



Guideline for the Management of Heart Failure

Derived From:

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Full-text guidelines available in both Circulation and JACC.

Overview

Top 10 Take-Home Messages:

- Guideline-directed medical therapy (GDMT) for heart failure (HF) with reduced ejection fraction (HFrEF) now includes 4 medication classes which include sodium-glucose cotransporter-2 inhibitors (SGLT2i).
- SGLT2 inhibitors have a 2a recommendation in heart failure with mildly reduced ejection fraction (HFmrEF). Weaker recommendations (2b) are made for ARNi, ACEi, ARB, MRA and beta blockers in this population.
- New recommendations for HFpEF are made for SGLT2 inhibitors
 (2a), MRAs (2b) and ARNi (2b). Several prior recommendations have
 been renewed including treatment of hypertension (1), treatment of
 atrial fibrillation (2a), use of ARBs (2b) avoidance of routine use of
 nitrates or phosphodiesterase-5 inhibitors (3-no benefit).
- Improved LVEF is used to refer to those patients with a previous HFrEF who now have an LVEF >40%. These patients should continue their HFrEF treatment.
- Value statements were created for select recommendations where high-quality cost-effectiveness studies of the intervention have been published.
- Amyloid heart disease has new recommendations for treatment including screening for serum and urine monoclonal light chains, bone scintigraphy, genetic sequencing, tetramer stabilizer therapy, and anticoagulation.
- Evidence supporting increased filling pressures is important for the diagnosis of HF if the LVEF is >40%. Evidence for increased filling pressures can be obtained from non-invasive (e.g., natriuretic peptide, diastolic function on imaging) or invasive testing (e.g., hemodynamic measurement).
- 8. Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF. A heart failure specialty team reviews HF management, assesses suitability for advanced HF therapies and uses palliative care including palliative inotropes where consistent with the patient's goals of care.
- Primary prevention is important for those at risk for HF (Stage A) or pre-HF (Stage B). Stages of HF were revised to emphasize the new terminologies of "at risk" for HF for Stage A and Pre-HF for Stage B.
- Recommendations are provided for select patients with HF and iron deficiency, anemia, hypertension, sleep disorders, diabetes type 2, atrial fibrillation, coronary artery disease and malignancy.

→ Assessment





Note: The numbering of the following tables differs from that of the Clinical Practice Guideline.

Colors in tables and figures correspond to Class of Recommendations and Level of Evidence tables on pages 78–79.

Table 3. Stages of HF		
Stages	Definition and Criteria	
Stage A: At Risk for HF	At risk for HF but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury (e.g., patients with hypertension, atherosclerotic CVD, diabetes, metabolic syndrome and obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or positive family history of cardiomyopathy).	
Stage B:	No symptoms or signs of HF and evidence of 1 of the following:	
Pre-HF	Structural heart disease* Reduced left or right ventricular systolic function Reduced ejection fraction, reduced strain Ventricular hypertrophy Chamber enlargement Wall motion abnormalities Valvular heart disease Evidence for increased filling pressures* By invasive hemodynamic measurements By noninvasive imaging suggesting elevated filling pressures (e.g., Doppler echocardiography) Patients with risk factors and Increased levels of BNPs* or Persistently elevated cardiac troponin in the absence of competing diagnoses resulting in such biomarker elevations such as acute coronary syndrome, CKD, pulmonary	
Stage C: Symptomatic HF	embolus, or myopericarditis Structural heart disease with current or previous symptoms of HF.	
Stage D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT.	

^{*} Abciximab may not be readily available to clinicians in the U.S.

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Figure 1. ACC/AHA Stages of HF

At-Risk for Heart STAGE A: Failure

Pre-Heart Failure STAGE B:

Symptomatic Heart STAGE C:

Patients without current signs of HF but evidence or previous symptoms/ Structural heart of 1 of the following:

signs of HF and without but without current or Patients at risk for HF

abnormal biomarkers structural/functional previous symptoms/

Evidence of increased

heart disease or

disease

or previous symptoms/ Patients with current signs of HF

> **Advanced Heart Failure** STAGE D:

that interfere with daily hospitalizations despite life and with recurrent attempts to optimize

Marked HF symptoms

agents, genetic variant for history of cardiomyopathy cardiomyopathy, or family exposure to cardiotoxic hypertension, CVD, diabetes, obesity, Patients with

Risk factors and filling pressures

- increased natriuretic peptide levels or
- in the absence of competing diagnoses persistently elevated cardiac troponin





Figure 2. Trajectory of Class C HF

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vo HF:

- Newly diagnosed HF
- No previous history of HF

Resolution of Symptoms:

- Resolution of symptoms/ signs of HF
 - dysfunction | heart disease* symptoms of HF with persistent previous C with Stage

of previous structural resolution

remission

with

functional

and/or

Persistent HF:

ongoing symptoms/signs and/or limited functional Persistent HF with capacity

Worsening HF:

signs/functional capacity Worsening symptoms/

*Full resolution of structural and functional cardiac abnormalities is uncommon.

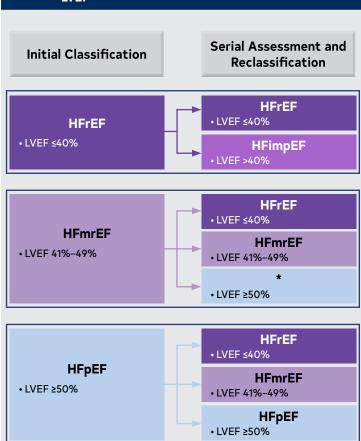
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Table 4. Classification of HF by LVEF		
Type of HF According to LVEF	Criteria	
HFrEF (HF with reduced EF)	• LVEF ≤40%	
HFimpEF (HF with improved EF)	• Previous LVEF ≤40% and a follow-up measurement of LVEF >40%	
HFmrEF (HF with mildly reduced EF)	LVEF 41%–49% Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)	
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)	





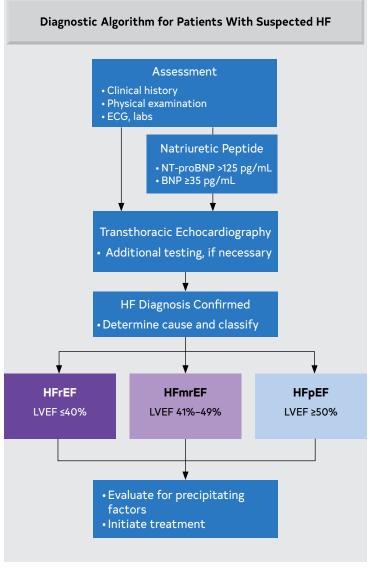
Figure 3. Classification and Trajectories of HF Based on LVEF



^{*} There is limited evidence to guide treatment for patients who improve their LVEF from mildly reduced (41%-49%) to ≥50%. It is unclear whether to treat these patients as HFpEF or HFmrEF.

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Figure 4. Diagnostic Algorithm for HF and EF-Based Classification







3. Epidemiology and Causes of HF

Beginning in 2012, the age-adjusted death rate per capita for HF increased for the first time in the United States. A recent U.S. evaluation found total deaths caused by HF have increased from 275,000 in 2009 to 310,000 in 2014.

➤ Death rate per capita by race and ethnicity:

- Non-Hispanic Black 92/100,000
- Non-Hispanic White 87/100,000
- Hispanic 53/100,000

Causes of heart failure:

- Risk Factors (in the United States):
 - ► 115 million have hypertension
 - ▶ 100 million are obese
 - ▶ 92 have prediabetes
 - ► 26 million have diabetes
 - ▶ 125 million have atherosclerotic CVD

• Other common causes:

- ► ischemic heart disease and myocardial infarction (MI)
- valvular heart disease (VHD)
- familial or genetic cardiomyopathies
- amyloidosis
- cardiotoxicity with cancer or other treatments
- ▶ substance abuse such as alcohol, cocaine, or methamphetamine
- ► tachycardia
- ► right ventricular (RV) pacing or stress-induced cardiomyopathies
- ► peripartum cardiomyopathy
- myocarditis
- autoimmune causes
- sarcoidosis
- ▶ iron overload including hemochromatosis
- ► thyroid disease
- other endocrine metabolic and nutritional causes

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4. Initial and Serial Evaluation

4.1. Clinical Assessment: History and Physical Examination		
COR	LOE	Recommendations
1	B-NR	In patients with HF, vital signs and evidence of clinical congestion should be assessed at each encounter to guide overall management, including adjustment of diuretics and other medications.
1	B-NR	2. In patients with symptomatic HF, clinical factors indicating the presence of advanced HF should be sought via the history and physical examination.
1	B-NR	3. In patients with cardiomyopathy, a 3-generation family history should be obtained or updated when assessing the cause of the cardiomyopathy to identify possible inherited disease.
1	B-NR	In patients presenting with HF, a thorough history and physical examination should direct diagnostic strategies to uncover specific causes that may warrant disease-specific management.
1	C-EO	5. In patients presenting with HF, a thorough history and physical examination should be obtained and performed to identify cardiac and noncardiac disorders, lifestyle and

Table 5. Other Potential Nonischemic Causes of HF

Chemotherapy and other cardiotoxic medications

HF

- · Rheumatologic or autoimmune
- Endocrine or metabolic (thyroid, acromegaly, pheochromocytoma, diabetes, obesity)

behavioral factors, and social determinants of health that might cause or accelerate the development or progression of

- · Familial cardiomyopathy or inherited and genetic heart disease
- Heart rhythm-related (e.g., tachycardia-mediated, PVCs, RV pacing)
- Hypertension
- Infiltrative cardiac disease (e.g., amyloid, sarcoid, hemochromatosis)
- Myocarditis (infectious, toxin or medication, immunological, hypersensitivity)
- · Peripartum cardiomyopathy
- Stress cardiomyopathy (Takotsubo)
- Substance abuse (e.g., alcohol, cocaine, methamphetamine)





4.1.1. Initial Laboratory and Electrocardiographic Testing		
COR	LOE	Recommendations
1	B-NR	For patients presenting with HF, the specific cause of HF should be explored using additional laboratory testing for appropriate management.
1	C-EO	For patients who are diagnosed with HF, laboratory evaluation should include complete blood count, urinalysis, serum electrolytes, blood urea nitrogen, serum creatinine, glucose, lipid profile, liver function tests, iron studies, and thyroid-stimulating hormone to optimize management.
1	C-EO	3. For all patients presenting with HF, a 12-lead ECG should be performed at the initial encounter to optimize management.

4.2. Use of Biomarkers for Prevention, Initial Diagnosis, and Risk Stratification		
COR	LOE	Recommendations
1	A	In patients presenting with dyspnea, measurement of B-type natriuretic peptide (BNP) or N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) is useful to support a diagnosis or exclusion of HF.
1	A	In patients with chronic HF, measurements of BNP or NT- proBNP levels are recommended for risk stratification.
1	A	In patients hospitalized for HF, measurement of BNP or NT-proBNP levels at admission is recommended to establish prognosis.
2a	B-R	In patients at risk of developing HF, BNP or NT-proBNP– based screening followed by team-based care, including a cardiovascular specialist, can be useful to prevent the development of LV dysfunction or new-onset HF.
2a	B-NR	In patients hospitalized for HF, a predischarge BNP or NT-proBNP level can be useful to inform the trajectory of the patient and establish a postdischarge prognosis.

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Table 6. Selected Potential Causes of Elevated Natriuretic Peptide Levels

Cardiac

- HF, including RV HF syndromes
- ACS
- Heart muscle disease, including LVH
- VHD
- Pericardial disease
- AF

- Myocarditis
- Cardiac surgery
- Cardioversion
- Toxic-metabolic myocardial insults, including cancer chemotherapy

Noncardiac

- Advancing age
- Anemia
- Renal failure
- Pulmonary: Obstructive sleep apnea, severe pneumonia
- Pulmonary embolism, pulmonary arterial hypertension
- Critical illness
- Bacterial sepsis
- Severe burns

4.3. Genetic Evaluation and Testing		
COR	LOE	Recommendations
1	B-NR	In first-degree relatives of selected patients with genetic or inherited cardiomyopathies, genetic screening and counseling are recommended to detect cardiac disease and prompt consideration of treatments to decrease HF progression and sudden death.
2a	B-NR	In select patients with nonischemic cardiomyopathy, referral for genetic counseling and testing is reasonable to identify conditions that could guide treatment for patients and family members.





