NR	In patients with chronic HF, measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, may be considered for additive risk stratification.	MODIFIED: 2013 recommendations have been combined into prognosis section, resulting in LOE change from A to B-NR.

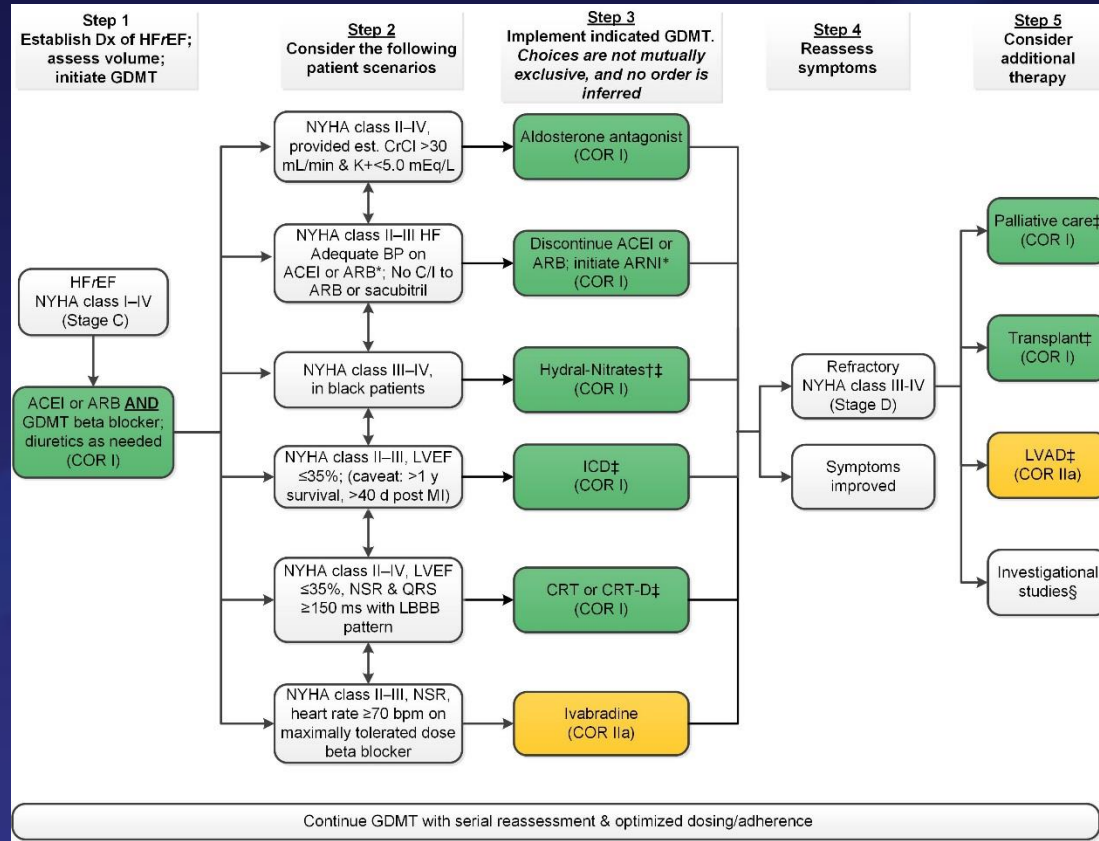
2017 Heart Failure Focused Update

Treatment of HF Stages A Through D

Treatment of HF Stages A Through D

Stage C

Treatment of HFrEF Stage C and D



†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored.

‡See 2013 HF guideline.

§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
I	ACE-I: A	The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (Level of Evidence: A), <u>OR</u> ARBs (Level of Evidence: A), <u>OR</u> ARNI (Level of Evidence: B-R) in conjunction with evidence-based beta blockers, and aldosterone antagonists in selected patients, is recommended for patients with chronic HF _r EF to reduce morbidity and mortality.	NEW: New clinical trial data prompted clarification and important updates.
	ARB: A		
	ARNI: B-R		

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
I	ACE-I: A	The use of ACE inhibitors is beneficial for patients with prior or current symptoms of chronic HF \neq EF to reduce morbidity and mortality.	2013 recommendation repeated for clarity in this section.
I	ARB: A	The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HF \neq EF who are intolerant to ACE inhibitors because of cough or angioedema.	2013 recommendation repeated for clarity in this section.

