

OHSU HEALTH SYSTEM OFFICE OF CLINICAL INTEGRATION AND EVIDENCE-BASED PRACTICE

GUIDELINE FOR THE MANAGEMENT OF HEART FAILURE

Background: Heart failure (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. 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. 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.[1, 2]

Epidemiology: The lifetime risk of developing HF is 20% for Americans ≥ 40 years of age. In the United States, HF incidence has largely remained stable over 7/16/2018 5:14:00 PM the past several decades, with $>650,000$ new HF cases diagnosed annually. 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. Approximately 5.1 million persons in the United States have clinically manifest HF, and the prevalence continues to rise. HFrEF and HFpEF each make up about half of the overall HF burden. One in 5 Americans will be >65 years of age by 2050. 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. Heart Failure 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.[1, 2]

Definitions:

HF with Reduced Ejection Fraction (HFrEF): In approximately half of patients with HFrEF, variable degrees of LV enlargement may accompany HFrEF. The definition of HFrEF has varied. For the present guideline, HFrEF is defined as the clinical diagnosis of HF and EF $\leq 40\%$. Those with LV systolic dysfunction commonly have elements of diastolic dysfunction as well. Although coronary artery disease (CAD) with antecedent myocardial infarction (MI) is a major cause of HFrEF, many other risk factors may lead to LV enlargement and HFrEF.[1, 2]

HF with Preserved Ejection Fraction (HFpEF)

In patients with clinical HF, studies estimate that the prevalence of HFpEF is approximately 50% (range 40% to 71%). The cutoff for HFpEF is classified as EF $>50\%$. Because some of these patients do not have entirely normal EF but also do not have major reduction in systolic function, the term preserved EF has been used. Patients with an EF in the range of 41% to 49% represent an intermediate group, with no guidelines specific to this group. These patients are often treated for underlying risk factors and comorbidities and with GDMT similar to that used in patients with HFrEF. The diagnosis of HFpEF is more challenging than the diagnosis of HFrEF because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. In the general population, patients with HFpEF are usually older women with a history of hypertension. [1, 2]

Guideline Eligibility Criteria: Adults being managed for heart failure in any clinical setting.

Guideline Exclusion Criteria:

- Children <18 years with heart failure
- Adults with congenital heart lesions

Clinical Practice Recommendations

OHSU Health System fully endorses the 2013 and 2017 American Heart Association Guidelines for the Management of Heart Failure. The AHA guideline summaries are listed below with specific aspects highlighted as they pertain to clinical practice throughout OHSU Health System.

Initial and Serial Evaluation of the Heart Failure Patient[1, 2]

History and Physical Examination: Recommendations

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.

-GRADE Strength of Recommendation (SoR): Strong; AHA Level of Evidence (LoE): C

In patients with idiopathic DCM, a 3-generational family history should be obtained to aid in establishing the diagnosis of familial DCM. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Diagnostic Tests: Recommendations

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Serial monitoring, when indicated, should include serum electrolytes and renal function. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

A 12-lead ECG should be performed initially on all patients presenting with HF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Biomarkers: Recommendations

The usefulness of BNP- or NT-proBNP-guided therapy for acutely decompensated HF is not well established. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

For patients at risk of developing HF, natriuretic peptide biomarker-based screening followed by team-based care, including a cardiovascular specialist optimizing GDMT, can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B-R*

In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

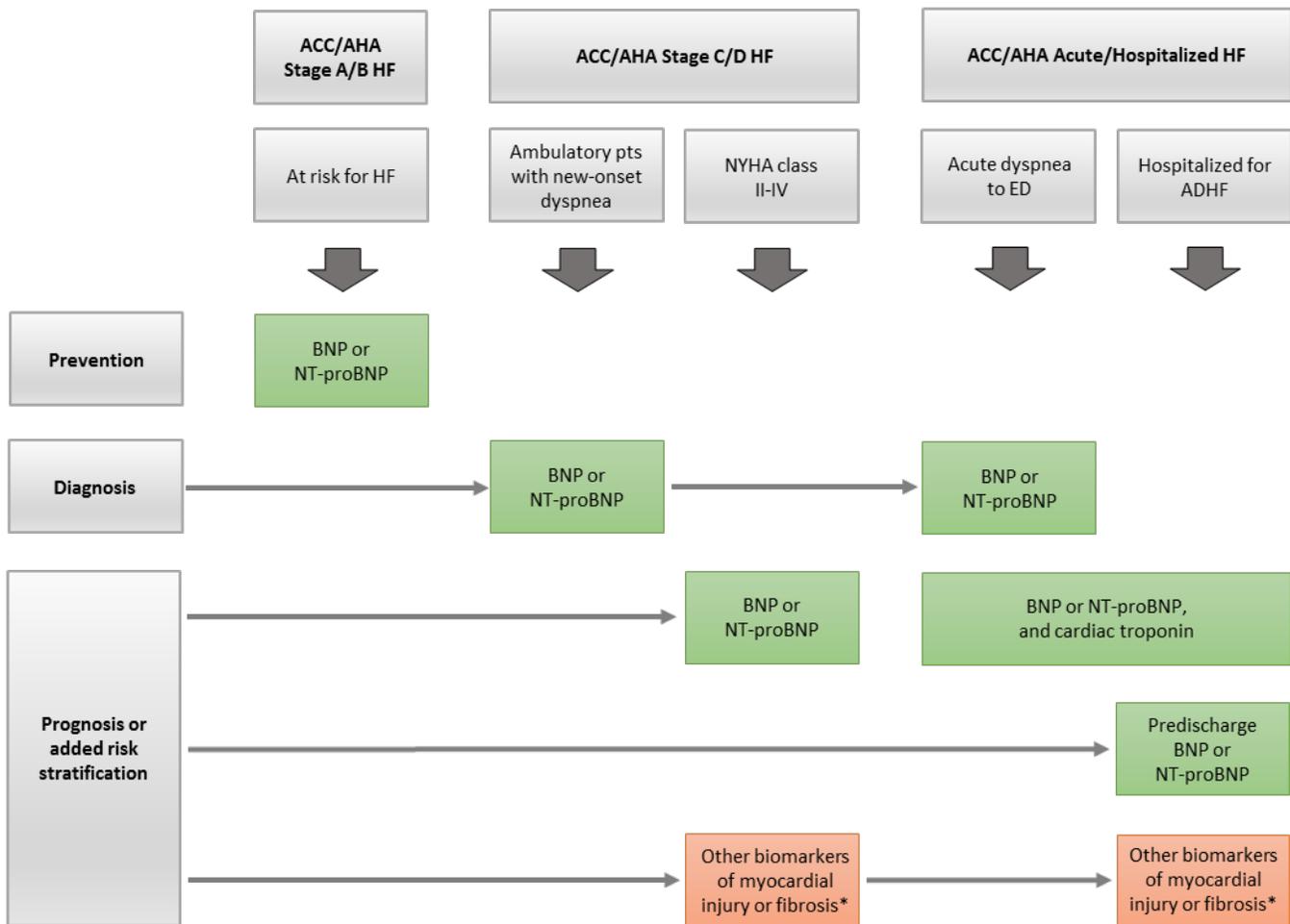
Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

During a HF hospitalization, a predischarge natriuretic peptide level can be useful to establish a post discharge prognosis. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B-R*

In patients with chronic HF, measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, may be considered for additive risk stratification. *-GRADE Strength of Recommendation: Conditional; AHA Level of Evidence: B-NR*

Figure 1. Biomarkers Indications for Use



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

Adapted from 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure; Yancy, et al.

Noninvasive Cardiac Imaging: Recommendations

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Noninvasive imaging to detect myocardial ischemia and viability is reasonable in patients presenting with de novo HF who have known CAD and no angina unless the patient is not eligible for revascularization of any kind. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Viability assessment is reasonable in select situations when planning revascularization in HF patients with CAD. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Radionuclide ventriculography or magnetic resonance imaging can be useful to assess LVEF and volume when echocardiography is inadequate. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Magnetic resonance imaging is reasonable when assessing myocardial infiltrative processes or scar burden. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Routine repeat measurement of LV function assessment in the absence of clinical status change or treatment interventions should not be performed. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Invasive Evaluation Recommendations

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

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 MCS or transplantation.