Table 7. Examples of Factors Implicating Possible Genetic Cardiomyopathy

Cardiomyopatny			
Phenotypic Category	Patient or Family Member Phenotypic Finding*	Ask Specifically About Family Members* With	
Cardiac morphology	Marked LV hypertrophy	Any mention of	
	LV noncompaction	cardiomyopathy, enlarged or weak heart, HF.	
	Ventricular thinning or fatty replacement on imaging or biopsy	Document even if attributed to other causes, such as alcohol or peripartum cardiomyopathy	
Findings on 12-lead ECG	Abnormal high or low voltage or conduction, and repolarization, altered RV forces	Recurrent syncope, long QT or Brugada syndrome	
Dysrhythmias	Frequent NSVT or very	ICD	
	frequent PVCs Sustained ventricular tachycardia or fibrillation	 Sudden death attributed to "massive heart attack" without known CAD 	
		Unexplained fatal event such as drowning or single- vehicle crash	
	Early onset AF	"Lone" AF before age 65 years	
	Early onset conduction disease	Pacemaker before age 65 years	
Extracardiac features	Skeletal myopathy Neuropathy Cutaneous stigmata Other possible manifestations of systemic syndromes	Any known skeletal muscle disease, including mention of Duchenne and Becker's, Emory-Dreifuss limbgirdle dystrophy Systemic syndromes: Dysmorphic features Mental retardation Congenital deafness Neurofibromatosis Renal failure with neuropathy	

^{*} Note that genetic cause is more likely when the person is younger at the onset of events. However, the cardiac morphology and peripheral manifestations of hereditary amyloidosis may present in later life, unlike most other inherited cardiomyopathies

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4.4. Evaluation With Cardiac Imaging		
COR	LOE	Recommendations
1	C-LD	In patients with suspected or new-onset HF, or those presenting with acute decompensated HF, a chest x-ray should be performed 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.
1	C-LD	In patients with suspected or newly diagnosed HF, transthoracic echocardiography (TTE) should be performed during initial evaluation to assess cardiac structure and function.
1	C-LD	In patients with HF who have had a significant clinical change, or who have received GDMT and are being considered for invasive procedures or device therapy, repeat measurement of EF, degree of structural remodeling, and valvular function are useful to inform therapeutic interventions.
1	C-LD	4. In patients for whom echocardiography is inadequate, alternative imaging (e.g., cardiac magnetic resonance [CMR], cardiac computed tomography [CT], radionuclide imaging) is recommended for assessment of LVEF.
2a	B-NR	In patients with HF or cardiomyopathy, CMR can be useful for diagnosis or management.
2a	B-NR	In patients with HF, an evaluation for possible ischemic heart disease can be useful to identify the cause and guide management.
2b	B-NR	7. In patients with HF and CAD who are candidates for coronary revascularization, noninvasive stress imaging (stress echocardiography, single-photon emission CT [SPECT], CMR, or positron emission tomography [PET]) may be considered for detection of myocardial ischemia to help guide coronary revascularization.
3: No Benefit	С-ЕО	8. In patients with HF in the absence of: 1) clinical status change, 2) treatment interventions that might have had a significant effect on cardiac function, or 3) candidacy for invasive procedures or device therapy, routine repeat assessment of LV function is not indicated.





4.5. Invasive Evaluation		
COR	LOE	Recommendations
2a	B-NR	In patients with HF, endomyocardial biopsy may be useful when a specific diagnosis is suspected that would influence therapy.
2a	С-ЕО	In selected patients with HF with persistent or worsening symptoms, signs, diagnostic parameters, and in whom hemodynamics are uncertain, invasive hemodynamic monitoring can be useful to guide management.
3: No Benefit	B-R	3. In patients with HF, routine use of invasive hemodynamic monitoring is <i>not</i> recommended.
3: Harm	C-LD	4. For patients undergoing routine evaluation of HF, endomyocardial biopsy should <i>not</i> be performed because of the risk of complications.

	4.6. Wearables and Remote Monitoring (Including Telemonitoring and Device Monitoring)		
COR	LOE	Recommendations	
2b	B-R	In selected adult patients with NYHA class III HF and history of a HF hospitalization in the past year or elevated natriuretic peptide levels, on maximally tolerated stable doses of GDMT with optimal device therapy, the usefulness of wireless monitoring of PA pressure by an implanted hemodynamic monitor to reduce the risk of subsequent HF hospitalizations is uncertain.	
Value Statement: Uncertain Value (B-NR)		In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the PA pressure by an implanted hemodynamic monitor provides uncertain value.	

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4.7. Exercise and Functional Capacity Testing		
COR	LOE	Recommendations
1	C-LD	In patients with HF, assessment and documentation of NYHA functional classification are recommended to determine eligibility for treatments.
1	C-LD	2. In selected ambulatory patients with HF, cardiopulmonary exercise testing (CPET) is recommended to determine appropriateness of advanced treatments (e.g., LVAD, heart transplant).
2a	C-LD	3. In ambulatory patients with HF, performing a CPET or 6-minute walk test is reasonable to assess functional capacity.
2a	C-LD	4. In ambulatory patients with unexplained dyspnea, CPET is reasonable to evaluate the cause of dyspnea.

4.8. Initial and Serial Evaluation: Clinical Assessment: HF Risk Scoring			
COR	LOE	Recommendation	
2a	B-NR	In ambulatory or hospitalized patients with HF, validated multivariable risk scores can be useful to estimate subsequent risk of mortality.	

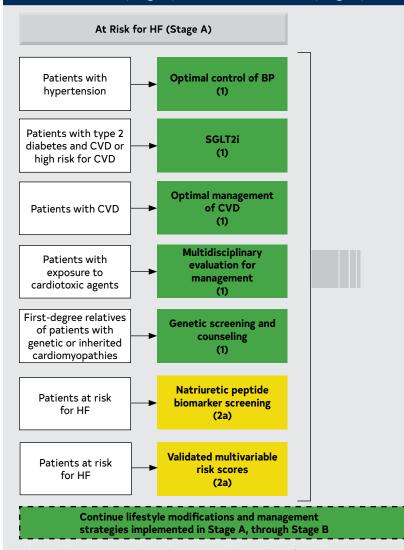




5. Stage A (Patients at Risk for HF)

5.1. Pa	5.1. Patients at Risk for HF (Stage A: Primary Prevention)		
COR	LOE	Recommendations	
1	A	In patients with hypertension, blood pressure should be controlled in accordance with GDMT for hypertension to prevent symptomatic HF.	
1	A	In patients with type 2 diabetes and either established CVD or at high cardiovascular risk, SGLT2i should be used to prevent hospitalizations for HF.	
1	B-NR	In the general population, healthy lifestyle habits such as regular physical activity, maintaining normal weight, healthy dietary patterns, and avoiding smoking are helpful to reduce future risk of HF.	
2a	B-R	4. 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 LV dysfunction (systolic or diastolic) or new-onset HF.	
2a	B-NR	5. In the general population, validated multivariable risk scores can be useful to estimate subsequent risk of incident HF.	

Figure 5. Recommendations (Class 1 and 2a) for Patients at Risk of HF (Stage A) and Those With Pre-HF (Stage B)

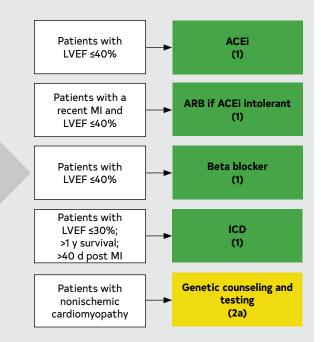


Class 1 and Class 2a recommendations for patients at risk for HF (stage A) and those with pre-HF (stage B) are shown. Management strategies implemented in patients at risk for HF (stage A) should be continued though stage B.





Pre-HF (Stage B)



Continue lifestyle modifications and management strategies implemented in Stage A, through Stage B

6. Stage B (Patients With Pre-HF)

6.1. Management of Stage B: Preventing the Syndrome of Clinical HF in Patients With Pre-HF

COR	LOE	Recommendations
1	A	 In patients with LVEF ≤40%, ACEi should be used to prevent symptomatic HF and reduce mortality.
1	A	In patients with a recent or remote history of MI or ACS, statins should be used to prevent symptomatic HF and adverse cardiovascular events.
1	B-R	 In patients with a recent MI and LVEF ≤40% who are intolerant to ACEi, ARB should be used to prevent symptomatic HF and reduce mortality.
1	B-R	 In patients with a recent or remote history of MI or acute coronary syndrome (ACS) and LVEF ≤40%, evidence-based beta blockers should be used to reduce mortality.
1	B-R	5. In patients who are at least 40 days post-MI with LVEF ≤30% and NYHA class I symptoms while receiving GDMT and have reasonable expectation of meaningful survival for >1 year, an ICD is recommended for primary prevention of sudden cardiac death (SCD) to reduce total mortality.
1	C-LD	6. In patients with LVEF ≤40%, beta blockers should be used to prevent symptomatic HF.
3: Harm	B-R	7. In patients with LVEF <50%, thiazolidinediones should not be used because they increase the risk of HF, including hospitalizations.
3: Harm	C-LD	8. In patients with LVEF <50%, nondihydropyridine calcium channel blockers with negative inotropic effects may be harmful.





7. Stage "C" HF

7.1.1. Nonpharmacological Interventions: Self-Care Support in HF		
COR	LOE	Recommendations
1	A	Patients with HF should receive care from multidisciplinary teams to facilitate the implementation of GDMT, address potential barriers to self-care, reduce the risk of subsequent rehospitalization for HF, and improve survival.
1	B-R	Patients with HF should receive specific education and support to facilitate HF self-care in a multidisciplinary manner.
2a	B-NR	3. In patients with HF, vaccinating against respiratory illnesses is reasonable to reduce mortality.
2a	B-NR	In adults with HF, screening for depression, social isolation, frailty, and low health literacy as risk factors for poor self-care is reasonable to improve management.

7.1.2. Dietary Sodium Restriction		
COR	LOE	Recommendation
2a	C-LD	For patients with stage C HF, avoiding excessive sodium intake is reasonable to reduce congestive symptoms.

	7.1.3. Management of Stage C HF: Activity, Exercise Prescription, and Cardiac Rehabilitation		
COR LOE Recommendations			
1	A	For patients with HF who are able to participate, exercise training (or regular physical activity) is recommended to improve functional status, exercise performance, and QOL.	
2a	B-NR	In patients with HF, a cardiac rehabilitation program can be useful to improve functional capacity, exercise tolerance, and health-related QOL.	

