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PRACTICE GUIDELINE

2013 ACCF/AHA Guideline for the Management of Heart Failure: Executive Summary

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

Developed in Collaboration With the American College of Chest Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

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Preamble

The medical profession should play a central role in evaluating the evidence related to drugs, devices, and procedures for the detection, management, and prevention of disease. When properly applied, expert analysis of available data on the benefits and risks of these therapies and procedures can improve the quality of care, optimize patient outcomes, and favorably affect costs by focusing resources on the most effective strategies. An organized and directed approach to a thorough review of evidence has resulted in the production of clinical practice guidelines that assist clinicians in selecting the best management strategy for an individual patient. Moreover, clinical practice guidelines can provide a foundation for other applications, such as performance measures, appropriate use criteria, and both quality improvement and clinical decision support tools.

The American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) have jointly produced guidelines in the area of cardiovascular disease since 1980. The ACCF/AHA Task Force on Practice Guidelines (Task Force), charged with developing, updating, and revising practice guidelines for cardiovascular diseases and procedures, directs and oversees this effort. Writing committees are charged with regularly reviewing and evaluating all available evidence to develop balanced, patient-centric recommendations for clinical practice.

Experts in the subject under consideration are selected by the ACCF and AHA to examine subject-specific data and write guidelines in partnership with representatives from other medical organizations and specialty groups. Writing committees are asked to perform a literature review; weigh the strength of evidence for or against particular tests, treatments, or procedures; and include estimates of expected outcomes where such data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of tests or therapies are considered. When available, information from studies on cost is considered, but data on efficacy and outcomes constitute the primary basis for the recommendations contained herein.

In analyzing the data and developing recommendations and supporting text, the writing committee uses evidence-based methodologies developed by the Task Force (1). The Class of Recommendation (COR) is an estimate of the size of the treatment effect considering risks versus benefits in addition to evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm. The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. The writing committee reviews and ranks evidence supporting each recommendation with the weight of evidence ranked as LOE A, B, or C according to specific definitions that are included in Table 1. Studies are identified as observational, retrospective, prospective, or randomized where appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and are ranked as LOE C. When recommendations at LOE C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available. For issues for which sparse data are available, a survey of current practice among the clinicians on the writing committee is the basis for LOE C recommendations and no references are cited. The schema for COR and LOE are summarized in Table 1, which also provides suggested phrases for writing recommendations within each COR. A new addition to this methodology is separation of the Class III recommendations to delineate whether the recommendation is determined to be of "no benefit" or is associated with "harm" to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment or strategy versus another have been added for COR I and IIa, LOE A or B only.

In view of the advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force has designated the term *guideline-directed medical therapy (GDMT)* to represent optimal medical therapy as defined by ACCF/AHA guideline–recommended therapies (primarily Class I). This new term, *GDMT*, will be used herein and throughout all future guidelines.

Because the ACCF/AHA practice guidelines address patient populations (and clinicians) residing in North America, drugs that are not currently available in North America are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside North America, each writing committee reviews the potential influence of different practice patterns and patient populations on the treatment effect and relevance to the ACCF/AHA target population to determine whether the findings should inform a specific recommendation.

The ACCF/AHA practice guidelines are intended to assist clinicians in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the clinician and patient in light of all the circumstances presented by that patient. As a result, situations may arise for which deviations from these guidelines may be appropriate. Clinical decision making should involve consideration of the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to inform patient care more effectively; these areas will be identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if followed. Because lack

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Table 1. Applying Classification of Recommendation and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT: CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

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

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

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

of patient understanding and adherence may adversely affect outcomes, clinicians should make every effort to engage the patient's active participation in prescribed medical regimens and lifestyles. In addition, patients should be informed of the risks, benefits, and alternatives to a particular treatment and be involved in shared decision making whenever feasible, particularly for COR IIa and IIb, for which the benefit-to-risk ratio may be lower.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the members of the writing committee. All writing committee members and peer reviewers of the guideline are required to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort. In December 2009, the ACCF and AHA implemented a new policy for relationship with industry and other entities (RWI) that requires the writing committee chair plus a minimum of 50% of the writing committee to have no *relevant* RWI (Appendix 1 includes the ACCF/AHA definition of

relevance). These statements are reviewed by the Task Force and all members during each conference call and/or meeting of the writing committee and are updated as changes occur. All guideline recommendations require a confidential vote by the writing committee and must be approved by a consensus of the voting members. Members are not permitted to draft or vote on any text or recommendations pertaining to their RWI. Members who recused themselves from voting are indicated in the list of writing committee members, and specific section recusals are noted in Appendix 1. Authors' and peer reviewers' RWI pertinent to this guideline are disclosed in Appendixes 1 and 2, respectively. Additionally, to ensure complete transparency, writing committee members' comprehensive disclosure information—including RWI not pertinent to this document—is available as an online supplement. Comprehensive disclosure information for the Task Force is also available online at http://www.cardiosource.org/en/ACC/About-ACC/Who-We-Are/Leadership/Guidelines-and-Documents-Task-Forces.aspx. The work of writing committees is supported exclusively by the ACCF and AHA without commercial support. Writing committee members volunteered their time for this activity.

In an effort to maintain relevance at the point of care for practicing clinicians, the Task Force continues to oversee an ongoing process improvement initiative. As a result, in response to pilot projects, several changes to these guidelines will be apparent, including limited narrative text, a focus on summary and evidence tables (with references linked to abstracts in PubMed), and more liberal use of summary recommendation tables (with references that support LOE) to serve as a quick reference.

In April 2011, the Institute of Medicine released 2 reports: *Clinical Practice Guidelines We Can Trust* and *Finding What Works in Health Care: Standards for Systematic Reviews* (2,3). It is noteworthy that the ACCF/AHA practice guidelines are cited as being compliant with many of the proposed standards. A thorough review of these reports and of our current methodology is under way, with further enhancements anticipated.

The recommendations in this guideline are considered current until they are superseded by a focused update or the full-text guideline is revised. Guidelines are official policy of both the ACCF and AHA. The reader is encouraged to consult the full-text guideline (4). for additional guidance and details about heart failure, because the Executive Summary contains only the recommendations.

Jeffrey L. Anderson, MD, FACC, FAHA
Chair, ACCF/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this document are, whenever possible, evidence based. An extensive evidence review was conducted through October 2011 and includes selected other references through April 2013. The relevant data are included in evidence tables in the Data Supplement. Searches were extended to studies, reviews, and other evidence conducted in human subjects and that were published in English from PubMed, EMBASE, Cochrane, Agency for Healthcare Research and Quality Reports, and other selected databases relevant to this guideline. Key search words included but were not limited to the following: *heart failure, cardiomyopathy, quality of life, mortality, hospitalizations, prevention, biomarkers, hypertension, dyslipidemia, imaging, cardiac catheterization, endomyocardial biopsy, angiotensin-converting enzyme inhibitors, angiotensin-receptor antagonists/blockers, beta blockers, cardiac, cardiac resynchronization therapy, defibrillator, device-based therapy, implantable cardioverter-defibrillator, device implantation, medical therapy, acute decompensated heart failure, preserved ejection fraction, terminal care and transplantation, quality measures,* and *performance measures*. Additionally, the committee reviewed documents related to the subject matter previously published by the ACCF and AHA. References selected and published in this document are representative and not all-inclusive.

1.2. Organization of the Writing Committee

The committee was composed of physicians and a nurse with broad expertise in the evaluation, care, and management of patients with heart failure (HF). The authors included general cardiologists, HF and transplant specialists, electrophysiologists, general internists, and physicians with methodological expertise. The committee included representatives from the ACCF, AHA, American Academy of Family Physicians, American College of Chest Physicians, American College of Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation.

1.3. Document Review and Approval

This document was reviewed by 2 official reviewers each nominated by both the ACCF and the AHA, as well as 1 to 2 reviewers each from the American Academy of Family Physicians, American College of Chest Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation, as well as 32 individual content reviewers (including members of the ACCF Adult Congenital and Pediatric Cardiology Council, ACCF Cardiovascular Team Council, ACCF Council on Cardiovascular Care for Older Adults, ACCF Electrophysiology Committee, ACCF Heart Failure and Transplant Council, ACCF Imaging Council, ACCF Prevention Committee, ACCF Surgeons' Scientific Council, and ACCF Task Force on Appropriate Use Criteria). All information on reviewers' RWI was distributed to the writing committee and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACCF and AHA and endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American College of Chest Physicians, Heart

Rhythm Society, and International Society for Heart and Lung Transplantation.

1.4. Scope of This Guideline With Reference to Other Relevant Guidelines or Statements

This guideline covers multiple management issues for the adult patient with HF. Although there is an abundance of evidence addressing HF, for many important clinical considerations, this writing committee was unable to identify sufficient data to properly inform a recommendation. The writing committee actively worked to reduce the number of LOE "C" recommendations, especially for Class I—recommended therapies. Despite these limitations, it is apparent that much can be done for HF. Adherence to the clinical practice guidelines herein reproduced should lead to improved patient outcomes.

Although of increasing importance, children with HF and adults with congenital heart lesions are not specifically addressed in this guideline. The reader is referred to publically available resources to address questions in these areas. However, this guideline does address HF with preserved ejection fraction (EF) in more detail and similarly revisits hospitalized HF. Additional areas of renewed interest are stage D HF, palliative care, transition of care, and quality of care for HF. Certain management strategies appropriate for the patient at risk for HF or already affected by HF are also reviewed in numerous relevant clinical practice guidelines and scientific statements published by the ACCF/AHA Task Force on Practice Guidelines, AHA, ACCF Task Force on Appropriate Use Criteria, European Society of Cardiology, Heart Failure Society of America, and the National Heart, Lung, and Blood Institute. The writing committee saw no need to reiterate the recommendations contained in those guidelines and chose to harmonize recommendations when appropriate and eliminate discrepancies. This is especially the case for device-based therapeutics, where complete alignment between the HF guideline and the device-based therapy guideline was deemed imperative (5). Some recommendations from earlier guidelines have been updated as warranted by new evidence or a better understanding of earlier evidence, whereas others that were no longer accurate or relevant or that were overlapping were modified; recommendations from previous guidelines that were similar or redundant were eliminated or consolidated when possible.

The present document recommends a combination of lifestyle modifications and medications that constitute GDMT. GDMT is specifically referenced in the recommendations for treatment of HF (Section 6.3.2). Both for GDMT and other recommended drug treatment regimens, the reader is advised to confirm dosages with product insert material and to evaluate carefully for contraindications and drug-drug interactions. Table 2 is a list of documents deemed pertinent to this effort and is intended for use as a resource; it obviates the need to repeat already extant guideline recommendations. Additional other HF guideline statements are highlighted as well for the purpose of comparison and completeness.

2. Definition of HF

HF is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral edema. Some patients have exercise intolerance but little evidence of fluid retention, whereas others complain primarily of edema, dyspnea, or fatigue. Because some patients present without signs or symptoms of volume overload, the term "heart failure" is preferred over "congestive heart failure." There is no single diagnostic test for HF because it is largely a clinical diagnosis based on a careful history and physical examination.

The clinical syndrome of HF may result from disorders of the pericardium, myocardium, endocardium, heart valves, or great vessels, or from certain metabolic abnormalities, but most patients with HF have symptoms due to impaired left ventricular (LV) myocardial function. It should be emphasized that HF is not synonymous with either cardiomyopathy or LV dysfunction; these latter terms describe possible structural or functional reasons for the development of HF. HF may be associated with a wide spectrum of LV functional abnormalities, which may range from patients with normal LV size and preserved EF to those with severe dilatation and/or markedly reduced EF. In most patients, abnormalities of systolic and diastolic dysfunction coexist, irrespective of EF. EF is considered important in classification of patients with HF because of differing patient demographics, comorbid conditions, prognosis, and response to therapies (36) and because most clinical trials selected patients based on EF. EF values are dependent on the imaging technique used, method of analysis, and operator. As other techniques may indicate abnormalities in systolic function among patients with a preserved EF, it is preferable to use the terms preserved or reduced EF over preserved or reduced systolic function. For the remainder of this guideline, we will consistently refer to HF with preserved EF and HF with reduced EF as HF*p*EF and HF*r*EF, respectively (Table 3).

3. HF Classifications

Both the ACCF/AHA stages of HF (37) and the New York Heart Association (NYHA) functional classification (37,38) provide useful and complementary information about the presence and severity of HF. The ACCF/AHA stages of HF emphasize the development and progression of disease and can be used to describe individuals and populations, whereas the NYHA classes focus on exercise capacity and the symptomatic status of the disease (Table 4).