-*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

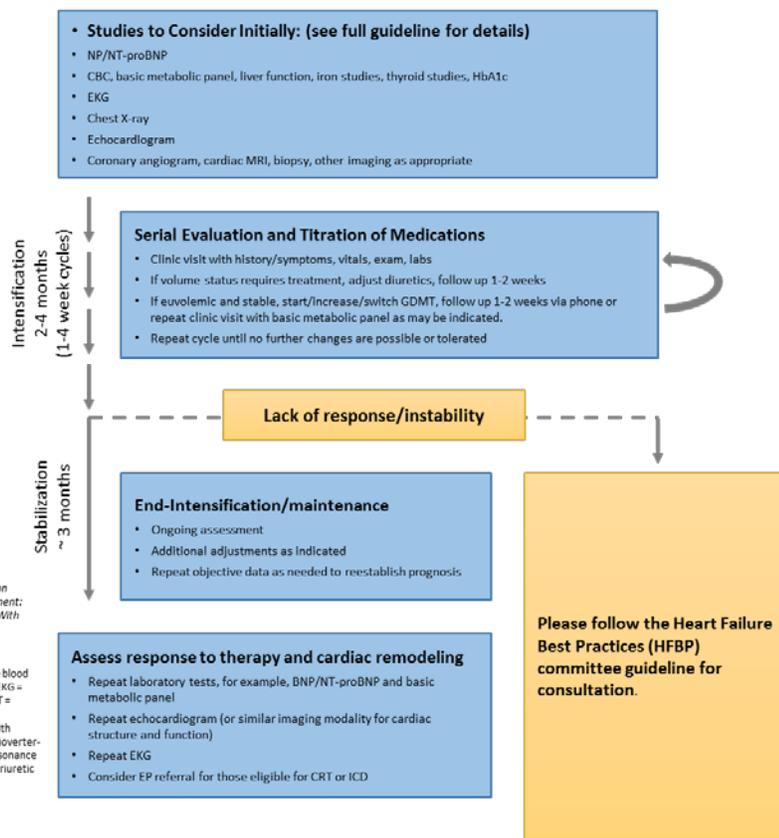
When ischemia may be contributing to HF, coronary arteriography is reasonable for patients eligible for revascularization. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Endomyocardial biopsy can be useful in patients presenting with HF when a specific diagnosis is suspected that would influence therapy. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Endomyocardial biopsy should not be performed in the routine evaluation of patients with HF. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

Figure 2. Testing and Medication Titration Following Diagnosis of HFrEF



[3]

Adapted from 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction, Yancy, et al. p. 13

BNP = B-type natriuretic peptide; CBC = complete blood count; CRT = cardiac resynchronization therapy; EKG = electrocardiogram; EP = electrophysiology; GDMT = guideline-directed medical therapy; HbA1c = hemoglobin A1c; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; IV = intravenous; MRI = magnetic resonance imaging; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

Treatment of Stages A to D[1, 2, 4]
Stage A: Recommendations

Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF. - GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

Evidence: C

Stage B: Recommendations

In all patients with a recent or remote history of MI or ACS and reduced EF, ACE inhibitors should be used to prevent symptomatic HF and reduce mortality. In patients intolerant of ACE inhibitors, ARBs are appropriate unless contraindicated. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

In all patients with a recent or remote history of MI or ACS, statins should be used to prevent symptomatic HF and cardiovascular events. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

To prevent sudden death, placement of an 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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Nondihydropyridine calcium channel blockers with negative inotropic effects may be harmful in asymptomatic patients with low LVEF and no symptoms of HF after MI. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

Stage C: Recommendations

Patients with HF should receive specific education to facilitate HF self-care. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Sodium restriction is reasonable for patients with symptomatic HF to reduce congestive symptoms. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

Unless contraindicated, all patients with HFrEF should be referred for cardiac rehabilitation. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Pharmacological Treatment for Stage C HF with Reduced Ejection Fraction (HFrEF): Recommendations

GDMT should be the mainstay of pharmacological therapy for HFrEF. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A



Diuretics are recommended in patients with HFrEF who have evidence of fluid retention, unless contraindicated, to improve symptoms. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (*LoE: A*) OR ARBs (*LoE:A*) OR ARNI (*LoE:B-R*) in conjunction with evidence-based beta blockers and aldosterone antagonists in selected patients is recommended for patients with chronic HFrEF to reduce morbidity and mortality. *-GRADE Strength of Recommendation: Strong*

The use of ACE inhibitors is beneficial for patients with prior or current symptoms of chronic HFrEF to reduce morbidity and mortality. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HFrEF who are intolerant to ACE inhibitors because of cough or angioedema. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: BR*

Routine combined use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful for patients with HFrEF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

ARNI should not be administered concomitantly with ACE inhibitors or within 36 hours of the last dose of an ACE inhibitor. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B-R*

ARNI should not be administered to patients with a history of angioedema. *-Consensus Statement*

Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF $\leq 35\%$) who are receiving guideline-directed management, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B-R*

Use of 1 of the 3 beta blockers proven to reduce mortality (i.e., bisoprolol, carvedilol, and sustained-release metoprolol succinate) is recommended for all patients with current or prior symptoms of HFrEF, unless contraindicated, to reduce morbidity and mortality. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

Aldosterone receptor antagonists [or mineralocorticoid receptor antagonists] are recommended in patients with NYHA class II-IV and who have LVEF of 35% or less, unless contraindicated, to reduce morbidity and mortality. Patients with NYHA class II 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 m²), 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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

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 who have a history of diabetes mellitus, unless contraindicated. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Inappropriate use of aldosterone receptor antagonists is potentially harmful because of life-threatening hyperkalemia or renal insufficiency when serum creatinine is more than 2.5 mg/dL in men or more than 2.0 mg/dL in women (or estimated glomerular filtration rate <30 mL/min/1.73 m²), and/or potassium more than 5.0 mEq/L. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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 HFrEF receiving optimal therapy with ACE inhibitors and beta blockers, unless contraindicated. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

A combination of hydralazine and isosorbide dinitrate can be useful to reduce morbidity or mortality in patients with current or prior symptomatic HFrEF who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency, unless contraindicated. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Patients with chronic HF with permanent/persistent/paroxysmal 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 in the absence of contraindications to anticoagulation. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

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 in the absence of contraindications to anticoagulation. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Anticoagulation is not recommended in patients with chronic HFrEF without AF, a prior thromboembolic event, or a cardioembolic source. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Statins are not beneficial as adjunctive therapy when prescribed solely for the diagnosis of HF in the absence of other indications for their use. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

Omega-3 polyunsaturated fatty acid (PUFA) supplementation is reasonable to use as adjunctive therapy in patients with NYHA class II–IV symptoms and HFrEF or HFpEF, unless contraindicated, to reduce mortality and cardiovascular hospitalizations. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Nutritional supplements as treatment for HF are not recommended in patients with current or prior symptoms of HFrEF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Hormonal therapies other than to correct deficiencies are not recommended for patients with current or prior symptoms of HFrEF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

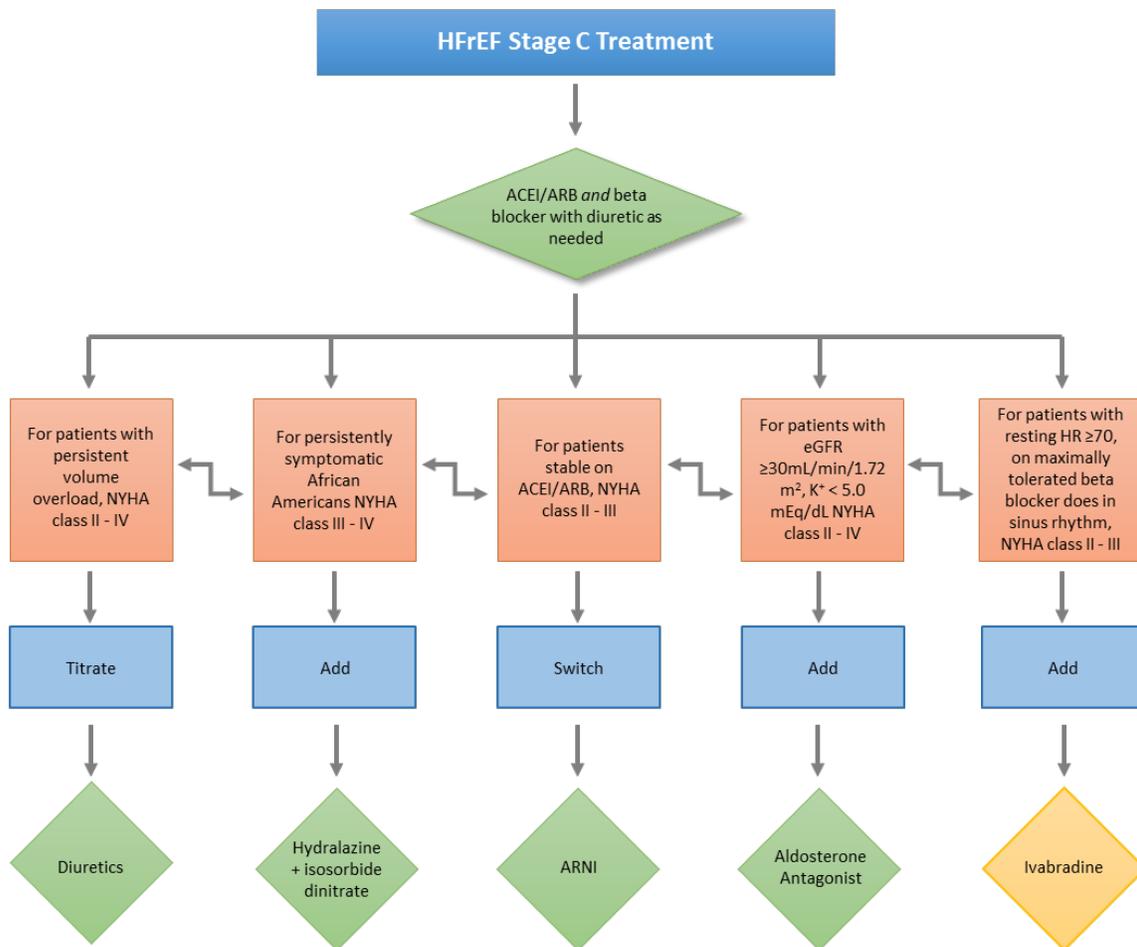
Drugs known to adversely affect the clinical status of patients with current or prior symptoms of HFrEF are potentially harmful and should be avoided or withdrawn whenever possible (e.g., most antiarrhythmic drugs, most calcium channel

blocking drugs (except amlodipine), NSAIDs, or thiazolidinediones). -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Long-term use of infused positive inotropic drugs is potentially harmful for patients with HFrEF, except as palliation for patients with end-stage disease who cannot be stabilized with standard medical treatment. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

