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AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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AIM: The "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure" replaces the "2013 ACCF/AHA Guideline for the Management of Heart Failure" and the "2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure." The 2022 guideline is intended to provide patient-centric recommendations for clinicians to prevent, diagnose, and manage patients with heart failure.

METHODS: A comprehensive literature search was conducted from May 2020 to December 2020, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from MEDLINE (PubMed), EMBASE, the Cochrane Collaboration, the Agency for Healthcare Research and Quality, and other relevant databases. Additional relevant clinical trials and research studies, published through September 2021, were also considered. This guideline was harmonized with other American Heart Association/American College of Cardiology guidelines published through December 2021.

STRUCTURE: Heart failure remains a leading cause of morbidity and mortality globally. The 2022 heart failure guideline provides recommendations based on contemporary evidence for the treatment of these patients. The recommendations present an evidence-based approach to managing patients with heart failure, with the intent to improve quality of care and align with patients' interests. Many recommendations from the earlier heart failure guidelines have been updated with new evidence, and new recommendations have been created when supported by published data. Value statements are provided for certain treatments with high-quality published economic analyses.

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*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 of the full guideline for detailed information. †ACC/AHA Representative. ‡ACC/AHA Joint Committee on Clinical Practice Guidelines Liaison. §ACC/AHA Task Force on Performance Measures Representative. ‖HFSA Representative.

ACC/AHA Joint Committee on Clinical Practice Guidelines Members, see page e888.

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Key Words: AHA Scientific Statements ■ heart failure ■ heart failure with reduced ejection fraction ■ heart failure with preserved ejection fraction ■ heart failure with mildly reduced ejection fraction ■ systolic heart failure ■ heart failure rehabilitation ■ cardiac failure ■ chronic heart failure ■ acute decompensated heart failure ■ cardiogenic shock ■ beta blockers ■ mineralocorticoid receptor antagonists ■ ACE inhibitors ■ angiotensin and neprilysin receptor antagonist ■ sacubitril valsartan ■ angiotensin receptor antagonist ■ sodium glucose co-transporter 2 ■ SGLT2 inhibitors ■ cardiac amyloidosis ■ atrial fibrillation ■ congestive heart failure ■ guideline-directed medical therapy ■ diabetes ■ cardiomyopathy ■ valvular heart disease ■ mitral regurgitation ■ cardiomyopathy in pregnancy ■ reduced ejection fraction ■ right heart pressure ■ palliative care ■ cardio-oncology ■ social determinants of health

TOP 10 TAKE-HOME MESSAGES

1. Guideline-directed medical therapy (GDMT) for heart failure (HF) with reduced ejection fraction (HFrEF) now includes 4 medication classes that include sodium-glucose cotransporter-2 inhibitors (SGLT2i).
2. SGLT2i have a Class of Recommendation 2a in heart failure with mildly reduced ejection fraction (HFmrEF). Weaker recommendations (Class of Recommendation 2b) are made for ARNi, ACEi, ARB, MRA, and beta blockers in this population.
3. New recommendations for HFpEF are made for SGLT2i (Class of Recommendation 2a), MRAs (Class of Recommendation 2b), and ARNi (Class of Recommendation 2b). Several prior recommendations have been renewed including treatment of hypertension (Class of Recommendation 1), treatment of atrial fibrillation (Class of Recommendation 2a), use of ARBs (Class of Recommendation 2b), and avoidance of routine use of nitrates or phosphodiesterase-5 inhibitors (Class of Recommendation 3: No Benefit).
4. 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.
5. Value statements were created for select recommendations where high-quality, cost-effectiveness studies of the intervention have been published.
6. 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.
7. 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 noninvasive (eg, natriuretic peptide, diastolic function on imaging) or invasive testing (eg, hemodynamic measurement).
8. Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF. A HF 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.
9. 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.
10. Recommendations are provided for select patients with HF and iron deficiency, anemia, hypertension, sleep disorders, type 2 diabetes, atrial fibrillation, coronary artery disease, and malignancy.

Purpose of the Executive Summary

The purpose of the "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure" (2022 HF guideline) is to provide an update and to consolidate the "2013 ACCF/AHA Guideline for the Management of Heart Failure"[1] for adults and the "2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure"[2] into a new document. Related ACC/AHA guidelines include recommendations relevant to HF and, in such cases, the HF guideline refers to these documents. For example, the 2019 primary prevention of cardiovascular disease guideline[3] includes recommendations that will be useful in preventing HF, and the 2021 valvular heart disease guideline[4] provides recommendations for mitral valve (MV) clipping in mitral regurgitation (MR).

Areas of focus include:

- Prevention of HF.
- Management strategies in stage C HF, including:
  - New treatment strategies in HF, including sodium-glucose cotransporter-2 inhibitors (SGLT2i) and angiotensin receptor-neprilysin inhibitors (ARNi).
  - Management of HF and atrial fibrillation (AF), including ablation of AF.
  - Management of HF and secondary MR, including MV transcatheter edge-to-edge repair.
- Specific management strategies, including:
  - Cardiac amyloidosis.
  - Cardio-oncology.
- Implantable devices.
- Left ventricular assist device (LVAD) use in stage D HF.

The intended primary target audience consists of clinicians who are involved in the care of patients with HF. The focus of the full clinical practice guideline[5] is to provide the most up-to-date evidence to direct the clinician in patient decision-making. This executive summary provides readers with the Top 10 items that they should

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Table 1. Applying American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
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	**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
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	**LEVEL B-R (Randomized)** • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
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	**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
CLASS 3: No Benefit (MODERATE) (Generally, LOE A or B use only) — **Benefit = Risk** **Suggested phrases for writing recommendations:** • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	**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
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 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 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

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

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

know about the 2022 HF guideline[5] and incorporates material from the full guideline along with each statement.