Table 2. Associated Guidelines and Statements

Title	Organization	Publication Year (Reference)
Guidelines		
Guidelines for the Management of Adults With Congenital Heart Disease	ACCF/AHA	2008 (6)
Guidelines for the Management of Patients With Atrial Fibrillation	ACCF/AHA/HRS	2011 (7–9)
Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults	ACCF/AHA	2010 (10)
Guideline for Coronary Artery Bypass Graft Surgery	ACCF/AHA	2011 (11)
Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities	ACCF/AHA/HRS	2013 (5)
Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy	ACCF/AHA	2011 (12)
Guideline for Percutaneous Coronary Intervention	ACCF/AHA/SCAI	2011 (13)
Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update	AHA/ACCF	2011 (14)
Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease	ACCF/AHA/ACP/AATS/PCNA/SCAI/STS	2012 (15)
Guideline for the Management of ST-Elevation Myocardial Infarction	ACCF/AHA	2013 (16)
Guidelines for the Management of Patients With Unstable Angina/ Non–ST-Elevation Myocardial Infarction	ACCF/AHA	2013 (17)
Guidelines for the Management of Patients With Valvular Heart Disease	ACCF/AHA	2008 (18)
Comprehensive Heart Failure Practice Guideline	HFSA	2010 (19)
Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure	ESC	2012 (20)
Chronic Heart Failure: Management of Chronic Heart Failure in Adults in Primary and Secondary Care	NICE	2010 (21)
Antithrombotic Therapy and Prevention of Thrombosis	ACCP	2012 (22)
Guidelines for the Care of Heart Transplant Recipients	ISHLT	2010 (23)
Statements		
Contemporary Definitions and Classification of the Cardiomyopathies	AHA	2006 (24)
Genetics and Cardiovascular Disease	AHA	2012 (25)
Appropriate Utilization of Cardiovascular Imaging in Heart Failure	ACCF	2013 (26)
Appropriate Use Criteria for Coronary Revascularization Focused Update	ACCF	2012 (27)
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure	NHLBI	2003 (28)
Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines	NHLBI	2002 (29)
Referral, Enrollment, and Delivery of Cardiac Rehabilitation/Secondary Prevention Programs at Clinical Centers and Beyond	AHA/AACVPR	2011 (30)
Decision Making in Advanced Heart Failure	AHA	2012 (31)
Recommendations for the Use of Mechanical Circulatory Support: Device Strategies and Patient Selection	AHA	2012 (32)
Advanced Chronic Heart Failure	ESC	2007 (33)
Oral Antithrombotic Agents for the Prevention of Stroke in Nonvalvular Atrial Fibrillation	AHA/ASA	2012 (34)
Third Universal Definition of Myocardial Infarction	ESC/ACCF/AHA/WHF	2012 (35)

AACVPR indicates American Association of Cardiovascular and Pulmonary Rehabilitation; AATS, American Association for Thoracic Surgery; ACCF, American College of Cardiology Foundation; ACCP, American College of Chest Physicians; ACP, American College of Physicians; AHA, American Heart Association; ASA, American Stroke Association; ESC, European Society of Cardiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; ISHLT, International Society for Heart and Lung Transplantation; NHLBI, National Heart, Lung, and Blood Institute; NICE, National Institute for Health and Clinical Excellence; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; STS, Society of Thoracic Surgeons; and WHF, World Heart Federation.

4. Epidemiology

The lifetime risk of developing HF is 20% for Americans ≥40 years of age (39). In the United States, HF incidence has largely remained stable over the past several decades, with >650,000 new HF cases diagnosed annually (40–42). HF incidence increases with age, rising from approximately 20 per 1,000 individuals 65 to 69 years of age to >80 per 1,000 individuals among those ≥85 years of age (41). Approximately 5.1 million persons in the United States have clinically manifest HF, and the

Table 3. Definitions of HF*r*EF and HF*p*EF

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.

EF indicates ejection fraction; HF, heart failure; HF*p*EF, heart failure with preserved ejection fraction; and HF*r*EF, heart failure with reduced ejection fraction.

prevalence continues to rise (40). In the Medicare-eligible population, HF prevalence increased from 90 to 121 per 1000 beneficiaries from 1994 to 2003 (41). HF*r*EF and HF*p*EF each make up about half of the overall HF burden (43). One in 5 Americans will be >65 years of age by 2050 (44). Because HF prevalence is highest in this group, the number of Americans with HF is expected to significantly worsen in the future. Disparities in the epidemiology of HF have been identified. Blacks have the highest risk for HF (45). In the ARIC (Atherosclerosis Risk in Communities) study, incidence rate per 1,000 person-years was lowest among white women, (41,42) and highest among black men, (46) with blacks having a greater 5-year mortality rate than whites (47). HF in non-Hispanic black males and females has a prevalence of 4.5% and 3.8%, respectively, versus 2.7% and 1.8% in non-Hispanic white males and females, respectively (40).

5. Initial and Serial Evaluation of the HF Patient: Recommendations

5.1. Clinical Evaluation

See Table 5 for multivariable clinical risk scores.

5.1.1. History and Physical Examination

CLASS I

1. **A thorough history and physical examination should be obtained/performed in patients presenting with HF to identify cardiac and noncardiac disorders or behaviors that might cause or accelerate the development or progression of HF. *(Level of Evidence: C)***
2. **In patients with idiopathic dilated cardiomyopathy, a 3-generational family history should be obtained to aid in establishing the diagnosis of familial dilated cardiomyopathy. *(Level of Evidence: C)***

Table 4. Comparison of ACCF/AHA Stages of HF and NYHA Functional Classifications

ACCF/AHA Stages of HF (37)		NYHA Functional Classification (38)	
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	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; HF, heart failure; and NYHA, New York Heart Association.

3. Volume status and vital signs should be assessed at each patient encounter. This includes serial assessment of weight, as well as estimates of jugular venous pressure and the presence of peripheral edema or orthopnea (48–51). *(Level of Evidence: B)*

5.1.2. Risk Scoring

CLASS IIa

1. Validated multivariable risk scores can be useful to estimate subsequent risk of mortality in ambulatory or hospitalized patients with HF (52–60). *(Level of Evidence: B)*

5.2. Diagnostic Tests

CLASS I

1. Initial laboratory evaluation of patients presenting with HF should include complete blood count, urinalysis, serum electrolytes (including calcium and magnesium), blood urea nitrogen, serum creatinine, glucose, fasting lipid profile, liver function tests, and thyroid-stimulating hormone. *(Level of Evidence: C)*
2. Serial monitoring, when indicated, should include serum electrolytes and renal function. *(Level of Evidence: C)*
3. A 12-lead electrocardiogram should be performed initially on all patients presenting with HF. *(Level of Evidence: C)*

CLASS IIa

1. Screening for hemochromatosis or HIV is reasonable in selected patients who present with HF (63). *(Level of Evidence: C)*
2. Diagnostic tests for rheumatologic diseases, amyloidosis, or pheochromocytoma are reasonable in patients presenting with HF in whom there is a clinical suspicion of these diseases. *(Level of Evidence: C)*

5.3. Biomarkers

See Table 6 for a summary of recommendations from this section.

A. Ambulatory/Outpatient

CLASS I

1. In ambulatory patients with dyspnea, measurement of B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP) is useful to support clinical decision making regarding the diagnosis of HF, especially in the setting of clinical uncertainty (64–70). *(Level of Evidence: A)*
2. Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF (69,71–76). *(Level of Evidence: A)*

CLASS IIa

1. BNP- or NT-proBNP–guided HF therapy can be useful to achieve optimal dosing of GDMT in select clinically euvolemic patients followed in a well-structured HF disease management program (77–84). *(Level of Evidence: B)*

CLASS IIb

1. The usefulness of serial measurement of BNP or NT-proBNP to reduce hospitalization or mortality in patients with HF is not well established (77–84). *(Level of Evidence: B)*
2. Measurement of other clinically available tests such as biomarkers of myocardial injury or fibrosis may be considered for additive risk stratification in patients with chronic HF (85–91). *(Level of Evidence: B)*

B. Hospitalized/Acute

CLASS I

1. Measurement of BNP or NT-proBNP is useful to support clinical judgment for the diagnosis of acutely decompensated HF, especially in the setting of uncertainty for the diagnosis (92–98). *(Level of Evidence: A)*

Table 5. Selected Multivariable Risk Scores to Predict Outcome in HF

Risk Score	Reference/Link
Chronic HF	
All patients with chronic HF	
Seattle Heart Failure Model	(56) http://SeattleHeartFailureModel.org
Heart Failure Survival Score	(52) http://handheld.softpedia.com/get/Health/Calculator/HFSS-Calc-37354.shtml
CHARM Risk Score	(59)
CORONA Risk Score	(60)
Specific to chronic HF*p*EF	
I-PRESERVE Score	(54)
Acutely decompensated HF	
ADHERE Classification and Regression Tree (CART) Model	(53)
American Heart Association Get With The Guidelines Score	(58) http://www.heart.org/HEARTORG/HealthcareProfessional/GetWithTheGuidelinesHFStroke/GetWithTheGuidelinesHeartFailureHomePage/Get-With-The-Guidelines-Heart-Failure-Home-%20Page_UCM_306087_SubHomePage.jsp
EFFECT Risk Score	(55) http://www.ccort.ca/Research/CHFRiskModel.aspx
ESCAPE Risk Model and Discharge Score	(61)
OPTIMIZE HF Risk-Prediction Nomogram	(62)

ADHERE indicates Acute Decompensated Heart Failure National Registry; CHARM, Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity; CORONA, Controlled Rosuvastatin Multinational Trial in Heart Failure; EFFECT, Enhanced Feedback for Effective Cardiac Treatment; ESCAPE, Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness; HF, heart failure; HF*p*EF, heart failure with preserved ejection fraction; I-PRESERVE, Irbesartan in Heart Failure with Preserved Ejection Fraction Study; and OPTIMIZE, Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure.

Table 6. Recommendations for Biomarkers in HF

Biomarker, Application	Setting	COR	LOE	References
Natriuretic peptides				
Diagnosis or exclusion of HF	Ambulatory, Acute	I	A	64–70,92–98
Prognosis of HF	Ambulatory, Acute	I	A	69,71–76,96,99–106
Achieve GDMT	Ambulatory	IIa	B	77–84
Guidance for acutely decompensated HF therapy	Acute	IIb	C	107,108
Biomarkers of myocardial injury				
Additive risk stratification	Acute, Ambulatory	I	A	85–88,96,101,104–115
Biomarkers of myocardial fibrosis				
Additive risk stratification	Ambulatory	IIb	B	89–91
	Acute	IIb	A	96,101,104,106–108,110,112–115

COR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; and LOE, Level of Evidence.

2. **Measurement of BNP or NT-proBNP and/or cardiac troponin is useful for establishing prognosis or disease severity in acutely decompensated HF (96,99–106). *(Level of Evidence: A)***

CLASS IIb

1. **The usefulness of BNP- or NT-proBNP–guided therapy for acutely decompensated HF is not well established (107,108). *(Level of Evidence: C)***
2. **Measurement of other clinically available tests such as biomarkers of myocardial injury or fibrosis may be considered for additive risk stratification in patients with acutely decompensated HF (96,101,104,105,109–115). *(Level of Evidence: A)***

5.4. Noninvasive Cardiac Imaging

See Table 7 for a summary of recommendations from this section.

CLASS I

1. **Patients with suspected or new-onset HF, or those presenting with acute decompensated HF, should undergo a chest x-ray to assess heart size and pulmonary congestion and to detect alternative cardiac, pulmonary, and other diseases that may cause or contribute to the patient's symptoms. *(Level of Evidence: C)***
2. **A 2-dimensional echocardiogram with Doppler should be performed during initial evaluation of patients presenting with HF to assess ventricular function, size, wall thickness, wall motion, and valve function. *(Level of Evidence: C)***
3. **Repeat measurement of EF and measurement of the severity of structural remodeling are useful to provide information in patients with HF who have had a significant change in clinical status; who have experienced or recovered from a clinical event; or who have received treatment, including GDMT, that might have had a significant effect on cardiac function; or who may be candidates for device therapy. *(Level of Evidence: C)***

CLASS IIa

1. **Noninvasive imaging to detect myocardial ischemia and viability is reasonable in patients presenting with de novo HF, who have known coronary artery disease (CAD) and no angina, unless the patient is not eligible for revascularization of any kind. *(Level of Evidence: C)***

Table 7. Recommendations for Noninvasive Cardiac Imaging

Recommendations	COR	LOE
Patients with suspected, acute, or new-onset HF should undergo a chest x-ray	I	C
A 2-dimensional echocardiogram with Doppler should be performed for initial evaluation of HF	I	C
Repeat measurement of EF is useful in patients with HF who have had a significant change in clinical status or received treatment that might affect cardiac function or for consideration of device therapy	I	C
Noninvasive imaging to detect myocardial ischemia and viability is reasonable in HF and CAD	IIa	C
Viability assessment is reasonable before revascularization in HF patients with CAD	IIa	B (117–121)
Radionuclide ventriculography or MRI can be useful to assess LVEF and volume	IIa	C
MRI is reasonable when assessing myocardial infiltration or scar	IIa	B (122–124)
Routine repeat measurement of LV function assessment should not be performed	III: No Benefit	B (125,126)

CAD indicates coronary artery disease; COR, Class of Recommendation; EF, ejection fraction; HF, heart failure; LOE, Level of Evidence; LV, left ventricular; LVEF, left ventricular ejection fraction; and MRI, magnetic resonance imaging.

2. Viability assessment is reasonable in select situations when planning revascularization in HF patients with CAD (117–121). *(Level of Evidence: B)*
3. Radionuclide ventriculography or magnetic resonance imaging can be useful to assess left ventricular ejection fraction (LVEF) and volume when echocardiography is inadequate. *(Level of Evidence: C)*
4. Magnetic resonance imaging is reasonable when assessing myocardial infiltrative processes or scar burden (122–124). *(Level of Evidence: B)*

CLASS III: NO BENEFIT

1. Routine repeat measurement of LV function assessment in the absence of clinical status change or treatment interventions should not be performed (125,126). *(Level of Evidence: B)*

5.5. Invasive Evaluation

See Table 8 for a summary of recommendations from this section.

CLASS I

1. Invasive hemodynamic monitoring with a pulmonary artery catheter should be performed to guide therapy in patients who have respiratory distress or clinical evidence of impaired perfusion in whom the adequacy or excess of intracardiac filling pressures cannot be determined from clinical assessment. *(Level of Evidence: C)*

CLASS IIa

1. Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF who have persistent symptoms despite empiric adjustment of standard therapies and
   a. whose fluid status, perfusion, or systemic or pulmonary vascular resistance is uncertain;
   b. whose systolic pressure remains low, or is associated with symptoms, despite initial therapy;
   c. whose renal function is worsening with therapy;
   d. who require parenteral vasoactive agents; or
   e. who may need consideration for mechanical circulatory support (MCS) or transplantation. *(Level of Evidence: C)*
2. When ischemia may be contributing to HF, coronary arteriography is reasonable for patients eligible for revascularization. *(Level of Evidence: C)*
3. Endomyocardial biopsy can be useful in patients presenting with HF when a specific diagnosis is suspected that would influence therapy. *(Level of Evidence: C)*

CLASS III: NO BENEFIT

1. Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute decompensated HF and congestion with symptomatic response to diuretics and vasodilators (127). *(Level of Evidence: B)*

CLASS III: HARM

1. Endomyocardial biopsy should not be performed in the routine evaluation of patients with HF. *(Level of Evidence: C)*

6. Treatment of Stages A to D: Recommendations

6.1. Stage A

CLASS I

1. Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF (28,128–132). *(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)*

6.2. Stage B

See Table 9 for a summary of recommendations from this section.