Table 11. Potential Barriers to Effective HF Self-Care and Example Interventions			
Potential Barrier	Example Screening Tools	Example Interventions	
Medical Barriers			
Cognitive impairment	Mini-Cog Mini-Mental State Examination (MMSE) Montreal Cognitive Assessment (MoCA)	 Home health aide Home meal deliveries Adult day care Geriatric psychiatry referral Memory care support groups 	
Depression	Hamilton Depression Rating Scale (HAM-D) Beck Depression Inventory-II (BDI-II) Patient Health Questionnaire-9 (PHQ-9)	Psychotherapy Selective serotonin reuptake inhibitors Nurse-led support	
Substance use disorders	Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	Referral to social work services and community support partners Referral for addiction psychiatry consultation	
Frailty	Fried frailty phenotype	Cardiac rehabilitation Registered dietitian nutritionist evaluation for malnutrition	
Social Barriers			
Financial burden of HF treatments	COmprehensive Score for financial Toxicity— Functional Assessment of Chronic Illness Therapy (COST-FACIT)	PharmD referral to review prescription assistance eligibilities	
Food insecurity	Hunger Vital Sign, 2 items U.S. Household Food Security Survey Module, 6 items	Determine eligibility for the Supplemental Nutrition Assistance Program (SNAP) Connect patients with community partners such as food pantries/food banks Home meal deliveries Registered dietitian nutritionist evaluation for potential malnutrition	
Homelessness or housing insecurity	Homelessness Screening Clinical Reminder (HSCR)	Referral to local housing services Connect patients with community housing partners	





Table 11. Potential Barriers to Effective HF Self-Care and Example Interventions (cont'd)

Potential Barrier	Example Screening Tools	Example Interventions
Intimate partner violence or elder abuse	Humiliation, Afraid, Rape, Kick (HARK) questionnaire Partner Violence Screen (PVS) Woman Abuse Screening Tool (WAST)	Referral to social work services and community support partners
Limited English proficiency or other language barriers	Routinely inquire in which language the patient is most comfortable conversing	Access to interpreter services covering a wide range of languages, ideally in person or, alternatively, via video platform Printed educational materials in a range of appropriate languages
Low health literacy	Short Assessment of Health Literacy (SAHL) Rapid Estimate of Adult Literacy in Medicine—Short Form (REALM-SF) Brief Health Literacy Screen (BHLS), 3 items	Agency for Healthcare Research and Quality (AHRQ) Health Literacy Universal Precautions Toolkit Written education tools provided at sixth grade reading level or below Graphic educational documents
Social isolation or low social support	Patient-Reported Outcomes Measurement Information System (PROMIS) Social Isolation Short Form	Determine eligibility for home care services Support group referral
Transport limitations	No validated tools currently available	Referral to social work services Determine eligibility for insurance or state-based transportation, or reduced-cost public transportation Maximize opportunities for telehealth visits and remote monitoring

	7.2. Diuretics and Decongestion Strategies in Patients With HF		
COR	LOE	Recommendations	
1	B-NR	In patients with HF who have fluid retention, diuretics are recommended to relieve congestion, improve symptoms, and prevent worsening HF.	
1	B-NR	For patients with HF and congestive symptoms, addition of a thiazide (e.g., metolazone) to treatment with a loop diuretic should be reserved for patients who do not respond to moderate- or high-dose loop diuretics to minimize electrolyte abnormalities.	

Table 12. Commonly Used Oral Diuretics in Treatment of Congestion for Chronic HF			
Drug	Initial Daily Dose	Maximum Total Daily Dose	Duration of Action
Loop diuretics			
Bumetanide	0.5–1.0 mg once or twice	10 mg	4–6 h
Furosemide	20–40 mg once or twice	600 mg	6–8 h
Torsemide	10-20 mg once	200 mg	12-16 h
Thiazide diuretics			
Chlorthiazide	250–500 mg once or twice	1000 mg	6–12 h
Chlorthalidone	12.5–25 mg once	100 mg	24–72 h
Hydrochlorothiazide	25 mg once or twice	200 mg	6–12 h
Indapamide	2.5 mg once	5 mg	36 h
Metolazone	2.5 mg once	20 mg	12-24 h





7.3. Pharmacological Treatment* for HFrEF

* See Section 7.2, "Diuretics and Decongestion Strategies in Patients with HF," for diuretic recommendations.

7.3.1. Renin-Angiotensin System Inhibition With ACEi or		
ARB or ARNi		
COR	LOE	Recommendations
1	A	In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality.
1	A	In patients with previous or current symptoms of chronic HFrEF, the use of ACEi is beneficial to reduce morbidity and mortality when the use of ARNi is not feasible.
1	A	3. In patients with previous or current symptoms of chronic HFrEF who are intolerant to ACEi because of cough or angioedema and when the use of ARNi is not feasible, the use of ARB is recommended to reduce morbidity and mortality.
Value Statement: High Value (A)		4. In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value.
1	B-R	5. In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNi is recommended to further reduce morbidity and mortality.
	atement: alue (A)	6. In patients with chronic symptomatic HFrEF, treatment with an ARNi instead of an ACEi provides high economic value.
3: Harm	B-R	7. ARNi should <i>not</i> be administered concomitantly with ACEi or within 36 hours of the last dose of an ACEi.
3: Harm	C-LD	8. ARNi should <i>not</i> be administered to patients with any history of angioedema.
3: Harm	C-LD	9. ACEi should <i>not</i> be administered to patients with any history of angioedema.

7.3.2. Beta Blockers		
COR	LOE	Recommendations
1	A	In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality (e.g., bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations.
	atement: alue (A)	2. In patients with HFrEF, with current or previous symptoms, beta-blocker therapy provides high economic value (4-8).

7.3.3.	Mineral	ocorticoid Receptor Antagonists (MRAs)		
COR LOE		Recommendations		
1	A	1. In patients with HFrEF and NYHA class II-IV symptoms, an MRA (spironolactone or eplerenone) is recommended to reduce morbidity and mortality, if eGFR is >30 mL/min/ 1.73 m² and serum potassium is <5.0 mEq/L. Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation and closely monitored thereafter to minimize risk of hyperkalemia and renal insufficiency.		
	atement: alue (A)	In patients with HFrEF and NYHA class II-IV symptoms, MRA therapy provides high economic value.		
3: Harm	B-NR	3. In patients taking MRA whose serum potassium cannot be maintained at <5.5 mEq/L, MRA should be discontinued to avoid life-threatening hyperkalemia.		
734	Sodium	-Glucose Cotransporter 2 Inhibitors		
COR	LOE	Recommendations		
1	A	In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.		
Intermed	atement: iate Value A)	In patients with symptomatic chronic HFrEF, SGLT2i therapy provides intermediate economic value.		
735	Hvdrala	zine and Isosorbide Dinitrate		
COR	LOE	Recommendations		
1	A	For patients self-identified as African American with NYHA class III-IV HFrEF who are receiving optimal medical therapy, the combination of hydralazine and isosorbide dinitrate is recommended to improve symptoms and reduce morbidity and mortality.		
Value Statement: High Value (B-NR)		2. For patients self-identified as African American with NYHA class III-IV HFrEF who are receiving optimal medical therapy with ACEi or ARB, beta blockers, and MRA, the combination of hydralazine and isosorbide dinitrate provides high economic value.		
2b	C-LD	3. In patients with current or previous symptomatic HFrEF		

who cannot be given first-line agents, such as ARNi, ACEi, or ARB, because of drug intolerance or renal insufficiency, a combination of hydralazine and isosorbide dinitrate might be

considered to reduce morbidity and mortality.

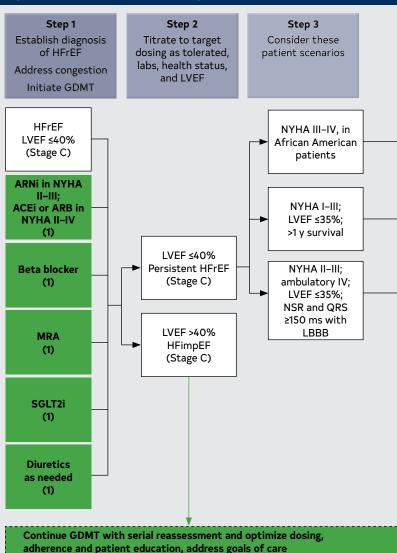




7.3.6.	7.3.6. Other Drug Treatment			
COR	LOE	Recommendations		
2b	B-R	In patients with HF class II to IV symptoms, omega-3 polyunsaturated fatty acid (PUFA) supplementation may be reasonable to use as adjunctive therapy to reduce mortality and cardiovascular hospitalizations.		
2b	B-R	2. In patients with HF who experience hyperkalemia (serum potassium level ≥5.5 mEq/L) while taking a reninangiotensin-aldosterone system inhibitor (RAASi), the effectiveness of potassium binders (patiromer, sodium zirconium cyclosilicate) to improve outcomes by facilitating continuation of RAASi therapy is uncertain.		
3: No Benefit	B-R	3. In patients with chronic HFrEF without a specific indication (e.g., venous thromboembolism [VTE], AF, a previous thromboembolic event, or a cardioembolic source), anticoagulation is <i>not</i> recommended.		

7.3.7. I	7.3.7. Drugs of Unproven Value or That May Worsen HF			
COR	LOE	Recommendations		
3: No Benefit	A	In patients with HFrEF, dihydropyridine calcium channel- blocking drugs are <i>not</i> recommended treatment for HF.		
3: No benefit	B-R	In patients with HFrEF, vitamins, nutritional supplements, and hormonal therapy are <i>not</i> recommended other than to correct specific deficiencies.		
3: Harm	A	3. In patients with HFrEF, nondihydropyridine calcium channel-blocking drugs are <i>not</i> recommended.		
3: Harm	A	In patients with HFrEF, class IC antiarrhythmic medications and dronedarone may increase the risk of mortality.		
3: Harm	A	5. In patients with HFrEF, thiazolidinediones increase the risk of worsening HF symptoms and hospitalizations.		
3: Harm	B-R	6. In patients with type 2 diabetes and high cardiovascular risk, the dipeptidyl peptidase-4 (DPP-4) inhibitors saxagliptin and alogliptin increase the risk of HF hospitalization and should be avoided in patients with HF.		
3: Harm	B-NR	7. In patients with HFrEF, NSAIDs worsen HF symptoms and should be avoided or withdrawn whenever possible.		

Figure 6. Treatment of HFrEF Stages C and D



^{*} Participation in investigational studies is appropriate for stage C, NYHA class II and III HF.





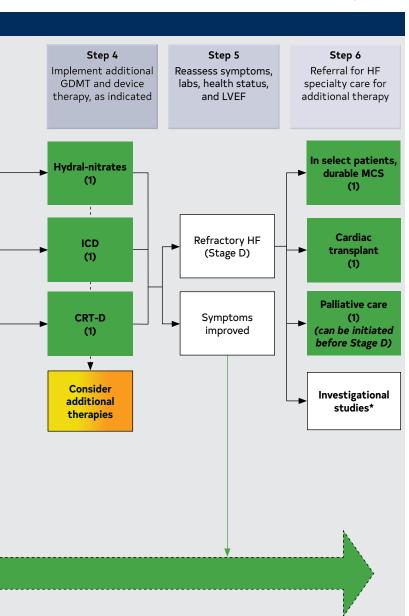


Table 13. Selected Prescription Medications That May Cause or Exacerbate HF

	Associated With HF		
Drug or Therapeutic Class	Causes Direct Myocardial Toxicity	Exacerbates Underlying Myocardial Dysfunction	Magnitude of HF Induction or Precipitation
COX, nonselective inhibitors (NSAIDs)		X	Major
COX, selective inhibitors (COX-2 inhibitors)		X	Major
Thiazolidinediones		X	Major
Saxagliptin		X	Major
Alogliptin		X	Major
Flecainide		X	Major
Disopyramide		X	Major
Sotalol		X	Major
Dronedarone		X	Major
Alpha-1 blockers			
Doxazosin		X	Moderate
Diltiazem		X	Major
Verapamil		X	Major
Nifedipine		X	Moderate





Level of Evidence for HF Induction or Precipitation	Possible Mechanism(s)	Onset	
В	Prostaglandin inhibition leading to sodium and water retention, increased	Immediate	
В	systemic vascular resistance, and blunted response to diuretics		
A	Possible calcium channel blockade	Intermediate	
A	Unknown	Intermediate to delayed	
A			
A	Negative inotrope,	Immediate to intermediate	
В	proarrhythmic effects		
A	Proarrhythmic properties, beta blockade	Immediate to intermediate	
A	Negative inotrope		
В	Beta-1-receptor stimulation with increases in renin and aldosterone	Intermediate to delayed	
В	Negative inotrope	Immediate to intermediate	
В			
С	Negative inotrope	Immediate to intermediate	

7.3.8.	7.3.8. GDMT Dosing: Sequencing and Uptitration				
COR	LOE	Recommendations			
1	A	In patients with HFrEF, titration of guideline-directed medication dosing to achieve target doses showed to be efficacious in RCTs is recommended, to reduce cardiovascular mortality and HF hospitalizations, unless not well tolerate.			
2a	С-ЕО	In patients with HFrEF, titration and optimization of guideline-directed medications as frequently as every 1 to 2 weeks depending on the patient's symptoms, vital signs, and laboratory findings can be useful to optimize management.			