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
I	ARNI: B-R	In patients with chronic symptomatic HF _r EF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.	NEW: New clinical trial data necessitated this recommendation.

Pharmacological Treatment for Stage C HF With Reduced EF

Renin-Angiotensin System Inhibition With ACE-Inhibitor or ARB or ARNI

COR	LOE	Recommendations	Comment/ Rationale
III: Harm	B-R	ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor.	NEW: Available evidence demonstrates a potential signal of harm for a concomitant use of ACE inhibitors and ARNI.
III: Harm	C-EO	ARNI should not be administered to patients with a history of angioedema.	NEW: New clinical trial data.

Pharmacological Treatment for Stage C HF With Reduced EF

Ivabradine

COR	LOE	Recommendations	Comment/ Rationale
Ila	B-R	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF rEF (LVEF \leq 35%) who are receiving GDEM*, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.	NEW: New clinical trial data.

*In other parts of the document, the term “GDMT” has been used to denote guideline-directed management and therapy. In this recommendation, however, the term “GDEM” has been used to denote this same concept in order to reflect the original wording of the recommendation that initially appeared in the “2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure”.

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
I	B	Systolic and diastolic blood pressure should be controlled in patients with HF _p EF in accordance with published clinical practice guidelines to prevent morbidity	2013 recommendation remains current.
I	C	Diuretics should be used for relief of symptoms due to volume overload in patients with HF _p EF.	2013 recommendation remains current.

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
Ila	C	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HF _p EF despite GDMT.	2013 recommendation remains current.
Ila	C	Management of AF according to published clinical practice guidelines in patients with HF _p EF is reasonable to improve symptomatic HF.	2013 recommendation remains current.
Ila	C	The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HF _p EF.	2013 recommendation remains current.

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
IIb	B-R	In appropriately selected patients with HF _p EF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations.	NEW: Current recommendation reflects new RCT data.
IIb	B	The use of ARBs might be considered to decrease hospitalizations for patients with HF _p EF.	2013 recommendation remains current.

Pharmacological Treatment for Stage C HF With Preserved EF

COR	LOE	Recommendations	Comment/ Rationale
III: No Benefit	B-R	Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HFpEF is ineffective.	NEW: Current recommendation reflects new data from RCTs.
III: No Benefit	C	Routine use of nutritional supplements is not recommended for patients with HFpEF.	2013 recommendation remains current.

2017 Heart Failure Focused Update

Important Comorbidities in HF

Important Comorbidities in HF

Anemia

Anemia

COR	LOE	Recommendations	Comment/ Rationale
IIb	B-R	In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL.	NEW: New evidence consistent with therapeutic benefit.
III: No Benefit	B-R	In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.	NEW: Current recommendation reflects new evidence demonstrating absence of therapeutic benefit.

Important Comorbidities in HF

Hypertension

Hypertension

Treating Hypertension to Reduce the Incidence of HF

COR	LOE	Recommendations	Comment/ Rationale
I	B-R	In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.	NEW: Recommendation reflects new RCT data.

Hypertension

Treating Hypertension in Stage C HF_rEF

COR	LOE	Recommendations	Comment/ Rationale
I	C-EO	Patients with HF _r EF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.	NEW: Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.

Hypertension

Treating Hypertension in Stage C HF_pEF

COR	LOE	Recommendations	Comment/ Rationale
I	C-LD	Patients with HF _p EF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.	NEW: New target goal blood pressure based on updated interpretation of recent clinical trial data.