CLASS I

1. In all patients with a recent or remote history of myocardial infarction (MI) or acute coronary syndrome (ACS) and reduced EF, angiotensin-converting enzyme (ACE) inhibitors should be used to prevent symptomatic HF and reduce mortality (133–135). In patients intolerant to ACE inhibitors, angiotensin-receptor blockers (ARBs) are appropriate unless contraindicated (132,136). *(Level of Evidence: A)*
2. In all patients with a recent or remote history of MI or ACS and reduced EF, evidence-based beta blockers should be used to reduce mortality (137–139). *(Level of Evidence: B)*

Table 8. Recommendations for Invasive Evaluation

Recommendations	COR	LOE
Monitoring with a pulmonary artery catheter should be performed in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate	I	C
Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF with persistent symptoms and/or when hemodynamics are uncertain	IIa	C
When ischemia may be contributing to HF, coronary arteriography is reasonable	IIa	C
Endomyocardial biopsy can be useful in patients with HF when a specific diagnosis is suspected that would influence therapy	IIa	C
Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute HF	III: No Benefit	B (127)
Endomyocardial biopsy should not be performed in the routine evaluation of HF	III: Harm	C

COR indicates Class of Recommendation; HF, heart failure; and LOE, Level of Evidence.

3. In all patients with a recent or remote history of MI or ACS, statins should be used to prevent symptomatic HF and cardiovascular events (140–146). *(Level of Evidence: A)*
4. In patients with structural cardiac abnormalities, including LV hypertrophy, in the absence of a history of MI or ACS, blood pressure should be controlled in accordance with clinical practice guidelines for hypertension to prevent symptomatic HF (28,128–131). *(Level of Evidence: A)*
5. ACE inhibitors should be used in all patients with a reduced EF to prevent symptomatic HF, even if they do not have a history of MI (135,147). *(Level of Evidence: A)*
6. Beta blockers should be used in all patients with a reduced EF to prevent symptomatic HF, even if they do not have a history of MI. *(Level of Evidence: C)*

CLASS IIa

1. To prevent sudden death, placement of an implantable cardioverter-defibrillator (ICD) is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 days post-MI, have an LVEF of 30% or less, are on appropriate medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 year (148). *(Level of Evidence: B)*

CLASS III: HARM

1. Nondihydropyridine calcium channel blockers with negative inotropic effects may be harmful in asymptomatic patients with low LVEF and no symptoms of HF after MI. *(Level of Evidence: C)*

6.3. Stage C

6.3.1. Nonpharmacological Interventions

CLASS I

1. Patients with HF should receive specific education to facilitate HF self-care (149–154). *(Level of Evidence: B)*
2. Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate to improve functional status (155–158). *(Level of Evidence: A)*

CLASS IIa

1. Sodium restriction is reasonable for patients with symptomatic HF to reduce congestive symptoms. *(Level of Evidence: C)*
2. Continuous positive airway pressure can be beneficial to increase LVEF and improve functional status in patients with HF and sleep apnea (159–162). *(Level of Evidence: B)*
3. Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional capacity, exercise duration, health-related quality of life, and mortality (155,157,158,163–166). *(Level of Evidence: B)*

6.3.2. Pharmacological Treatment for Stage C HF*r*EF

CLASS I

1. Measures listed as Class I recommendations for patients in stages A and B are recommended where appropriate for patients in stage C. *(Levels of Evidence: A, B, and C as appropriate)*
2. GDMT as depicted in Figure 1 should be the mainstay of pharmacological therapy for HF*r*EF (134,136,137,167–182). *(Level of Evidence: A)*

6.3.2.1. DIURETICS

See Table 10 for oral diuretics recommended for use in the treatment of chronic HF.

CLASS I

1. Diuretics are recommended in patients with HF*r*EF who have evidence of fluid retention, unless contraindicated, to improve symptoms. *(Level of Evidence: C)*

6.3.2.2. ACE INHIBITORS

See Table 11 for drugs commonly used for HF*r*EF (stage C HF).

CLASS I

1. ACE inhibitors are recommended in patients with HF*r*EF and current or prior symptoms, unless contraindicated, to reduce morbidity and mortality (134,167–169). *(Level of Evidence: A)*

Table 9. Recommendations for Treatment of Stage B HF

Recommendations	COR	LOE	References
In patients with a history of MI and reduced EF, ACE inhibitors or ARBs should be used to prevent HF	I	A	132–136
In patients with MI and reduced EF, evidence-based beta blockers should be used to prevent HF	I	B	137–139
In patients with MI, statins should be used to prevent HF	I	A	140–146
Blood pressure should be controlled to prevent symptomatic HF	I	A	28,128–131
ACE inhibitors should be used in all patients with a reduced EF to prevent HF	I	A	135,147
Beta blockers should be used in all patients with a reduced EF to prevent HF	I	C	N/A
An ICD is reasonable in patients with asymptomatic ischemic cardiomyopathy who are at least 40 d post-MI, have an LVEF $\leq$30%, and on GDMT	IIa	B	148
Nondihydropyridine calcium channel blockers may be harmful in patients with low LVEF	III: Harm	C	N/A

ACE indicates angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; COR, Class of Recommendation; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and N/A, not available.

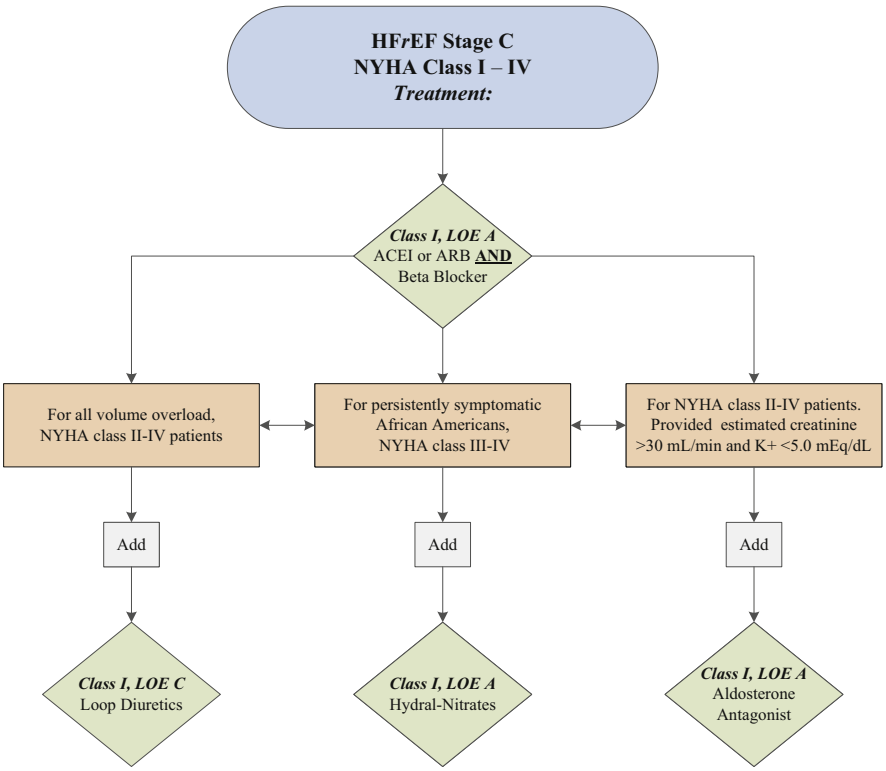

Figure 1. Stage C HF*r*EF: evidence-based, guideline-directed medical therapy. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; HF*r*EF, heart failure with reduced ejection fraction; Hydral-Nitrates, hydralazine and isosorbide dinitrate; LOE, Level of Evidence; and NYHA, New York Heart Association.

6.3.2.3. ANGIOTENSIN-RECEPTOR BLOCKERS

CLASS I

1. **ARBs are recommended in patients with HF*r*EF with current or prior symptoms who are ACE inhibitor intolerant, unless contraindicated, to reduce morbidity and mortality (136,170,171,189). *(Level of Evidence: A)***

CLASS IIa

1. **ARBs are reasonable to reduce morbidity and mortality as alternatives to ACE inhibitors as first-line therapy for patients with HF*r*EF, especially for patients already taking ARBs for other indications, unless contraindicated (190–195). *(Level of Evidence: A)***

CLASS IIb

1. **Addition of an ARB may be considered in persistently symptomatic patients with HF*r*EF who are already being treated with an ACE inhibitor and a beta blocker in whom an aldosterone antagonist is not indicated or tolerated (176,196). *(Level of Evidence: A)***

CLASS III: HARM

1. **Routine combined use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful for patients with HF*r*EF. *(Level of Evidence: C)***

6.3.2.4. BETA BLOCKERS

CLASS I

1. **Use of 1 of the 3 beta blockers proven to reduce mortality (e.g., bisoprolol, carvedilol, and sustained-release metoprolol succinate) is recommended for all patients with current or prior symptoms of HF*r*EF, unless contraindicated, to reduce morbidity and mortality (137,172–175,187). *(Level of Evidence: A)***

6.3.2.5. ALDOSTERONE RECEPTOR ANTAGONISTS

See Table 12 for aldosterone receptor antagonists drug dosing.

CLASS I

1. **Aldosterone receptor antagonists (or mineralocorticoid receptor antagonists) are recommended in patients with NYHA class II–IV HF and who have LVEF of 35% or less, unless contraindicated, to reduce morbidity and mortality. Patients with NYHA class II HF should have a history of prior cardiovascular hospitalization or elevated plasma natriuretic peptide levels to be considered for aldosterone receptor antagonists. Creatinine should be 2.5 mg/dL or less in men or 2.0 mg/dL or less in women (or estimated glomerular filtration rate >30 mL/min/1.73 m^2), and potassium should be less than 5.0 mEq/L. Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation and closely followed thereafter to minimize risk of hyperkalemia and renal insufficiency (181,182,197). *(Level of Evidence: A)***
2. **Aldosterone receptor antagonists are recommended to reduce morbidity and mortality following an acute MI in patients who have LVEF of 40% or less who develop symptoms of HF or have a history of diabetes mellitus, unless contraindicated (184). *(Level of Evidence: B)***

CLASS III: HARM

1. **Inappropriate use of aldosterone receptor antagonists is potentially harmful because of life-threatening hyperkalemia or renal insufficiency when serum creatinine is greater than**

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Table 10. Oral Diuretics Recommended for Use in the Treatment of Chronic HF

Drug	Initial Daily Dose(s)	Maximum Total Daily Dose	Duration of Action
Loop diuretics			
Bumetanide	0.5 to 1.0 mg once or twice	10 mg	4 to 6 h
Furosemide	20 to 40 mg once or twice	600 mg	6 to 8 h
Torsemide	10 to 20 mg once	200 mg	12 to 16 h
Thiazide diuretics			
Chlorothiazide	250 to 500 mg once or twice	1000 mg	6 to 12 h
Chlorthalidone	12.5 to 25.0 mg once	100 mg	24 to 72 h
Hydrochlorothiazide	25 mg once or twice	200 mg	6 to 12 h
Indapamide	2.5 mg once	5 mg	36 h
Metolazone	2.5 mg once	20 mg	12 to 24 h
Potassium-sparing diuretics*			
Amiloride	5 mg once	20 mg	24 h
Spironolactone	12.5 to 25.0 mg once	50 mg†	1 to 3 h
Triamterene	50 to 75 mg twice	200 mg	7 to 9 h
Sequential nephron blockade			
Metolazone‡	2.5 to 10.0 mg once plus loop diuretic	N/A	N/A
Hydrochlorothiazide	25 to 100 mg once or twice plus loop diuretic	N/A	N/A
Chlorothiazide (IV)	500 to 1,000 mg once plus loop diuretic	N/A	N/A

*Eplerenone, although also a diuretic, is primarily used in chronic HF.
†Higher doses may occasionally be used with close monitoring.
‡See Section 7.3.
HF indicates heart failure; IV, intravenous; and N/A, not applicable.

2.5 mg/dL in men or greater than 2.0 mg/dL in women (or estimated glomerular filtration rate <30 mL/min/1.73 m^2), and/or potassium greater than 5.0 mEq/L (198,199). *(Level of Evidence: B)*

6.3.2.6. HYDRALAZINE AND ISOSORBIDE DINITRATE

CLASS I

1. **The combination of hydralazine and isosorbide dinitrate is recommended to reduce morbidity and mortality for patients self-described as African Americans with NYHA class III–IV HF*r*EF receiving optimal therapy with ACE inhibitors and beta blockers, unless contraindicated (179,180). *(Level of Evidence: A)***

CLASS IIa

1. **A combination of hydralazine and isosorbide dinitrate can be useful to reduce morbidity or mortality in patients with current or prior symptomatic HF*r*EF who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency, unless contraindicated (188). *(Level of Evidence: B)***

See Table 13 for a summary of the treatment benefit of GDMT in HF*r*EF.

6.3.2.7. DIGOXIN

CLASS IIa

1. **Digoxin can be beneficial in patients with HF*r*EF, unless contraindicated, to decrease hospitalizations for HF (202–209). *(Level of Evidence: B)***

6.3.2.8. OTHER DRUG TREATMENT

6.3.2.8.1. Anticoagulation

CLASS I

1. **Patients with chronic HF with permanent/persistent/paroxysmal atrial fibrillation (AF) and an additional risk factor for cardioembolic stroke (history of hypertension, diabetes mellitus, previous stroke or transient ischemic attack, or ≥75 years of age) should receive chronic anticoagulant therapy* (210–216). *(Level of Evidence: A)***
2. **The selection of an anticoagulant agent (warfarin, dabigatran, apixaban, or rivaroxaban) for permanent/persistent/paroxysmal AF should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including time in the international normalized ratio therapeutic range if the patient has been taking warfarin. *(Level of Evidence: C)***

CLASS IIa

1. **Chronic anticoagulation is reasonable for patients with chronic HF who have permanent/persistent/paroxysmal AF but are without an additional risk factor for cardioembolic stroke* (211–213,217–219). *(Level of Evidence: B)***

CLASS III: NO BENEFIT

1. **Anticoagulation is not recommended in patients with chronic HF*r*EF without AF, a prior thromboembolic event, or a cardioembolic source (220–222). *(Level of Evidence: B)***

6.3.2.8.2. Statins

CLASS III: NO BENEFIT

1. **Statins are not beneficial as adjunctive therapy when prescribed solely for the diagnosis of HF in the absence of other indications for their use (223–228). *(Level of Evidence: A)***

6.3.2.8.3. Omega-3 Fatty Acids

CLASS IIa

1. **Omega-3 polyunsaturated fatty acid supplementation is reasonable to use as adjunctive therapy in patients with NYHA class II–IV symptoms and HF*r*EF or HF*p*EF, unless contraindicated, to reduce mortality and cardiovascular hospitalizations (229,230). *(Level of Evidence: B)***

*In the absence of contraindications to anticoagulation.