Calcium channel blocking drugs are not recommended as routine treatment for patients with HFrEF. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A

Figure 3. Treatment Algorithm for Guideline-Directed Medical Therapy Including Novel Therapies

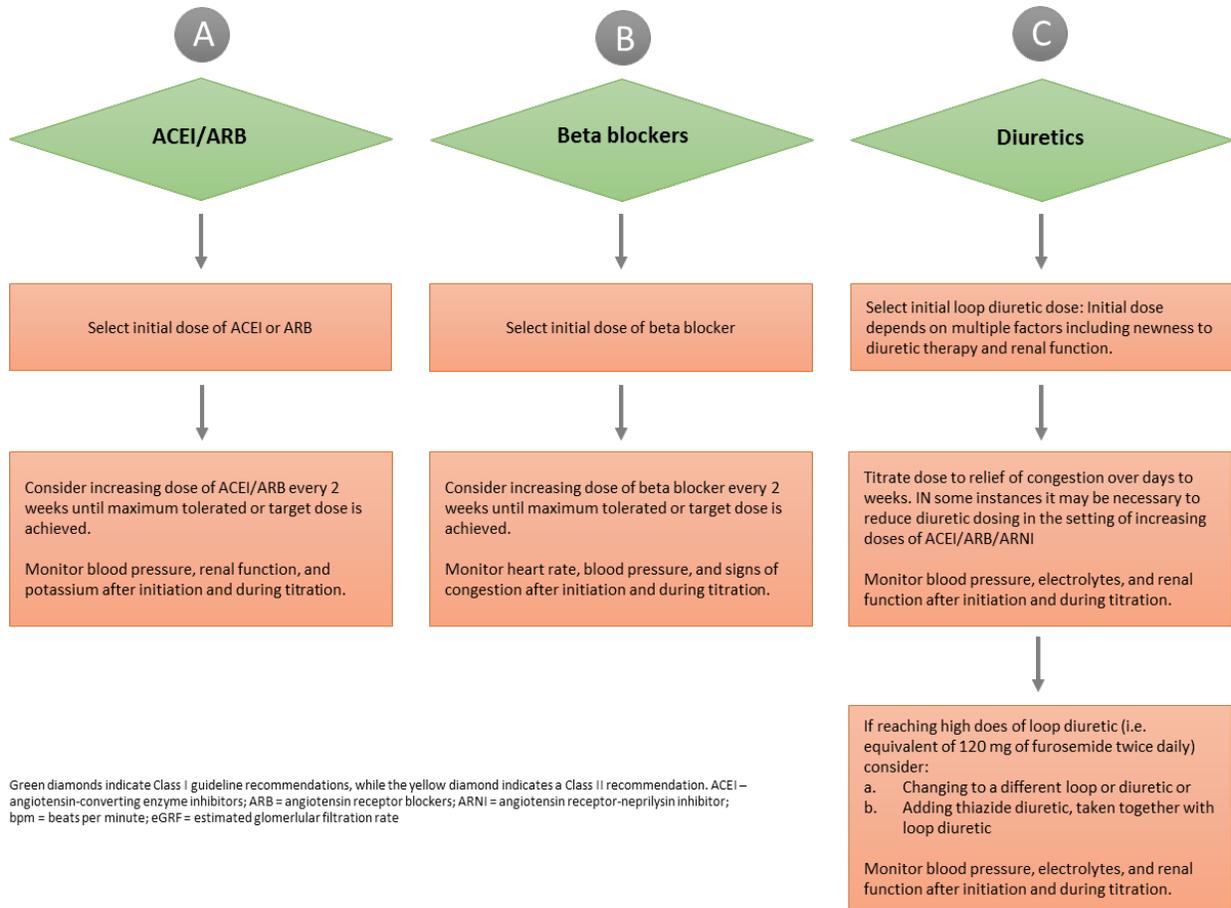


Green diamonds indicate Class I guideline recommendations, while the yellow diamond indicates a Class II recommendation. ACEI – angiotensin-converting enzyme inhibitors; ARB – angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitor; eGFR = estimated glomerular filtration rate; HFrEF = HF with reduced ejection fraction; HR = heart rate; NYHA = New York Heart Association.

Adapted from 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction, Yancy, et al. p.6

[3]

Figure 4. Guideline-Directed Medical Therapy Including Novel Therapies in the Expert Consensus Decision Pathway for Chronic Heart Failure



Green diamonds indicate Class I guideline recommendations, while the yellow diamond indicates a Class II recommendation. ACEI – angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitor; bpm = beats per minute; eGFR = estimated glomerular filtration rate