Document Review and Approval

The full clinical practice guideline was reviewed by 2 official reviewers nominated by the AHA; 1 official reviewer nominated by the ACC; 2 official reviewers from the Heart Failure Society of America; 1 official Joint Committee on Clinical Practice Guidelines reviewer; and 32 individual content reviewers. Authors' relationships with industry and other entities information is published in Appendix 1 of the full guideline.[5] Reviewers' relationships with industry and other entities information is published in Appendix 2 of the full guideline.[5]

CLASS OF RECOMMENDATION AND LEVEL OF EVIDENCE

The Class of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 1).[6]

TAKE-HOME MESSAGE NO. 1

Guideline-directed medical therapy (GDMT) for HF with reduced ejection fraction (HFrEF) now includes 4 medication

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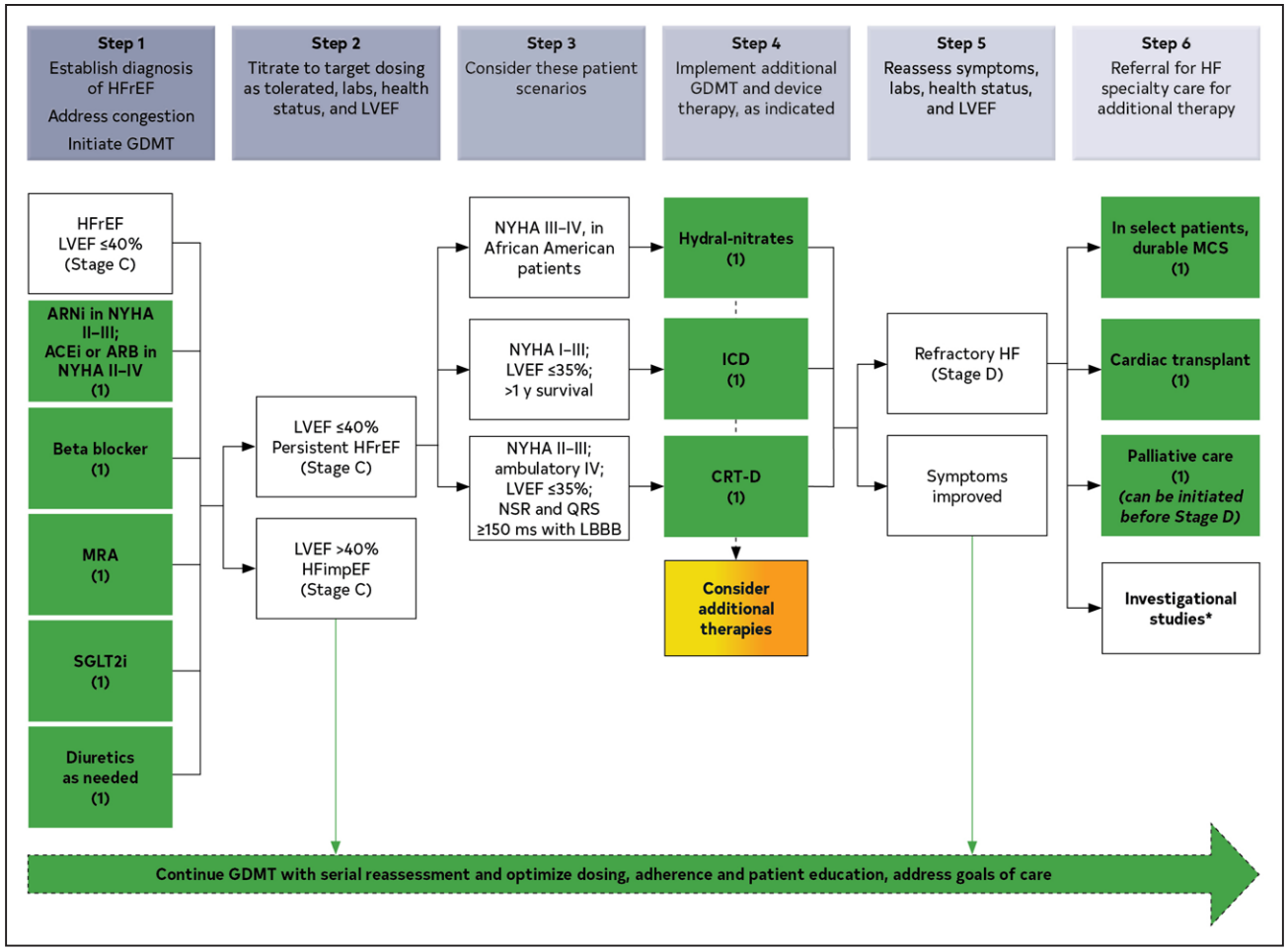

Figure 1. Treatment of HFrEF Stages C and D.
Colors correspond to COR in Table 1. Treatment recommendations for patients with HFrEF are displayed. Step 1 medications may be started simultaneously at initial (low) doses recommended for HFrEF. Alternatively, these medications may be started sequentially, with sequence guided by clinical or other factors, without need to achieve target dosing before initiating next medication. Medication doses should be increased to target as tolerated. ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; COR, Class of Recommendation; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; HFimpEF, heart failure with improved ejection fraction; HFrEF, heart failure with reduced ejection fraction; hydral-nitrates, hydralazine and isosorbide dinitrate; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MRA, mineralocorticoid receptor antagonist; NSR, normal sinus rhythm; NYHA, New York Heart Association; and SGLT2i, sodium-glucose cotransporter 2 inhibitor.
*Participation in investigational studies is appropriate for stage C, NYHA class II and III HF.

classes that include SGLT2i. The 4 groups are: 1) renin-angiotensin system inhibition with angiotensin receptor-neprilysin inhibitors (ARNi), angiotensin-converting enzyme inhibitors (ACEi), or angiotensin (II) receptor blockers (ARB) alone; 2) beta blockers; 3) mineralocorticoid receptor antagonists (MRAs); and 4) the new group, SGLT2i (Figure 1).