Table 11. Drugs Commonly Used for Stage C HF*r*EF

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 (178)
Enalapril	2.5 mg twice	10 to 20 mg twice	16.6 mg/d (168)
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 (183)
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 (176)
Losartan	25 to 50 mg once	50 to 150 mg once	129 mg/d (177)
Valsartan	20 to 40 mg twice	160 mg twice	254 mg/d (170)
Aldosterone antagonists			
Spironolactone	12.5 to 25.0 mg once	25 mg once or twice	26 mg/d (181)
Eplerenone	25 mg once	50 mg once	42.6 mg/d (184)
Beta blockers			
Bisoprolol	1.25 mg once	10 mg once	8.6 mg/d (185)
Carvedilol	3.125 mg twice	50 mg twice	37 mg/d (186)
Carvedilol CR	10 mg once	80 mg once	N/A
Metoprolol succinate extended release (metoprolol CR/XL)	12.5 to 25.0 mg once	200 mg once	159 mg/d (187)
Hydralazine and isosorbide dinitrate			
Fixed-dose combination (180)	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 (188)	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*r*EF, heart failure with reduced ejection fraction; and N/A, not applicable.

6.3.2.9. DRUGS OF UNPROVEN VALUE OR THAT MAY WORSEN HF

CLASS III: NO BENEFIT

1. **Nutritional supplements as treatment for HF are not recommended in patients with current or prior symptoms of HF*r*EF (231,232). *(Level of Evidence: B)***
2. **Hormonal therapies other than to correct deficiencies are not recommended for patients with current or prior symptoms of HF*r*EF. *(Level of Evidence: C)***

CLASS III: HARM

1. **Drugs known to adversely affect the clinical status of patients with current or prior symptoms of HF*r*EF are potentially harmful and should be avoided or withdrawn**

Table 12. Drug Dosing for Aldosterone Receptor Antagonists

	Eplerenone		Spironolactone	
eGFR (mL/min/1.73 m^2)	≥50	30 to 49	≥50	30 to 49
Initial dose (only if K^+ ≤5 mEq/L)	25 mg once daily	25 mg once every other day	12.5 to 25.0 mg once daily	12.5 mg once daily or every other day
Maintenance dose (after 4 wk for K^+ ≤5 mEq/L)*	50 mg once daily	25 mg once daily	25 mg once or twice daily	12.5 to 25.0 mg once daily

*After dose initiation for K^+, increase≤6.0 mEq/L, or worsening renal function, hold until K^+<5.0 mEq/L. Consider restarting reduced dose after confirming resolution of hyperkalemia/renal insufficiency for at least 72 h.

eGFR indicates estimated glomerular filtration rate; and K^+, potassium.

Adapted from Butler et al. (200).

Table 13. Medical Therapy for Stage C HF*r*EF: Magnitude of Benefit Demonstrated in RCTs

GDMT	RR Reduction in Mortality (%)	NNT for Mortality Reduction (Standardized to 36 mo)	RR Reduction in HF Hospitalizations (%)
ACE inhibitor or ARB	17	26	31
Beta blocker	34	9	41
Aldosterone antagonist	30	6	35
Hydralazine/nitrate	43	7	33

ACE indicates angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; NNT, number needed to treat; RCTs, randomized controlled trials; and RR, relative risk.

Adapted with permission from Fonarow et al. (201).

whenever possible (e.g., most antiarrhythmic drugs, most calcium channel–blocking drugs [except amlodipine], nonsteroidal anti-inflammatory drugs, or thiazolidinediones) (233–244). *(Level of Evidence: B)*

2. **Long-term use of infused positive inotropic drugs is potentially harmful for patients with HF*r*EF, except as palliation for patients with end-stage disease who cannot be stabilized with standard medical treatment (see recommendations for stage D). *(Level of Evidence: C)***

6.3.2.9.1. Calcium Channel Blockers

CLASS III: NO BENEFIT

1. **Calcium channel–blocking drugs are not recommended as routine treatment for patients with HF*r*EF (238,245,246). *(Level of Evidence: A)***

See Table 14 for a summary of recommendations from this section and Table 15 for strategies for achieving optimal GDMT.

6.3.3. Pharmacological Treatment for Stage C HF*p*EF

See Table 16 for a summary of recommendations from this section.

CLASS I

1. **Systolic and diastolic blood pressure should be controlled in patients with HF*p*EF in accordance with published clinical practice guidelines to prevent morbidity (28,247). *(Level of Evidence: B)***
2. **Diuretics should be used for relief of symptoms due to volume overload in patients with HF*p*EF. *(Level of Evidence: C)***

CLASS IIa

1. **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. *(Level of Evidence: C)***
2. **Management of AF according to published clinical practice guidelines in patients with HF*p*EF is reasonable to improve symptomatic HF. *(Level of Evidence: C)***
3. **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. *(Level of Evidence: C)***

CLASS IIb

1. **The use of ARBs might be considered to decrease hospitalizations for patients with HF*p*EF (248). *(Level of Evidence: B)***

CLASS III: NO BENEFIT

1. **Routine use of nutritional supplements is not recommended for patients with HF*p*EF. *(Level of Evidence: C)***

6.3.4. Device Therapy for Stage C HF*r*EF

See Table 17 for a summary of recommendations from this section.

CLASS I

1. **ICD therapy is recommended for primary prevention of sudden cardiac death to reduce total mortality in selected patients with nonischemic dilated cardiomyopathy or ischemic heart disease at least 40 days post-MI with LVEF of 35% or less and NYHA class II or III symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for more than 1 year† (148,249). *(Level of Evidence: A)***
2. **Cardiac resynchronization therapy (CRT) is indicated for patients who have LVEF of 35% or less, sinus rhythm, left bundle-branch block (LBBB) with a QRS duration of 150 ms or greater, and NYHA class II, III, or ambulatory IV symptoms on GDMT. *(Level of Evidence: A for NYHA class III/IV (37,250–252); Level of Evidence: B for NYHA class II (253,254).***
3. **ICD therapy is recommended for primary prevention of sudden cardiac death to reduce total mortality in selected patients at least 40 days post-MI with LVEF of 30% or less and NYHA class I symptoms while receiving GDMT, who have reasonable expectation of meaningful survival for more than 1 year† (255–257). *(Level of Evidence: B)***

CLASS IIa

1. **CRT can be useful for patients who have LVEF of 35% or less, sinus rhythm, a non-LBBB pattern with a QRS duration of 150 ms or greater, and NYHA class III/ambulatory class IV symptoms on GDMT (250–252,254). *(Level of Evidence: A)***
2. **CRT can be useful for patients who have LVEF of 35% or less, sinus rhythm, LBBB with a QRS duration of 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT (250–254,258). *(Level of Evidence: B)***
3. **CRT can be useful in patients with AF and LVEF of 35% or less on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) atrioventricular nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT (259–264). *(Level of Evidence: B)***
4. **CRT can be useful for patients on GDMT who have LVEF of 35% or less and are undergoing placement of a new or replacement device implantation with anticipated requirement for significant (>40%) ventricular pacing (261,265–267). *(Level of Evidence: C)***

†Counseling should be specific to each individual patient and should include documentation of a discussion about the potential for sudden death and nonsudden death from HF or noncardiac conditions. Information should be provided about the efficacy, safety, and potential complications of an ICD and the potential for defibrillation to be inactivated if desired in the future, notably when a patient is approaching end of life. This will facilitate shared decision making between patients, families, and the medical care team about ICDs (31).

Table 14. Recommendations for Pharmacological Therapy for Management of Stage C HF*r*EF

Recommendations	COR	LOE	References
Diuretics			
Diuretics are recommended in patients with HF*r*EF with fluid retention	I	C	N/A
ACE inhibitors			
ACE inhibitors are recommended for all patients with HF*r*EF	I	A	134,167–169
ARBs			
ARBs are recommended in patients with HF*r*EF who are ACE inhibitor intolerant	I	A	136,170,171,189
ARBs are reasonable as alternatives to ACE inhibitors as first-line therapy in HF*r*EF	IIa	A	190–195
Addition of an ARB may be considered in persistently symptomatic patients with HF*r*EF on GDMT	IIb	A	176,196
Routine *combined* use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful	III: Harm	C	N/A
Beta blockers			
Use of 1 of the 3 beta blockers proven to reduce mortality is recommended for all stable patients	I	A	137,172–175,187
Aldosterone receptor antagonists			
Aldosterone receptor antagonists are recommended in patients with NYHA class II–IV who have LVEF $\leq$35%	I	A	181,182,197
Aldosterone receptor antagonists are recommended in patients following an acute MI who have LVEF $\leq$40% with symptoms of HF or DM	I	B	184
Inappropriate use of aldosterone receptor antagonists may be harmful	III: Harm	B	198,199
Hydralazine and isosorbide dinitrate			
The combination of hydralazine and isosorbide dinitrate is recommended for African Americans with NYHA class III–IV HF*r*EF on GDMT	I	A	179,180
A combination of hydralazine and isosorbide dinitrate can be useful in patients with HF*r*EF who cannot be given ACE inhibitors or ARBs	IIa	B	188
Digoxin			
Digoxin can be beneficial in patients with HF*r*EF	IIa	B	202–209
Anticoagulation			
Patients with chronic HF with permanent/persistent/paroxysmal AF and an additional risk factor for cardioembolic stroke should receive chronic anticoagulant therapy*	I	A	210–216
The selection of an anticoagulant agent should be individualized	I	C	N/A
Chronic anticoagulation is reasonable for patients with chronic HF who have permanent/persistent/paroxysmal AF but are without an additional risk factor for cardioembolic stroke*	IIa	B	211–213,217–219
Anticoagulation is not recommended in patients with chronic HF*r*EF without AF, a prior thromboembolic event, or a cardioembolic source	III: No Benefit	B	220–222
Statins			
Statins are not beneficial as adjunctive therapy when prescribed solely for HF	III: No Benefit	A	223–228
Omega-3 fatty acids			
Omega-3 PUFA supplementation is reasonable to use as adjunctive therapy in HF*r*EF or HF*p*EF patients	IIa	B	229,230
Other drugs			
Nutritional supplements as treatment for HF are not recommended in HF*r*EF	III: No Benefit	B	231,232
Hormonal therapies other than to correct deficiencies are not recommended in HF*r*EF	III: No Benefit	C	N/A
Drugs known to adversely affect the clinical status of patients with HF*r*EF are potentially harmful and should be avoided or withdrawn	III: Harm	B	233–244
Long-term use of an infusion of a positive inotropic drug is not recommended and may be harmful except as palliation	III: Harm	C	N/A
Calcium channel blockers			
Calcium channel–blocking drugs are not recommended as routine treatment in HF*r*EF	III: No Benefit	A	238,245,246

*In the absence of contraindications to anticoagulation.

ACE indicates angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin-receptor blocker; COR, Class of Recommendation; DM, diabetes mellitus; GDMT, guideline-directed medical therapy; HF, heart failure; HF*p*EF, heart failure with preserved ejection fraction; HF*r*EF, heart failure with reduced ejection fraction; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; MI, myocardial infarction; N/A, not available; NYHA, New York Heart Association; and PUFA, polyunsaturated fatty acids.

Table 15. Strategies for Achieving Optimal GDMT

1. *Uptitrate in small increments* to the recommended target dose or the highest tolerated dose for those medications listed in Table 11 with an appreciation that some patients cannot tolerate the full recommended doses of all medications, particularly patients with low baseline heart rate or blood pressure or with a tendency to postural symptoms.
2. Certain patients (e.g., the elderly, patients with chronic kidney disease) may require *more frequent visits and laboratory monitoring during dose titration* and more gradual dose changes. However, such vulnerable patients may accrue considerable benefits from GDMT. Inability to tolerate optimal doses of GDMT may change after disease-modifying interventions such as CRT.
3. *Monitor vital signs closely* before and during uptitration, including postural changes in blood pressure or heart rate, particularly in patients with orthostatic symptoms, bradycardia, and/or "low" systolic blood pressure (e.g., 80 to 100 mm Hg).
4. *Alternate adjustments of different medication classes* (especially ACE inhibitors/ARBs and beta blockers) listed in Table 11. Patients with elevated or normal blood pressure and heart rate may tolerate faster incremental increases in dosages.
5. *Monitor renal function and electrolytes* for rising creatinine and hyperkalemia, recognizing that an initial rise in creatinine may be expected and does not necessarily require discontinuation of therapy; discuss tolerable levels of creatinine above baseline with a nephrologist if necessary.
6. Patients may complain of *symptoms of fatigue and weakness* with dosage increases; in the absence of instability in vital signs, reassure them that these symptoms are often transient and usually resolve within a few days of changes in therapy.
7. *Discourage sudden spontaneous discontinuation of GDMT* medications by the patient and/or other clinicians without discussion with managing clinicians.
8. *Carefully review doses of other medications* for HF symptom control (e.g., diuretics, nitrates) during uptitration.
9. *Consider temporary adjustments in dosages of GDMT* during acute episodes of noncardiac illnesses (e.g., respiratory infections, risk of dehydration, etc).
10. *Educate patients, family members, and other clinicians* about the expected benefits of achieving GDMT, including an understanding of the potential benefits of myocardial reverse remodeling, increased survival, and improved functional status and HRQOL.

ACE indicates angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; and HRQOL, health-related quality of life.

Table 16. Recommendations for Treatment of HF*p*EF

Recommendations	COR	LOE
Systolic and diastolic blood pressure should be controlled according to published clinical practice guidelines	I	B (28,247)
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 (248)
Nutritional supplementation is not recommended in HF*p*EF	III: No Benefit	C

ACE indicates angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; COR, Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; HF*p*EF, heart failure with preserved ejection fraction; and LOE, Level of Evidence.

