MedStar Health

Guidelines for the Management of Heart Failure
Clinical Practice Guideline Endorsement
MedStar Health

"These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication but should be used with the clear understanding that continued research may result in new knowledge and recommendations".

MedStar Ambulatory Best Practice Committee endorses the 2021 American College of Cardiology Expert Consensus Decision Pathway for the Optimization of Heart Failure Treatment[1] and its two companion prior publications from 2013[2] and 2017[3].

With this latest 2021 update, the American College of Cardiology (ACC) hopes to provide clinicians with "actionable knowledge" and to this end, this document contains many Expert Consensus Decision Pathways. These pathways are intended to guide clinicians, not define the one correct answer.

It is an update to the 2013 and 2017 documents cited in the references and is an interim document to bring the latest clinical evidence into practice. A complete and definitive updated guideline is under development by the ACC.

This guideline focuses specifically on the clinical care of individuals with Heart Failure with Reduced Ejection Fraction (HFrEF). Heart Failure with Preserved Ejection Fraction is a topic for a different guideline.

What follows below is a summary and key figures and tables. Practitioners are encouraged to review the primary document for a better understanding of this summary and endorsement.

The 2021 Update addresses Ten Pivotal Issues in the care of patients with heart failure with reduced ejection fraction and incorporates the latest evidence from clinical trials and expert opinion presented as a series of tables and treatment algorithms. For the purposes of the update, HFrEF is defined as a left ventricular ejection fraction of $\leq$ 40%. The document focuses on the ambulatory management of these patients.

The Ten Pivotal Issues addressed are:

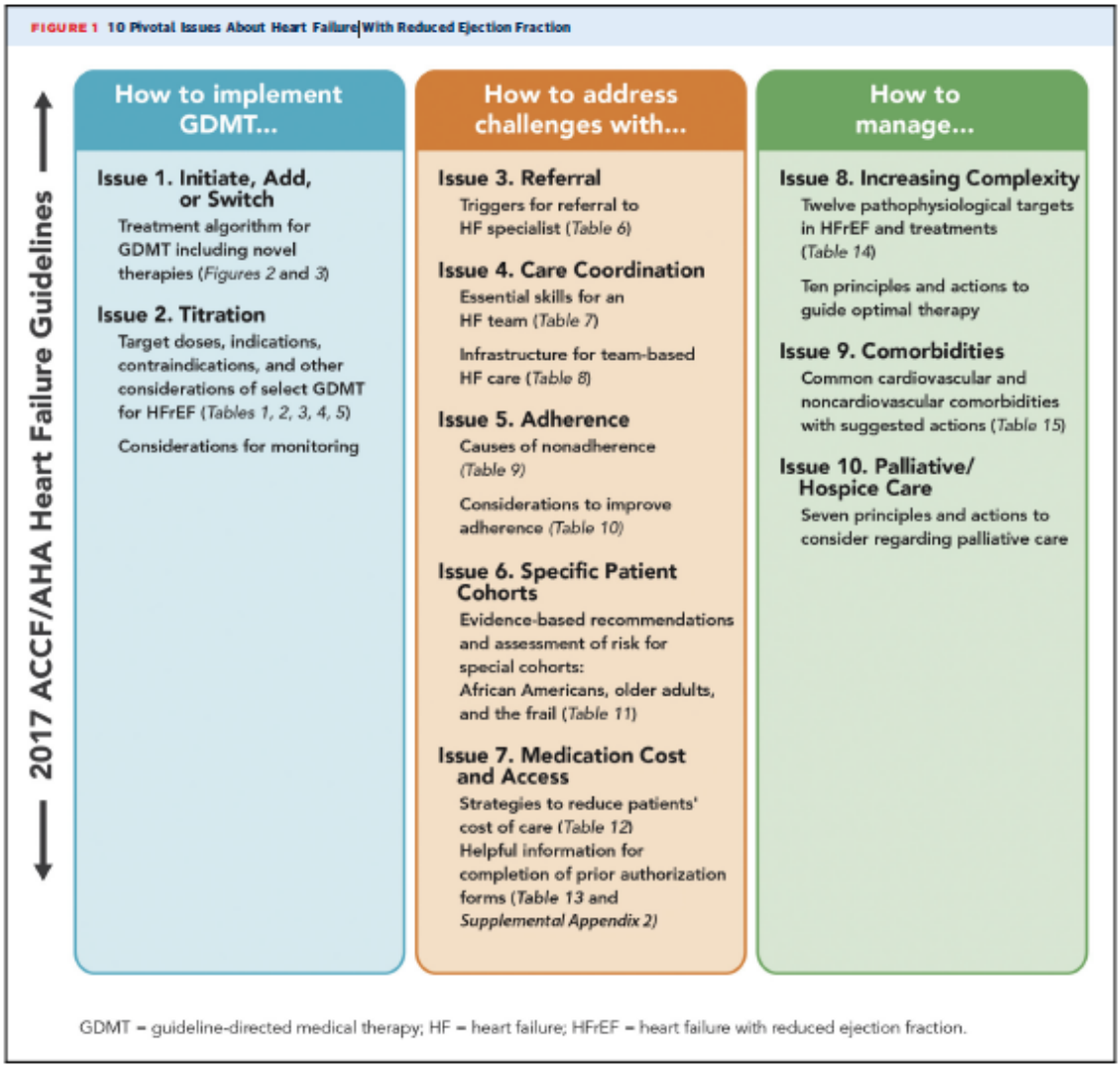
1. How to initiate, add, or switch therapies to new evidence-based guideline-directed treatments for HFrEF.
2. How to achieve optimal therapy given multiple drugs for heart failure including augmented clinical assessment (e.g., imaging data, biomarkers, and filling pressures) that may trigger additional changes in guideline-directed therapy.
3. When to refer to a heart failure specialist.
4. How to address challenges of care coordination.
5. How to improve medication adherence