Recommendations for Renin-Angiotensin System Inhibition With ACEi or ARB or ARNi Referenced studies that support the recommendations are summarized in the Online Data Supplements.		
COR	**LOE**	**Recommendations**
1	A	1. In patients with HFrEF and New York Heart Association (NYHA) class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality.[7–11]

Recommendations for Renin-Angiotensin System Inhibition With ACEi or ARB or ARNi (Continued)		
1	A	2. 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.[12–19]
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.[20–24]
1	B-R	4. 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.[7–11]

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Recommendation for Beta Blockers
Referenced studies that support the recommendation are summarized in the Online Data Supplements.

COR	LOE	Recommendation
1	A	1. In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality (eg, bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations.[25–27]

Recommendation for MRAs
Referenced studies that support the recommendation are summarized in the Online Data Supplements.

COR	LOE	Recommendation
1	A	1. In patients with HFrEF and NYHA class II to IV symptoms, an MRA (spironolactone or eplerenone) is recommended to reduce morbidity and mortality, if estimated glomerular filtration rate is >30 mL/min/1.73 m^2 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.[28–30]

Recommendation for SGLT2i
Referenced studies that support the recommendation are summarized in the Online Data Supplements.

COR	LOE	Recommendation
1	A	1. 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.[31,32]

TAKE-HOME MESSAGE NO. 2

Mildly reduced LVEF has new medication recommendations, including use of SGLT2i (Figure 2). SGLT2i have a COR 2a in HF with mildly reduced EF (HFmrEF). Weaker recommendations (COR 2b) are made for ARNi, ACEi, ARB, MRA and beta blockers in this population.

Recommendations for HFmrEF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
2a	B-R	1. In patients with HFmrEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.[33]
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.[34–41]

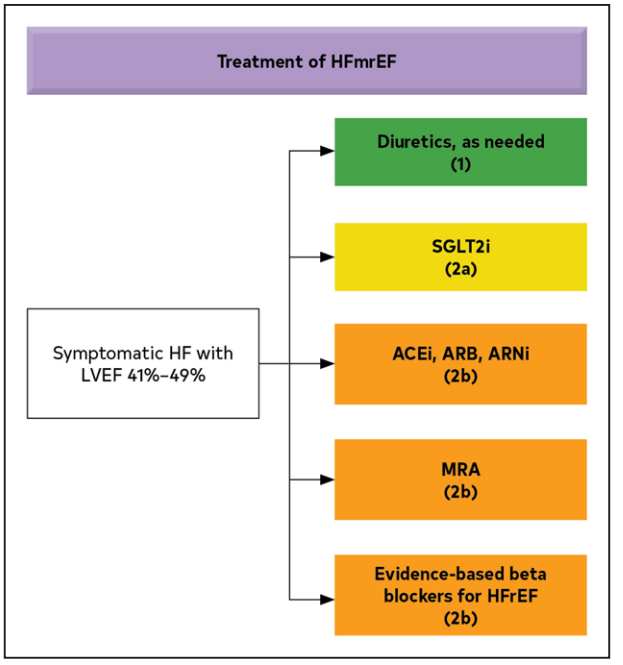

Figure 2. Recommendations for Patients with Mildly Reduced LVEF (41%–49%).
Colors correspond to COR in Table 1. Medication recommendations for HFmrEF are displayed.
ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HRmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium- glucose cotransporter 2 inhibitor.

TAKE-HOME MESSAGE NO. 3

Preserved LVEF has new medication recommendations, including use of SGLT2i (Figure 3). New recommendations for HF with preserved EF (HFpEF) are made for SGLT2i (COR 2a), MRAs (COR 2b), and ARNi (COR 2b). Several previous recommendations have been renewed, including treatment of hypertension (COR 1), treatment of AF (COR 2a), use of ARB (COR 2b), and avoidance of routine use of nitrates or phosphodiesterase-5 inhibitors (COR 3: No Benefit).

New Recommendations for HFpEF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
2a	B-R	1. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.[33]
2b	B-R	2. In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[38,42,43]
2b	B-R	3. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[35,40]

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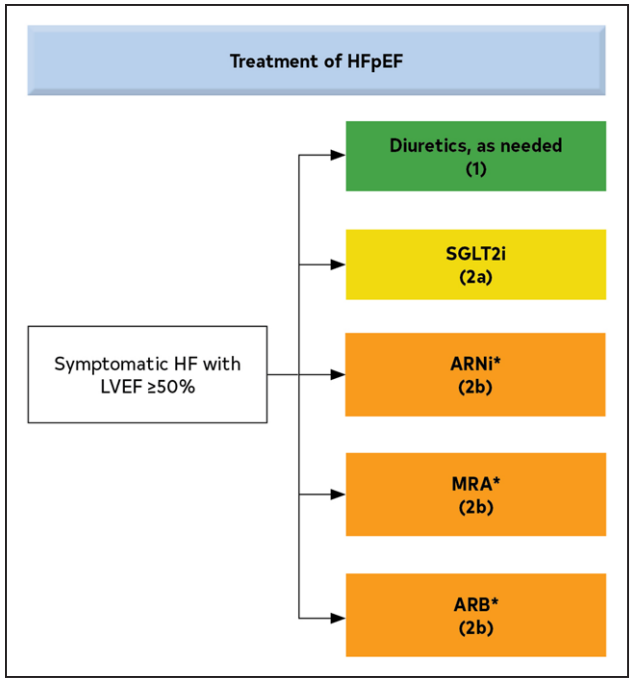

Figure 3. Recommendations for Patients with Preserved LVEF (≥50%).
Colors correspond to COR in Table 1. Medication recommendations for HFpEF are displayed.
ARB indicates angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium-glucose cotransporter-2 inhibitor.
*Greater benefit in patients with LVEF closer to 50%.