Table 14. Drugs Commonly Used for HFrEF (Stage C HF)			
Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
ACEi			
Captopril	6.25 mg 3 times daily	50 mg 3 times daily	122.7 mg total daily
Enalapril	2.5 mg twice daily	10–20 mg twice daily	16.6 mg total daily
Fosinopril	5–10 mg once daily	40 mg once daily	NA
Lisinopril	2.5–5 mg once daily	20–40 mg once daily	32.5-35.0 mg total daily
Perindopril	2 mg once daily	8–16 mg once daily	NA
Quinapril	5 mg twice daily	20 mg twice daily	NA
Ramipril	1.25–2.5 mg once daily	10 mg once daily	NA
Trandolapril	1 mg once daily	4 mg once daily	NA
ARB			
Candesartan	4–8 mg once daily	32 mg once daily	24 mg total daily
Losartan	25–50 mg once daily	50–150 mg once daily	129 mg total daily
Valsartan	20–40 mg once daily	160 mg twice daily	254 mg total daily





Table 14. Drugs Commonly Used for HFrEF (Stage C HF) (cont'd)

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials
ARNi			
Sacubitril-valsartan	49 mg sacubitril and 51 mg valsartan twice daily (therapy may be initiated at 24 mg sacubitril and 26 mg valsartan twice daily)	97 mg sacubitril and 103 mg valsartan twice daily	182 mg sacubitril and 193 mg valsartan total daily
Beta blockers			
Bisoprolol	1.25 mg once daily	10 mg once daily	8.6 mg total daily
Carvedilol	3.125 mg twice daily	25–50 mg twice daily	37 mg total daily
Carvedilol CR	10 mg once daily	80 mg once daily	NA
Metoprolol succinate extended release (metoprolol CR/XL) 12.5–25 mg once daily		200 mg once daily	159 mg total daily
Mineralocorticoid r	eceptor antagonists		
Spironolactone	12.5–25 mg once daily	25–50 mg once daily	26 mg total daily
Eplerenone	25 mg once daily	50 mg once daily	42.6 mg total daily
SGLT2i			
Dapagliflozin	10 mg once daily	10 mg once daily	9.8 mg total daily
Empagliflozin	10 mg once daily	10 mg once daily	NR
Isosorbide dinitrate	and hydralazine		
Fixed dose combination	20 mg isosorbide dinitrate and 37.5 mg hydralazine 3 times daily	40 mg isosorbide dinitrate and 75 mg hydralazine 3 times daily	90 mg isosorbide dinitrate and ~175 mg hydralazine total daily
Isosorbide dinitrate and hydralazine	20–30 mg isosorbide dinitrate and 25–50 mg hydralazine 3–4 times daily	120 mg isosorbide dinitrate total daily in divided doses and 300 mg hydralazine total daily in divided doses	NA

Table 14. Drugs	Table 14. Drugs Commonly Used for HFrEF (Stage C HF) (cont'd)			
Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials	
I _f Channel inhibitor				
Ivabradine	5 mg twice daily	7.5 mg twice daily	12.8 total daily	
Soluble guanylate cy	clase stimulator			
Vericiguat	2.5 mg once daily	10 mg once daily	9.2 mg total daily	
Digoxin	0.125–0.25 mg daily (modified according to monogram)	Individualized variable dose to achieve serum digoxin concentration 0.5–<0.9 ng/mL	NA	

	Table 15. Benefits of Evidence-Based Therapies for Patients With HFrEF				
Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal RCTs, %	NNT to Prevent All-Cause Mortality Over Time*	NNT for All-Cause Mortality (Standardized to 12 mo)	NNT for All-Cause Mortality (Standardized to 36 mo)	
ACEi or ARB	17	22 over 42 mo	77	26	
ARNi [†]	16	36 over 27 mo	80	27	
Beta blocker	34	28 over 12 mo	28	9	
Mineralocorticoid receptor antagonist	30	9 over 24 mo	18	6	
SGLT2i	17	43 over 18 mo	63	22	
Hydralazine or nitrate [‡]	43	25 over 10 mo	21	7	
CRT	36	12 over 24 mo	24	8	
ICD	23	14 over 60 mo	70	23	

^{*} Median duration follow-up in the respective clinical trial.

[†] Benefit of ARNi therapy incremental to that achieved with ACEi therapy. For the other medications shown, the benefits are based on comparisons to placebo control.

[‡] Benefit of hydralazine-nitrate therapy was limited to African American patients in this trial.





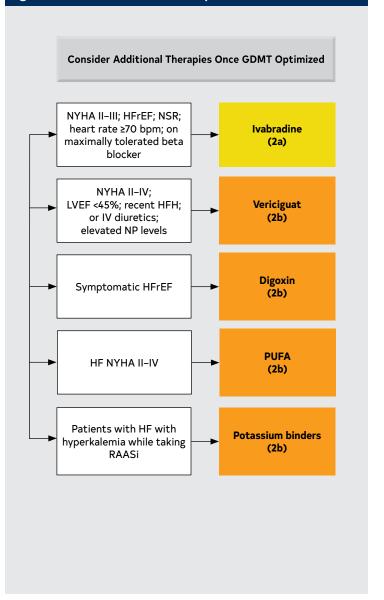
7.3.9. Additional Medical Therapies

7.3.9.1	7.3.9.1. Management of Stage C HF: Ivabradine			
COR	LOE	Recommendation		
2a	B-R	1. For patients with symptomatic (NYHA class II to III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDMT, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of ≥70 bpm at rest, ivabradine can be beneficial to reduce HF hospitalizations and cardiovascular death.		

7.3.9.2. Pharmacological Treatment for Stage C HFrEF (Digoxin)			
COR	LOE	Recommendation	
2b	B-R	In patients with symptomatic HFrEF despite GDMT (or who are unable to tolerate GDMT), digoxin might be considered to decrease hospitalizations for HF.	

7.3.9.3. Pharmacological Treatment for Stage C HFrEF: Soluble Guanylyl Cyclase Stimulators		
COR	LOE	Recommendation
2b	B-R	In selected high-risk patients with HFrEF and recent worsening of HF already on GDMT, an oral soluble guanylate cyclase stimulator (vericiguat) may be considered to reduce HF hospitalization and cardiovascular death.

Figure 7. Additional Medical Therapies for Patients With HFrEF







7.4. Device and Interventional Therapies for HFrEF

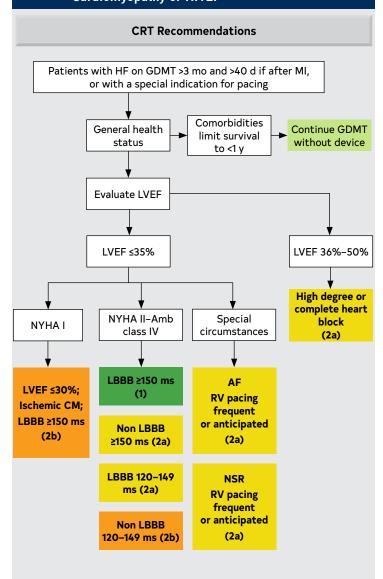
7.4.1.	7.4.1. ICDs and CRTs		
COR	LOE	Recommendations	
1	A	In patients with nonischemic DCM or ischemic heart disease at least 40 days post-MI with LVEF ≤35% and NYHA class II or III symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for >1 year, ICD therapy is recommended for primary prevention of SCD to reduce total mortality.	
Value Statement: High Value (A)		A transvenous ICD provides high economic value in the primary prevention of SCD particularly when the patient's risk of death caused by ventricular arrythmia is deemed high and the risk of nonarrhythmic death (either cardiac or noncardiac) is deemed low based on the patient's burden of comorbidities and functional status.	
1	B-R	3. In patients at least 40 days post-MI with LVEF ≤30% and NYHA class I symptoms while receiving GDMT, who have reasonable expectation of meaningful survival for >1 year, ICD therapy is recommended for primary prevention of SCD to reduce total mortality.	
1	B-R	4. For patients who have LVEF ≤35%, sinus rhythm, left bundle branch block (LBBB) with a QRS duration ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT is indicated to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.	
Value Statement: High Value (B-NR)		5. For patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration of ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT implantation provides high economic value.	
2a	B-R	6. For patients who have LVEF ≤35%, sinus rhythm, a non- LBBB pattern with a QRS duration ≥150 ms, and NYHA class II, III, or ambulatory class IV symptoms on GDMT, CRT can be useful to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.	
2a	B-R	7. In patients with high-degree or complete heart block and LVEF of 36% to 50%, CRT is reasonable to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.	

7.4.1. ICDs and CRTs (cont'd)		
COR	LOE	Recommendations
2a	B-NR	8. For patients who have LVEF ≤35%, sinus rhythm, LBBB with a QRS duration of 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT can be useful to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.
2a	B-NR	9. In patients with AF and LVEF ≤35% on GDMT, CRT can be useful to reduce total mortality, improve symptoms and QOL, and increase LVEF, 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.
2a	B-NR	10. For patients on GDMT who have LVEF ≤35% and are undergoing placement of a new or replacement device implantation with anticipated requirement for significant (>40%) ventricular pacing, CRT can be useful to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.
2a	B-NR	11. In patients with genetic arrhythmogenic cardiomyopathy with high-risk features of sudden death, with EF ≤45%, implantation of ICD is reasonable to decrease sudden death.
2b	B-NR	12. For patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration of 120 to 149 ms, and NYHA class III or ambulatory class IV on GDMT, CRT may be considered to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL.
2b	B-NR	13. For patients who have LVEF ≤30%, ischemic cause of HF, sinus rhythm, LBBB with a QRS duration ≥150 ms, and NYHA class I symptoms on GDMT, CRT may be considered to reduce hospitalizations and improve symptoms and QOL.
3: No Benefit	B-R	14. In patients with QRS duration <120 ms, CRT is <i>not</i> recommended.
3: No Benefit	B-NR	15. For patients with NYHA class I or II symptoms and non- LBBB pattern with QRS duration <150 ms, CRT is <i>not</i> recommended.
3: No Benefit	C-LD	16. For patients whose comorbidities or frailty limit survival with good functional capacity to <1 year, ICD and cardiac resynchronization therapy with defibrillation (CRT-D) are not indicated.

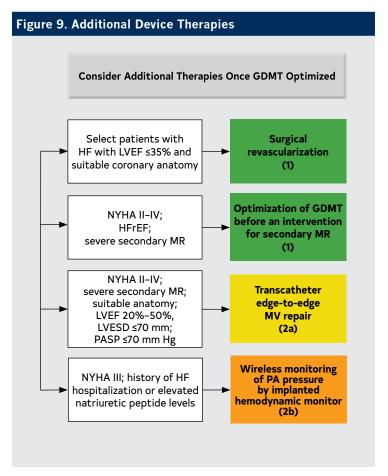




Figure 8. Algorithm for CRT Indications in Patients With Cardiomyopathy or HFrEF



7.4.3. Revascularization for CAD			
COR	LOE	Recommendation	
1	B-R	In selected patients with HF, reduced EF (EF ≤35%), and suitable coronary anatomy, surgical revascularization plus GDMT is beneficial to improve symptoms, cardiovascular hospitalizations, and long-term all-cause mortality.	

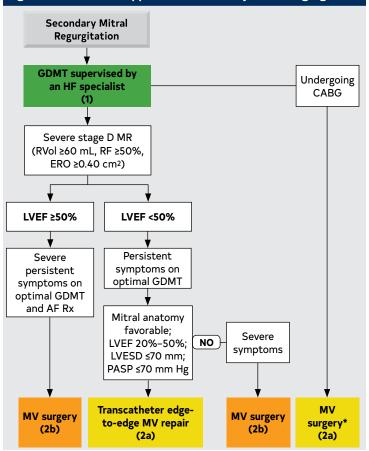






7.5. Va	7.5. Valvular Heart Disease		
COR	LOE	Recommendations	
1	B-R	In patients with HF, VHD should be managed in a multidisciplinary manner in accordance with clinical practice guidelines for VHD to prevent worsening of HF and adverse clinical outcomes.	
1	C-LD	In patients with chronic severe secondary MR and HFrEF, optimization of GDMT is recommended before any intervention for secondary MR related to LV dysfunction.	