CLASS IIb

1. **The usefulness of implantation of an ICD is of uncertain benefit to prolong meaningful survival in patients with a high risk of nonsudden death as predicted by frequent hospitalizations, advanced frailty, or comorbidities such as systemic malignancy or severe renal dysfunction† (268–271). *(Level of Evidence: B)***
2. **CRT may be considered for patients who have LVEF of 35% or less, sinus rhythm, a non-LBBB pattern with a QRS duration of 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT (254,272). *(Level of Evidence: B)***
3. **CRT may be considered for patients who have LVEF of 35% or less, sinus rhythm, a non-LBBB pattern with a QRS duration of 150 ms or greater, and NYHA class II symptoms on GDMT (253,254). *(Level of Evidence: B)***
4. **CRT may be considered for patients who have LVEF of 30% or less, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration of 150 ms or greater, and NYHA class I symptoms on GDMT (253,254). *(Level of Evidence: C)***

CLASS III: NO BENEFIT

1. **CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with a QRS duration of less than 150 ms (253,254,272). *(Level of Evidence: B)***
2. **CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year (37). *(Level of Evidence: C)***

See Figure 2, indications for CRT therapy algorithm.

†Counseling should be specific to each individual patient and should include documentation of a discussion about the potential for sudden death and nonsudden death from HF or noncardiac conditions. Information should be provided about the efficacy, safety, and potential complications of an ICD and the potential for defibrillation to be inactivated if desired in the future, notably when a patient is approaching end of life. This will facilitate shared decision making between patients, families, and the medical care team about ICDs (31).

Table 17. Recommendations for Device Therapy for Management of Stage C HF

Recommendations	COR	LOE	References
ICD therapy is recommended for primary prevention of SCD in selected patients with HF*r*EF at least 40 d post-MI with LVEF ≤35% and NYHA class II or III symptoms on chronic GDMT, who are expected to live >1 y*	I	A	148,249
CRT is indicated for patients who have LVEF ≤35%, sinus rhythm, and LBBB with a QRS ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT	I	A (NYHA class III/IV)	37,250–252
		B (NYHA class II)	253,254
ICD therapy is recommended for primary prevention of SCD in selected patients with HF*r*EF at least 40 d post-MI with LVEF ≤30% and NYHA class I symptoms while receiving GDMT, who are expected to live >1 y*	I	B	255–257
CRT can be useful for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with a QRS ≥150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT	IIa	A	250–252,254
CRT can be useful for patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT	IIa	B	250–254,258
CRT can be useful in patients with AF and LVEF ≤35% on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or rate control allows near 100% ventricular pacing with CRT	IIa	B	259–264
CRT can be useful for patients on GDMT who have LVEF ≤35% and are undergoing new or replacement device implantation with anticipated ventricular pacing (>40%)	IIa	C	261,265–267
An ICD is of uncertain benefit to prolong meaningful survival in patients with a high risk of nonsudden death such as frequent hospitalizations, frailty, or severe comorbidities*	IIb	B	268–271
CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT	IIb	B	254,272
CRT may be considered for patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with a QRS ≥150 ms, and NYHA class II symptoms on GDMT	IIb	B	253,254
CRT may be considered for patients who have LVEF ≤30%, ischemic etiology of HF, sinus rhythm, LBBB with QRS ≥150 ms, and NYHA class I symptoms on GDMT	IIb	C	253,254
CRT is not recommended for patients with NYHA class I or II symptoms and a non-LBBB pattern with QRS <150 ms	III: No Benefit	B	253,254,272
CRT is not indicated for patients whose comorbidities and/or frailty limit survival to <1 y	III: No Benefit	C	37

*Counseling should be specific to each individual patient and should include documentation of a discussion about the potential for sudden death and nonsudden death from HF or noncardiac conditions. Information should be provided about the efficacy, safety, and potential complications of an ICD and the potential for defibrillation to be inactivated if desired in the future, notably when a patient is approaching end of life. This will facilitate shared decision making between patients, families, and the medical care team about ICDs (31).

AF indicates atrial fibrillation; AV, atrioventricular; COR, Class of Recommendation; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; LBBB, left bundle-branch block; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; and SCD, sudden cardiac death.

6.4. Stage D

See Table 18 for the European Society of Cardiology definition of advanced HF and Table 19 for clinical events and findings useful for identifying patients with advanced HF.

6.4.1. Water Restriction

CLASS IIa

1. **Fluid restriction (1.5 to 2 L/d) is reasonable in stage D, especially in patients with hyponatremia, to reduce congestive symptoms. *(Level of Evidence: C)***

6.4.2. Inotropic Support

See Table 20 for inotropic agents used in HF management and Table 21 for a summary of recommendations from this section.

CLASS I

1. **Until definitive therapy (e.g., coronary revascularization, MCS, heart transplantation) or resolution of the acute precipitating problem, patients with cardiogenic shock should receive temporary intravenous inotropic support to maintain systemic perfusion and preserve end-organ performance. *(Level of Evidence: C)***

CLASS IIa

1. **Continuous intravenous inotropic support is reasonable as "bridge therapy" in patients with stage D HF refractory to GDMT and device therapy who are eligible for and awaiting MCS or cardiac transplantation (275,276). *(Level of Evidence: B)***

CLASS IIb

1. **Short-term, continuous intravenous inotropic support may be reasonable in those hospitalized patients presenting with documented severe systolic dysfunction who present with low blood pressure and significantly depressed cardiac output to maintain systemic perfusion and preserve end-organ performance (277–279). *(Level of Evidence: B)***
2. **Long-term, continuous intravenous inotropic support may be considered as palliative therapy for symptom control in select patients with stage D HF despite optimal GDMT and device therapy who are not eligible for either MCS or cardiac transplantation (280–282). *(Level of Evidence: B)***

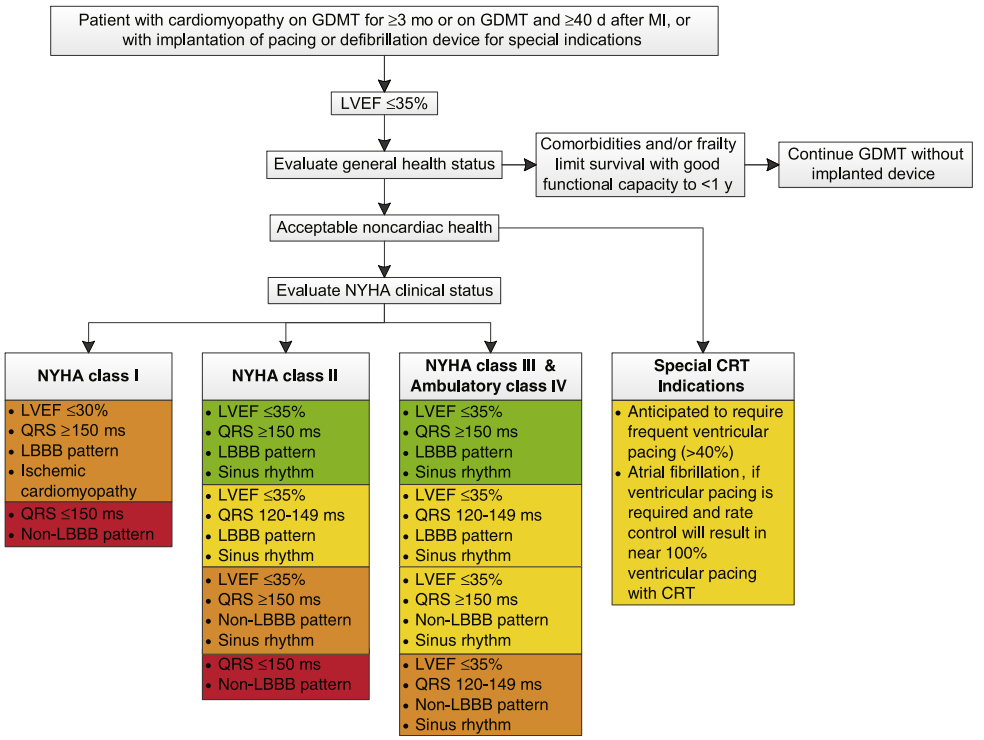

Figure 2. Indications for CRT therapy algorithm. CRT indicates cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy-defibrillator; GDMT, guideline-directed medical therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LBBB, left bundle-branch block; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and NYHA, New York Heart Association.

Table 18. ESC Definition of Advanced HF

1. Severe symptoms of HF with dyspnea and/or fatigue at rest or with minimal exertion (NYHA class III or IV)
2. Episodes of fluid retention (pulmonary and/or systemic congestion, peripheral edema) and/or reduced cardiac output at rest (peripheral hypoperfusion)
3. Objective evidence of severe cardiac dysfunction shown by at least 1 of the following:
   a. LVEF <30%
   b. Pseudonormal or restrictive mitral inflow pattern
   c. Mean PCWP >16 mm Hg and/or RAP >12 mm Hg by PA catheterization
   d. High BNP or NT-proBNP plasma levels in the absence of noncardiac causes
4. Severe impairment of functional capacity shown by 1 of the following:
   a. Inability to exercise
   b. 6-Minute walk distance ≤300 m
   c. Peak $\dot{V}o_2$ <12 to 14 mL/kg/min
5. History of ≥1 HF hospitalization in past 6 mo
6. Presence of all the previous features despite "attempts to optimize" therapy, including diuretics and GDMT, unless these are poorly tolerated or contraindicated, and CRT when indicated

BNP indicates B-type natriuretic peptide; CRT, cardiac resynchronization therapy; ESC, European Society of Cardiology; GDMT, guideline-directed medical therapy; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure; and RAP, right atrial pressure.

Adapted from Metra et al. (33).

Table 19. Clinical Events and Findings Useful for Identifying Patients With Advanced HF

Repeated (≥2) hospitalizations or ED visits for HF in the past year
Progressive deterioration in renal function (e.g., rise in BUN and creatinine)
Weight loss without other cause (e.g., cardiac cachexia)
Intolerance to ACE inhibitors due to hypotension and/or worsening renal function
Intolerance to beta blockers due to worsening HF or hypotension
Frequent systolic blood pressure <90 mm Hg
Persistent dyspnea with dressing or bathing requiring rest
Inability to walk 1 block on the level ground due to dyspnea or fatigue
Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose over 160 mg/d and/or use of supplemental metolazone therapy
Progressive decline in serum sodium, usually to <133 mEq/L
Frequent ICD shocks

ACE indicates angiotensin-converting enzyme; BUN, blood urea nitrogen; ED, emergency department; HF, heart failure; and ICD, implantable cardioverter-defibrillator.

Adapted from Russell et al. (274).

Table 20. Intravenous Inotropic Agents Used in Management of HF

Inotropic Agent	Dose (mcg/kg)		Drug Kinetics and Metabolism	Effects				Adverse Effects	Special Considerations
	Bolus	Infusion (/min)		CO	HR	SVR	PVR		
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

BP indicates blood pressure; CI, contraindication; CO, cardiac output; F, fever; H, hepatic; HA, headache; HF, heart failure; HR, heart rate; LFT, liver function test; MAO-I, monoamine oxidase inhibitor; N, nausea; N/A, not applicable; N/R, not recommended; P, plasma; PDE, phosphodiesterase; PVR, pulmonary vascular resistance; R, renal; SVR, systemic vascular resistance; T, tachyarrhythmias; and $t_{1/2}$, elimination half-life.

CLASS III: HARM

1. **Long-term use of either continuous or intermittent, intravenous parenteral positive inotropic agents, in the absence of specific indications or for reasons other than palliative care, is potentially harmful in the patient with HF (172,283–288). *(Level of Evidence: B)***

2. **Use of parenteral inotropic agents in hospitalized patients without documented severe systolic dysfunction, low blood pressure, or impaired perfusion and evidence of significantly depressed cardiac output, with or without congestion, is potentially harmful (277–279). *(Level of Evidence: B)***

Table 21. Recommendations for Inotropic Support, MCS, and Cardiac Transplantation

Recommendations	COR	LOE	References
Inotropic support			
Cardiogenic shock pending definitive therapy or resolution	I	C	N/A
BTT or MCS in stage D refractory to GDMT	IIa	B	275,276
Short-term support for threatened end-organ dysfunction in hospitalized patients with stage D and severe HF*r*EF	IIb	B	277–279
Long-term support with continuous infusion palliative therapy in select stage D HF	IIb	B	280–282
Routine intravenous use, either continuous or intermittent, is potentially harmful in stage D HF	III: Harm	B	172,283–288
Short-term intravenous use in hospitalized patients without evidence of shock or threatened end-organ performance is potentially harmful	III: Harm	B	277–279
MCS			
MCS is beneficial in carefully selected* patients with stage D HF in whom definitive management (e.g., cardiac transplantation) is anticipated or planned	IIa	B	289–296
Nondurable MCS is reasonable as a "bridge to recovery" or a "bridge to decision" for carefully selected* patients with HF and acute profound disease	IIa	B	297–300
Durable MCS is reasonable to prolong survival for carefully selected* patients with stage D HF*r*EF	IIa	B	301–304
Cardiac transplantation			
Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management	I	C	305

*Although optimal patient selection for MCS remains an active area of investigation, general indications for referral for MCS therapy include patients with LVEF <25% and NYHA class III–IV functional status despite GDMT, including, when indicated, CRT, with either high predicted 1- to 2-year mortality (e.g., as suggested by markedly reduced peak oxygen consumption and clinical prognostic scores) or dependence on continuous parenteral inotropic support. Patient selection requires a multidisciplinary team of experienced advanced HF and transplantation cardiologists, cardiothoracic surgeons, nurses, and ideally, social workers and palliative care clinicians.

BTT indicates bridge to transplant; COR, Class of Recommendation; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; N/A, not applicable; and NYHA, New York Heart Association.