Renewed Recommendations for HFpEF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	C-LD	1. Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity.[44–46]
2a	C-EO	2. In patients with HFpEF, management of AF can be useful to improve symptoms.
2b	B-R	3. 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.[47,48]
3: No Benefit	B-R	4. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life is ineffective.[49,50]

TAKE-HOME MESSAGE NO. 4

Improved LVEF is used to refer to those with a previous HFrEF who now have an LVEF >40% (Figure 4). These patients should continue their HFrEF treatment.

Recommendation for HF With Improved EF (HFimpEF)
Referenced studies that support the recommendation are summarized in the Online Data Supplements.

COR	LOE	Recommendation
1	B-R	1. In patients with HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and left ventricular dysfunction, even in patients who may become asymptomatic.[36]

TAKE-HOME MESSAGE NO. 5

Value statements have been created for many treatments. In accordance with ACC/AHA methodology,[51] value statements were created for select recommendations where high-quality, cost-effectiveness studies of the intervention have been published. High value is defined as <$60 000/quality-adjusted life year gained (<1 US GDP/capita/QALY). Low value is defined as >$180 000/quality-adjusted life year gained (>3 US GDP/capita/QALY). High-value therapies include ARNi, ACEi, ARB, beta blocker, MRA, implantable cardioverter-defibrillator, and cardiac resynchronization therapy. Intermediate-value therapies include SGLT2i and cardiac transplantation. The only therapy identified as low value was tafamidis for cardiac amyloidosis. The value of mechanical circulatory support and pulmonary pressure monitoring was considered uncertain.

Value Statements	
Level	**Statements**
High	1. 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.[52–58]
High	2. In patients with chronic symptomatic HFrEF, treatment with an ARNi instead of an ACEi provides high economic value.[59–62]
High	3. In patients with HFrEF, with current or previous symptoms, beta-blocker therapy provides high economic value.[52,63–66]
High	4. In patients with HFrEF and NYHA class II to IV symptoms, MRA therapy provides high economic value.[52,67–69]
High	5. For patients self-identified as African American with NYHA class III to 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.[70]
High	6. A transvenous implantable cardioverter-defibrillator provides high economic value in the primary prevention of sudden cardiac death 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.[71–76]
High	7. For patients who have LVEF ≤35%, sinus rhythm, left bundle branch block with a QRS duration of ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, cardiac resynchronization therapy implantation provides high economic value.[77–82]

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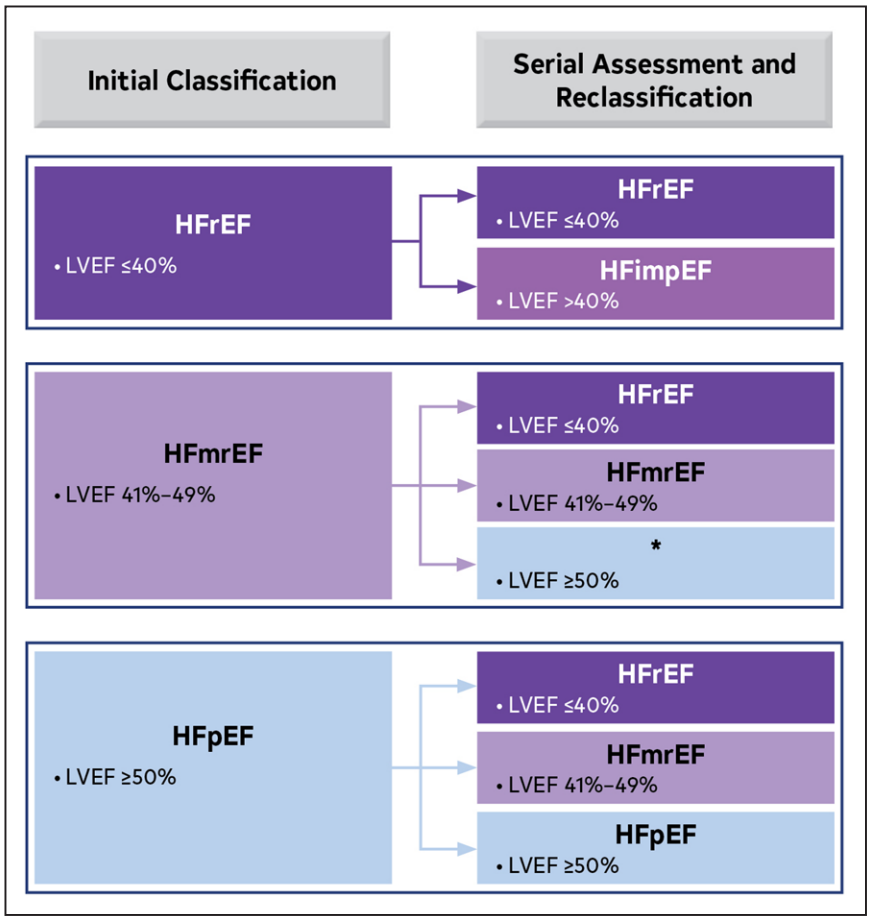

Figure 4. Classification and Trajectories of HF Based on LVEF.
See Appendix 1 for suggested thresholds for laboratory findings. The classification for baseline and subsequent LVEF is shown. Patients with HFrEF who improve their LVEF to >40% are considered to have HFimpEF and should continue HFrEF treatment. HF indicates 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; and LVEF, left ventricular ejection fraction. It is unclear whether to treat these patients as HFpEF or HFmrEF.
*There is limited evidence to guide therapy for patients who improve their LVEF from mildly reduced (41%–49%) to ≥50%.