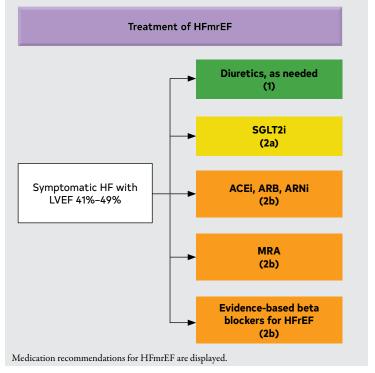
Figure 10. Treatment Approach in Secondary Mitral Regurgitation



7.6. Mildly Reduced EF (HFmrEF) and Improved EF (HFimpHF)

7.6.1. HF With Mildly Reduced Ejection Fraction		
COR	LOE	Recommendations
2a	B-R	In patients with HFmrEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.
2b	B-NR	2. Among patients with current or previous symptomatic HFmrEF (LVEF 41%–49%), use of evidence-based beta blockers for HFrEF, ARNi, ACEi or ARB, and MRAs may be considered to reduce the risk of HF hospitalization and cardiovascular mortality, particularly among patients with LVEF on the lower end of this spectrum.

Figure 11. Recommendations for Patients With Mildly Reduced LVEF (41%–49%)







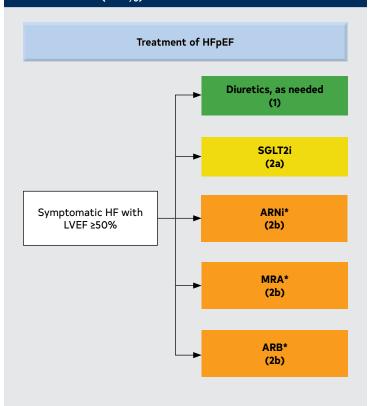
7.6.2. HF With Improved Ejection Fraction			
COR	LOE	Recommendation	
1	B-R	In HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic.	

7.7. Preserved EF (HFpEF)

7.7.1. HF With Preserved Ejection Fraction*		
COR	LOE	Recommendations
1	C-LD	Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity.
2a	B-R	In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.
2a	C-EO	3. In patients with HFpEF, management of AF can be useful to improve symptoms.
2b	B-R	In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.
2b	B-R	5. In selected patients with HFpEF, the use of ARB may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.
2b	B-R	6. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.
3: No- Benefit	B-R	7. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QOL is ineffective.

^{*} See Section 7.2 ("Diuretics and Decongestion Strategies in Patients with HF") and Section 10.2 ("Management of Atrial Fibrillation (AF) in HF") for recommendations for use of diuretics and management of AF in HF.

Figure 12. Recommendations for Patients With Preserved LVEF (≥50%)



Medication recommendations for HFpEF are displayed.

^{*} Greater benefit in patients with LVEF closer to 50%.





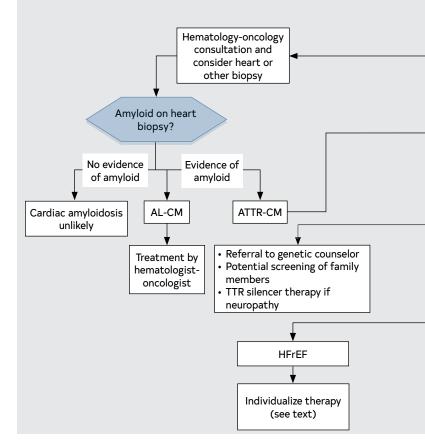
7.8. Cardiac Amyloidosis

7.8.1.	7.8.1. Diagnosis of Cardiac Amyloidosis		
COR	LOE	Recommendations	
1	B-NR	Patients for whom there is a clinical suspicion for cardiac amyloidosis* should have screening for serum and urine monoclonal light chains with serum and urine immunofixation electrophoresis and serum free light chains.	
1	B-NR	In patients with high clinical suspicion for cardiac amyloidosis, without evidence of serum or urine monoclonal light chains, bone scintigraphy should be performed to confirm the presence of transthyretin cardiac amyloidosis.	
1	B-NR	3. In patients for whom a diagnosis of transthyretin cardiac amyloidosis is made, genetic testing with TTR gene sequencing is recommended to differentiate hereditary variant from wild-type transthyretin cardiac amyloidosis.	

^{*} LV wall thickness ≥ 14 mm in conjunction with fatigue, dyspnea, or edema, especially in the context of discordance between wall thickness on echocardiogram and QRS voltage on ECG, and in the context of aortic stenosis, HFpEF, carpal tunnel syndrome, spinal stenosis, and autonomic or sensory polyneuropathy.

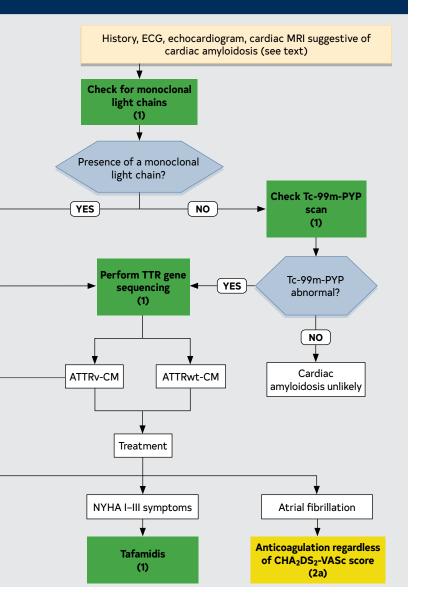
7.8.2.	7.8.2. Treatment of Cardiac Amyloidosis		
COR	LOE	Recommendations	
1	B-R	In select patients with wild-type or variant transthyretin cardiac amyloidosis and NYHA class I to III HF symptoms, transthyretin tetramer stabilizer therapy (tafamidis) is indicated to reduce cardiovascular morbidity and mortality.	
Value Statement: Low Value (B-NR)		At 2020 list prices, tafamidis provides low economic value (>\$180,000 per QALY gained) in patients with HF with wild-type or variant transthyretin cardiac amyloidosis.	
2a	C-LD	3. In patients with cardiac amyloidosis and AF, anticoagulation is reasonable to reduce the risk of stroke regardless of the CHA₂DS₂-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack [TIA], vascular disease, age 65 to 74 years, sex category) score.	

Figure 13. Diagnostic and Treatment of Transthyretin Cardiac Amyloidosis Algorithm









8. Stage D (Advanced) HF

8.1. Specialty Referral for Advanced HF

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COR	LOE	Recommendation	
1	C-LD	In patients with advanced HF, when consistent with the patient's goals of care, timely referral for HF specialty care is recommended to review HF management and assess suitability for advanced HF therapies (e.g., LVAD, cardiac transplantation, palliative care, and palliative inotropes).	

Table 16. ESC Definition of Advanced HF

All of these criteria must be present despite optimal guideline-directed treatment:

- 1. Severe and persistent symptoms of HF (NYHA class III [advanced] or IV)
- 2. Severe cardiac dysfunction defined by ≥1 of these:
 - LVEF ≤30%
 - Isolated RV failure
 - Nonoperable severe valve abnormalities
 - Nonoperable severe congenital heart disease
 - EF ≥40%, elevated natriuretic peptide levels and evidence of significant diastolic dysfunction
- 3. Hospitalizations or unplanned visits in the past 12 mo for episodes of:
 - Congestion requiring high-dose intravenous diuretics or diuretic combinations
 - Low output requiring inotropes or vasoactive medications
 - Malignant arrhythmias
- 4. Severe impairment of exercise capacity with inability to exercise or low 6-minute walk test distance (<300 m) or peak VO_2 (<12–14 mL/kg/min) estimated to be of cardiac origin

Criteria 1 and 4 can be met in patients with cardiac dysfunction (as described in criterion 2) but who also have substantial limitations as a result of other conditions (e.g., severe pulmonary disease, noncardiac cirrhosis, renal disease). The therapeutic options for these patients may be more limited.





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

Table 18. Clinical Indicators of Advanced HF

Repeated hospitalizations or emergency department visits for HF in the past 12 mo.

Need for intravenous inotropic therapy.

Persistent NYHA functional class III to IV symptoms despite therapy.

Severely reduced exercise capacity (peak VO₂, <14 mL/kg/min or <50% predicted, 6-minute walk test distance <300 m, or inability to walk 1 block on level ground because of dyspnea or fatigue).

Intolerance to RAAS inhibitors because of hypotension or worsening renal function.

Intolerance to beta blockers as a result of worsening HF or hypotension.

Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose > 160 mg/d or use of supplemental metolazone therapy.

Refractory clinical congestion.

Progressive deterioration in renal or hepatic function.

Worsening right HF or secondary pulmonary hypertension.

Frequent SBP ≤90 mm Hg.

Cardiac cachexia.

Persistent hyponatremia (serum sodium, <134 mEq/L).

Refractory or recurrent ventricular arrhythmias; frequent ICD shocks.

Increased predicted 1-year mortality (e.g., >20%) according to HF survival models (e.g., MAGGIC, SHFM).

8.2. Nonpharmacological Management: Advanced HF COR LOE Recommendation 2b C-LD 1. For patients with advanced HF and hyponatremia, the benefit of fluid restriction to reduce congestive symptoms is uncertain.





Table 19. Indications and Contraindications to Durable Mechanical Support

Indications (combination of these):

- · Frequent hospitalizations for HF
- NYHA class IIIb to IV functional limitations despite maximal therapy
- Intolerance of neurohormonal antagonists
- Increasing diuretic requirement
- Symptomatic despite CRT
- Inotrope dependence
- Low peak VO₂ (<14-16)
- End-organ dysfunction attributable to low cardiac output

Contraindications:

Absolute

- Irreversible hepatic disease
- Irreversible renal disease
- Irreversible neurological disease
- Medical nonadherence
- Severe psychosocial limitations

Relative

- Age >80 y for destination therapy
- · Obesity or malnutrition
- Musculoskeletal disease that impairs rehabilitation
- Active systemic infection or prolonged intubation
- Untreated malignancy
- Severe PVD
- Active substance abuse
- Impaired cognitive function
- Unmanaged psychiatric disorder
- Lack of social support

8.3. In	8.3. Inotropic Support		
COR	LOE	Recommendations	
2a	B-NR	In patients with advanced (stage D) HF refractory to GDMT and device therapy who are eligible for and awaiting MCS or cardiac transplantation, continuous intravenous inotropic support is reasonable as "bridge therapy".	
2Ь	B-NR	In select patients with stage D HF, despite optimal GDMT and device therapy who are ineligible for either MCS or cardiac transplantation, continuous intravenous inotropic support may be considered as palliative therapy for symptom control and improvement in functional status.	
3: Harm	B-R	3. In patients with HF, long-term use of either continuous or intermittent intravenous inotropic agents, for reasons other than palliative care or as a bridge to advanced therapies, is potentially harmful.	

8.4. M	echanica	al Circulatory Support
COR	LOE	Recommendations
1	A	In select patients with advanced HFrEF with NYHA class IV symptoms who are deemed to be dependent on continuous intravenous inotropes or temporary MCS, durable LVAD implantation is effective to improve functional status, QOL, and survival.
2a	B-R	In select patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS can be beneficial to improve symptoms, improve functional class, and reduce mortality.
Value Statement: Uncertain Value (B-NR)		3. In patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS devices provide low to intermediate economic value based on current costs and outcomes.
2a	B-NR	4. In patients with advanced HFrEF and hemodynamic compromise and shock, temporary MCS, including percutaneous and extracorporeal ventricular assist devices, are reasonable as a "bridge to recovery" or "bridge to decision".