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date: April 2021**	**Next Scheduled Review Date:**
April 2021		April 2023

6. What is needed in specific patient cohorts: African Americans, older adults, and the frail.
7. How to manage your patients' costs and access to heart failure medications.
8. How to manage the increasing complexity of heart failure.
9. How to manage common comorbidities.
10. How to integrate palliative care and the transition into hospice care.

The 2021 Update reviews how to:

- ❖ Implement guideline directed medical treatment – how to select, initiate and titrate medications
- ❖ How to address challenges with referrals, care coordination, adherence, specific patient cohorts and medication cost and access
- ❖ How to manage increasing complexity of care, comorbidities and palliative and hospice care.



The 2021 Update continues with the same definitions of Stages and Functional Classification

ACC/AHA Stages of HF:
Stage A: At high risk for HF but without structural heart disease or symptoms of HF.
Stage B: Structural heart disease but without signs or symptoms of HF.
Stage C: Structural heart disease with prior or current symptoms of HF.
Stage D: Refractory HF requiring specialized interventions.

New York Heart Association (NYHA) functional classification:
Class I: No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
Class II: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
Class IV: Unable to perform any physical activity without symptoms of HF, or symptoms of HF at rest.

In an accompanying article, Dr. Supriya Shore summarized the ACC update like this:

The following are key points to remember from the 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment:

1. For patients with newly diagnosed Stage C heart failure with reduced ejection fraction (HFrEF), a beta-blocker and an angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB)/angiotensin receptor-neprilysin inhibitor (ARNI) should be started in any order. Each agent should be up-titrated to maximally tolerated or target dose. Initiation of a beta-blocker is better tolerated when patients are dry and an ACEI/ARB/ARNI when patients are wet.
2. Only guideline-recommended beta-blockers (i.e., carvedilol, metoprolol succinate, or bisoprolol) should be used in patients with HFrEF. Among angiotensin antagonists, ARNIs are preferred agents. Renal function and potassium should be checked within 1-2 weeks of initiation or dose up-titration of ACEI/ARB/ARNI.
3. Diuretics should be added as needed and dose should be titrated to achieve decongestion. If doses in excess of furosemide 80 mg twice daily are needed, either a different loop diuretic should be considered, or a thiazide should be added.
4. After initiation of beta-blocker and angiotensin antagonist, addition of an aldosterone antagonist should be considered with close monitoring of electrolytes. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors should also be considered for HFrEF with New York Heart Association (NYHA) class II-IV patients.