Value Statements Continued	
Level	**Statements**
Intermediate	8. In patients with symptomatic chronic HFrEF, SGLT2i therapy provides intermediate economic value.[83,84]
Intermediate	9. In patients with stage D (advanced) HF despite GDMT, cardiac transplantation provides intermediate economic value.[85]
Low	10. 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.[86]
Uncertain	11. In patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable mechanical circulatory support devices provide low to intermediate economic value based on current costs and outcomes.[85,87–90]
Uncertain	12. In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the pulmonary artery pressure by an implanted hemodynamic monitor provides uncertain value.[62,91–93]

TAKE-HOME MESSAGE NO. 6

Amyloid heart disease has new recommendations for treatment. Specific strategies for diagnosis and treatment of cardiac amyloidosis are recommended (Figure 5). In patients with a clinical suspicion for cardiac amyloidosis, screening for serum and urine monoclonal light chains with serum and urine immunofixation electrophoresis and serum free light chains are recommended. If there is no evidence of serum or urine monoclonal light chains, bone scintigraphy is recommended to confirm the presence of transthyretin cardiac amyloidosis. If transthyretin cardiac amyloidosis is identified, genetic sequencing of the *TTR* gene is recommended to differentiate hereditary variant from wild-type transthyretin cardiac amyloidosis because confirmation of a hereditary variant would trigger genetic counseling and potential screening of family members. Transthyretin tetramer stabilizer therapy (tafamidis) is recommended in select patients with wild-type or variant transthyretin cardiac amyloidosis. Anticoagulation is a reasonable treatment strategy to reduce the risk of stroke in patients with cardiac amyloidosis and AF.

Recommendations for Diagnosis of Cardiac Amyloidosis Referenced studies that support the recommendations are summarized in the Online Data Supplements.		
COR	**LOE**	**Recommendations**
1	B-NR	1. Patients for whom there is a clinical suspicion for cardiac amyloidosis*[94–98] should have screening for serum and urine monoclonal light chains with serum and urine immunofixation electrophoresis and serum free light chains.[99]

*Left ventricular 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.

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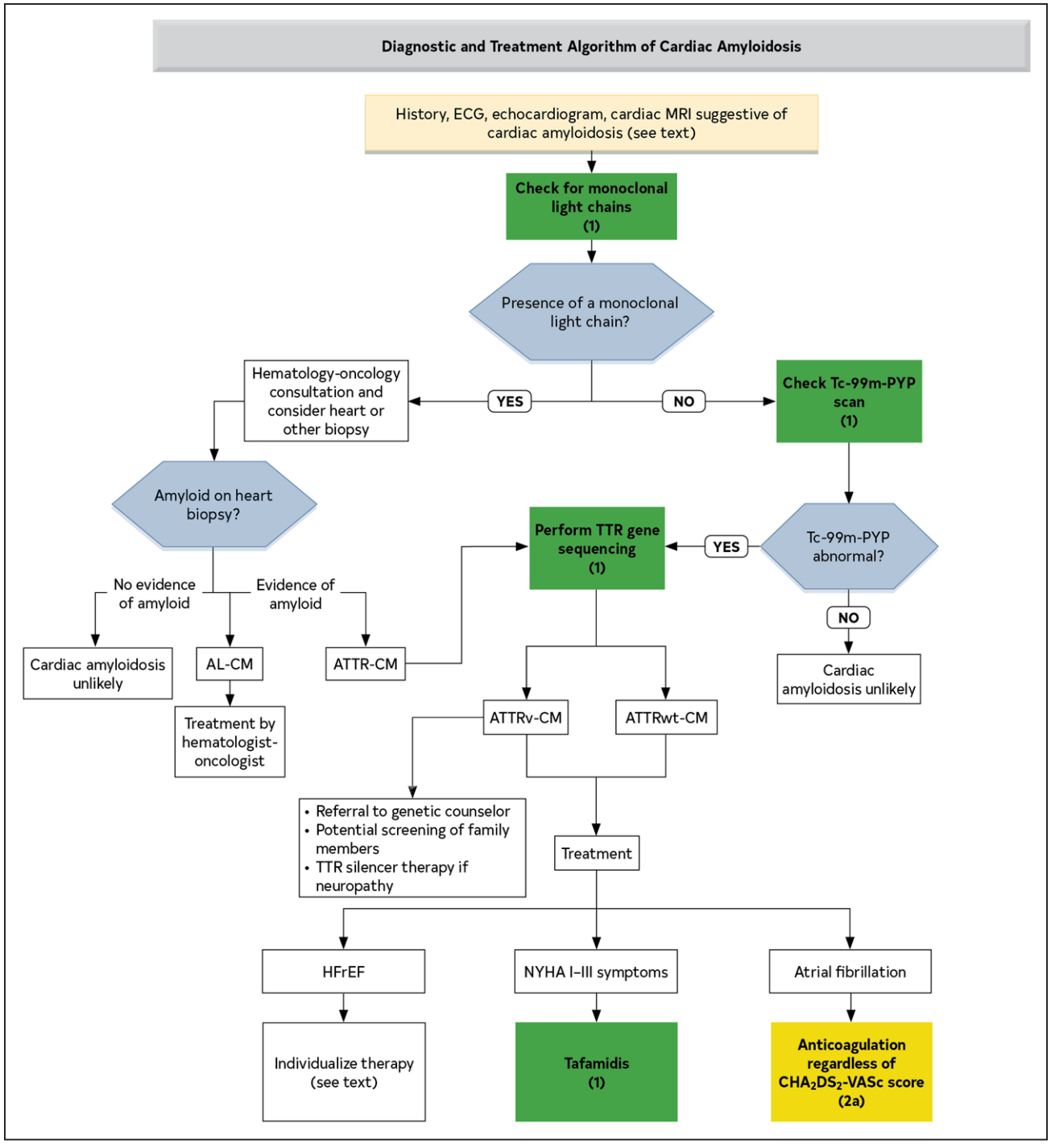

Figure 5. Diagnostic and Treatment of Transthyretin Cardiac Amyloidosis Algorithm.
Colors correspond to COR in Table 1.
AF indicates atrial fibrillation; AL-CM, amyloid cardiomyopathy; ATTR-CM, transthyretin amyloid cardiomyopathy; ATTRv, variant transthyretin amyloidosis; ATTRwt, wild-type transthyretin amyloidosis; CHA_2DS_2-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; ECG, electrocardiogram; H/CL, heart to contralateral chest; HFrEF, heart failure with reduced ejection fraction; IFE, immunofixation electrophoresis; MRI, magnetic resonance imaging; NYHA, New York Heart Association; PYP, pyrophosphate; Tc, technetium; and TTR, transthyretin.