Important Comorbidities in HF

Sleep Disorders

Sleep Disorders

COR	LOE	Recommendations	Comment/ Rationale
IIa	C-LD	In patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable.	NEW: Recommendation reflects clinical necessity to distinguish obstructive versus central sleep apnea.
IIb	B-R	In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness.	NEW: New data demonstrate the limited scope of benefit expected from CPAP for obstructive sleep apnea.
III: Harm	B-R	In patients with NYHA class II–IV HF/rEF and central sleep apnea, adaptive servo-ventilation causes harm.	NEW: New data demonstrate a signal of harm when adaptive servo-ventilation is used for central sleep apnea.



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ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

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Angiotensin Receptor-Neprilysin Inhibition in Patients Hospitalized With Acute Decompensated Heart Failure

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Background

- **Acute decompensated heart failure (ADHF) accounts for over 1M hospitalizations in the US annually**
- **Guideline-directed therapy for ADHF is limited**
 - **Decongestion with diuretics and hemodynamic support with vasodilators remain the standards of care**

Rationale

- **PARADIGM-HF trial in chronic HFrEF: sacubitril/valsartan → ↓ CV death or HF hospitalization compared to enalapril**
 - Patients with ADHF requiring IV therapy were excluded
 - Stable HF therapy with adequate doses for >4 weeks
 - Required sequential run-in with high dose enalapril and sacubitril/valsartan before randomization
- **It is unknown if in-hospital initiation of sacubitril/valsartan compared to enalapril is safe and effective in ADHF**

Conclusions

Among hemodynamically stabilized acute heart failure patients with reduced EF, compared with enalapril, sacubitril/valsartan administered over 8 weeks ...

- Led to greater reduction in NT-proBNP
- Reduced re-hospitalization for heart failure
- Was well tolerated with comparable rates of worsening renal function, hyperkalemia, symptomatic hypotension, and angioedema

Clinical Implications

These results support the in-hospital initiation of sacubitril/valsartan in stabilized patients with acute decompensated heart failure and reduced EF, irrespective of prior ACEi/ARB use, or prior HF diagnosis.

Heart Failure Therapies During Hospitalization


JACC: Heart Failure

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 PDF Article

Initiation, Continuation, Switching, and Withdrawal of Heart Failure Medical Therapies During Hospitalization

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Heart Failure Therapies During Hospitalization

Hospitalization in patients with heart failure and reduced ejection fraction (HFrEF) provides a key opportunity to re-address guideline-directed medical therapies (GDMT). Pre-discharge initiation of GDMT is associated with improved rates of post-discharge use.

Landmark trials with beta-blockers in HFrEF patients showed that they were safely tolerated with a low risk for deterioration and demonstrated an early mortality benefit by week 8 of initiation. Small randomized trials suggest that pre-discharge initiation of low-dose beta-blockers in *hemodynamically stable patients* was well tolerated and reduced re-hospitalization and improved functional status at 6 months. Switching from nonevidence-based beta-blockers to evidence-based beta-blockers has not been studied, but based on clinical experience, is well tolerated.

Observational studies show that continuation of beta-blockers during HFrEF hospitalization is associated with lower risk for re-hospitalization and post-discharge mortality. Withdrawal or dose reduction of beta-blockers should be considered in patients with hemodynamic intolerance, borderline perfusion, cardiogenic shock, or inotrope requirement. Careful attention should be paid to patients with bradycardia due to risk for progression to heart block and tachycardia, which may be a compensatory mechanism for low stroke volume.

Heart Failure Therapies During Hospitalization

There are no randomized data assessing in-hospital initiation or continuation of angiotensin-converting enzyme inhibitor (ACEI)/angiotensin-receptor blocker (ARB). However, observational studies suggest that in-hospital initiation of ACEI/ARB correlate with lower 30-day re-hospitalization and mortality rates, which persist at 12 months as well.

Similarly, in-hospital continuation of ACEI/ARB was associated with lower post-discharge mortality and re-hospitalization. Common reasons for their discontinuation are hyperkalemia and renal dysfunction. In particular, caution should be used in initiating ACEI/ARB in hypovolemic patients, as this may be associated with hypotension.