Figure 4. Continued

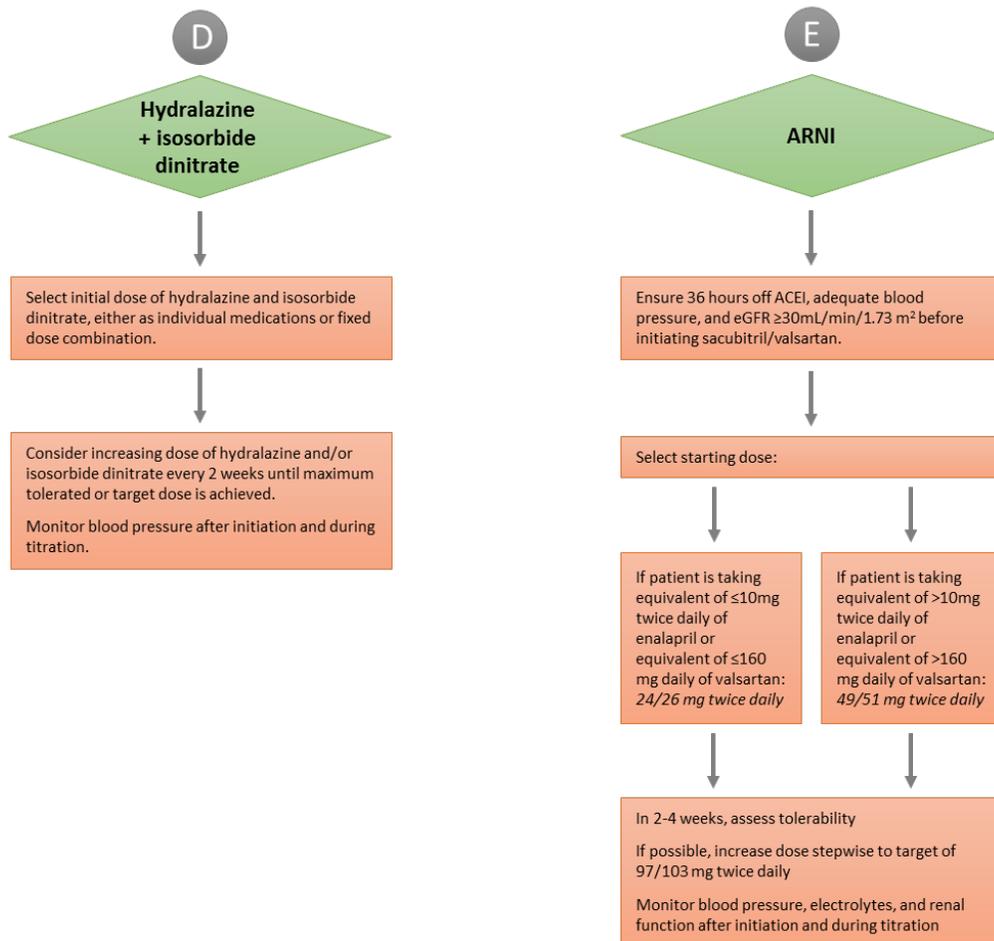
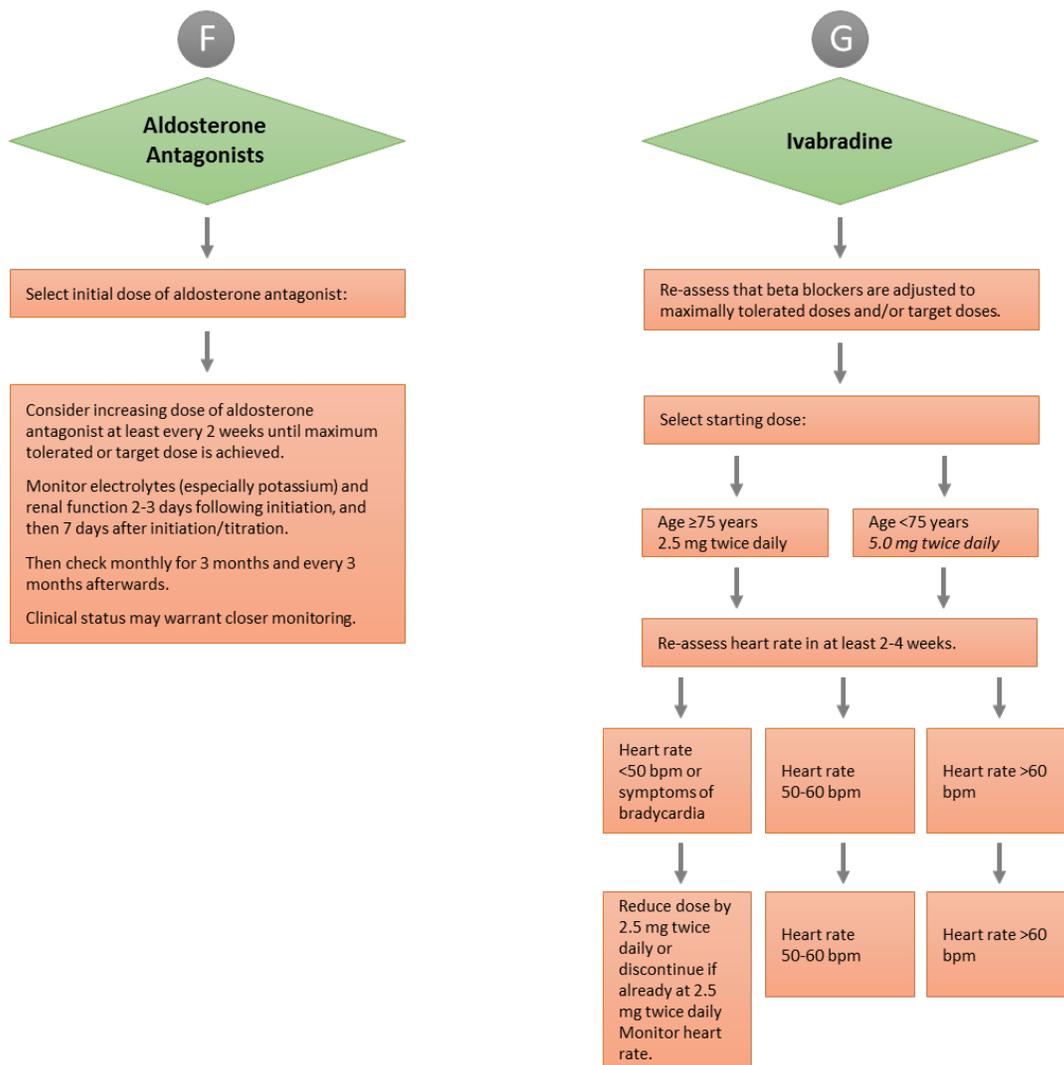


Figure 4. Continued



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Pharmacological Treatment for Stage C HF with Preserved Ejection Fraction (HFpEF): Recommendations

Systolic and diastolic blood pressure should be controlled in patients with HFpEF in accordance with published clinical practice guidelines to prevent morbidity. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Diuretics should be used for relief of symptoms due to volume overload in patients with HFpEF. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable myocardial ischemia is judged to be having an adverse effect on symptomatic HFpEF despite guideline-directed management. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Management of AF according to published clinical practice guidelines in patients with HFpEF is reasonable to improve symptomatic HF. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

The use of beta-blocking agents, ACE inhibitors, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HFpEF. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

In appropriately selected patients with HFpEF (with EF \geq 45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate $>$ 30 mL/min, creatinine $<$ 2.5 mg/dL, potassium $<$ 5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations. - *GRADE Strength of Recommendation: Conditional; AHA Level of Evidence: B-R*

The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF. - *GRADE Strength of Recommendation: Conditional; AHA Level of Evidence: B-R*

Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HFpEF is ineffective. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B-R*

Routine use of nutritional supplements is not recommended for patients with HFpEF. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Device Therapy for Stage C HFrEF: Recommendations

ICD therapy is recommended for primary prevention of SCD to reduce total mortality in selected patients with nonischemic DCM 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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

ICD therapy is recommended for primary prevention of SCD 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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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 with anticipated requirement for significant ($>$ 40%) ventricular pacing. - *GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*



DATE: July 2018

The usefulness of implantation of an ICD is of uncertain benefit to prolong meaningful survival in patients with a high risk of non-sudden death as predicted by frequent hospitalizations, advanced frailty, or comorbidities such as systemic malignancy or severe renal dysfunction. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

CRT may be considered for patients who have LVEF of 35% or less, sinus rhythm, a non-LBBB pattern with QRS duration of 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

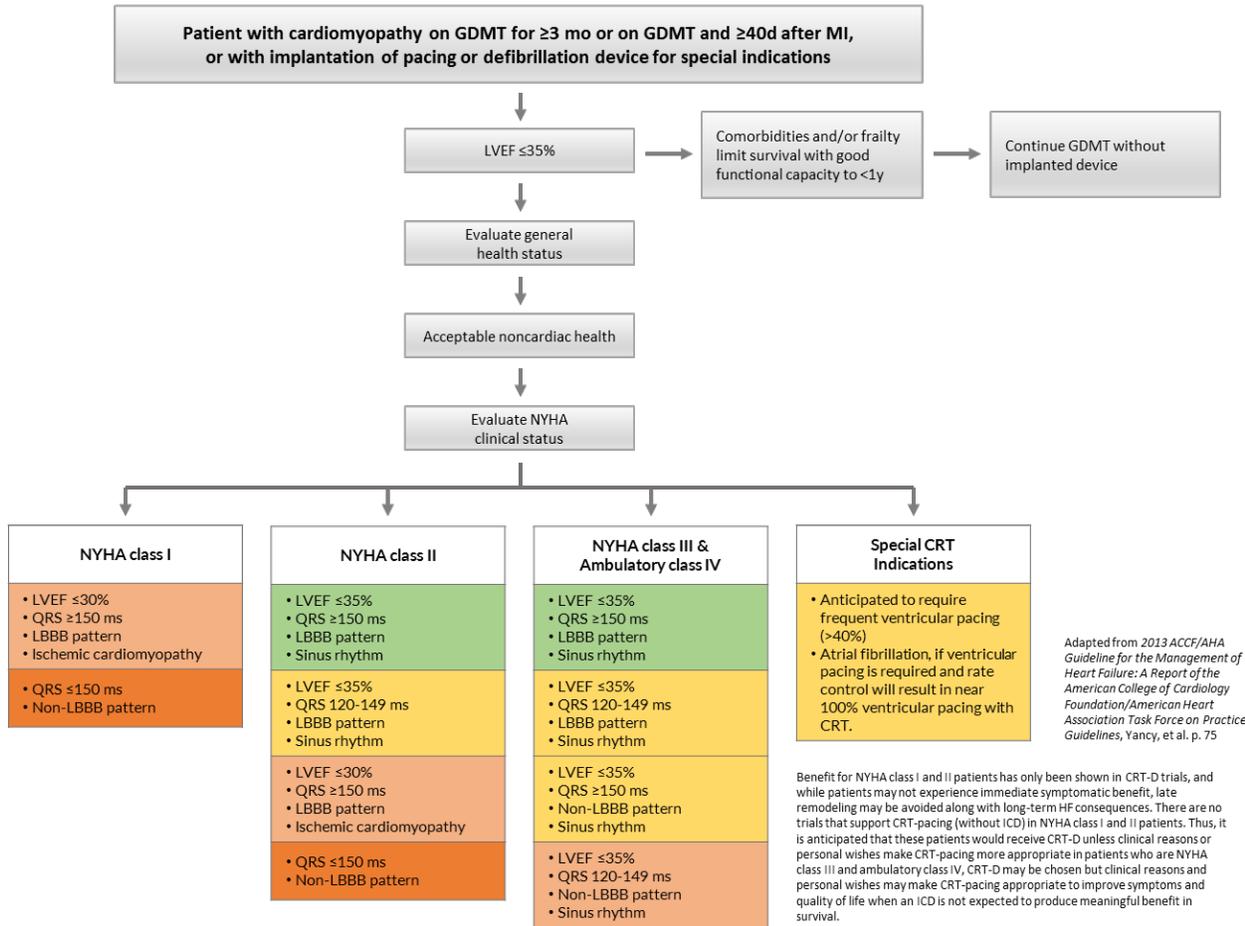
CRT may be considered for patients who have LVEF of 35% or less, sinus rhythm, a non-LBBB pattern with a QRS duration of 150 ms or greater, and NYHA class II symptoms on GDMT. *--GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. *--GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Figure 5. Indications for CRT Therapy Algorithm