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Recommendations for Diagnosis of Cardiac Amyloidosis (Continued)		
1	B-NR	2. 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.[100]
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.[101]

Recommendations for Treatment of Cardiac Amyloidosis Referenced studies that support the recommendations are summarized in the Online Data Supplements.		
COR	LOE	Recommendations
1	B-R	1. 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.[102]
2a	C-LD	2. In patients with cardiac amyloidosis and AF, anticoagulation is reasonable to reduce the risk of stroke regardless of the CHA_2DS_2-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.[103,104]

TAKE-HOME MESSAGE NO. 7

Evidence supporting increased filling pressures is important for the diagnosis of HF if the LVEF is >40% (Table 2). The signs and symptoms of HF are nonspecific and thus a diagnosis of HF requires supporting evidence. Increased cardiac filling pressure is a feature of HF, and this is assumed for patients with an LVEF ≤40%. However, if the LVEF is 41% to 49% (mildly reduced) or ≥50% (preserved), evidence of spontaneous or provokable increased LV filling pressures is needed to confirm a diagnosis of HF. Evidence for increased filling pressures can be obtained from noninvasive (eg, natriuretic peptide, diastolic function on imaging) or invasive testing (eg, hemodynamic measurement).

Table 2. 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 (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)

Please see Appendix 1 for suggested thresholds for structural heart disease and evidence of increased filling pressures.

HF indicates heart failure; LV, left ventricular; and LVEF, left ventricular ejection fraction.

TAKE-HOME MESSAGE NO. 8

Patients with advanced HF who wish to prolong survival should be referred to a team specializing in HF. A HF specialty team, typically located at an advanced HF center, reviews HF management, assesses suitability for advanced HF therapies (eg, left ventricular assist devices, cardiac transplantation), and uses palliative care including palliative inotropes where consistent with the patient's goals of care.

Recommendation for Specialty Referral for Advanced HF		
COR	LOE	Recommendation
1	C-LD	1. 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 (eg, left ventricular assist devices, cardiac transplantation, palliative care, and palliative inotropes).[105–110]

TAKE-HOME MESSAGE NO. 9

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 (Figure 6, Table 3). In the full guideline, primary prevention included all health care strategies that prevent the development of symptomatic HF (stage C). Healthy lifestyle habits, such as maintaining regular physical activity, maintaining normal weight, and a healthy diet, are recommended. Blood pressure should be controlled in accordance with published clinical practice guidelines. SGLT2i are recommended in patients with type 2 diabetes and either established cardiovascular disease or at high cardiovascular risk. Natriuretic peptide biomarker–based screening followed by team-based care, including a cardiovascular specialist, can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF (pre-HF, stage B). Validated multivariable risk scores can also be useful to estimate subsequent risk of incident HF. In asymptomatic patients with LVEF ≤40% (pre-HF, stage B), ACEi, ARB, evidence-based beta blockers, statins, and implantable cardioverter-defibrillators are recommended in certain patients.

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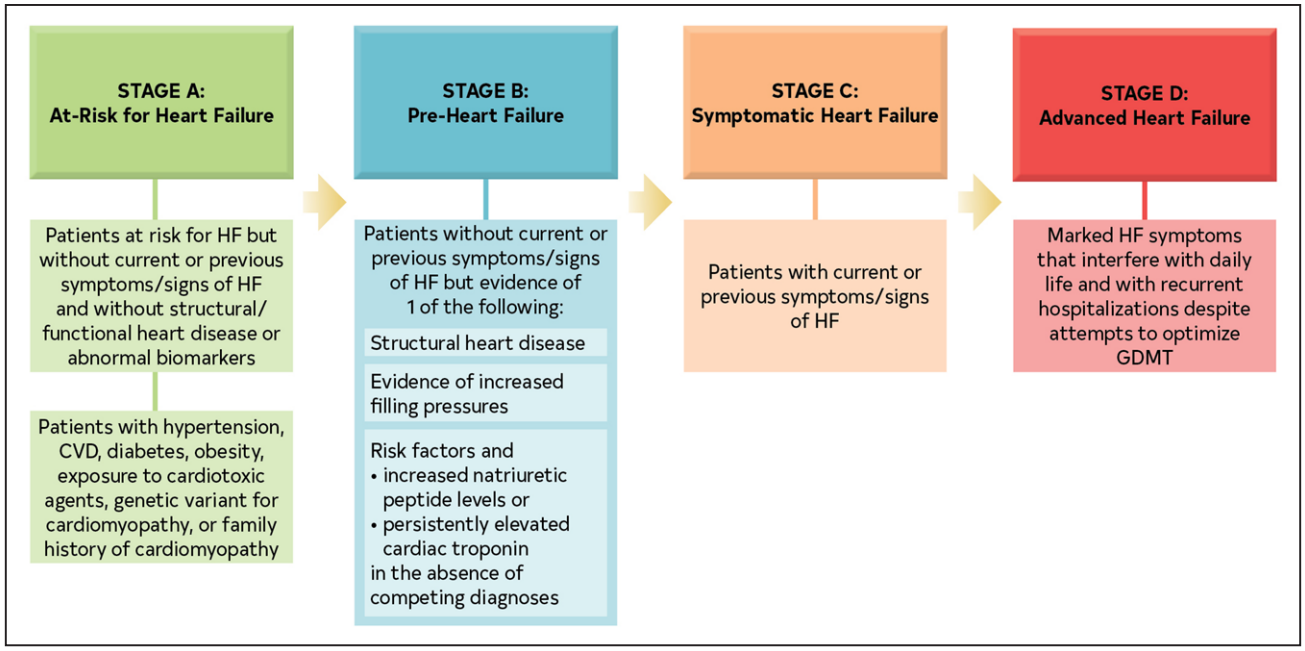

Figure 6. ACC/AHA Stages of HF.
The ACC/AHA stages of HF are shown.
ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.