Heart Failure Therapies During Hospitalization

Benefits of angiotensin receptor/neprilysin inhibitor (ARNI) therapy over ACEI are consistent across a wide spectrum of patients with HFrEF including patients with recent hospitalizations. This suggests clinical benefit with in-hospital switching from ACEI/ARB to ARNI. Inpatient initiation of ARNI therapy in euvolemic patients tolerating ACEI/ARB can be considered and will increase rates of post-discharge use. ACEI must be held for 36 hours prior to ARNI initiation and ARNI should not be used in patients with prior hypersensitivity or angioedema to ACEI/ARB.

Smaller trials with spironolactone show in-hospital initiation is associated with reduced rates for arrhythmia and greater congestion relief. These benefits have not been consistently demonstrated in observational studies, likely due to confounding with selection bias. In-hospital initiation of spironolactone correlates with higher post-discharge adherence.

Heart Failure Therapies During Hospitalization

Continuation of spironolactone during hospitalization has not been well studied. However, subgroup analysis of a randomized trial showed that patients initiated or continued on spironolactone had a lower 30-day mortality. It is safe and well tolerated in most hemodynamically stable patients.

Reasons for low use rates of spironolactone therapy at hospital discharge are not well understood. Nonetheless, based on randomized data, their safety profile has been favorable. Patients who are unable or unwilling to comply with post-discharge clinical and laboratory monitoring should not be considered for initiation or up-titration of spironolactone.

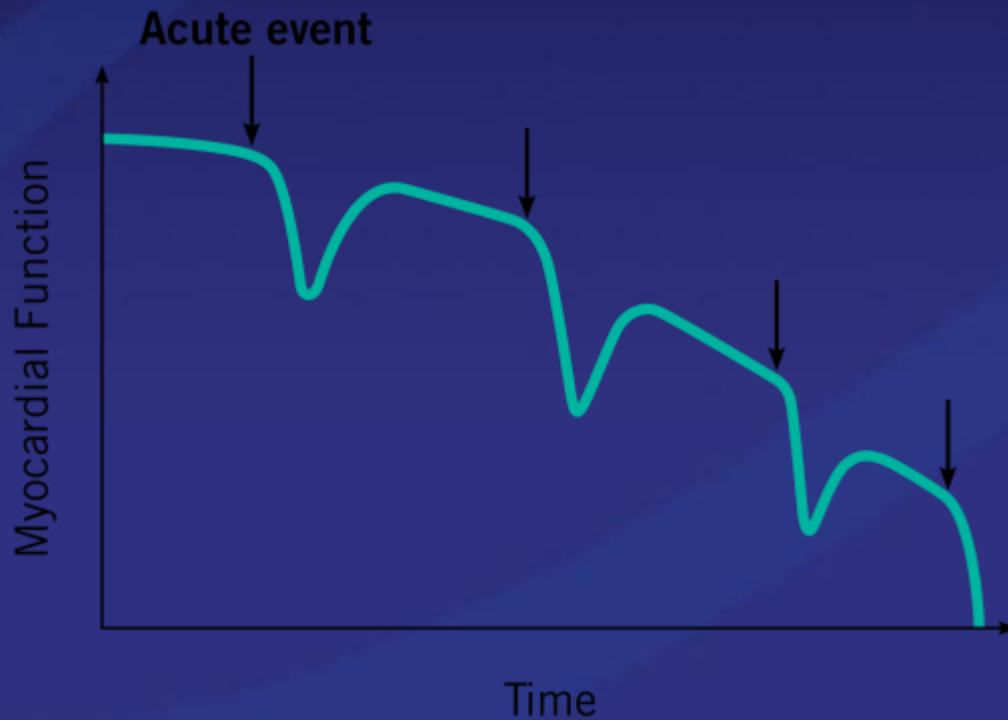
Patients in the hospital with HFrEF should be counseled and educated regarding need for GDMT and anticipated side effects. Close follow-up after discharge with lab monitoring is mandatory, especially in treatment-naïve patients.