5. For persistently symptomatic Black patients despite above therapies, hydralazine and isosorbide dinitrate should be considered. In addition, if despite maximally tolerated beta-blocker, resting HR is ≥70 bpm in sinus rhythm, ivabradine may be considered.
6. An ideal time to consider therapy optimization is during hospitalization for HFrEF. As an outpatient, adjustment of therapies should be considered every 2 weeks to achieve guideline-directed medical therapy (GDMT) within 3-6 months of initial diagnosis. An echocardiogram should be repeated 3-6 months after achieving target doses of therapy for consideration of an implantable cardioverter-defibrillator (ICD)/cardiac resynchronization therapy (CRT).
7. Surgical treatment is recommended for patients with severe primary chronic mitral regurgitation. For severe chronic functional mitral regurgitation, optimization of GDMT is recommended prior to consideration of percutaneous transcatheter repair in symptomatic patients only.
8. Hyperkalemia and/or abnormal renal function are common barriers to achieving target medication doses. Patients with hyperkalemia should be educated about a low potassium diet. Potassium binders may be considered.
9. Socioeconomic barriers pose a major barrier to use of ARNI, SGLT-2 inhibitors, and ivabradine. In these cases, financially feasible options should be considered. This may include virtual care and visiting home nursing services particularly during the coronavirus disease 2019 (COVID-19) pandemic.
10. For patients with recovery of left ventricular ejection fraction (LVEF) to >40%, GDMT should be resumed in the absence of a defined, reversible cause.
11. Repeat echocardiograms should be considered in the context of change in clinical status or other high-risk features only. Measuring B-type natriuretic peptide (BNP) or N-terminal–proBNP (NT-proBNP) is useful for risk assessment and decision making regarding referral to a HF specialist or assessing need for other imaging studies. BNP levels may rise with use of ARNI therapy, but NT-proBNP levels are not impacted.
12. Right heart catheterizations should be considered when symptoms persist despite adequate diuretic dose, worsening renal function with attempts to use higher dose therapies including diuretics or those with repeated hospitalizations for decompensation. In highly selected patients with recurrent congestion, an implantable sensor to guide filling pressure assessment (e.g., CardioMEMS) in ambulatory HF patients may be considered.
13. Referral to a HF specialist should be considered in patients needing inotropes, NYHA class IIIB/IV symptoms or persistently elevated natriuretic peptides, end-organ dysfunction, EF ≤35%, ICD shocks, recurrent hospitalizations, congestion despite escalating diuretics, low blood pressure and/or high heart rate, and progressive intolerance to GDMT needing down-titration.
14. Delivering care for HF requires a team-based approach. Infrastructure such as provision of patient monitoring devices (e.g., Scales) or smartphones or electronic health records can support such team-based care.
15. Medication adherence should be assessed regularly. Interventions helping with adherence include patient education, medication management, pharmacist co-management,

cognitive behavioral therapies, medication taking reminders, and incentives to improve adherence.

16. Goals of care should be addressed during the course of illness with HF and expectations should be calibrated to guide timely decisions. When feasible, decision support tools should be used. End-of-life care in HF involves meticulous management of HF therapies, and palliative care consultation may help with other noncardiac symptoms such as pain.

The 2021 document includes the following principles which are reproduced here verbatim:

- Principle 1: Guideline directed medical therapy (GDMT) is the foundation of HF care, and the GDMT with the highest expected benefit should be prioritized.
- Principle 2: Target doses are associated with best outcomes.
- Principle 3: Start GDMT immediately. Delayed initiation of GDMT is associated with never initiating GDMT.
- Principle 4: Attention to the clinical, social, and financial barriers to achieving GDMT should be prioritized.
- Principle 5: Diligent management of volume status will reduce patient symptoms.
- Principle 6: Tolerability and side effects depend, in part, on how and when GDMT is prescribed.
- Principle 7: Primary prevention implantable cardioverter-defibrillator and cardiac resynchronization therapy should be considered after consistent use of optimal doses of all GDMTs for at least 3 to 6 months, followed by reassessment of EF and other indications for device therapy.
- Principle 8: Transcatheter mitral valve repair may be considered among symptomatic patients with chronic moderate-severe to severe mitral regurgitation despite optimal doses of all GDMTs.
- Principle 9: Focus on the patient's symptoms, functional capacity, and cardiac function.
- Principle 10: The value of a therapy to a patient is the combination of benefits and burdens as they relate to that patient's values, goals, and preferences.
- Principle 11: Team-based care is critical to optimizing GDMT and may include frequent follow-up visits, telehealth visits, and remote monitoring.