Water Restriction: Recommendation

Fluid restriction (1.5 to 2 L/d) is reasonable in stage D, especially in patients with hyponatremia, to reduce congestive symptoms. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

Inotropic Support: Recommendations

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C

Continuous intravenous inotropic support is reasonable as “bridge therapy” in patients with stage D refractory to GDMT and device therapy who are eligible for and awaiting MCS or cardiac transplantation. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

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. -GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Long-term, continuous intravenous inotropic support may be considered as palliative therapy for symptom control in select patients with stage D despite optimal GDMT and device therapy who are not eligible for either MCS or cardiac transplantation. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Mechanical Circulatory Support: Recommendations

MCS is beneficial in carefully selected patients with stage D HFrEF in whom definitive management (e.g., cardiac transplantation) or cardiac recovery is anticipated or planned. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Nondurable MCS, including the use of percutaneous and extracorporeal ventricular assist devices (VADs), is reasonable as a “bridge to recovery” or “bridge to decision” for carefully selected patients with HFrEF with acute, profound hemodynamic compromise. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Durable MCS is reasonable to prolong survival for carefully selected* patients with stage D HFrEF. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Cardiac Transplantation: Recommendation

Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

The Hospitalized Patient[1, 2]

Precipitating Causes of Decompensated HF: Recommendations

ACS precipitating acute HF decompensation should be promptly identified by ECG and serum biomarkers, including cardiac troponin testing, and treated optimally as appropriate to the overall condition and prognosis of the patient. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Common precipitating factors for acute HF should be considered during initial evaluation, as recognition of these conditions is critical to guide appropriate therapy. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Maintenance of GDMT During Hospitalization: Recommendations

In patients with HFrEF 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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Diuretics in Hospitalized Patients: Recommendations

Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to reduce morbidity. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. For example, oral furosemide has about 50% bioavailability so giving the same mg dose IV, doubles the effective dose. 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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

When diuresis is inadequate to relieve symptoms, it is reasonable to intensify the diuretic regimen using either:

- a. higher doses of intravenous loop diuretics;
- b. addition of a second (e.g., thiazide) diuretic

-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Renal Replacement Therapy—Ultrafiltration: Recommendations

Ultrafiltration may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Ultrafiltration may be considered for patients with refractory congestion not responding to medical therapy. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Parenteral Therapy in Hospitalized HF: Recommendation

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: A*

Venous Thromboembolism Prophylaxis in Hospitalized Patients: Recommendation

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Arginine Vasopressin Antagonists: Recommendation

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

V2 receptor selective or a nonselective vasopressin antagonist. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Inpatient and Transitions of Care Recommendations

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. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Throughout the hospitalization as appropriate, before hospital discharge, at the first post-discharge visit, and in subsequent follow-up visits, the following should be addressed:

- a. initiation of GDMT if not previously established and not contraindicated;
- b. precipitant causes of HF, barriers to optimal care transitions, and limitations in post-discharge 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.

-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B

Multidisciplinary HF disease-management programs are recommended for all HF patients, to facilitate the implementation of GDMT, to address different barriers to behavioral change, and to reduce the risk of hospitalizations and rehospitalizations for HF. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Scheduling an early follow-up visit (within 7 days) and early telephone follow-up (within 3 days) of hospital discharge is reasonable. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Use of clinical risk-prediction tools and/or biomarkers to identify patients at higher risk for post-discharge clinical events is reasonable. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Important Comorbidities in HF[1, 2]

Anemia: Recommendations

In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

In patients with HF and anemia, erythropoietin stimulating agents should not be used to improve morbidity and mortality. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: BR*

Hypertension: Recommendations

In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg. *-GRADE Strength of Recommendation: Strong; AHA Level of Evidence: BR*

Patients with HFrEF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg. *-Consensus Statement*



Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: CLD*

Sleep Disordered Breathing: Recommendations

In patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: CLD*

In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness. -*GRADE Strength of Recommendation: Conditional; AHA Level of Evidence: BR*

Continuous positive airway pressure (CPAP) can be beneficial to increase LVEF and improve functional status in patients with HF and sleep apnea. —*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

In patients with NYHA class II–IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: BR*

Table 1. Common Cardiac and Noncardiac Comorbidities Encountered in Patients With HFrEF

Common Cardiac and Noncardiac Comorbidities Encountered in Patients With HFrEF			
Comorbidity	Association With Heart Failure Outcomes	Clinical Trial Evidence for Modulating Comorbidity	Suggested Action
Cardiovascular			
Coronary Artery Disease	Strong	Strong	Evaluate and revascularize in appropriate patients
Atrial Fibrillation/Flutter	Strong	Intermediate	Treat according to current ACC/AHA/HRS Guideline for the Management of Patients with Atrial Fibrillation (94)
Mitral Regurgitation	Strong	Intermediate	Refer to structural heart disease expert & treat according to current AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (95)
Aortic Stenosis	Strong	Strong	Refer to structural heart disease expert & treat according to current AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (95)
Hypertension	Uncertain	Strong for prevention	Treat according to current ACC/AHA hypertension guidelines
Dyslipidemia	Uncertain	Strong for prevention	Treat according to ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults (96). Also see the nonstatin treatment of dyslipidemia clinical pathways (97)
Peripheral Vascular Disease	Moderate	None	Treat according to current AHA/ACC vascular guidelines (98)
Cerebrovascular Disease	Moderate	Weak	Treat according to current AHA stroke guidelines (99)
Noncardiovascular			
Obesity	Moderate (inverse association)	Weak	Further data needed
Chronic Lung Disease	Strong	Weak	Optimize therapy, consider pulmonary consultation
Diabetes Mellitus	Strong	Intermediate	Optimize therapy, consider SGLT2 inhibitors, consider endocrine consult and follow current American Diabetes Association Standards of Medical Care in Diabetes
Chronic Renal Disease	Strong	Weak	Optimize RAASi therapy, consider nephrology consult

Anemia	Moderate	Weak	Evaluate secondary causes, consider transfusing in severe cases
Iron Deficiency	Strong	Intermediate	Consider intravenous iron replacement for symptom improvement
Thyroid Disorder—hypo or hyper	Strong	Weak	Consider referral to endocrinologist and/or treatment
Sleep Disordered Breathing	Strong	Intermediate	Consider sleep study and treat severe obstructive sleep apnea to improve sleep quality, consider referring to sleep specialist

ACC = American College of Cardiology; AHA = American Heart Association; HRS = Heart Rhythm Society; RAASi = renin-angiotensin-aldosterone system inhibitor; SGLT2 = sodiumglucose co-transporter 2.

[3]

Surgical/Percutaneous/Transcatheter Interventional Treatments of HF Recommendations[1, 2]:

Coronary artery revascularization via CABG or percutaneous intervention is indicated for patients (HFpEF and HFrEF) on GDMT with angina and suitable coronary anatomy, especially for a left main stenosis (>50%) or left main equivalent disease. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

CABG or medical therapy is reasonable to improve morbidity and cardiovascular mortality for patients with severe LV dysfunction (EF <35%), HF, and significant CAD. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Surgical aortic valve replacement is reasonable for patients with critical aortic stenosis and a predicted surgical mortality of no greater than 10%. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Transcatheter aortic valve replacement after careful candidate consideration is reasonable for patients with critical aortic stenosis who are deemed inoperable. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Surgical reverse remodeling or LV aneurysmectomy may be considered in carefully selected patients with HFrEF for specific indications, including intractable HF and ventricular arrhythmias. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*

Coordinating Care for Patients with Chronic HF Recommendations:[1, 2]

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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*



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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. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: C*

Palliative and supportive care is effective for patients with symptomatic advanced HF to improve quality of life. -*GRADE Strength of Recommendation: Strong; AHA Level of Evidence: B*



Quality Measures:

Structure-

- Get with the Guideline Program implemented at Tuality and Adventist

Process-

- ACEI/ARB or ARNi for low EF prescribed
- Beta Blocker for low EF prescribed
- Spironolactone for low EF prescribed
- Follow-up appointment within one week scheduled
- Advanced Directive discussed with patient
- Measure LV function
- Anticoagulant for AF
- DVT prophylaxis
- ICD placed or prescribed
- CRT placed
- Influenza vaccine administered
- Pneumococcal vaccine administered
- Hydralazine/nitrate prescribed
- Referral for cardiac rehab
- Education and counseling

Outcome-

- 30 Day Related and All Cause Readmissions to OHSU for adults Discharged with Heart Failure Primary Diagnosis
- Mortality
- Patient Experience
- Length of Stay
- Post-discharge follow-up