Hemodynamic Monitoring for Heart Failure Management

- **Managing Pressures in the Heart Failure Patient**
- **CardioMEMS™ HF System**
- **CHAMPION Clinical Trial**

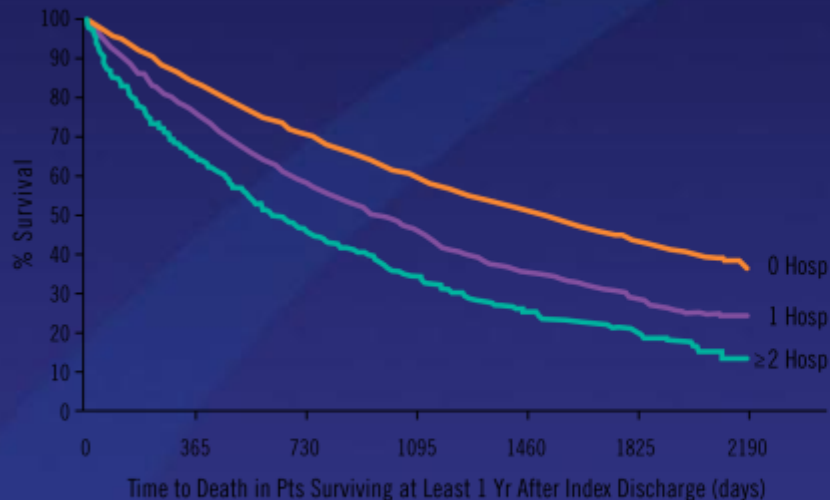
Worsening Heart Failure Leading to HF Hospitalizations Contributes to Disease Progression

With each subsequent HF-related admission, the patient leaves the hospital with a further decrease in cardiac function.