8.5. Ca	ardiac T	ransplantation
COR	LOE	Recommendations
1	C-LD	For selected patients with advanced HF despite GDMT, cardiac transplantation is indicated to improve survival and QOL.
Intermed	atement: liate Value LD)	2. In patients with stage D (advanced) HF despite GDMT, cardiac transplantation provides intermediate economic value.





	j.	Dose (mcg/kg)	Drug		Eff	Effects			
Inotropic Agent Bolus Infusion (/min) Metabolism	Bolus	Infusion (/min)	Metabolism	8	뚶	CO HR SVR	PVR	Adverse Effects	Special Considerations
Adrenergic agonists	ts								
Dopamine	NA	NA 5-10	t½: 2–20 min	←	←	1	1	$\uparrow \qquad \uparrow \qquad \longleftrightarrow \qquad T, HA, N, \text{ tissue necrosis} \qquad \text{Caution: MAO-I}$	Caution: MAO-I
	NA	NA 10–15	R, H, P	←	←	←	1		
Dobutamine	NA	NA 2.5–20	t½: 2–3 min H	←	←	↓ ← ←	1	←→ ↑/↓BP, HA, T, N, F, hypersensitivity	Caution: MAO-I; CI: sulfite allergy
PDE 3 inhibitor									
Milrinone	NR	NR 0.125-0.75 t½: 2.5 h H	t½: 2.5 h H	←	←	→	\rightarrow	Т, ЏВР	Accumulation may occur in setting of renal failure; monitor kidney function and LFTs

of renal failure; monitor kidney function and LFTs		Caution: MAO-I	Caution: MAO-I	is Caution: MAO-I
1, tbr		$\uparrow \qquad \uparrow \qquad \downarrow \downarrow \downarrow \downarrow \qquad \downarrow \qquad \downarrow \downarrow \uparrow \downarrow \uparrow \downarrow \downarrow \uparrow \downarrow \uparrow$	$\uparrow\uparrow \uparrow\uparrow \qquad \leftrightarrow \qquad \text{HA, T.}$	\leftrightarrow \uparrow \uparrow \leftrightarrow \downarrow HR, tissue necrosis
→		\$	1	1
→		(1)1	←	1
_		Ţ	←	←
_		+	←	1
		NR 5–15 mcg/ t½: 2–3 min min	t½: 2–3 min	t½: 2.5 min
		5–15 mcg/ min	15-20 mcg/min	
***		NR		NR
	Vasopressors	Epinephrine		Norepinephrine NR 0.5–30 mcg/min

9. Patients Hospitalized With Acute Decompensated HF

9.1. Assessment of Patients Hospitalized With Decompensated HF

D€	ecompe	nsated HF		
COR	LOE	Recommendations		
1	C-LD	In patients hospitalized with HF, severity of congestion and adequacy of perfusion should be assessed to guide triage and initial therapy.		
1	C-LD	2. In patients hospitalized with HF, the common precipitating factors and the overall patient trajectory should be assessed to guide appropriate therapy.		
	Goals for Optimization and Continuation of GDMT			
1	C-LD	For patients admitted with HF, treatment should address reversible factors, establish optimal volume status, and advance GDMT toward targets for outpatient therapy.		

Table 21. Common Factors Precipitating HF Hospitalization With Acute Decompensated HF

- ACS
- Uncontrolled hypertension
- · AF and other arrhythmias
- Additional cardiac disease (e.g., endocarditis)
- Acute infections (e.g., pneumonia, urinary tract)
- · Nonadherence with medication regimen or dietary intake
- Anemia
- Hyper- or hypothyroidism
- Medications that increase sodium retention (e.g., NSAID)
- Medications with negative inotropic effect (e.g., verapamil)





9.2. Maintenance or Optimization of GDMT During Hospitalization

	<u> </u>	
COR	LOE	Recommendations
1	B-NR	In patients with HFrEF requiring hospitalization, preexisting GDMT should be continued and optimized to improve outcomes, unless contraindicated.
1	B-NR	In patients experiencing mild decrease of renal function or asymptomatic reduction of blood pressure during HF hospitalization, diuresis and other GDMT should not routinely be discontinued.
1	B-NR	3. In patients with HFrEF, GDMT should be initiated during hospitalization after clinical stability is achieved.
1	B-NR	4. In patients with HFrEF, if discontinuation of GDMT is necessary during hospitalization, it should be reinitiated and further optimized as soon as possible.

	uretics rategy	in Hospitalized Patients: Decongestion
COR	LOE	Recommendations
1	B-NR	Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to improve symptoms and reduce morbidity.
1	B-NR	2. For patients hospitalized with HF, therapy with diuretics and other guideline-directed medications should be titrated with a goal to resolve clinical evidence of congestion to reduce symptoms and rehospitalizations.
1	B-NR	For patients requiring diuretic treatment during hospitalization for HF, the discharge regimen should include a plan for adjustment of diuretics to decrease rehospitalizations.
2a	B-NR	4. In patients hospitalized with HF when diuresis is inadequate to relieve symptoms and signs of congestion, it is reasonable to intensify the diuretic regimen using either: a. higher doses of intravenous loop diuretics; or b. addition of a second diuretic.

9.4a. Parenteral Vasodilation Therapy in Patients Hospitalized With HF

COR	LOE	Recommendation
2b	B-NR	In patients who are admitted with decompensated HF, in the absence of systemic hypotension, intravenous nitroglycerin or nitroprusside may be considered as an adjuvant to diuretic therapy for relief of dyspnea.

9.4b. V	TE Pro	phylaxis in Hospitalized Patients
COR	LOE	Recommendation
1	B-R	In patients hospitalized with HF, prophylaxis for VTE is recommended to prevent venous thromboembolic disease.

9.5. Ev	aluatior	and Management of Cardiogenic Shock
COR	LOE	Recommendations
1	B-NR	In patients with cardiogenic shock, intravenous inotropic support should be used to maintain systemic perfusion and preserve end-organ performance.
2a	B-NR	In patients with cardiogenic shock, temporary MCS is reasonable when end-organ function cannot be maintained by pharmacologic means to support cardiac function.
2a	B-NR	In patients with cardiogenic shock, management by a multidisciplinary team experienced in shock in reasonable.
2b	B-NR	4. In patients presenting with cardiogenic shock, placement of a PA line may be considered to define hemodynamic subsets and appropriate management strategies.
2b	C-LD	For patients who are not rapidly responding to initial shock measures, triage to centers that can provide temporary MCS may be considered to optimize management.





Table 22. Suggested Shock Clinical Criteria*

SBP <90 mm Hg for >30 min:

- a. Or mean BP < 60 mm Hg for > 30 min
- b. Or requirement of vasopressors to maintain systolic BP ≥90 mm Hg or mean BP ≥60 mm Hg

Hypoperfusion defined by:

- c. Decreased mentation
- d. Cold extremities, livedo reticularis
- e. Urine output <30 mL/h
- f. Lactate > 2 mmol/L
- * Systolic BP and hypoperfusion criteria need to be met for the shock diagnosis.

Table 23. Suggested Shock Hemodynamic Criteria*

- 1. SBP <90 mm Hg or mean BP <60 mm Hg
- 2. Cardiac index <2.2 L/min/m²
- Pulmonary capillary wedge pressure >15 mm Hg
- 4. Other hemodynamic considerations
 - a. Cardiac power output ([CO x MAP]/451) < 0.6 W
 - b. Shock index (HR/systolic BP) >1.0
 - c. RV shock
 - i. Pulmonary artery pulse index [(PASP-PADP)/CVP] < 1.0
 - ii. CVP > 15 mm Hg
 - iii. CVP-PCW > 0.6

^{*} Diagnosis of shock requires ≥1 criteria to be present along with cardiac index <2.0 L/min/m² and SBP <90 mm Hg.

Table 24. Society for Cardiovascular Angiography and Interventions (SCAI) Cardiogenic Shock Criteria

Stage	Bedside Findings	Selected Laboratory Markers	Hemodynamics
A: At risk Normotensive Normal perfusion Cause for risk for shock such as large myocardial infarction or HF	Normal venous pressure Clear lungs Warm extremities Strong palpable pulses Normal mentation	Normal renal function Normal lactate	SBP >100 mm Hg Hemodynamics: Normal
B: Beginning shock ("pre-shock") • Hypotension • Normal perfusion	Elevated venous pressure Rales present Warm extremities Strong pulses Normal mentation	Preserved renal function Normal lactate Elevated BNP	a. SBP <90 mm Hg b. MAP <60 mm Hg or c. >30 mm Hg decrease from baseline SBP • HR >100 bpm • Hemodynamics: CI ≥2.2 L/min/m²
C: Classic cardiogenic shock • Hypotension • Hypoperfusion	Elevated venous pressure Rales present Cold, ashen, livedo Weak or nonpalpable pulses Altered mentation Decreased urine output Respiratory distress	Impaired renal function Increased lactate Elevated BNP Increased LFTs Acidosis	SBP <90 mm Hg; MAP <60 mm Hg; >30 mm Hg from baseline SBP despite drugs and temporary MCS HR >100 bpm Hemodynamics: CI ≤2.2 L/min/m²; PCW >15 mm Hg; CPO <0.6 W; PAPi <2.0; CVP-PCW >1.0
D: Deteriorating • Worsening hypotension • Worsening hypoperfusion	Same as stage C	Persistent or worsening values of stage C	Escalating use of pressors or MCS to maintain SBP and end-organ perfusion in setting of stage C hemodynamics
E: Extremis • Refractory hypotension • Refractory hypoperfusion	Cardiac arrest CPR	Worsening values of stage C laboratories	SBP only with resuscitation PEA Recurrent VT/VF





9.6 Inte	egration	of Care: Transitions and Team-Based Approaches
COR	LOE	Recommendations
1	B-R	In patients with high-risk HF, particularly those with recurrent hospitalizations for HFrEF, referral to multidisciplinary HF disease management programs is recommended to reduce the risk of hospitalization.
1	B-NR	In patients hospitalized with worsening HF, patient-centered discharge instructions with a clear plan for transitional care should be provided before hospital discharge.
2a	B-NR	3. In patients hospitalized with worsening HF, participation in systems that allow benchmarking to performance measures is reasonable to increase use of evidence-based therapy, and to improve quality of care.
2a	B-NR	4. In patients being discharged after hospitalization for worsening HF, an early follow-up, generally within 7 days of hospital discharge, is reasonable to optimize care and reduce rehospitalization.

Table 25. Important Components of a Transitional Care Plan

A transitional care plan, communicated with the patient and their outpatient clinicians before hospital discharge, should clearly outline plans for:

- Addressing any precipitating causes of worsening HF identified in the hospital;
- Adjusting diuretics based on volume status (including weight) and electrolytes;
- Coordination of safety laboratory checks (e.g., electrolytes after initiation or intensification of GDMT);
- Further changes to optimize GDMT, including:
 - a. Plans for resuming medications held in the hospital;
 - b. Plans for initiating new medications;
 - c. Plans for titration of GDMT to goal doses as tolerated;
- Reinforcing HF education and assessing compliance with medical therapy and lifestyle modifications, including dietary restrictions and physical activity;
- Addressing high-risk characteristics that may be associated with poor postdischarge clinical outcomes, such as:
 - a. Comorbid conditions (e.g., renal dysfunction, pulmonary disease, diabetes, mental health, and substance use disorders);
 - b. Limitations in psychosocial support;
 - c. Impaired health literacy, cognitive impairment;
- Additional surgical or device therapy, referral to cardiac rehabilitation in the future, where appropriate;
- Referral to palliative care specialists and/or enrollment in hospice in selected patients.

10. Comorbidities in Patients With HF

10.1. Management of Comorbidities in Patients With HF			
COR	LOE	Recommendations	
		Management of Anemia or Iron Deficiency	
2a	B-R	In patients with HFrEF and iron deficiency with or without anemia, intravenous iron replacement is reasonable to improve functional status and QOL.	
3: Harm	B-R	In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.	
	Management of Hypertension		
1	C-LD	3. In patients with HFrEF and hypertension, uptitration of GDMT to the maximally tolerated target dose is recommended.	
Management of Sleep Disorders			
2a	C-LD	4. In patients with HF and suspicion of sleep-disordered breathing, a formal sleep assessment is reasonable to confirm the diagnosis and differentiate between obstructive and central sleep apnea.	
2a	B-R	5. In patients with HF and obstructive sleep apnea, continuous positive airway pressure may be reasonable to improve sleep quality and decrease daytime sleepiness.	
3: Harm	B-R	6. In patients with NYHA class II to IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm.	
		Management of Diabetes	
1	A	7. In patients with HF and type 2 diabetes, the use of SGLT2i is recommended for the management of hyperglycemia and to reduce HF-related morbidity and mortality.	