Heart Failure Existing External Guidelines

External Guideline	Organization and Author	Last Update
Guideline for the Management of Heart Failure	American College of Cardiology (ACCF) and American Heart Association (AHA)	2013
Focused Update on New Pharmacological Therapy for Heart Failure: an update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure	American College of Cardiology (ACC), American Heart Association (AHA), Heart Failure Society of America (HFSA)	2016
Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure	American College of Cardiology (ACC), American Heart Association (AHA), Heart Failure Society of America (HFSA)	2017

The two published clinical guidelines were evaluated for this review using the **University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale**. The scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

Guideline Issuer	ACCF/AHA 2013	ACC/AHA/HFSA 2016	ACC/AHA/HFSA 2017
1. Transparency	A	A	A
2. Conflict of interest	A	A	A
3. Development group	A	A	A
4. Systematic Review	A	A	A
5. Supporting evidence	A	A	A
6. Recommendations	A	A	A
7. External Review	A	A	A
8. Currency and updates	A	A	A

Appendix 1. Abbreviations[1, 2]

ACE = angiotensin-converting enzyme	HFpEF = heart failure with preserved ejection fraction
ACS = acute coronary syndrome	HFrEF = heart failure with reduced ejection fraction
AF = arterial fibrillation	HRQOL = heart- related quality of life
ARB = angiotensin-receptor blocker	ICD = implantable cardioverter-defibrillator
ARNI = angiotensin receptor-neprilysin inhibitor	LBBB = left bundle-branch block
BMI = body mass index	LOE= level of evidence
BNP = B-type natriuretic peptide	LV = left ventricular
BP = blood pressure	LVEF = left ventricular ejection fraction
BTT = bridge to transplantation	MCS = mechanical circulatory support
CABG = coronary artery bypass graft	MI = myocardial infarction
CAD = coronary artery disease	NSAIDS = nonsteroidal anti-inflammatory drugs
CPAP = continuous positive airway pressure	NT-proBNP = N-terminal pro-B-type natriuretic peptide
CRT = cardiac resynchronization therapy	NYHA = New York Heart Association
DCM = dilated cardiomyopathy	PUFA = polyunsaturated fatty acids
ECG = electrocardiogram	RCT = randomized controlled trial
EF = ejection fraction	SCD = sudden cardiac death
GDMT = guideline-directed medical therapy	SOR= strength of recommendation
HbA1c = hemoglobin A1c	VAD = ventricular assist device
HF = heart failure	

Appendix 2. Recommended Medications and Dosing Information for use in the Treatment of Chronic HF[1-3]

Oral Diuretics Recommended for Use in the Treatment of Chronic HF			
	Initial Daily Dose	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	1,000 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.

HF indicates heart failure; IV, intravenous; and N/A, not applicable.

Intravenous Inotropic Agents Used in Management of HF									
Inotropic Agent	Dose		Drug Kinetics and Metabolism	Effects				Adverse Events	Special Considerations
	Bolus	Infusion (/min)		CO	HR	SVR	PVR		
Adrenergic agonists									
Dopamine	N/A	5 to 10	t ½: 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 5.0	t ½: 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 ½: 2.5 h H	↑	↑	↓	↓	T, ↓BP	Renal dosing, monitor LFTs

t ½ Indicates elimination half-life; BP, 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; and T, tachyarrhythmias.

Starting and Target Doses of Select Guideline-Directed Medical Therapy for HF		
	Starting dose	Target dose
Beta Blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5-25 mg/d	200 mg daily
ARNI		
Sacubitril/valsartan	24/26 mg - 49/51 mg twice daily	97/103 mg twice daily
ACEI		
Captopril	6.25 mg 3x daily	50 mg 3x daily
Enalapril	2.5 mg twice daily	10-20 mg twice daily
Lisinopril	2.5-5 mg daily	20-40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARB		
Candesartan	4/8 mg daily	32 mg daily
Losartan	25-50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily
Aldosterone antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5-25 mg daily	25-50 mg daily
Vasodilators		
Hydralazine	25 mg 3x daily	75 mg 3x daily
Isosorbide dinitrate*	20 mg 3x daily	40 mg 3x daily
Fixed-dose combination isosorbide dinitrate/hydralazine†	20 mg/37.5 mg (one tab) 3x daily	2 tabs 3x daily
Ivabradine		
Ivabradine	2.5-5 mg twice daily	Titrate to heart rate 50-60 bpm. Maximum dose 7.5 mg twice daily

Digoxin remains indicated for HFrEF, but there are no contemporary data to warrant additional comment in this document. The reader is referred to already available guideline statements (2).
 *Isosorbide mononitrate is not recommended by the ACC/AHA/HFSA guideline. †The ACC/AHA/HFSA guideline considers either the fixed dose combination or the separate combination of isosorbide dinitrate and hydralazine as appropriate guideline directed therapy for HF. ACEI = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor neprilysin inhibitor; ARB = angiotensin receptor blocker; bpm = beats per minute; HF = heart failure; HFrEF = heart failure with reduced ejection fraction.

Recommended Starting Dose of Sacubitril/Valsartan	
Population	Initial Dose
Moderate- or high-dose ACEI <i>Equivalent of enalapril ≥10 mg twice daily</i>	49/51 mg twice daily
Moderate- or high-dose ARB <i>Equivalent of valsartan ≥80 mg twice daily</i>	
Low dose ACEI <i>Equivalent of <10 mg of enalapril twice daily</i>	24/26 mg twice daily
Low dose ARB <i>Equivalent of valsartan ≤80 mg twice daily</i>	
ACEI/ARB naïve	
Severe renal impairment† (eGFR <30 mL/min/1.73 m ²)	
Moderate hepatic impairment (Child-Pugh Class B)	
Elderly (age ≥75 years)	

†This population was not studied in PARADIGM HF.

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate.



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Recommended Starting Dose of Ivabradine	
Population	Initial Dose
Maximally tolerated beta-blocker dose with persistent resting heart rate \geq 70 bpm	5 mg twice daily
History of conduction defects	2.5 mg twice daily
Age \geq 75 years	

bpm = beats per minute.

Appendix 3. Indications and Contraindication for Drugs Commonly Used for HFrEF Stage C

Guideline-Recommended Indications for ARNI and Ivabradine Use
Indications for Use of an ARNI
<ul style="list-style-type: none"> ▪ HFrEF (EF ≤40%) ▪ NYHA class II or III HF
Indications for Use of Ivabradine
<ul style="list-style-type: none"> ▪ HFrEF (EF ≤35%) ▪ On maximum tolerated doses of beta blocker ▪ Sinus rhythm with a resting heart rate ≥70 bpm ▪ NYHA class II or III HF

ARNI = angiotensin receptor-neprilysin inhibitor; bpm = beats per minute; EF = ejection fraction; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; NYHA = New York Heart Association.

Contraindications and Cautions for Sacubitril/Valsartan and Ivabradine	
A) Sacubitril/Valsartan	
Contraindications	Cautions
<ul style="list-style-type: none"> ▪ Within 36 hours of ACEI use ▪ Angioedema with an ACEI or ARB previously ▪ Pregnancy ▪ Lactation (not recommended) ▪ Severe hepatic impairment (Child-Pugh C) ▪ Concomitant aliskiren use in patients with diabetes ▪ Known hypersensitivity to either ARB or ARNI 	<ul style="list-style-type: none"> ▪ Renal impairment: <ul style="list-style-type: none"> - Mild-to-moderate (eGFR ≥30 mL/min/1.73 m²): No starting dose adjustment required - Severe* eGFR <30 mL/min/1.73 m²): Reduce starting dose to 24 mg/26 mg twice daily; double the dose every 2–4 weeks to target maintenance dose of 97 mg/103 mg twice daily as tolerated ▪ Hepatic impairment: <ul style="list-style-type: none"> - Mild (Child-Pugh A): No starting dose adjustment required - Moderate (Child-Pugh B): Reduce starting dose to 24 mg/26 mg twice daily; double the dose every 2–4 weeks to target maintenance dose of 97 mg/103 mg twice daily as tolerated. - Severe (Child-Pugh C): contraindicated ▪ Renal artery stenosis ▪ Hypotension ▪ Volume depletion ▪ Hyponatremia ▪ Post myocardial infarction
B) Ivabradine	
Contraindications	Cautions
<ul style="list-style-type: none"> ▪ HFpEF ▪ Presence of angina with normal EF ▪ Hypersensitivity ▪ Severe hepatic impairment ▪ Acute decompensated HF ▪ Blood pressure <90/50 mm Hg ▪ Sick sinus syndrome without a pacemaker ▪ Sinoatrial node block ▪ 2nd or 3rd degree block without a pacemaker ▪ Resting heart rate <60 bpm ▪ Atrial fibrillation or flutter ▪ Atrial pacemaker dependence 	<ul style="list-style-type: none"> ▪ Bradycardia ▪ Sinus node disease ▪ Cardiac conduction defects ▪ Prolonged QT interval

*This population was not studied in PARADIGM HF. The statement is consistent with Food and Drug Administration–approved labeling indications.