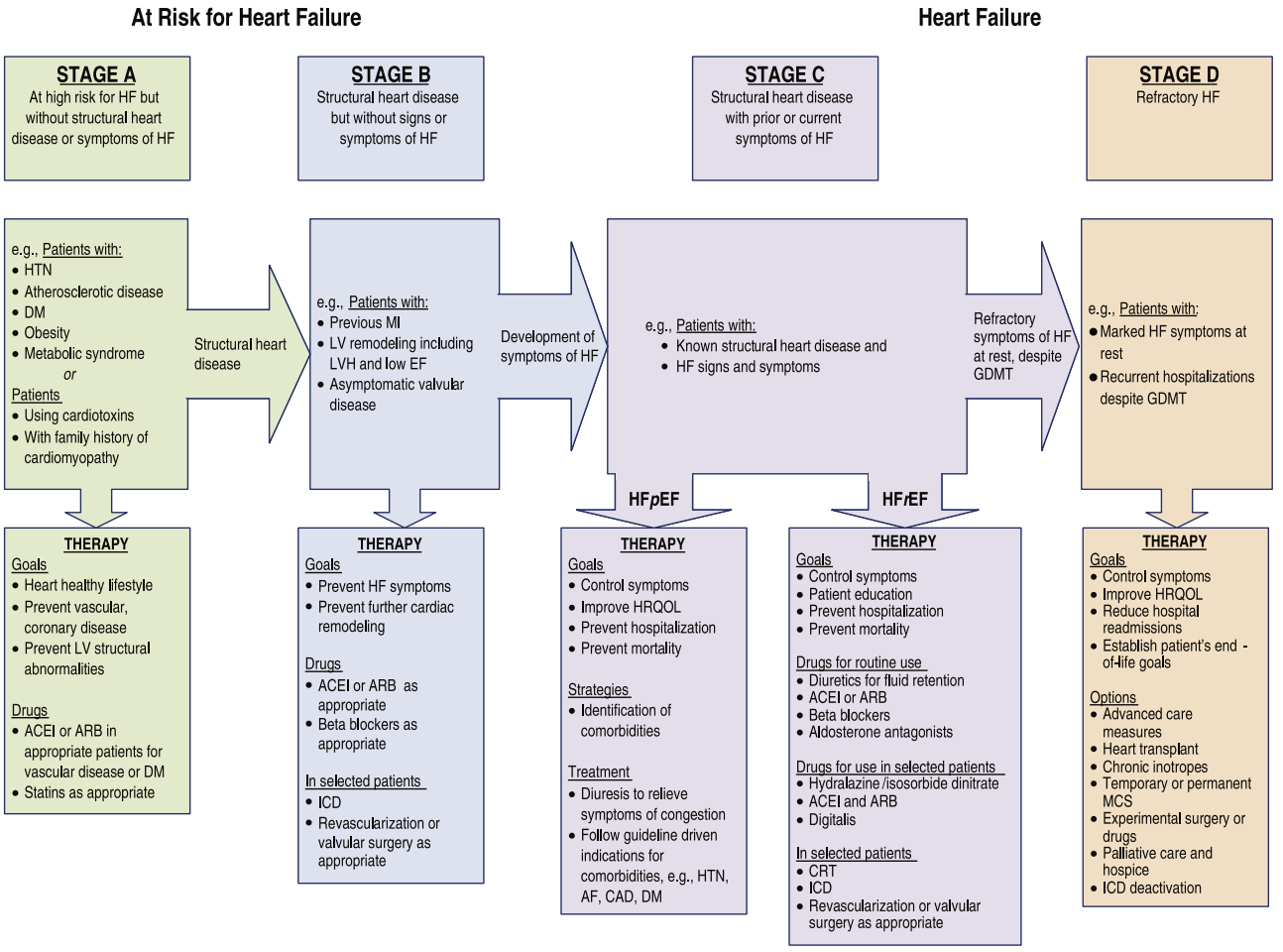

Figure 3. Stages in the development of HF and recommended therapy by stage. ACEI indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; DM, diabetes mellitus; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HF*p*EF, heart failure with preserved ejection fraction; HF*r*EF, heart failure with reduced ejection fraction; HRQOL, health-related quality of life; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LV, left ventricular; LVH, left ventricular hypertrophy; MCS, mechanical circulatory support; and MI, myocardial infarction. Adapted from Hunt et al (37).

6.4.3. Mechanical Circulatory Support

CLASS IIa

1. **MCS is beneficial in carefully selected‡ patients with stage D HF*r*EF in whom definitive management (e.g., cardiac transplantation) or cardiac recovery is anticipated or planned (289–296). *(Level of Evidence: B)***
2. **Nondurable MCS, including the use of percutaneous and extracorporeal ventricular assist devices, is reasonable as a "bridge to recovery" or a "bridge to decision" for carefully selected‡ patients with HF*r*EF with acute, profound hemodynamic compromise (297–300). *(Level of Evidence: B)***
3. **Durable MCS is reasonable to prolong survival for carefully selected‡ patients with stage D HF*r*EF (301–304). *(Level of Evidence: B)***

6.4.4. Cardiac Transplantation

CLASS I

1. **Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management (305). *(Level of Evidence: C)***

See Figure 3 for the stages in the development of HF.

7. The Hospitalized Patient: Recommendations

See Table 22 for a summary of recommendations from this section and Figure 4 for the classification of patients presenting with acutely decompensated HF.

‡Although optimal patient selection for MCS remains an active area of investigation, general indications for referral for MCS therapy include patients with LVEF <25% and NYHA class III–IV functional status despite GDMT, including, when indicated, CRT, with either high predicted 1- to 2-year mortality (e.g., as suggested by markedly reduced peak oxygen consumption and clinical prognostic scores) or dependence on continuous parenteral inotropic support. Patient selection requires a multidisciplinary team of experienced advanced HF and transplantation cardiologists, cardiothoracic surgeons, nurses, and ideally, social workers and palliative care clinicians.

Table 22. Recommendations for Therapies in the Hospitalized HF Patient

Recommendations	COR	LOE	References
HF patients hospitalized with fluid overload should be treated with intravenous diuretics	I	B	310,311
HF patients receiving loop diuretic therapy should receive an initial parenteral dose greater than or equal to their chronic oral daily dose; then dose should be serially adjusted	I	B	312
HF*r*EF patients requiring HF hospitalization on GDMT should continue GDMT except in cases of hemodynamic instability or where contraindicated	I	B	307–309
Initiation of beta-blocker therapy at a low dose is recommended after optimization of volume status and discontinuation of intravenous agents	I	B	307–309
Thrombosis/thromboembolism prophylaxis is recommended for patients hospitalized with HF	I	B	22,324–328
Serum electrolytes, urea nitrogen, and creatinine should be measured during titration of HF medications, including diuretics	I	C	N/A
When diuresis is inadequate, it is reasonable to	IIa		
a. give higher doses of intravenous loop diuretics; or		B	37,312
b. add a second diuretic (e.g., thiazide)		B	313–316
Low-dose dopamine infusion may be considered with loop diuretics to improve diuresis	IIb	B	317,318
Ultrafiltration may be considered for patients with obvious volume overload	IIb	B	319
Ultrafiltration may be considered for patients with refractory congestion	IIb	C	N/A
Intravenous nitroglycerin, nitroprusside, or nesiritide may be considered an adjuvant to diuretic therapy for stable patients with HF	IIb	A	320–323
In patients hospitalized with volume overload and severe hyponatremia, vasopressin antagonists may be considered	IIb	B	330,331

COR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; LOE, Level of Evidence; and N/A, not available.

7.1. Precipitating Causes of Decompensated HF

CLASS I

1. **ACS precipitating acute HF decompensation should be promptly identified by electrocardiogram and serum biomarkers, including cardiac troponin testing, and treated optimally as appropriate to the overall condition and prognosis of the patient. *(Level of Evidence: C)***
2. **Common precipitating factors for acute HF should be considered during initial evaluation, as recognition of these conditions is critical to guide appropriate therapy. (*Level of Evidence: C*)**

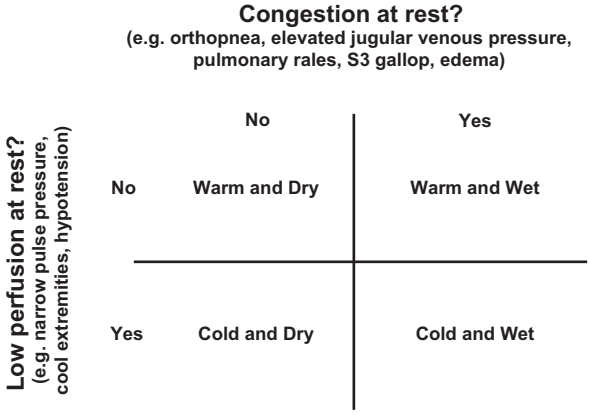

Figure 4. Classification of patients presenting with acutely decompensated heart failure. Adapted with permission from Nohria et al. (306).

7.2. Maintenance of GDMT During Hospitalization

CLASS I

1. **In patients with HF*r*EF experiencing a symptomatic exacerbation of HF requiring hospitalization during chronic maintenance treatment with GDMT, it is recommended that GDMT be continued in the absence of hemodynamic instability or contraindications (307–309). *(Level of Evidence: B)***
2. **Initiation of beta-blocker therapy is recommended after optimization of volume status and successful discontinuation of intravenous diuretics, vasodilators, and inotropic agents. Beta-blocker therapy should be initiated at a low dose and only in stable patients. Caution should be used when initiating beta blockers in patients who have required inotropes during their hospital course (307–309). *(Level of Evidence: B)***

7.3. Diuretics in Hospitalized Patients

CLASS I

1. **Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to reduce morbidity (310,311). *(Level of Evidence: B)***
2. **If patients are already receiving loop diuretic therapy, the initial intravenous dose should equal or exceed their chronic oral daily dose and should be given as either intermittent boluses or continuous infusion. Urine output and signs and symptoms of congestion should be serially assessed, and the diuretic dose should be adjusted accordingly to relieve symptoms, reduce volume excess, and avoid hypotension (312). *(Level of Evidence: B)***

3. The effect of HF treatment should be monitored with careful measurement of fluid intake and output, vital signs, body weight that is determined at the same time each day, and clinical signs and symptoms of systemic perfusion and congestion. Daily serum electrolytes, urea nitrogen, and creatinine concentrations should be measured during the use of intravenous diuretics or active titration of HF medications. *(Level of Evidence: C)*

CLASS IIa

1. When diuresis is inadequate to relieve symptoms, it is reasonable to intensify the diuretic regimen using either:
   a. higher doses of intravenous loop diuretics (37,312) *(Level of Evidence: B);*
   b. addition of a second (e.g., thiazide) diuretic (313–316). *(Level of Evidence: B)*

CLASS IIb

1. Low-dose dopamine infusion may be considered in addition to loop diuretic therapy to improve diuresis and better preserve renal function and renal blood flow (317,318). *(Level of Evidence: B)*

7.4. Renal Replacement Therapy—Ultrafiltration

CLASS IIb

1. Ultrafiltration may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight (319). *(Level of Evidence: B)*
2. Ultrafiltration may be considered for patients with refractory congestion not responding to medical therapy. *(Level of Evidence: C)*

7.5. Parenteral Therapy in Hospitalized HF

CLASS IIb

1. If symptomatic hypotension is absent, intravenous nitroglycerin, nitroprusside, or nesiritide may be considered an adjuvant to diuretic therapy for relief of dyspnea in patients admitted with acutely decompensated HF (320–323). *(Level of Evidence: A)*

7.6. Venous Thromboembolism Prophylaxis in Hospitalized Patients

CLASS I

1. A patient admitted to the hospital with decompensated HF should receive venous thromboembolism prophylaxis with an anticoagulant medication if the risk−benefit ratio is favorable (22,324–328). *(Level of Evidence: B)*

7.7. Arginine Vasopressin Antagonists

CLASS IIb

1. In patients hospitalized with volume overload, including HF, who have persistent severe hyponatremia and are at risk for or having active cognitive symptoms despite water restriction and maximization of GDMT, vasopressin antagonists may be considered in the short term to improve serum sodium concentration in hypervolemic, hyponatremic states with either a V_2 receptor selective or a nonselective vasopressin antagonist (330,331). *(Level of Evidence: B)*

7.8. Inpatient and Transitions of Care

See Table 23 for a summary of recommendations from this section.

CLASS I

1. The use of performance improvement systems and/or evidence-based systems of care is recommended in the hospital and early postdischarge outpatient setting to identify appropriate HF patients for GDMT, provide clinicians with useful reminders to advance GDMT, and assess the clinical response (151,332–338). *(Level of Evidence: B)*
2. Throughout the hospitalization as appropriate, before hospital discharge, at the first postdischarge visit, and in

Table 23. Recommendations for Hospital Discharge

Recommendations or Indications	COR	LOE	References
Performance improvement systems in the hospital and early postdischarge outpatient setting to identify HF for GDMT	I	B	151,332–338
Before hospital discharge, at the first postdischarge visit, and in subsequent follow-up visits, the following should be addressed: a. initiation of GDMT if not done or contraindicated; b. causes of HF, barriers to care, and limitations in support; c. assessment of volume status and blood pressure with adjustment of HF therapy; d. optimization of chronic oral HF therapy; e. renal function and electrolytes; f. management of comorbid conditions; g. HF education, self-care, emergency plans, and adherence; and h. palliative or hospice care	I	B	57,337,339–341
Multidisciplinary HF disease management for patients at high risk for hospital readmission	I	B	336,342–344
A follow-up visit within 7 to 14 d and a telephone follow-up within 3 d of hospital discharge are reasonable	IIa	B	345,346
Use of clinical risk-prediction tools and/or biomarkers to identify higher-risk patients are reasonable	IIa	B	62

OR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; and LOE, Level of Evidence.

subsequent follow-up visits, the following should be addressed (57,337,339–341). *(Level of Evidence: B):*

a. initiation of GDMT if not previously established and not contraindicated;
b. precipitant causes of HF, barriers to optimal care transitions, and limitations in postdischarge support;
c. assessment of volume status and supine/upright hypotension with adjustment of HF therapy as appropriate;
d. titration and optimization of chronic oral HF therapy;
e. assessment of renal function and electrolytes where appropriate;
f. assessment and management of comorbid conditions;
g. reinforcement of HF education, self-care, emergency plans, and need for adherence; and
h. consideration for palliative care or hospice care in selected patients.