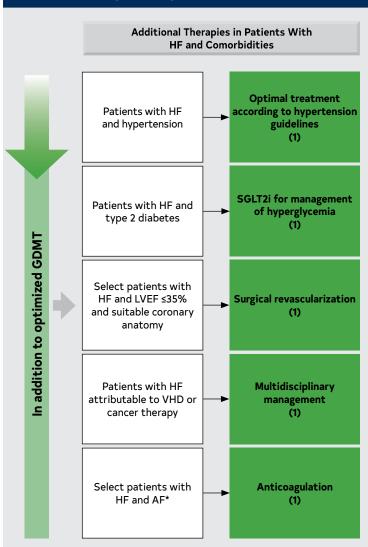
Table 26. Most Common Co-Occurring Chronic Conditions Among Medicare Beneficiaries With HF (N=4,947,918), 2011

Beneficiaries Age ≥65 y (n=4,376,150)*			Beneficiaries Age <65 y (n=571,768) [†]		
	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	CKD	257,015	45.0
CKD	1,851,812	42.3	Depression	207,082	36.2
COPD	1,311,118	30.0	Arthritis	201,964	35.3
AF	1,247,748	28.5	COPD	191,016	33.4
Alzheimer's disease or dementia	1,207,704	27.6	Asthma	88,816	15.5

^{*} Mean No. of conditions is 6.1; median is 6.

 $^{^{\}dagger}$ Mean No. of conditions is 5.5; median is 5.

Figure 14. Recommendations for Treatment of Patients With HF and Selected Comorbidities



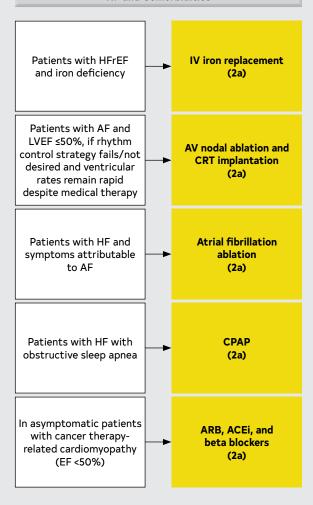
Recommendations for treatment of patients with HF and select comorbidities are displayed.

^{*} Patients with chronic HF with permanent-persistent-paroxysmal AF and a CHA2DS2-VASc score of ≥ 2 (for men) and ≥ 3 (for women).





Additional Therapies in Patients With HF and Comorbidities



10.2. N	10.2. Management of AF in HF		
COR	LOE	Recommendations	
1	A	 Patients with chronic HF with permanent-persistent- paroxysmal AF and a CHA2DS2-VASc score of ≥2 (for men) and ≥3 (for women) should receive chronic anticoagulant therapy. 	
1	A	For patients with chronic HF with permanent-persistent- paroxysmal AF, DOAC is recommended over warfarin in eligible patients.	
2a	B-R	3. For patients with HF and symptoms caused by AF, AF ablation is reasonable to improve symptoms and QOL.	
2a	B-R	4. For patients with AF and LVEF ≤50%, if a rhythm control strategy fails or is not desired, and ventricular rates remain rapid despite medical therapy, atrioventricular nodal ablation with implantation of a CRT device is reasonable.	
2a	B-NR	For patients with chronic HF and permanent/persistent/ paroxysmal AF, chronic anticoagulant therapy is reasonable for men and women without additional risk factors.	

11. Special Populations

11.1. [11.1. Disparities and Vulnerable Populations*		
COR	LOE	LOE Recommendations	
1	C-LD	In vulnerable patient populations at risk for health disparities, HF risk assessments and multidisciplinary management strategies should target both known risks for CVD and social determinants of health, as a means toward elimination of disparate HF outcomes.	
1	C-LD	Evidence of health disparities should be monitored and addressed at the clinical practice and the health care system levels.	

^{*} This section crosslinks to Section 7.1.1, "Stage C Nonpharmacological Interventions and Self-Care Support in HF," where screening and interventions for social determinants of health are now addressed.





Table 27. Risk	of HF and Outcomes in	Special Populations
Vulnerable Population	Risk of HF	HF Outcomes
Women	The lifetime risk of HF is equivalent between sexes, but HFpEF risk is higher in women—in FHS participants with new-onset HF, odds of HfpEF (EF >45%) are 2.8-fold higher in women than in men. Sex-specific differences in the predictive value of cardiac biomarkers for incident HF. Nontraditional cardiovascular risk factors, including anxiety, depression, caregiver stress, and low household income may contribute more toward incident heart disease in women than men.	Overall, more favorable survival with HF than men. In the OPTIMIZE-HF registry, women with acute HF had a lower 1-y mortality (HR, 0.93; 95% CI, 0.89–0.97), although women are more likely not to receive optimal GDMT. Lower patient-reported quality of life for women with HFrEF, compared with men. Greater transplant waitlist mortality for women but equivalent survival after heart transplantation or LVAD implantation.
Older adults	Per FHS, at 40 y of age, the lifetime risk of incident HF is 20% for both sexes; at 80 y of age, the risk remains 20% for men and women despite the shorter life expectancy. LVEF is preserved in at least two-thirds of older adults with the diagnosis of HF.	Among 1233 patients with HF aged ≥80 y, 40% mortality during mean 27-mo follow- up; survival associated with prescription of GDMT.
Lower socioeconomic status populations	Among 27,078 White and Black adults of low income (70% earned <\$15,000/y) participating from 2002–2009 in the Southern Community Cohort Study, a 1 interquartile increase in neighborhood deprivation index was associated with a 12% increase in risk of HF (adjusted HR, 1.12; 95% CI, 1.07–1.18).	Age-adjusted 1999–2018 HF mortality (deaths/100,000; mean and 95% CI) was higher with increasing quartiles of ADI, which is based on 17 indicators of employment, poverty, and education: Quartile 1, 20.0 (19.4–20.5); Quartile 2, 23.3 (22.6–24.0); Quartile 3, 26.4 (25.5–27.3); Quartile 4, 33.1 (31.8–34.4)

Table 27. Risk of HF and Outcomes in Special Populations (cont'd)				
Risk of HF	HF Outcomes			
In MESA, patients of Black race had highest risk of incident HF (4.6/1000 personyears) and highest proportion of nonischemic incident HF. Higher prevalence of HF risk factors including hypertension, obesity, and diabetes, compared with White populations.	CDC data show race-based differences in HF mortality over time: Black men had a 1.16-fold versus 1.43-fold higher age-adjusted HF-related CVD death rate compared with White men in 1999 versus 2017; Black women had a 1.35-fold versus 1.54-fold higher age-adjusted HF-related CVD death rate compared with White women in 1999 versus 2017. Gap in outcomes is more pronounced among younger adults (35–64 y of age) versus older adults (65–84 y of age); age-adjusted HF-related CVD death rates were 2.60-fold and 2.97-fold higher in young Black versus White men and women, respectively. Higher rates of hospitalization (3) and mortality among patients with HFpEF. Lower 5-year survival after heart transplant.			
	Risk of HF In MESA, patients of Black race had highest risk of incident HF (4.6/1000 personyears) and highest proportion of nonischemic incident HF. Higher prevalence of HF risk factors including hypertension, obesity, and diabetes, compared			





Table 27. Risk of HF and Outcomes in Special Populations (cont'd)

Vulnerable Population	Risk of HF	HF Outcomes
Hispanic populations	MESA study showed higher HF incidence in Hispanic compared with non-Hispanic White groups (3.5 versus 2.4 per 1000 person-years) but lower than for African Americans (4.6/1000 person-years).	Despite higher rates of hospitalization for HF compared with non-Hispanic Whites, Hispanic patients with HF have shown lower short-term mortality rates. In GWTG, Hispanic patients with HfpEF had lower mortality (OR, 0.50; 95% CI, 0.31–0.81) than non-Hispanic Whites, but this was not the case for Hispanic patients with HFrEF (OR, 0.94; 95% CI, 0.62–1.43). Lower risk of developing AF in the setting of HF, compared with White patients.
Asian and Pacific Islander populations	Limited population-specific data for Asian and pacific Islander subgroups in the United States.	High rates of preventable HF hospitalization observed in some Asian and Pacific Islander populations. Lower mortality rates from HF for Asian subgroups when listed as the primary cause of death, compared with non-Hispanic White groups.
Native American and Alaskan Native populations	Limited population-specific data, with cardiovascular risk factor trends best characterized by the Strong Heart Study and Strong Heart Family Study, demonstrating high rates of hypertension and diabetes.	Limited data suggest HF mortality rates in American Indians and Alaska Natives are similar to those in White populations.

11.2. Cardio-Oncology			
COR	LOE	Recommendations	
1	B-NR	In patients who develop cancer therapy-related cardiomyopathy or HF, a multidisciplinary discussion involving the patient about the risk-benefit ratio of cancer therapy interruption, discontinuation, or continuation is recommended to improve management.	
2a	B-NR	2. In asymptomatic patients with cancer therapy-related cardiomyopathy (EF <50%), ARB, ACEi, and beta blockers are reasonable to prevent progression to HF and improve cardiac function.	
2a	B-NR	In patients with cardiovascular risk factors or known cardiac disease being considered for potentially cardiotoxic anticancer therapies, pretherapy evaluation of cardiac function is reasonable to establish baseline cardiac function and guide the choice of cancer therapy.	
2a	B-NR	In patients with cardiovascular risk factors or known cardiac disease receiving potentially cardiotoxic anticancer therapies, monitoring of cardiac function is reasonable for the early identification of drug-induced cardiomyopathy.	
2b	B-R	In patients at risk of cancer therapy-related cardiomyopathy, initiation of beta blockers and ACEi/ARB for the primary prevention of drug-induced cardiomyopathy is of uncertain benefit.	
2b	C-LD	6. In patients being considered for potentially cardiotoxic therapies, serial measurement of cardiac troponin might be reasonable for further risk stratification.	

reasonable for further risk stratification.				
Table 29. Risk Factors for Cancer Therapy–Related Cardiomyopathy				
Age ≥60 y				
Black race				
CAD				
Hypertension				
Diabetes				
Preexisting cardiomyopathy				
Previous exposure to anthracyclines				
Previous chest radiation				
Elevated troponin pretherapy				





Table 28. Cancer Therapies Known to Be Associated With Cardiomyopathy

Cardiac Function Monitoring Often Performed in Clinical Practice

Class	Agent(s)	Pretherapy	Serial
Anthracyclines	Doxorubicin, epirubicin	Х	Х
Alkylating agents	Cyclophosphamide, ifosfamide, melphalan	Х	
Antimicrotubule agents	Docetaxel		
Antimetabolites	Fluorouracil, capecitabine, fludarabine, decitabine		
Anti-HER2 agents	Trastuzumab, pertuzumab	Х	Х
Monoclonal antibodies	Rituximab		
Tyrosine-kinase inhibitors	Dabrafenib, dasatinib, lapatinib, pazopanib, ponatinib, sorafenib, trametinib, sunitinib, vandetanib, imatinib, vandetanib		
Immune checkpoint inhibitors	Nivolumab, ipilimumab, pembrolizumab		
Protease inhibitors	Bortezomib, carfilzomib		
Endocrine therapy	Goserelin, leuprolide, flutamide, bicalutamide, nilutamide		
Chimeric antigen receptor T-cell therapy	Tisagenlecleucel, axicabtageneciloleucel	Х	
Hematopoietic stem cell transplantation	Hematopoietic stem cell transplantation	Х	
Radiation	Chest		

Table 30. HF Management Strategies Across the Pregnancy Continuum

Preconception

Nonpharmacological strategies

Preconception genetic counseling and testing for potentially heritable cardiac conditions.

Use of pregnancy cardiovascular risk tools, and echocardiography for myocardial structure and function assessment, to provide information that facilitates informed counseling.

For women planning a pregnancy, provide personalized counseling that promotes the autonomy and goals of the patient (and her partner, as applicable), the patient's ability for self-care and risk awareness, and ensures adequate psychosocial support for decision-making.

For women not currently planning a pregnancy but who might conceive, discuss HF-specific considerations regarding pregnancy and refer to gynecology or primary care for contraceptive counseling.





During Pregnancy

Close maternal monitoring for HF signs or symptoms or other cardiovascular instability by cardiology and obstetric and maternal-fetal medicine teams; close fetal monitoring by the obstetric and maternal-fetal medicine teams.

Consideration of routine echocardiographic screening in the third trimester for reassessment of myocardial structure and function before labor; echocardiography for any significant changes in HF symptoms or signs during pregnancy, or if HF medications are reduced or discontinued.

BNP or NT-proBNP monitoring during pregnancy may have some value for prediction of cardiovascular events.

Close maternal monitoring by obstetrics and maternal-fetal medicine teams for preeclampsia, which has shared risk factors and pathogenesis with PPCM.