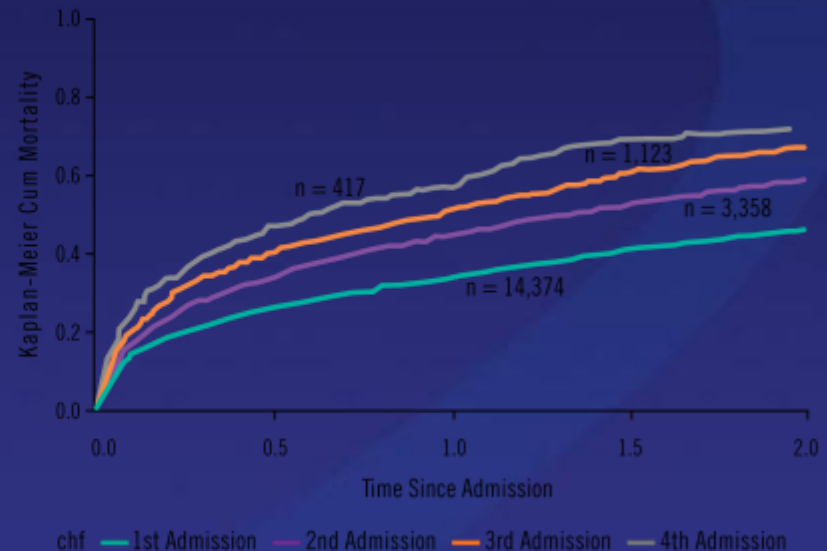


HF Hospitalizations are a Strong Predictor of Mortality^{1,2}

- Data from the EFFECT study, n = 9138 patients¹



- Data from the Setoguchi et al., n = 14,374 patients²

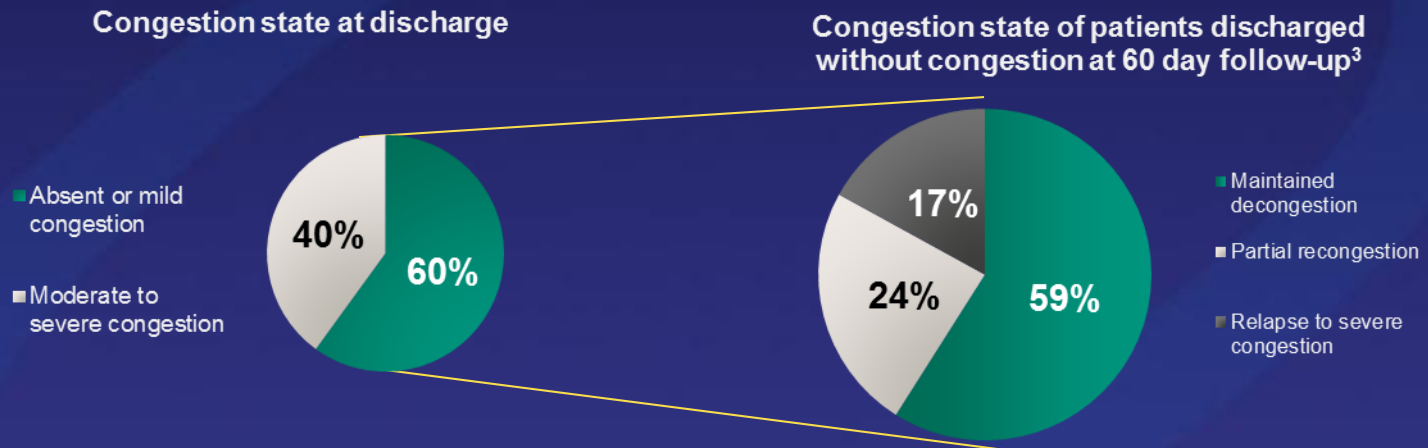


Studies show each admission decreases a patient's chance of survival.

1. Lee DS, et al. Am J of Med, 2009.
2. Setoguchi S, et al. Am Heart J, 2007.

How well do our current tools work?

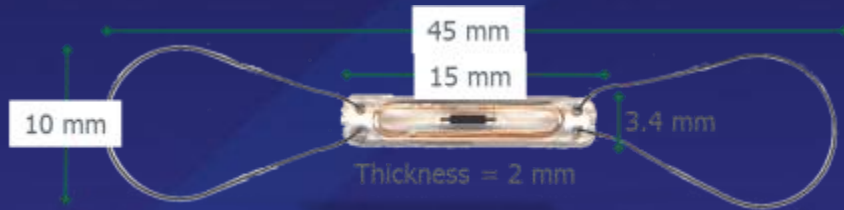
1,000,000 hospitalizations for heart failure
>3,000,000 hospitalizations include heart failure as contributor
25% of patients are readmitted in 30 days 50% in 6 months



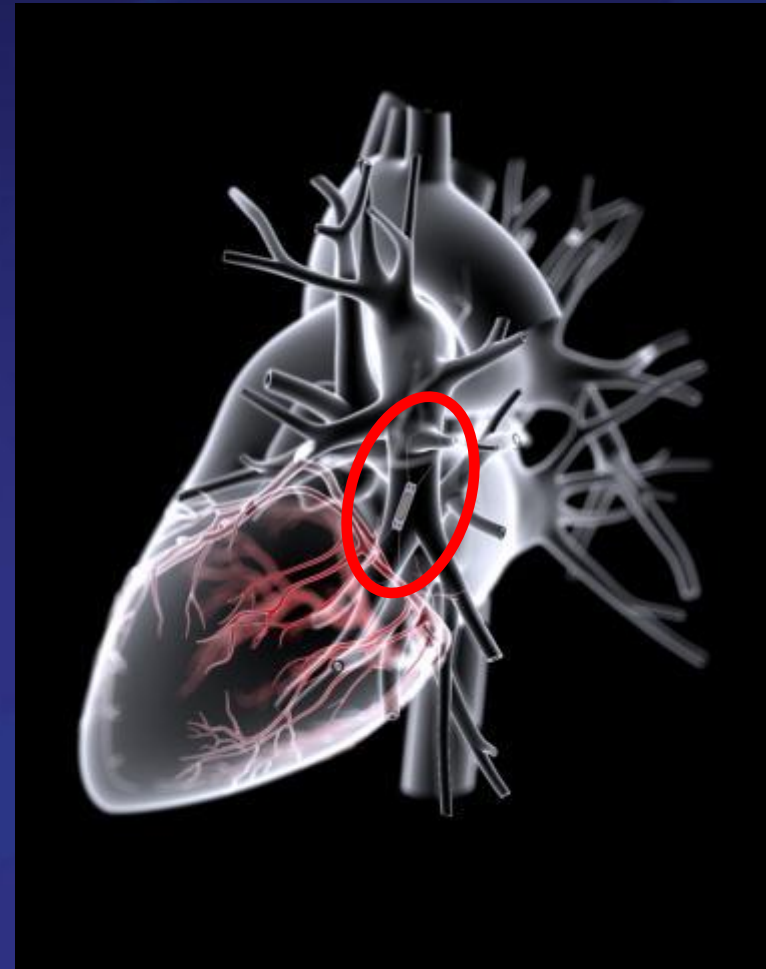
- Post hoc analysis of 463 acute decompensated HF patients from DOSE-HF and CARRESS-HF trials showed:
 - 40% of patients are discharged with moderate to severe congestion.¹
 - Of patients decongested at discharge, 41% had severe or partial re-congestion by 60 days.¹