The following are the Key Tables and Figures from the ACC Update.

Adapted from Table 1: Guideline Directed Medication Therapy:

Medication*	**Starting Dose**	**Target Dose**	**Common Adverse Effects**	**Additional Clinical Information**
Beta Blockers				
Bisoprolol ($68)	1.25mg once daily	10mg once daily	Headache Fatigue	May mask symptoms of hypoglycemia in diabetics

Carvedilol *Coreg®* ($257)	3.125mg twice daily	Weight <85kg: 25mg twice daily Weight 85+kg: 50mg twice daily	Dizziness Fatigue Weight gain Erectile dysfunction	Take with food to decrease risk of orthostatic hypotension May mask symptoms of hypoglycemia in diabetics
Metoprolol Succinate *Toprol XL®* ($92)	12.5-25mg daily	200mg daily	Dizziness Fatigue Headache Depression	Tartrate form should not be used in heart failure May be split in half but not crushed or chewed Do not discontinue abruptly May mask symptoms of hypoglycemia in diabetics
ARNIs				
Sacubitril/valsartan *Entresto®* ($350 – brand only)	24/26mg-49/51mg daily	97/103mg daily	Hyperkalemia Dizziness	Avoid in pregnant patients
ACEIs				
Captopril ($261)	6.25mg 3x/day	50mg 3x/day	Hyperkalemia Angioedema	Take at least 1 hour before meals Avoid in pregnant patients
Enalapril *Vasotec®* ($166)	2.5mg twice daily	10-20mg twice daily	Hyperkalemia Dizziness Angioedema	If SCr > 1.6, start at 2.5mg daily Avoid in pregnant patients
Lisinopril *Prinvil®, Zestril®* ($47)	2.5-5mg daily	20-40mg daily	Dizziness Headache Hyperkalemia Angioedema	Avoid in pregnant patients
Ramipril *Altace®* ($67)	1.25mg daily	10mg daily	Dizziness Headache Angioedema	Avoid in pregnant patients
ARBs				
Candesartan *Atacand®* ($136)	4-8mg daily	32mg daily	Dizziness Headache	Avoid in pregnant patients
Losartan *Cozaar®* ($167)	25-50mg daily	150mg daily	Dizziness	Avoid in pregnant patients
Valsartan *Dioven®*	40mg twice daily	160mg twice daily	Dizziness Headache	Avoid in pregnant patients

($197)				
Aldosterone Antagonists				
Eplerenone *Inspra®* ($130)	25mg daily	50mg daily	Hyperkalemia	
Spironolactone *Aldactone®* ($26)	12.5-25mg daily	25-50mg daily	Hyperkalemia Gynecomastia	
SGLT2 Inhibitors				
Dapagliflozin *Farxiga®* ($639 – brand only)	10mg daily	10mg daily	Urinary tract infection Diabetic ketoacidosis Hypotension	Must maintain adequate hydration
Empagliflozin *Jardiance®* ($658 – brand only)	10mg daily	10mg daily	Urinary tract infection Diabetic ketoacidosis Hypotension	Must maintain adequate hydration
Vasodilators				
Hydralazine ($96)	25mg 3x/day	75mg 3x/day	Diarrhea Loss of appetite	
Isosorbide dinitrate *Isordil Titradose ®* ($214)	20mg 3x/day	40mg 3x/day	Headache Lightheadedness	PDE 5 inhibitors contraindicated in patients on nitrates
Isosorbide dinitrate/hydralazine combination (20/37.5mg) *BiDil®* ($828)	1 tab 3x/day	2 tab 3x/day	See individual agents	
Other				
Ivabradine *Corlanor®* ($590)	2.5-5mg twice daily	Titrated to goal heart rate 50-60bpm Max dose 7.5mg twice daily	Atrial fibrillation Phosphenes	Take with food Available as oral solution if patient unable to swallow tabs

*AWP for 30 days of medication at maximum target dose unless specified otherwise

Figure 2 below outlines the strategies for medication management. Note in the upper diamond that all patients should be started on either an ARNI, or ACEI/ARB and a beta blocker with proven efficacy (carvedilol, metoprolol succinate or bisoprolol.)