For women presenting with decompensated HF or cardiogenic shock, hemodynamic monitoring and MCS, as appropriate, within a multidisciplinary collaborative approach that supports prompt decision-making about the timing and mechanism of delivery.

Postpartum

Multidisciplinary recommendations from obstetrics and neonatology and pediatrics teams and shared decision-making regarding the maternal and neonatal risks and benefits of breastfeeding.

For women presenting with decompensated HF or cardiogenic shock, HF management should include hemodynamic monitoring and mechanical circulatory support as appropriate

Table 30. HF Management Strategies Across the Pregnancy Continuum (cont'd) Preconception Review of all current medications. Pharmacological strategies For women planning pregnancy imminently, modification of HF pharmacotherapy including. discontinuation of any ACEi, ARB, ARNi, MRA, or SGLT2i or ivabradine medications; within a construct of multidisciplinary shared decision-making, continuation of a beta blocker (most commonly metoprolol), hydralazine, and nitrates; adjustment of diuretic dosing to minimize the risk of placental hypoperfusion. Ideally, repeat echocardiography approximately 3 mo after preconception HF medication adjustments to ensure stability of myocardial structure and function before conception. Multidisciplinary Consultation with genetics, gynecology, and maternal-fetal care beyond the medicine teams, as appropriate to the outcome of shared cardiology team decision-making.

^{*} An initial open-label pilot RCT in South Africa suggested addition of bromocriptine to GDMT was associated with greater LVEF improvement and a lower rate of the composite endpoint at 6 mo.





During Pregnancy Postpartum

Close monitoring of maternal blood pressure, heart rate, and volume status, with adjustment of the modified HF regimen as appropriate to avoid hypotension (systemic vasodilation peaks in the second trimester) and placental hypoperfusion.

For women with HF or cardiomyopathy presenting during pregnancy without preconception counseling and assessment, urgent discontinuation of any GDMT pharmacotherapies with fetal toxicities; within a construct of multidisciplinary shared decision-making, continuation of a beta blocker (most commonly metoprolol succinate), hydralazine, and nitrates; adjustment of diuretic dosing to minimize the risk of placental hypoperfusion.

For women with acute HF caused by PPCM and LVEF <30%, consideration of anticoagulation until 6–8 wk postpartum, although the efficacy and safety remain uncertain at this time.

For postpartum women with severe acute HF caused by PPCM and LVEF <35%, in GDMT pharmacotherapy and prophylactic anticoagulation, to improve LVEF recovery (6,31,36-41,76); the efficacy and safety of bromocriptine for acute PPCM treatment remains uncertain at this time, particularly in the setting of contemporary HF GDMT and cardiogenic shock management.*

For women who choose to breastfeed, review medications with neonatology and pediatrics teams for neonatal safety during lactation, ideally with pharmacist consultation if available.

Within a construct of multidisciplinary shared decision-making, medications that may be appropriate during breastfeeding include ACEi (enalapril or captopril preferred, monitor neonatal weight), beta blockers (metoprolol preferred, monitor neonatal heart rate).

Diuretics can suppress lactation, but with neonatal follow-up the use of furosemide may be appropriate.

Multidisciplinary management with obstetrics and maternal-fetal medicine teams during pregnancy.

For women with decompensated HF or evidence of hemodynamic instability antepartum, delivery planning will include obstetrics and maternal-fetal medicine, anesthesia, and neonatology teams.

Multidisciplinary management with obstetrics, maternal-fetal medicine, neonatology, and pediatrics teams, especially for multidisciplinary recommendations regarding lactation.

Consultation with gynecology team for ongoing contraceptive planning.

11.3. H	11.3. HF and Pregnancy		
COR	LOE	Recommendations	
1	C-LD	In women with a history of HF or cardiomyopathy, including previous peripartum cardiomyopathy, patient-centered counseling regarding contraception and the risks of cardiovascular deterioration during pregnancy should be provided.	
2b	C-LD	In women with acute HF caused by peripartum cardiomyopathy and LVEF < 30%, anticoagulation may be reasonable at diagnosis, until 6 to 8 weeks postpartum, although the efficacy and safety are uncertain.	
3: Harm	C-LD	3. In women with HF or cardiomyopathy who are pregnant or currently planning for pregnancy, ACEi, ARB, ARNi, MRA, SGLT2i, ivabradine, and vericiguat should <i>not</i> be administered because of significant risks of fetal harm.	

12. Quality Metrics and Reporting

12.1. Performance Measurement			
COR	LOE	Recommendations	
1	B-NR	Performance measures based on professionally developed clinical practice guidelines should be used with the goal of improving quality of care for patients with HF.	
2a	B-NR	2. Participation in quality improvement programs, including patient registries that provide benchmark feedback on nationally endorsed, clinical practice guideline–based quality and performance measures can be beneficial in improving the quality of care for patients with HF.	





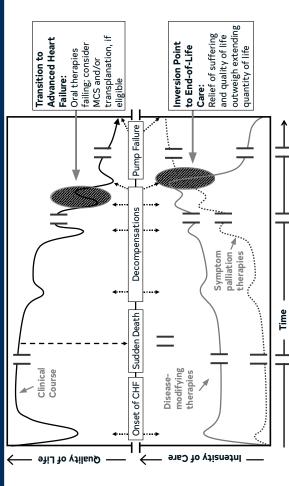
13. Goals of Care

13.1. Palliative and Supportive Care, Shared Decision-Making, and End-of-Life

making, and the or the			
COR	LOE	Recommendations	
1	C-LD	For all patients with HF, palliative and supportive care—including high-quality communication, conveyance of prognosis, clarifying goals of care, shared decision-making, symptom management, and caregiver support—should be provided to improve QOL and relieve suffering.	
1	C-LD	For patients with HF being considered for, or treated with, life-extending therapies, the option for discontinuation should be anticipated and discussed through the continuum of care, including at the time of initiation, and reassessed with changing medical conditions and shifting goals of care.	
2 a	B-R	3. For patients with HF—particularly stage D HF patients being evaluated for advanced therapies, patients requiring inotropic support or temporary mechanical support, patients experiencing uncontrolled symptoms, major medical decisions, or multimorbidity, frailty, and cognitive impairment—specialist palliative care consultation can be useful to improve QOL and relieve suffering.	
2a	C-LD	4. For patients with HF, execution of advance care directives can be useful to improve documentation of treatment preferences, delivery of patient-centered care, and dying in preferred place.	
2a	C-LD	5. In patients with advanced HF with expected survival <6 months, timely referral to hospice can be useful to improve QOL.	

Table 32.	Palliative and Supportive Care Domains to Improve	,
	Processes of Care and Patient Outcomes	

Palliative and Supportive Domains of Care	What Palliative Care Adds to Overall HF Management
High-quality communication	Central to palliative care approaches are communication and patient-caregiver engagement techniques.
Conveyance of prognosis	Palliative care specifically addresses patient and caregiver understanding of disease, treatment, and prognosis. Research suggests that patients tend to overestimate their survival and overestimate the potential benefits of treatment. Objective risk models can calibrate expectations, but discussion of uncertainty should accompany prognostic conversations, often summarized as "hope for the best, plan for the worst."
Clarifying goals of care	Management of patients with HF as their disease becomes end-stage and death seems near includes decisions about when to discontinue treatments designed primarily to prolong life (e.g., ICD, hospitalization, tube feeding), decisions on when to initiate treatments to reduce pain and suffering that may hasten death (e.g., narcotics), and decisions about the location of death, home services, and hospice care. Exploring patients' expressed preferences, values, needs, concerns, means and desires through clinician-led discussion can clarify valuestreatment concordance and improve medical decision-making.
Shared decision- making	Shared decision-making is a process by which patients and clinicians work together to make optimal health care decisions from medically reasonable options that align with what matters most to patients. Shared decision-making requires: unbiased medical evidence about the risks, benefits, and burdens of each alternative, including no intervention; clinician expertise in communication and tailoring that evidence for individual patients; and patient goals and informed preferences.
Symptom management	Dyspnea, fatigue, pain, nausea, depression, anxiety, and other symptoms of HF refractory to cardiovascular therapies can be partially remediated through palliative and supportive approaches in addition to GDMT.
Caregiver support	Care of the patient with heart failure should extend to their loved ones, including beyond their death, to offer support to families and help them cope with loss.



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Class of Recommendations and Level of Evidence

CLASS (STRENGTH) OF RECOMMENDATION

CLASS 1 (STRONG) Benefit >>> Risk

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should 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

CLASS 2a (MODERATE)

Benefit >> Risk

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases[†]:
 - Treatment/strategy A is probably recommended/indicated in preference to treatment B
 - It is reasonable to choose treatment A over treatment B

CLASS 2b (WEAK)

Benefit ≥ Risk

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

CLASS 3: No Benefit (MODERATE)

Benefit = Risk

(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS 3: Harm (STRONG)

Risk > Benefit

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other





LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A

- High-quality evidence[‡] from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)

- Moderate-quality evidence[‡] from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)

- Moderate-quality evidence[‡] from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)

- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

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

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

- * The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).
- † For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
- * The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

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

Abbreviations

AF, atrial fibrillation; AL-CM, immunoglobulin light chain amyloid cardiomyopathy; ATTR-CM, transthyretin amyloid cardiomyopathy; ATTRv, variant transthyretin amyloidosis; ATTRwt, wildtype transthyretin amyloidosis; BNP, B-type natriuretic peptide; CABG, coronary artery bypass graft; CAD, coronary artery disease; CCM, cardiac contractility modulation; CHA2DS2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack [TIA], vascular disease, age 65 to 74 years, sex category; CHF, congestive heart failure; CKD, chronic kidney disease; CMR, cardiovascular magnetic resonance; COVID-19, coronavirus disease 2019; CPET, cardiopulmonary exercise test; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy with defibrillation; CRT-P, cardiac resynchronization therapy with pacemaker; CT, computed tomography; CVD, cardiovascular disease; CVP, central venous pressure; DOAC, direct-acting oral anticoagulants; DPP-4, dipeptidyl peptidase-4; ECG, electrocardiogram; EF, ejection fraction; eGFR, estimated glomerular filtration rate; ERO, effective regurgitant orifice; FDA, U.S. Food and Drug Administration; FLC, free light chain; GDMT, guideline-directed medical therapy; HF, heart failure; HFimpEF, heart failure with improved ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; IFE, immunofixation electrophoresis; LBBB, left bundle branch block; LV, left ventricular; LVAD, left ventricular assist device; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVH, left ventricular hypertrophy; MCS, mechanical circulatory support; MI, myocardial infarction; MR, mitral regurgitation; MRA, mineralocorticoid receptor antagonist; MRI, magnetic resonance imaging; MV, mitral valve; NSAID, nonsteroidal anti-inflammatory drug; NSVT, nonsustained ventricular tachycardia; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; NYHA, New York Heart Association; QALY, quality-adjusted life year; QOL, quality of life; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; PET, positron emission tomography; PPAR-γ, peroxisome proliferator-activated receptor gamma; PUFA, polyunsaturated fatty acid; RA, right atrial; RAASi, renin-angiotensin-aldosterone system inhibitor; RCT, randomized controlled trial; RF, radiofrequency; RV, right ventricular; Rx, prescription; RVol, regurgitant volume; SCD, sudden cardiac death; SGLT2i, sodium-glucose cotransporter-2 inhibitors; SPECT, single photon emission CT; 99mTc-PYP, technetium pyrophosphate; TEE, transesophageal echocardiogram; TEER, transcatheter mitral edge-to-edge repair; TIA, transient ischemic attack; TTE, transthoracic echocardiogram; VA, ventricular arrhythmia; VF, ventricular fibrillation; VHD, valvular heart disease; VO2, oxygen consumption/oxygen uptake; VT, ventricular tachycardia

Source

Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published online ahead of print April 1, 2022]. *J Am Coll Cardiol*. doi: 10.1016/j.jacc.2021.12.012

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Disclaimer

This pocket guide attempts to define principles of practice that should produce high-quality patient care. It is applicable to specialists, primary care, and providers at all levels. This pocket guide should not be considered exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment concerning the propriety of any course of conduct must be made by the clinician after consideration of each individual patient situation. Neither IGC, the medical associations, nor the authors endorse any product or service associated with the distributor of this clinical reference tool.

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