CardioMEMS™ HF System

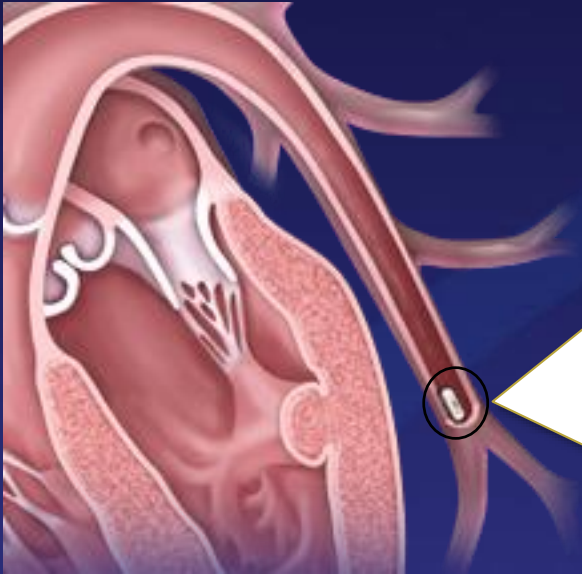
The pulmonary artery pressure sensor is implanted via a right heart catheterization procedure via femoral vein approach.



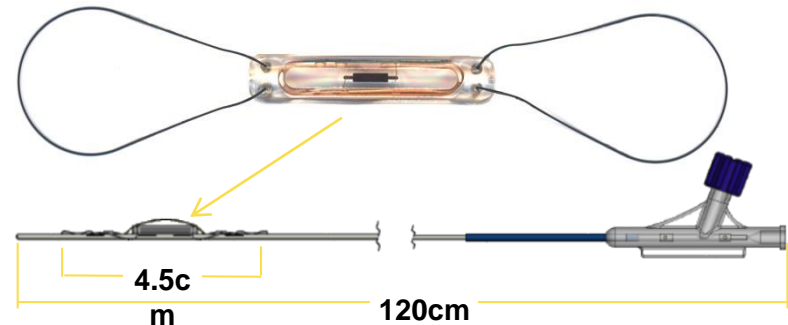
Target location for pulmonary artery pressure sensor



Cardiomems™ HF System



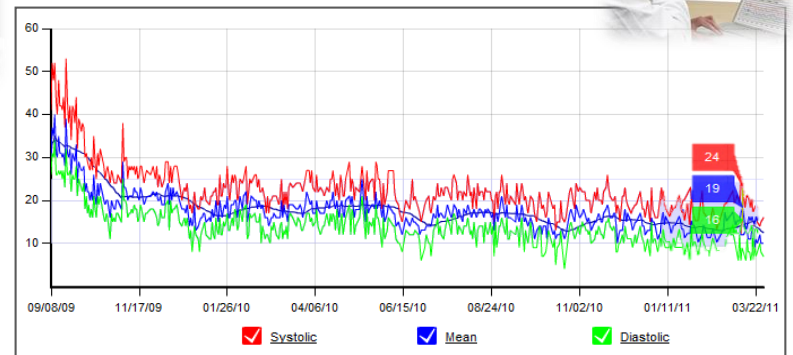
PA Pressure Sensor on Catheter Delivery System