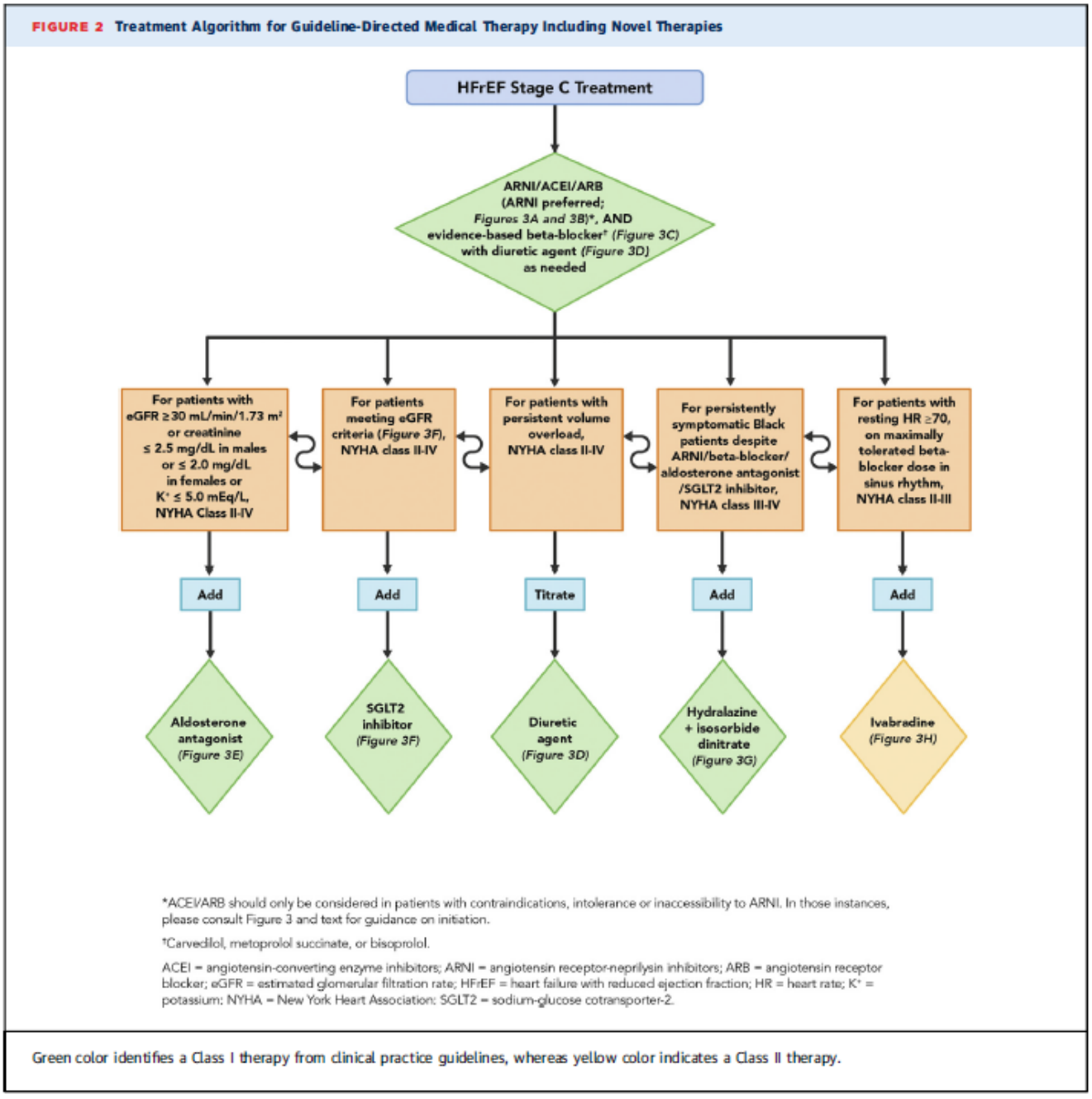