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 (eg, 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: Pre-HF	No symptoms or signs of HF and evidence of 1 of the following:
	*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 (eg, Doppler echocardiography)
	Patients with risk factors and *Increased levels of B-type natriuretic peptides* or* *Persistently elevated cardiac troponin* in the absence of competing diagnoses resulting in such biomarker elevations such as acute coronary syndrome, CKD, pulmonary embolus, or myopericarditis
Stage C: Symptomatic HF	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.

CKD indicates chronic kidney disease; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.
*For thresholds of cardiac structural, functional changes, elevated filling pressures, and biomarker elevations, refer to Appendix 1.

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Recommendations for Patients at Risk for HF (Stage A: Primary Prevention)
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	A	1. In patients with hypertension, blood pressure should be controlled in accordance with GDMT for hypertension to prevent symptomatic HF.[46,111–118]
1	A	2. In patients with type 2 diabetes and either established cardiovascular disease or at high cardiovascular risk, SGLT2i should be used to prevent hospitalizations for HF.[119–121]
1	B-NR	3. 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.[122–130]
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.[131,132]
2a	B-NR	5. In the general population, validated multivariable risk scores can be useful to estimate subsequent risk of incident HF.[133–135]

Recommendations for Management of Stage B: Preventing the Syndrome of Clinical HF in Patients With Pre-HF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	A	1. In patients with LVEF ≤40%, ACEi should be used to prevent symptomatic HF and reduce mortality.[15,17,136,137]
1	A	2. In patients with a recent or remote history of myocardial infarction or acute coronary syndrome, statins should be used to prevent symptomatic HF and adverse cardiovascular events.[138–142]
1	B-R	3. In patients with a recent myocardial infarction and LVEF ≤40% who are intolerant to ACEi, ARB should be used to prevent symptomatic HF and reduce mortality.[143]
1	B-R	4. In patients with a recent or remote history of myocardial infarction or acute coronary syndrome and LVEF ≤40%, evidence-based beta blockers should be used to reduce mortality.[144–146]
1	B-R	5. In patients who are at least 40 days post–myocardial infarction with LVEF ≤30% and NYHA class I symptoms while receiving GDMT and have reasonable expectation of meaningful survival for >1 year, an implantable cardioverter-defibrillator is recommended for primary prevention of sudden cardiac death to reduce total mortality.[147]
1	C-LD	6. In patients with LVEF ≤40%, beta blockers should be used to prevent symptomatic HF.[145,146]
3: Harm	B-R	7. In patients with LVEF <50%, thiazolidinediones should not be used because they increase the risk of HF, including hospitalizations.[148]
3: Harm	C-LD	8. In patients with LVEF <50%, nondihydropyridine calcium channel blockers with negative inotropic effects may be harmful.[149,150]

TAKE-HOME MESSAGE NO. 10

Specific-treatment recommendations are provided for patients with HF and certain comorbidities (Figure 7). Recommendations are provided for select patients with HF and iron deficiency, anemia, hypertension, sleep disorders, type 2 diabetes, AF, coronary artery disease, and malignancy.

Recommendations for the Management of Comorbidities in Patients With HF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
Management of Anemia or Iron Deficiency		
2a	B-R	1. In patients with HFrEF and iron deficiency with or without anemia, intravenous iron replacement is reasonable to improve functional status and quality of life.[151–154]
3: Harm	B-R	2. In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality.[155,156]
Management of Hypertension		
1	C-LD	3. In patients with HFrEF and hypertension, uptitration of GDMT to the maximally tolerated target dose is recommended.[157–159]
Management of Sleep Disorders		
2a	B-R	4. In patients with HF and obstructive sleep apnea, continuous positive airway pressure may be reasonable to improve sleep quality and decrease daytime sleepiness.[160–163]
2a	C-LD	5. 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.[160,164]
3: Harm	B-R	6. In patients with NYHA class II to IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm.[162,163]
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.[31,32,165,166]

Recommendations for Management of AF in HF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	A	1. Patients with chronic HF with permanent-persistent-paroxysmal AF and a CHA_2DS_2-VASc score of ≥2 (for men) and ≥3 (for women) should receive chronic anticoagulant therapy.[167–171]
1	A	2. For patients with chronic HF with permanent-persistent-paroxysmal AF, a direct-acting oral anticoagulant is recommended over warfarin in eligible patients.[168–176]
2a	B-R	3. For patients with HF and symptoms caused by AF, AF ablation is reasonable to improve symptoms and quality of life.[177–180]