3. Multidisciplinary HF disease-management programs are recommended for patients at high risk for hospital readmission, to facilitate the implementation of GDMT, to address different barriers to behavioral change, and to reduce the risk of subsequent rehospitalization for HF (336,342–344). *(Level of Evidence: B)*

CLASS IIa

1. Scheduling an early follow-up visit (within 7 to 14 days) and early telephone follow-up (within 3 days) of hospital discharge are reasonable (345,346). *(Level of Evidence: B)*
2. Use of clinical risk-prediction tools and/or biomarkers to identify patients at higher risk for postdischarge clinical events are reasonable (62). *(Level of Evidence: B)*

8. Important Comorbidities in HF

Although there are additional and important comorbidities that occur in patients with HF as referenced in Table 24, it remains uncertain how best to generate specific recommendations, given the status of current evidence.

9. Surgical/Percutaneous/Transcatheter Interventional Treatments of HF: Recommendations

See Table 25 for a summary of recommendations from this section.

CLASS I

1. Coronary artery revascularization via coronary artery bypass graft surgery (CABG) or percutaneous intervention is indicated for patients (HF*p*EF and HF*r*EF) on GDMT with angina and suitable coronary anatomy, especially for a left main stenosis (>50%) or left main equivalent disease (11,13,15,348). *(Level of Evidence: C)*

CLASS IIa

1. CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction (EF 35% to 50%) and significant (≥70% diameter stenosis) multivessel CAD or proximal left anterior descending coronary artery stenosis when viable myocardium is present in the region of intended revascularization (348–350). *(Level of Evidence: B)*
2. CABG or medical therapy is reasonable to improve morbidity and cardiovascular mortality for patients with severe LV dysfunction (EF <35%), HF, and significant CAD (351,352). *(Level of Evidence: B)*
3. Surgical aortic valve replacement is reasonable for patients with critical aortic stenosis and a predicted surgical mortality of no greater than 10% (353). *(Level of Evidence: B)*
4. Transcatheter aortic valve replacement after careful candidate consideration is reasonable for patients with critical aortic stenosis who are deemed inoperable (354). *(Level of Evidence: B)*

CLASS IIb

1. CABG may be considered with the intent of improving survival in patients with ischemic heart disease with severe LV systolic dysfunction (EF <35%) and operable coronary anatomy whether or not viable myocardium is present (352,355,356). *(Level of Evidence: B)*

Table 24. Ten Most Common Co-Occurring Chronic Conditions Among Medicare Beneficiaries With Heart Failure (N = 4,947,918), 2011

Beneficiaries Age ≥65 y (N=4,376,150)*			Beneficiaries Age <65 y (N=5,71,768)†		
	N	%		N	%
Hypertension	3,685,373	84.2	Hypertension	461,235	80.7
Ischemic heart disease	3,145,718	71.9	Ischemic heart disease	365,889	64.0
Hyperlipidemia	2,623,601	60.0	Diabetes	338,687	59.2
Anemia	2,200,674	50.3	Hyperlipidemia	325,498	56.9
Diabetes	2,027,875	46.3	Anemia	284,102	49.7
Arthritis	1,901,447	43.5	Chronic kidney disease	257,015	45.0
Chronic kidney disease	1,851,812	42.3	Depression	207,082	36.2
COPD	1,311,118	30.0	Arthritis	201,964	35.3
Atrial fibrillation	1,247,748	28.5	COPD	191,016	33.4
Alzheimer's disease/dementia	1,207,704	27.6	Asthma	888,16	15.5

*Mean No. of conditions is 6.1; median is 6.
†Mean No. of conditions is 5.5; median is 5.
COPD indicates chronic obstructive pulmonary disease.
Data source: Centers for Medicare and Medicaid Services administrative claims data, January 2011–December 2011, from the Chronic Condition Warehouse (CCW), ccwdata.org (347).

Table 25. Recommendations for Surgical/Percutaneous/Transcatheter Interventional Treatments of HF

Recommendations	COR	LOE	References
CABG or percutaneous intervention is indicated for HF patients on GDMT with angina and suitable coronary anatomy, especially significant left main stenosis or left main equivalent	I	C	11,13,15,348
CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction and significant multivessel CAD or proximal LAD stenosis when viable myocardium is present	IIa	B	348–350
CABG or medical therapy is reasonable to improve morbidity and mortality for patients with severe LV dysfunction (EF <35%), HF, and significant CAD	IIa	B	351,352
Surgical aortic valve replacement is reasonable for patients with critical aortic stenosis and a predicted surgical mortality of no greater than 10%	IIa	B	353
Transcatheter aortic valve replacement is reasonable for patients with critical aortic stenosis who are deemed inoperable	IIa	B	354
CABG may be considered in patients with ischemic heart disease, severe LV systolic dysfunction, and operable coronary anatomy whether or not viable myocardium is present	IIb	B	352,355,356
Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit	IIb	B	357–360
Surgical reverse remodeling or LV aneurysmectomy may be considered in HF*r*EF for specific indications, including intractable HF and ventricular arrhythmias	IIb	B	361

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; COR, Class of Recommendation; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; LAD, left anterior descending; LOE, Level of Evidence; and LV, left ventricular.

2. **Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit and should only be considered after careful candidate selection and with a background of GDMT (357–360). *(Level of Evidence: B)***
3. **Surgical reverse remodeling or LV aneurysmectomy may be considered in carefully selected patients with HF*r*EF for specific indications, including intractable HF and ventricular arrhythmias (361). *(Level of Evidence: B)***

10. Coordinating Care for Patients With Chronic HF: Recommendations

CLASS I

1. **Effective systems of care coordination with special attention to care transitions should be deployed for every patient with chronic HF that facilitate and ensure effective care that is designed to achieve GDMT and prevent hospitalization (333,336,362–377). *(Level of Evidence: B)***
2. **Every patient with HF should have a clear, detailed, and evidence-based plan of care that ensures the achievement of GDMT goals, effective management of comorbid conditions, timely follow-up with the healthcare team, appropriate dietary and physical activities, and compliance with secondary prevention guidelines for cardiovascular disease. This plan of care should be updated regularly and made readily available to all members of each patient's healthcare team (14). *(Level of Evidence: C)***
3. **Palliative and supportive care is effective for patients with symptomatic advanced HF to improve quality of life (31,378–381). *(Level of Evidence: B)***

11. Quality Metrics/Performance Measures: Recommendations

CLASS I

1. **Performance measures based on professionally developed clinical practice guidelines should be used with the goal of improving quality of care for HF (334,343,382). *(Level of Evidence: B)***

CLASS IIa

1. **Participation in quality improvement programs and patient registries based on nationally endorsed, clinical practice guideline–based quality and performance measures can be beneficial in improving quality of HF care (334,343). *(Level of Evidence: B)***

See Table 26 for a revised ACCF/AHA/PCPI 2011 HF measurement set.

12. Evidence Gaps and Future Research Directions

Despite the objective evidence compiled by the writing committee on the basis of hundreds of clinical trials, there are huge gaps in our knowledge base about many fundamental aspects of HF care. Some key examples include an effective management strategy for patients with HF*p*EF beyond blood pressure control; a convincing method to use biomarkers in the optimization of medical therapy; the recognition and treatment of cardiorenal syndrome; and the critical need for improving patient adherence to therapeutic regimens. Even the widely embraced dictum of sodium restriction in HF is not well supported by current evidence. Moreover, the majority of the clinical trials that inform GDMT were designed around the primary endpoint of mortality, so that there is less certainty about the impact of therapies on the health-related quality of life of patients. It is also of major concern that the majority of randomized controlled trials failed to randomize a sufficient number of the elderly, women, and underrepresented minorities, thus limiting our insight into these important patient cohorts. A growing body of studies on patient-centered outcomes research is likely to address some of these deficiencies, but time will be required.

HF is a syndrome with a high prevalence of comorbidities and multiple chronic conditions, but most guidelines are developed for patients with a single disease. Nevertheless, the coexistence of additional diseases such as arthritis, renal

Table 26. ACCF/AHA/AMA-PCPI 2011 HF Measurement Set

Measure	Description*	Care Setting	Level of Measurement
1. LVEF assessment	Percentage of patients aged ≥18 y with a diagnosis of HF for whom the quantitative or qualitative results of a recent or prior (any time in the past) LVEF assessment is documented within a 12-mo period	Outpatient	Individual practitioner
2. LVEF assessment	Percentage of patients aged ≥18 y with a principal discharge diagnosis of HF with documentation in the hospital record of the results of an LVEF assessment performed either before arrival or during hospitalization, OR documentation in the hospital record that LVEF assessment is planned for after discharge	Inpatient	• Individual practitioner • Facility
3. Symptom and activity assessment	Percentage of patient visits for patients aged ≥18 y with a diagnosis of HF with quantitative results of an evaluation of both current level of activity and clinical symptoms documented	Outpatient	Individual practitioner
4. Symptom management†	Percentage of patient visits for patients aged ≥18 y with a diagnosis of HF and with quantitative results of an evaluation of both level of activity AND clinical symptoms documented in which patient symptoms have improved or remained consistent with treatment goals since last assessment OR patient symptoms have demonstrated clinically important deterioration since last assessment with a documented plan of care	Outpatient	Individual practitioner
5. Patient self-care education†‡	Percentage of patients aged ≥18 y with a diagnosis of HF who were provided with self-care education on ≥3 elements of education during ≥1 visits within a 12-mo period	Outpatient	Individual practitioner
6. Beta-blocker therapy for LVSD (outpatient and inpatient setting)	Percentage of patients aged ≥18 y with a diagnosis of HF with a current or prior LVEF <40% who were prescribed beta-blocker therapy with bisoprolol, carvedilol, or sustained-release metoprolol succinate either within a 12-mo period when seen in the outpatient setting or at hospital discharge	Inpatient and outpatient	• Individual practitioner • Facility
7. ACE inhibitor or ARB therapy for LVSD (outpatient and inpatient setting)	Percentage of patients aged ≥18 y with a diagnosis of HF with a current or prior LVEF <40% who were prescribed ACE inhibitor or ARB therapy either within a 12-mo period when seen in the outpatient setting or at hospital discharge	Inpatient and outpatient	• Individual practitioner • Facility
8. Counseling about ICD implantation for patients with LVSD on combination medical therapy†‡	Percentage of patients aged ≥18 y with a diagnosis of HF with current LVEF ≤35% despite ACE inhibitor/ARB and beta-blocker therapy for at least 3 mo who were counseled about ICD placement as a treatment option for the prophylaxis of sudden death	Outpatient	Individual practitioner
9. Postdischarge appointment for HF patients	Percentage of patients, regardless of age, discharged from an inpatient facility to ambulatory care or home health care with a principal discharge diagnosis of HF for whom a follow-up appointment was scheduled and documented, including location, date, and time for a follow-up office visit or home health visit (as specified)	Inpatient	Facility

N.B., Regarding test measure no. 8, implantation of an ICD must be consistent with published guidelines. This measure is intended to promote counseling only.

*Refer to the complete measures for comprehensive information, including measure exception.

†Test measure designated for use in internal quality improvement programs only. These measures are not appropriate for any other purpose (e.g., pay for performance, physician ranking, or public reporting programs).

‡New measure.

ACCF indicates American College of Cardiology Foundation; ACE, angiotensin-converting enzyme; AHA, American Heart Association; AMA-PCPI, American Medical Association–Physician Consortium for Performance Improvement; ARB, angiotensin-receptor blocker; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; and LVSD, left ventricular systolic dysfunction.

Adapted from Bonow et al. (383).

insufficiency, diabetes mellitus, or chronic lung disease with the HF syndrome should logically require a modification of treatment, outcome assessment, or follow-up care. About 25% of Americans have multiple chronic conditions; this figure rises to 75% in those >65 years of age, including the diseases referred to above, as well as asthma, hypertension, cognitive disorders, or depression (347). Most randomized controlled trials in HF specifically excluded patients with significant

other comorbidities from enrollment, thus limiting our ability to generalize our recommendations to many real-world patients. Therefore, the clinician must, as always, practice the art of using the best of the guideline recommendations as they apply to a specific patient.

Future research will need to focus on novel pharmacological therapies, especially for patients hospitalized with HF; regenerative cell-based therapies to restore myocardium; and new device platforms that will either improve existing technologies (e.g., CRT, ICD, left ventricular assist device) or introduce simpler, less morbid devices that are capable of changing the natural history of HF. What is critically needed is an evidence base that clearly identifies best processes of care, especially in the transition from hospital to home. Finally, preventing the burden of this disease through more successful risk modification, sophisticated screening, perhaps using specific omics technologies (i.e., systems biology), or effective treatment interventions that reduce the progression from stage A to stage B is an urgent need.

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Key Words: ACCF/AHA Practice Guidelines ■ cardio-renal physiology/pathophysiology ■ congestive heart failure ■ CV surgery: transplantation, ventricular assistance, cardiomyopathy ■ epidemiology ■ health policy and outcome research ■ heart failure ■ other heart failure.