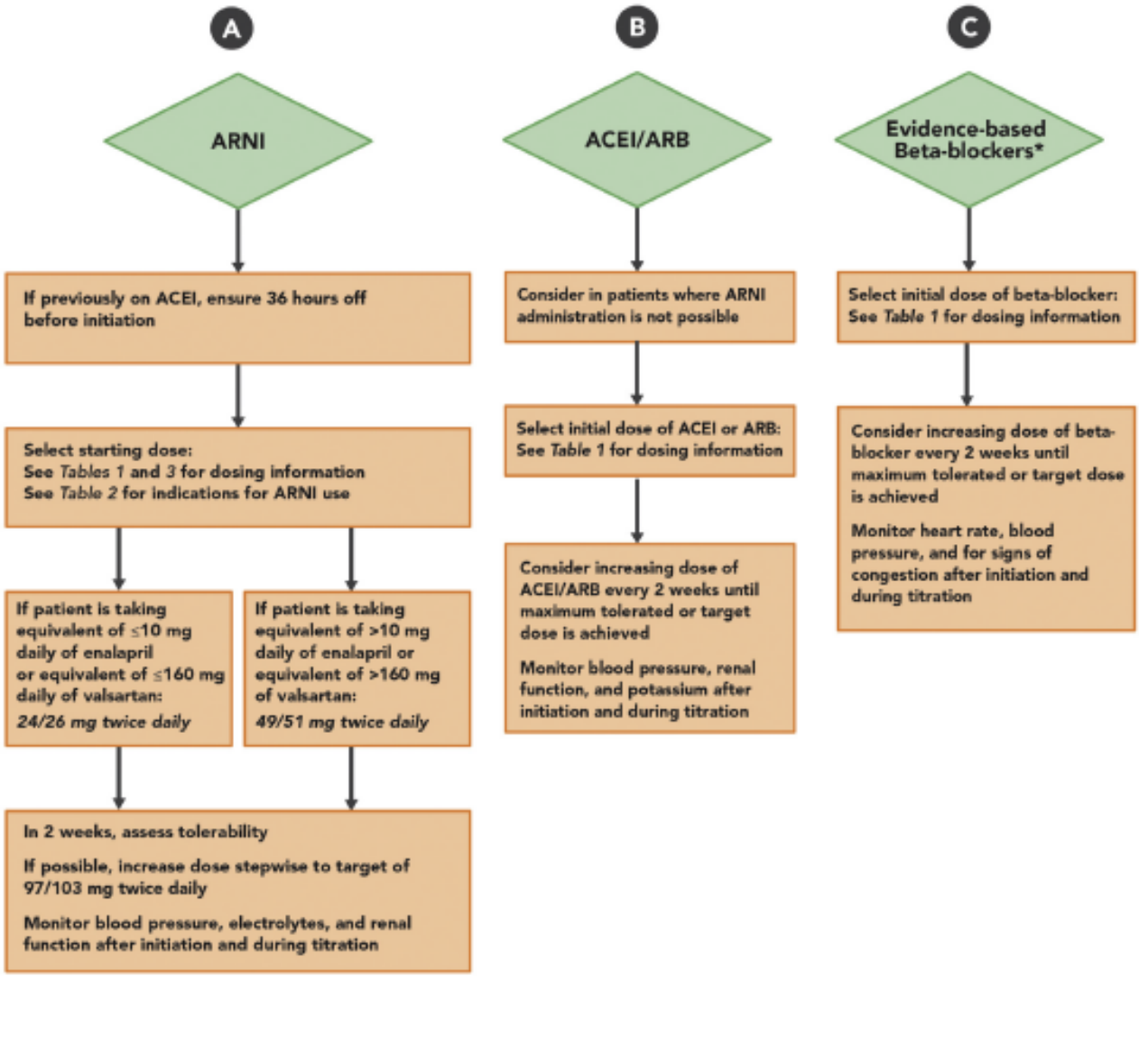