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; bpm = beats per minute; EF = ejection fraction; eGFR = estimated glomerular filtration rate; HF = heart failure; HFpEF = heart failure with preserved ejection fraction.

Appendix 4. Triggers for HF Patient Referral to a Specialist/Program[3]

Triggers for HF Patient Referral to a Specialist/Program
1. New onset HF (regardless of EF) for evaluation of etiology, guideline-directed evaluation and management of recommended therapies, and assistance in disease management.
2. Chronic HF with high-risk features, such as development of 1 or more of the following risk factors: <ul style="list-style-type: none"> ▪ Need for chronic IV inotropes ▪ Persistent NYHA functional class III–IV symptoms of congestion or profound fatigue ▪ Systolic blood pressure ≤ 90 mm Hg or symptomatic hypotension ▪ Creatinine ≥ 1.8 mg/dL or BUN ≥ 43 mg/dL ▪ Onset of atrial fibrillation or ventricular arrhythmias or repetitive ICD shocks ▪ Two or more emergency department visits or hospitalizations for worsening HF in prior 12 months ▪ Inability to tolerate optimally-dosed beta blockers and/or ACEI/ARB/ARNI and/or aldosterone antagonists ▪ Clinical deterioration as indicated by worsening edema, rising biomarkers (BNP, NT-proBNP, others), worsened exercise testing, decompensated hemodynamics, or evidence of progressive remodeling on imaging ▪ High mortality risk using validated risk model for further assessment and consideration of advanced therapies (http://www.onlinejacc.org/content/62/16/e147/T10)
3. To assist with management of GDMT, including replacement of ACEI or ARB therapy with ARNI for eligible patients, or to address comorbid conditions such as chronic renal disease or hyperkalemia, which may complicate treatment.
4. Persistently reduced LVEF $\leq 35\%$ despite GDMT for ≥ 3 months for consideration of device therapy in those patients without prior placement of ICD or CRT, unless device therapy contraindicated.
5. Second opinion regarding etiology of HF; for example: <ul style="list-style-type: none"> ▪ Evaluation for potential ischemic etiology ▪ Suspected myocarditis ▪ Established or suspected specific cardiomyopathies, e.g., hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, Chagas disease, restrictive cardiomyopathy, cardiac sarcoidosis, amyloid, aortic stenosis ▪ Valvular heart disease with or without HF symptoms
6. Annual review for patients with established advanced HF in which patients/caregivers and clinicians discuss current and potential therapies for both anticipated and unanticipated events, possible HF disease trajectory and prognosis, patient preferences, and advanced care planning.
7. Assess the possibility of participation in a clinical trial.

ACEI = angiotensin converting enzyme inhibitors; ARB = angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitor; BNP = B-type natriuretic peptide; BUN = blood urea nitrogen; CRT = cardiac resynchronization therapy; EF = ejection fraction; GDMT = guideline-directed medical therapy; HF = heart failure; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NTproBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

Appendix 5. Specific Patient Cohorts in HF Care[3]

Specific Patient Cohorts in HF Care				
Patient Cohorts	Description	Evidence-Based Recommendations	Risks	Uncertainties
African Americans	Self-Identified	GDMT	ACEI, ARB, and ARNI: higher risk of angioedema compared with Caucasian patients Uncertain risk of hypotension when combining new drugs with HYD/ISDN	Expected outcomes of ARNI and/or ivabradine in those treated with HYD/ISDN
Older adults	≥75 years	Attempt to establish GDMT; however, doses utilized might need to be lower. Device therapy should be carefully considered due to possibly higher risk for complications in older patients	Falls, worsening of renal function, polypharmacy, costs, comorbidity	Efficacy of lower-dose GDMT on outcomes
Frail	Meets established frailty criteria (83)	GDMT as tolerated	Uncertain response to GDMT, increase risk for adverse drug reactions	Ability to impact natural history in the frail with HF

ACEI = angiotensin converting enzyme inhibitors; ARB = angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitor; GDMT = guideline-directed medical therapy; HF = heart failure; HYD/ISDN = hydralazine/isosorbide dinitrate.



Appendix 6. Important Pathophysiologic Targets in HFrEF and Treatments[3]

Important Pathophysiologic Targets in HFrEF and Treatments	
Target	Therapy
Renin-angiotensin-aldosterone system	ACEI, ARBs, ARNI, aldosterone antagonists
Sympathetic nervous system	Beta blockers
Natriuretic and other vasodilator peptides	ARNI
Elevated heart rate (in sinus rhythm, on optimal beta-blocker dose)	Ivabradine, beta blocker
Balanced vasodilation and oxidative stress modulation in African Americans	HYD/ISDN
Arrhythmic sudden death	Implantable cardioverter-defibrillators
Ventricular dyssynchrony due to conduction abnormalities	Cardiac resynchronization therapy
Congestion	Diuretics (with chronic ambulatory pulmonary artery pressure monitoring in select patients)
Reduced aerobic capacity	Exercise training/cardiac rehabilitation

ACEI = angiotensin converting enzyme inhibitors; ARB = angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitor; HYD/ISDN = hydralazine/isosorbide dinitrate.

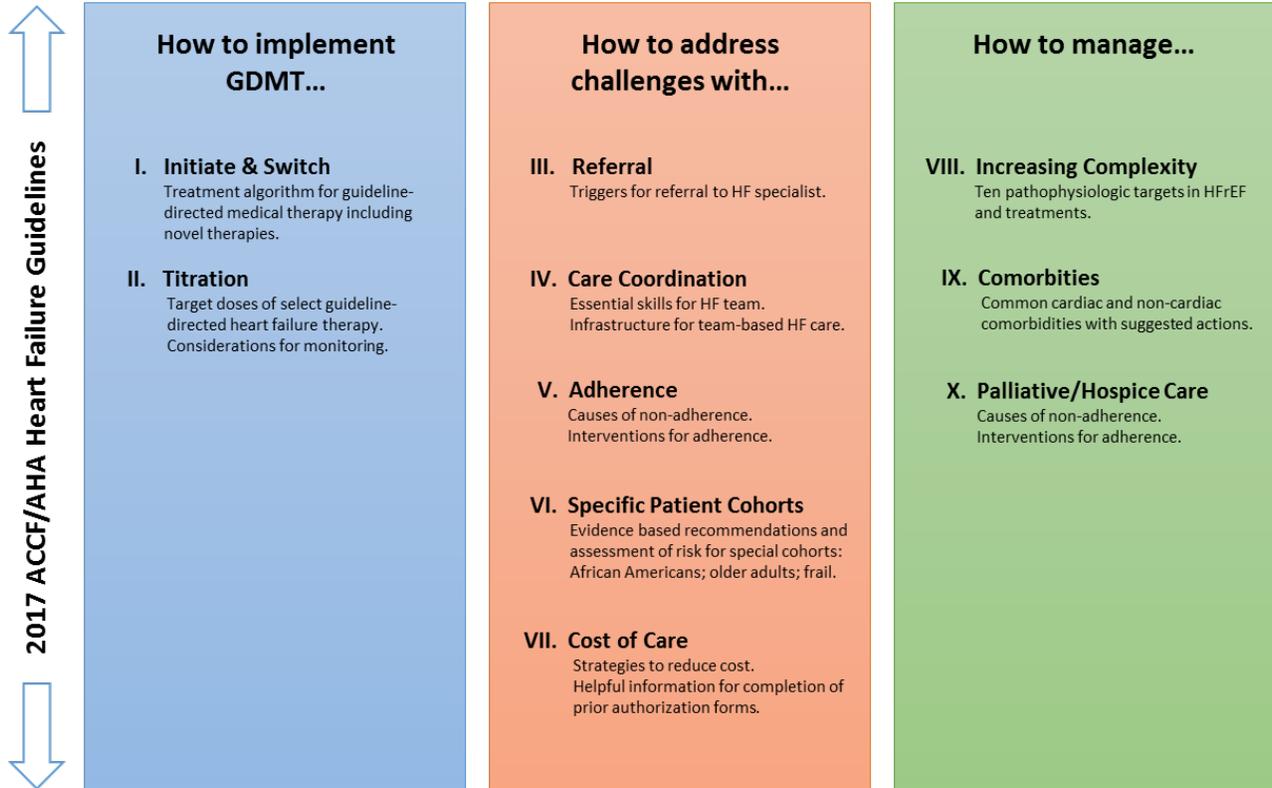


Appendix 7. Comparison of ACCF/AHA Stages of HF and NYHA Functional Classifications[1, 2]

Comparison of ACCF/AHA Stages of HF and NYHA Functional Classifications			
ACCF/ AHA Stages of HF		NYHA Functional Classification	
A	At 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.