Patient Home Electronics Unit

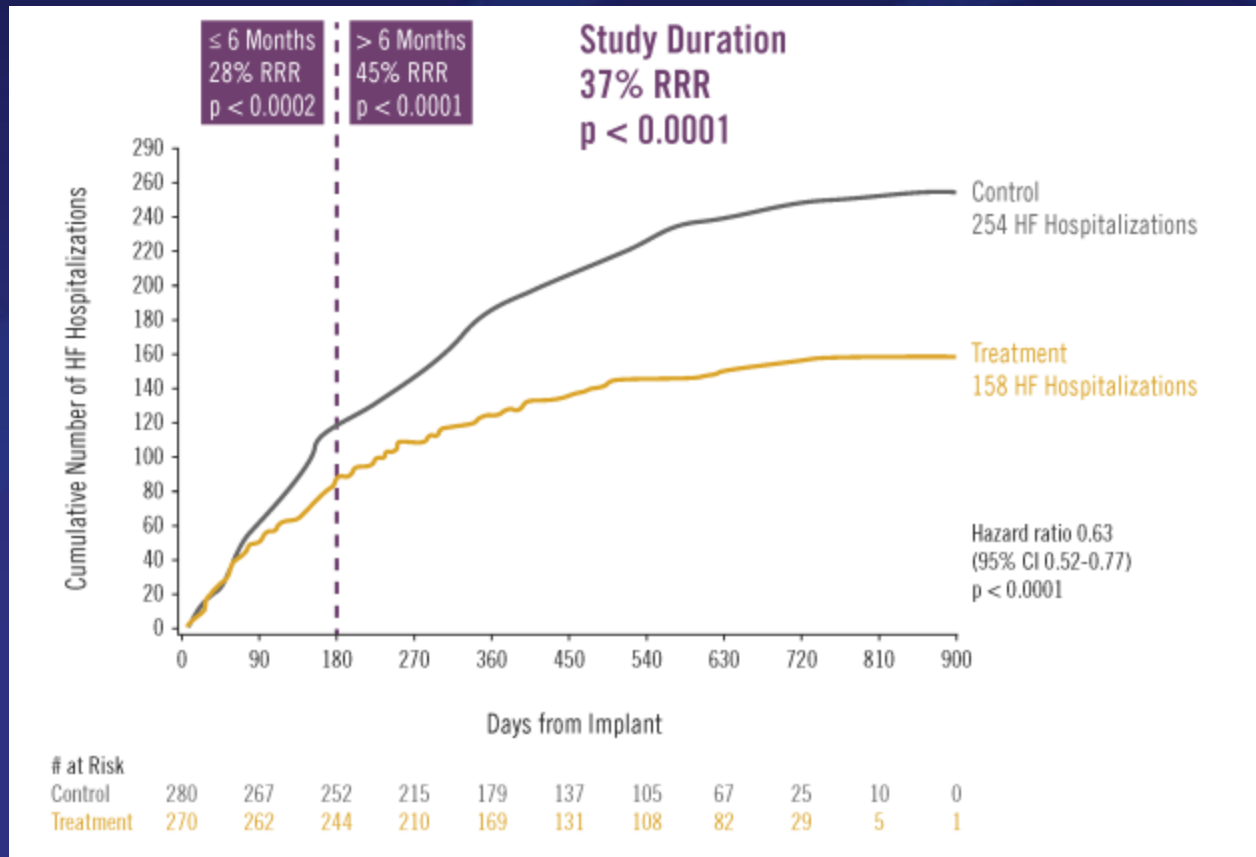


PA Pressure Database



Physician Access Via Secure Website

CHAMPION Clinical Trial: PA Pressure-guided Therapy Reduces HF Hospitalizations



Patients managed with PA pressure data had **significantly fewer HF hospitalizations** as compared to the control group.

Thank you!

References

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