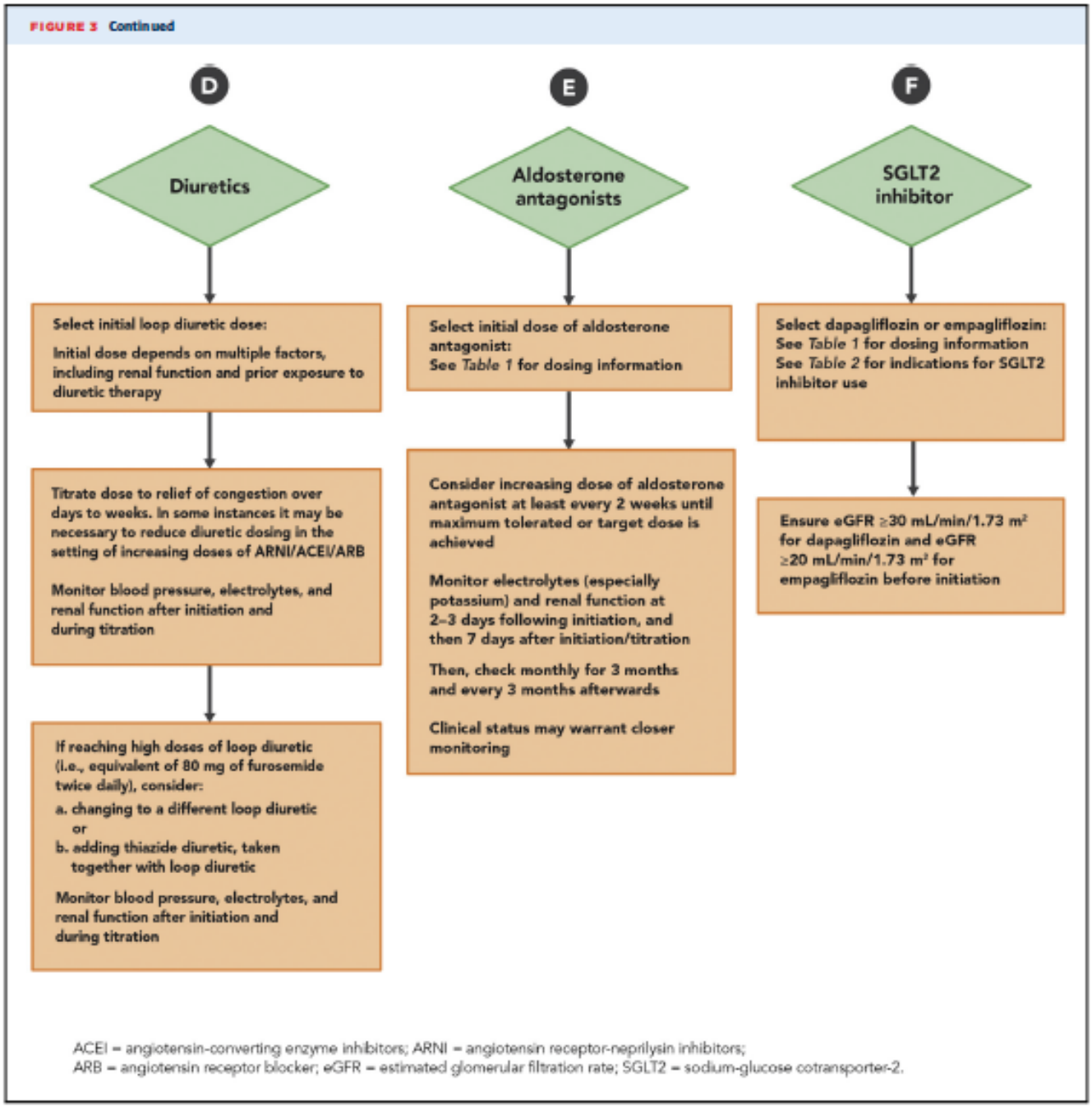
FIGURE 3 Guideline-Directed Medical Therapy Including Novel Therapies in the Expert Consensus Decision Pathway for Chronic Heart Failure