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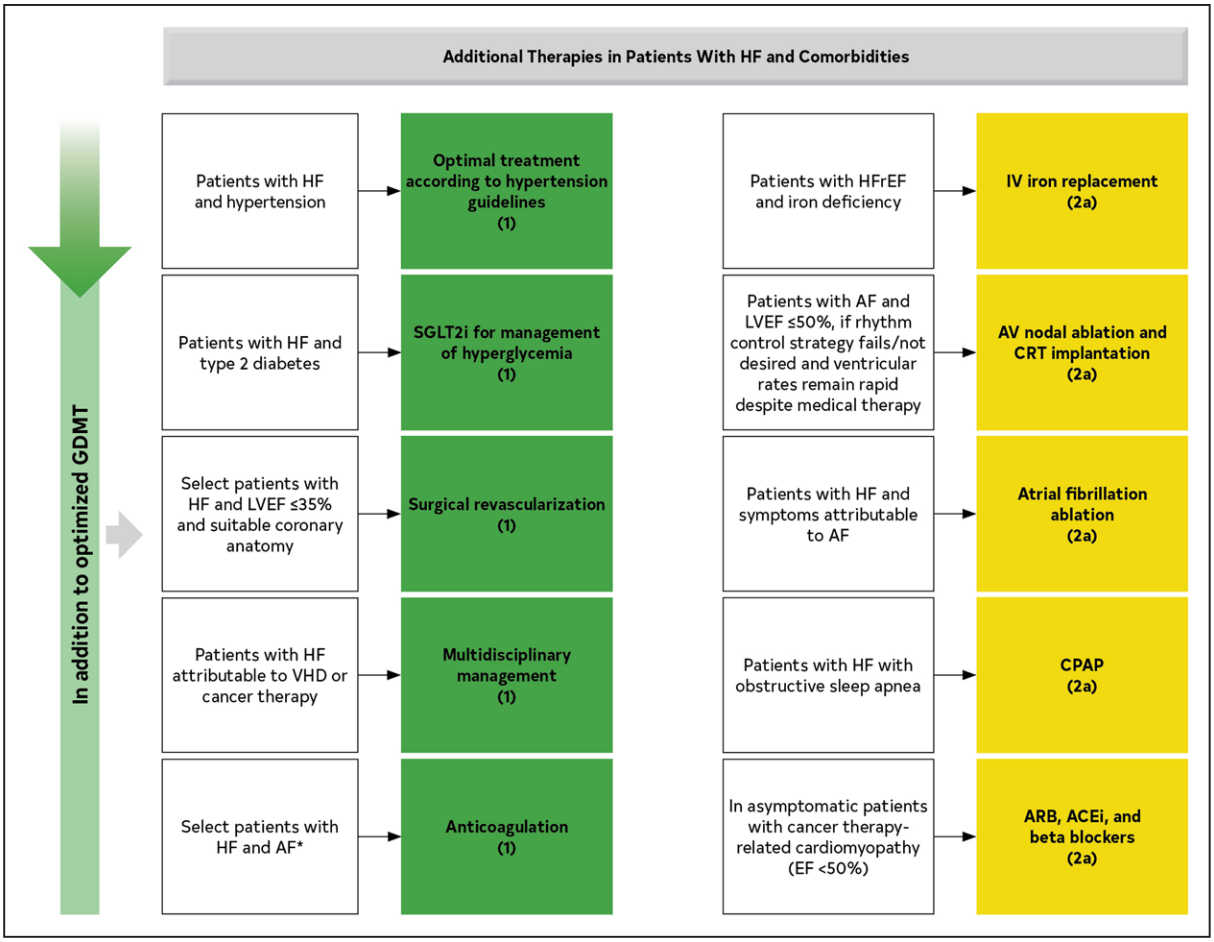

Figure 7. Recommendations for Treatment of Patients with HF and Selected Comorbidities.
Colors correspond to COR in Table 1. Recommendations for treatment of patients with HF and select comorbidities are displayed. ACEi indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; AV, atrioventricular; CHA_2DS_2-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; CPAP, continuous positive airway pressure; CRT, cardiac resynchronization therapy; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SGLT2i, sodium-glucose cotransporter 2 inhibitor; and VHD, valvular heart disease.
*Patients with chronic HF with permanent-persistent-paroxysmal AF and a CHA_2DS_2-VASc score of ≥2 (for men) and ≥3 (for women).

Recommendations for Management of AF in HF (Continued)

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 cardiac resynchronization therapy device is reasonable.[181–188]
2a	B-NR	5. For patients with chronic HF and permanent-persistent-paroxysmal AF, chronic anticoagulant therapy is reasonable for men and women without additional risk factors.[189–192]

Recommendation for Revascularization for Coronary Artery Disease
Referenced studies that support the recommendation are summarized in the Online Data Supplements.

COR	LOE	Recommendation
1	B-R	1. 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.[193–200]

Recommendations for Cardio-Oncology
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	B-NR	1. 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.[201,202]
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.[202–204]
2a	B-NR	3. 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.[202,205–216]

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Recommendations for Cardio-Oncology (Continued)		
2a	B-NR	4. 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.[202,204,206,208]
2b	B-R	5. 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.[217–228]
2b	C-LD	6. In patients being considered for potentially cardiotoxic therapies, serial measurement of cardiac troponin might be reasonable for further risk stratification.[229–232]

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ARTICLE INFORMATION

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*Former Joint Committee member; current member during the writing effort.

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Appendix 1. Appendix for Tables 2 and 3: Suggested Thresholds for Structural Heart Disease and Evidence of Increased Filling Pressures

Morphology	• LAVI ≥29 mL/m^2 • LVMI >116/95 g/m^2 • RWT >0.42 • LV wall thickness ≥12 mm
Ventricular systolic function	• LVEF <50% • GLS <16%
Ventricular diastolic function	• Average E/e′ ≥15 for increased filling pressures • Septal e′ <7 cm/s • Lateral e′ <10 cm/s • TR velocity >2.8 m/s • Estimated PA systolic pressure >35 mm Hg
Biomarker	• BNP ≥35 pg/mL* • NT-proBNP ≥125 pg/mL*

AF indicates atrial fibrillation; BNP, brain natriuretic peptide; CKD, chronic kidney disease; GLS, global longitudinal strain; HF, heart failure; LAVI, left atrial volume index; LVMI, left ventricular mass index; NT-proBNP, natriuretic peptide tests; PA, pulmonary artery; RWT, relative wall thickness; and TR, tricuspid regurgitation.

Usually, higher cutoff values are recommended for the diagnosis of HF in these patients. Natriuretic peptide cutoffs selected for population screening for pre-HF (stage B HF) may be <99% reference limits and need to be defined according to the population at risk. *Cutoffs provided for natriuretic peptide levels may have lower specificity, especially in older patients or in patients with AF or CKD.

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