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2013 ACCF/AHA Guideline for the Management of Heart Failure

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Clyde W. Yancy, *Chair*	Northwestern University—Chief, Division of Cardiology and Magerstadt Professor of Medicine	None	None	None	None	None	None	None
Mariell Jessup, *Vice Chair*	University of Pennsylvania—Professor of Medicine	None	None	None	• Amgen • Celladon • HeartWare	None	None	7.4.4 7.4.5 7.4.6 10
Biykem Bozkurt	Michael E. DeBakey VA Medical Center—The Mary and Gordon Cain Chair and Professor of Medicine	None	None	None	None	None	None	None
Javed Butler	Emory Healthcare—Director of Heart Failure Research; Emory University School of Medicine—Professor of Medicine	• Amgen • CardioMEMS • Gambro • Takeda	None	None	None	• Amgen • Biotronic • Boston Scientific • CardioMEMS • Corthera† • FoldRx • iOcopsys • Johnson & Johnson • Medtronic • Thoratec • World Heart	None	6.4 7.1 7.2 7.3.2 7.3.3 7.3.4 7.4.4 7.4.5 7.4.6 8.6 8.7 10
Donald E. Casey, Jr	Clinically Integrated Physician Network, NYU Langone Medical Center—Vice President and Medical Director	None	None	None	None	None	None	None
Mark H. Drazner	University of Texas Southwestern Medical Center—Professor, Internal Medicine	None	None	None	• HeartWare • Scios/Johnson & Johnson†	• Medtronic • Thoratec†	None	7.1 7.2 7.3.2 7.3.4 7.4.4 7.4.5 7.4.6 8.6 8.7 10
Gregg C. Fonarow	Director Ahmanson—UCLA Cardiomyopathy Center; Co-Chief—UCLA Division of Cardiology	• Gambro (formerly CHF Solutions) • Medtronic • Novartis† • Takeda	None	None	• Gambro (formerly CHF Solutions) • Novartis†	• Medtronic	None	7.1 7.2 (Class IIa) 7.3.2 7.3.4 8.3 8.4 8.7 10
Stephen A. Geraci	Quillen College of Medicine/East Tennessee State University—Chairman of Internal Medicine	None	None	None	None	None	None	None

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Appendix 1. Continued

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Tamara Horwich	Ahmanson—UCLA Cardiomyopathy Center—Assistant Professor of Medicine, Cardiology	None	None	None	None	None	None	None
James L. Januzzi	Harvard Medical School—Associate Professor of Medicine; Massachusetts General Hospital—Director, Cardiac Intensive Care Unit	• Critical Diagnostics† • Roche Diagnostics†	None	None	• Critical Diagnostics† • Roche Diagnostics†	None	None	6.2 6.3
Maryl R. Johnson	University of Wisconsin–Madison, Professor of Medicine, Director Heart Failure and Transplantation	None	None	None	None	None	None	None
Edward K. Kasper	Johns Hopkins Hospital—E. Cowles Andrus Professor in Cardiology, Director, Clinical Cardiology	None	None	None	None	None	None	None
Wayne C. Levy	University of Washington—Professor of Medicine, Division of Cardiology	• Cardiac Dimensions† • CardioMEMS • GE/Scios/ Johnson & Johnson	• Amarin • Boehringer Ingelheim • GlaxoSmithKline	None	• Amgen† • HeartWare†	• Amgen • Epocrates • GE Healthcare • HeartWare • Thoratec	None	6.4 6.5 7.1 7.2 7.3.1 7.3.2 7.3.4 7.4.5 8.3 8.6 8.7 10
Frederick A. Masoudi	University of Colorado, Denver—Associate Professor of Medicine, Division of Cardiology	None	None	None	None	None	None	None
Patrick E. McBride	University of Wisconsin School of Medicine and Public Health—Professor of Medicine and Family Medicine, Associate Dean for Students, Associate Director, Preventive Cardiology	None	None	None	None	None	None	None
John J.V. McMurray	University of Glasgow, Scotland, BHF Glasgow Cardiovascular Research Center—Professor of Medical Cardiology	None	None	None	• GlaxoSmithKline† • Novartis • Roche (DSMB)	• Novartis (PARADIGM–PI)	None	6.2 6.3 7.1 7.2 (Class I and Class III) 7.3.2 8.3 8.7
Judith E. Mitchell	SUNY Downstate Medical Center—Director, Heart Failure Center; Associate Professor of Medicine	None	None	None	None	None	None	None

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Appendix 1. Continued

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Pamela N. Peterson	University of Colorado, Denver Health Medical Center—Associate Professor of Medicine, Division of Cardiology	None	None	None	None	None	None	None
Barbara Riegel	University of Pennsylvania School of Nursing—Professor	None	None	None	None	None	None	None
Flora Sam	Boston University School of Medicine, Whitaker Cardiovascular Institute—Associate Professor of Medicine, Division of Cardiology/ Cardiomyopathy Program	None	None	None	None	None	None	None
Lynne W. Stevenson	Brigham and Women's Hospital Cardiovascular Division—Director, Cardiomyopathy and Heart Failure Program	None	None	None	• Biosense Webster	None	None	7.3.4
W.H. Wilson Tang	Cleveland Clinic Foundation—Associate Professor of Medicine, Research Director for Heart Failure/Transplant	• Medtronic • St. Jude Medical	None	None	• Abbott† • FoldRx • Johnson & Johnson • Medtronic† • St. Jude Medical†	None	None	6.2 6.3 7.1 7.2 7.3.2 7.3.3 7.3.4 8.6 8.7 10
Emily J. Tsai	Temple University School of Medicine—Assistant Professor of Medicine, Cardiology	None	None	None	None	None	None	None
Bruce L. Wilkoff	Cleveland Clinic—Director, Cardiac Pacing and Tachyarrhythmia Devices; Director, Clinical EP Research	None	None	None	• Biotronic • Boston Scientific • Medtronic • St. Jude Medical	None	None	7.2 (Class IIa) 7.3.4 10

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of $\geq$5% of the voting stock or share of the business entity, or ownership of $\geq$\$10,000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACCF/AHA, a person has a *relevant* relationship IF: a) The *relationship or interest relates* to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) The *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the document, or makes a competing drug or device addressed in the *document*; or c) The *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the document.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply. Section numbers pertain to those in the full-text guideline.

†Indicates significant relationship.

DSMB indicates Data Safety Monitoring Board; EP, electrophysiology; NYU, New York University; PARADIGM, a Multicenter, Randomized, Double-blind, Parallel Group, Active-controlled Study to Evaluate the Efficacy and Safety of LCZ696 Compared to Enalapril on Morbidity and Mortality in Patients With Chronic Heart Failure and Reduced Ejection Fraction; PI, Principal Investigator; SUNY, State University of New York; UCLA, University of California, Los Angeles; and VA, Veterans Affairs.

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Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)—2013 ACCF/AHA Guideline for the Management of Heart Failure

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Nancy Albert	Official Reviewer—ACCF/AHA Task Force on Practice Guidelines	Kaufman Center for Heart Failure—Senior Director of Nursing Research	• BG Medicine • Medtronic • Merck†	None	None	None	None	None
Kathleen Grady	Official Reviewer—AHA	Bluhm Cardiovascular Institute— Administrative Director, Center for Heart Failure	None	None	None	None	None	None
Paul Hauptman	Official Reviewer—AHA	St Louis University School of Medicine—Professor of Internal Medicine, Division of Cardiology	• BG Medicine • BioControl Medical • Otsuka*	None	None	None	• EvaHeart†	None
Hector Ventura	Official Reviewer—ACCF Board of Governors	Ochsner Clinic Foundation—Director, Section of Cardiomyopathy and Heart Transplantation	• Otsuka	• Actelion	None	None	None	None
Mary Norine Walsh	Official Reviewer—ACCF Board of Trustees	St. Vincent Heart Center of Indiana—Medical Director	• United Healthcare	None	None	None	None	None
Jun Chiong	Organizational Reviewer—ACCP	Loma Linda University—Associate Clinical Professor of Medicine	None	None	None	None	• Otsuka (DSMB)	None
David DeLurgio	Organizational Reviewer—HRS	The Emory Clinic—Associate Professor, Director of EP Laboratory	None	None	None	None	None	None
Folashade Omole	Organizational Reviewer—AAFP	Morehouse School of Medicine—Associate Professor of Clinical Family Medicine	None	None	None	None	None	None
Robert Rich, Jr	Organizational Reviewer—AAFP	Bladen Medical Associates—Family Practice	None	None	None	None	None	None
David Taylor	Organizational Reviewer—ISHLT	Cleveland Clinic, Department of Cardiology—Professor of Medicine	None	None	None	None	• Biotronix† • Genentech† • HeartWare† • ISHLT • Novartis† • St. Jude's Medical†	None
Kimberly Birtcher	Content Reviewer—ACCF Cardiovascular Team Council	University of Houston College of Pharmacy—Clinical Professor	None	None	None	None	None	None
Kay Blum	Content Reviewer—ACCF Cardiovascular Team Council	Medstar Southern Maryland Hospital Center—Nurse Practitioner	None	None	None	None	None	None

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Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Michael Chan	Content Reviewer—ACCF Cardiovascular Team Council	Royal Alexandra Hospital—Co-Director, Heart Function Program; University of Alberta—Associate Clinical Professor of Medicine	None	None	None	None	• Medtronic	None
Jane Chen	Content Reviewer—ACCF EP Committee	Washington University School of Medicine—Assistant Professor of Medicine	• Medtronic • St. Jude Medical	None	None	None	None	None
Michael Clark	Content Reviewer—ACCF Cardiovascular Team Council	North Texas Cardiology and EP—Associate Professor	None	• Abbott Pharma	None	None	None	None
Marco Costa	Content Reviewer—ACCF Imaging Council	University Hospital for Cleveland—Professor of Medicine	• Abbott Vascular • Boston Scientific • Cardiokinetix* • Medtronic • St. Jude Medical	• Daiichi-Sankyo • Eli Lilly • Sanofi	None	None	• Abbott Vascular* • Boston Scientific • Cardiokinetix† • Medtronic* • St. Jude Medical	None
Anita Deswal	Content Reviewer	Baylor College of Medicine—Associate Professor of Medicine	None	None	None	• Amgen† • Novartis†	None	None
Steven Dunn	Content Reviewer—ACCF Prevention Committee	University of Virginia Health System—Clinical Pharmacy Specialist	None	None	None	None	None	None
Andrew Epstein	Content Reviewer	University of Pennsylvania—Professor of Medicine	• Biotronic • Boehringer Ingelheim • Medtronic • Zoll	None	None	• Biosense Webster* • Boston Scientific* • Cameron Health*	• Boston Scientific* • St. Jude Medical*	None
Justin Ezekowitz	Content Reviewer—AHA	Mazankowski Alberta Heart Institute—Director, Heart Function Clinic	• Abbott Labs • AstraZeneca • Pfizer	None	None	• Amgen • Bristol-Myers Squibb	None	None
Gerasimos Filippatos	Content Reviewer	University of Athens—Department of Cardiology	None	None	None	None	• Corthera • Vifor	None
Linda Gillam	Content Reviewer—ACCF Imaging Council	Morristown Medical Center—Professor of Cardiology	None	None	None	None	• Edwards Lifesciences†	None
Paul Heidenreich	Content Reviewer	Stanford VA Palo Alto Medical Center—Assistant Professor of Medicine	None	None	None	• Medtronic†	None	None
Paul Hess	Content Reviewer—ACCF EP Committee	Duke University School of Medicine—Fellow	None	None	None	None	None	None
Sharon Ann Hunt	Content Reviewer	Stanford University Medical Center—Professor, Department of Cardiovascular Medicine	None	None	None	None	None	None

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Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Charles McKay	Content Reviewer—ACCF Council on Cardiovascular Care for Older Adults	Harbor-UCLA Medical Center—Professor of Medicine	None	None	None	None	None	None
James McClurken	Content Reviewer—ACCF Surgeons' Scientific Council	Temple University School of Medicine—Director of Cardiothoracic Perioperative Services	None	None	None	None	None	None
Wayne Miller	Content Reviewer—ACCF Heart Failure and Transplant Council	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None
Rick Nishimura	Content Reviewer	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None
Donna Petruccelli	Content Reviewer—ACCF Heart Failure and Transplant Council	Lehigh Valley Health Network—Heart Failure Nurse Practitioner/Clinical Nurse Specialist, Center for Advanced Heart Failure	None	None	None	None	None	None
Geetha Raghuveer	Content Reviewer—ACCF Board of Governors	Children's Mercy Hospital—Associate Professor of Pediatrics	None	None	None	None	None	None
Pasala Ravichandran	Content Reviewer—ACCF Surgeons' Scientific Council	Oregon Health & Science University—Associate Professor	None	None	None	None	None	None
Michael Rich	Content Reviewer—ACCF Council on Cardiovascular Care for Older Adults	Washington University School of Medicine—Professor of Medicine	None	None	None	None	None	None
Anitra Romfh	Content Reviewer—ACCF Adult Congenital and Pediatric Cardiology Council	Children's Hospital Boston—Clinical Fellow in Pediatrics	None	None	None	None	None	None
Andrea Russo	Content Reviewer—ACCF Task Force on Appropriate Use Criteria	Cooper University Hospital—Professor of Medicine	• Biotronik • Boston Scientific • Cameron Health • Medtronic • St. Jude Medical	None	None	• Cameron Health • Medtronic	None	None
Dipan Shah	Content Reviewer—ACCF Imaging Council	Methodist DeBakey Heart Center—Director	None	• AstraZeneca* • Lantheus Medical Imaging	None	None	• Astellas Pharma • Siemens Medical Solutions*	None
Randy Starling	Content Reviewer	Cleveland Clinic, Department of Cardiovascular Medicine—Vice Chairman	• Novartis	None	None	None	• Biotronik • Medtronic	None
Karen Stout	Content Reviewer—ACCF Adult Congenital and Pediatric Cardiology Council	University of Washington—Director, Adult Congenital Heart Disease Program	None	None	None	None	None	None

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Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
John Teerlink	Content Reviewer	San Francisco VA Medical Center—Professor of Medicine	• Amgen* • Anexon • CardioMEMS* • Cytokinetics • Novartis* • Scios/ Johnson & Johnson • St. Jude Medical* • Trevena	None	None	None	• Amgen* • Merck • Novartis*	None
Robert Touchon	Content Reviewer—ACCF Prevention Committee	Marshall University, Joan C. Edwards School of Medicine—Professor of Medicine	None	None	None	None	None	None
Hiroyuki Tsutsui	Content Reviewer	Hokkaido University—Professor of Medicine	• Daiichi-Sankyo* • Novartis* • Pfizer • Takeda*	None	None	None	None	None
Robert Vincent	Content Reviewer—ACCF Adult Congenital and Pediatric Cardiology Council	Emory University School of Medicine—Professor of Pediatrics	None	None	None	None	• AGA	None

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant to this document. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$10,000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review.

According to the ACCF/AHA, a person has a *relevant* relationship IF: a) The *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) The *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) The *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Significant relationship.

†No financial benefit.

AAFP indicates American Academy of Family Physicians; ACCF, American College of Cardiology Foundation; ACCP, American College of Chest Physicians AHA, American Heart Association; DSMB, data safety monitoring board; EP, electrophysiology; HRS, Heart Rhythm Society; ISHLT, International Society for Heart and Lung Transplantation; UCLA, University of California, Los Angeles; and VA, Veterans Affairs.