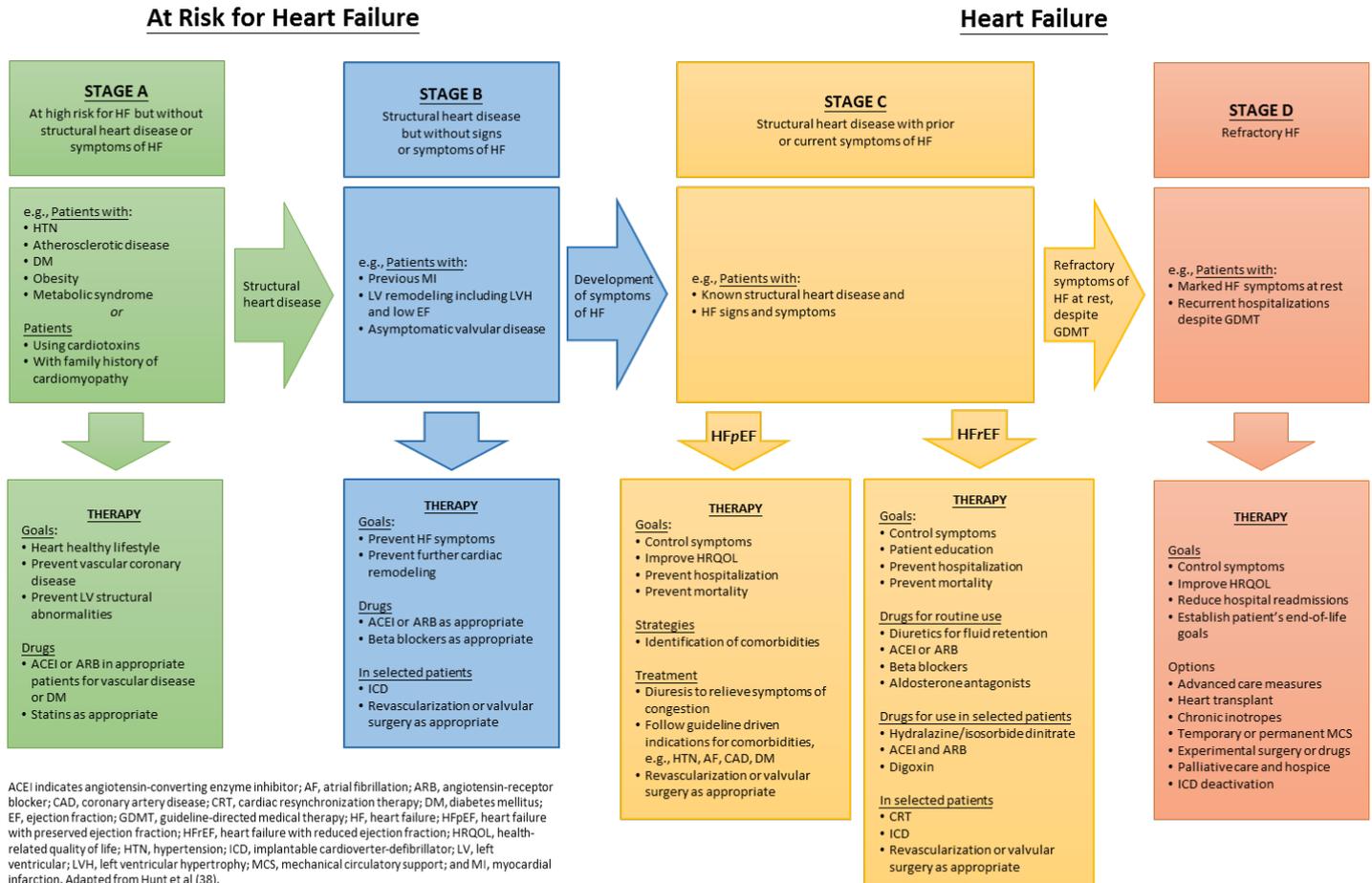
Appendix 8. Ten Principles for Successful Treatment of Heart Failure[3]



ACCF = American College of Cardiology Foundation; AHA = American Heart Association; GDMT = guideline-directed medical therapy; HF = heart failure; HFrEF = HF with reduced ejection fraction.

Adapted from 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction, Yancy, et al. p. 5

Appendix 9. Stages in the development of HF and recommended therapy by stage[1, 2]



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; HFpEF, heart failure with preserved ejection fraction; HFrEF, 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 (38).

Adapted from 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, Yancy, C.W., et al., p. 84

Appendix 10. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

A	Guideline development methods are fully disclosed.
B	Guideline development methods are partially disclosed.
C	Guideline development methods are not disclosed.

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:

Who wrote the initial draft

How the committee voted on or otherwise approved recommendations

Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

A	Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).
B	Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.
C	Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.
NR	Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

A	Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.
B	Guideline development group includes one of the above, but not both.

C	Guideline developers all from one specialty or organization, and no methodologists.
NR	Affiliations of guideline developers not reported

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

A	Guideline includes a systematic review of the evidence or links to a current review.
B	Guideline is based on a review which may or may not meet systematic review criteria.
C	Guideline is not based on a review of the evidence.

In order to qualify as a systematic review, the review must do all of the following:

Describe itself as systematic or report search strategies using multiple databases

Define the scope of the review (including key questions and the applicable population)

Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

A	Specific supporting evidence (or lack thereof) for each recommendation is cited and graded
B	Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.
C	Recommendations are not supported by specific evidence.

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

A	Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.
B	Either one or the other of the above criteria is met.
C	Neither of the above criteria are met

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

A	Guideline was made available to external groups for review.
B	Guideline was reviewed by members of the sponsoring body only.
C	Guideline was not externally reviewed.
NR	No external review process is described.

8. Updating and currency of guideline

A	Guideline is current and an expiration date or update process is specified.
B	Guideline is current but no expiration date or update process is specified.
C	Guideline is outdated.

A guideline is considered current if it is within the developers' stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst's discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.



Guideline Preparation

This guideline was prepared by the Office of Clinical Integration (CI) and Evidence-Based Practice (EBP) in collaboration with content experts at Oregon Health and Science University, Tuality, and Adventist Health.

Heart Failure Best Practice Committee Content Expert Team- Reviewed 5/15/2018

Clinical Integration and EBP Team

Elizabeth Crabtree, MPH, PhD (c) Director of Clinical Integration and EBP
 Andrew Hamilton, MS/MLS, Liaison Librarian
 Tovah Kohl MA, EBP Guideline Development Program Manager

Development Process

This guideline was developed by translating the AHA guidelines into OHSU Department of Clinical Integration and EBP guideline template. The AHA’s recommendation process was adopted to fit GRADE while keeping their rubric for evaluating the quality of evidence.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **University of Pennsylvania’s Trustworthy Guideline Rating Scale**. The summary of these guidelines are included in the evidence summary. The rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains. This scale evaluates a guideline’s transparency, conflict of interest, development group, systematic review, supporting evidence, recommendations, external review and currency and updates. The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated).

The **GRADE (Grading of Recommendations, Assessment, Development and Evaluation)** criteria were utilized to make clinical recommendations.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects

The **AHA Level of Evidence Rubric** was used evaluate the body of evidence.

AHA Levels of Evidence from 2013 and 2017 Guidelines			
AHA 2013		AHA 2017	
A	Multiple populations evaluated Data derived from multiple randomized clinical trials of meta-analyses	A	High-quality evidence from more than 1 RCT Meta-analysis of high quality RCTs One or more RCTs corroborated by high-quality registry studies
B	Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	B-R	Moderate-quality evidence from 1 or more RCTs Meta-analysis of moderate quality RCTs
C	Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care Refractory HF requiring specialized interventions	B-NR	Moderate-quality evidence from 1 or more well-designed, well-executed non randomized studies, observational studies, or registry studies. Meta-analysis of such studies
		C-LD	Randomized or nonrandomized observational or registry studies with limitations of design or execution. Meta-analysis of such studies. Physiological or mechanistic studies in human subjects.
		C-EO	Consensus of expert opinion based on clinical experience.

Recommendations

Recommendations for the guidelines were directed by the existing evidence, content experts, and consensus. Patient and family preference were included when possible. When evidence is lacking, options in care are provided in the guideline and the order sets that accompany the guideline.

Approval Process

Guidelines are reviewed and approved by the Content Expert Team, Office of CI and EBP, Knowledge Management and Therapeutics Committee, Professional Board, and other appropriate hospital committees as



DATE: July 2018

deemed appropriate for the guideline's intended use. Guidelines are reviewed and updated as necessary every 2 to 3 years within the Office of CI and EBP at OHSU. Content Expert Teams will be involved with every review and update.

Conflict of Interest

None of the content expert team members has any affiliations or financial involvement that conflicts with the material presented in this guideline.

Disclaimer

Guideline recommendations are made from the best evidence, clinical expertise and consensus, in addition to

thoughtful consideration for the patients and families cared for within the Integrated Delivery System. When evidence was lacking or inconclusive, content experts made recommendations based on consensus. Expert consensus is implied when a reference is not otherwise indicated.

The guideline is not intended to impose standards of care preventing selective variation in practice that is necessary to meet the unique needs of individual patients. The physician must consider each patient and family's circumstance to make the ultimate judgment regarding best care.

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