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

*Carvedilol, metoprolol succinate, or bisoprolol.

ARNIs are the preferred agents, but for patients in whom ARNI administration is not possible, an ACEI/ARB is recommended.



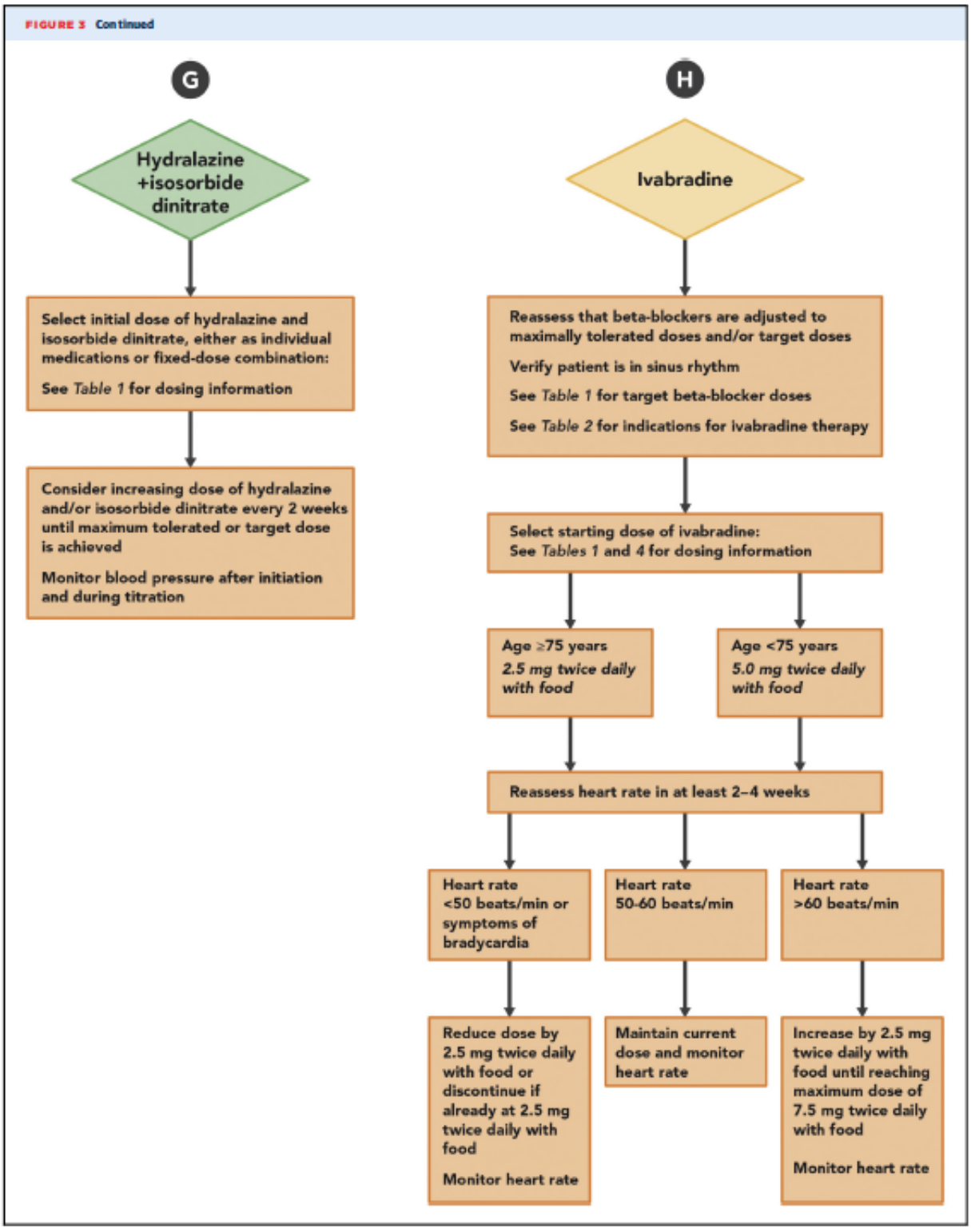


Table 4: Reviews the contraindications of the relatively new therapies – ARNI, Ivabradine and SGLT2 inhibitors

Table 5: Describes the recommended starting doses for Ivabradine

Figure 4: Offers guidance on the evaluation and management – short and long term.

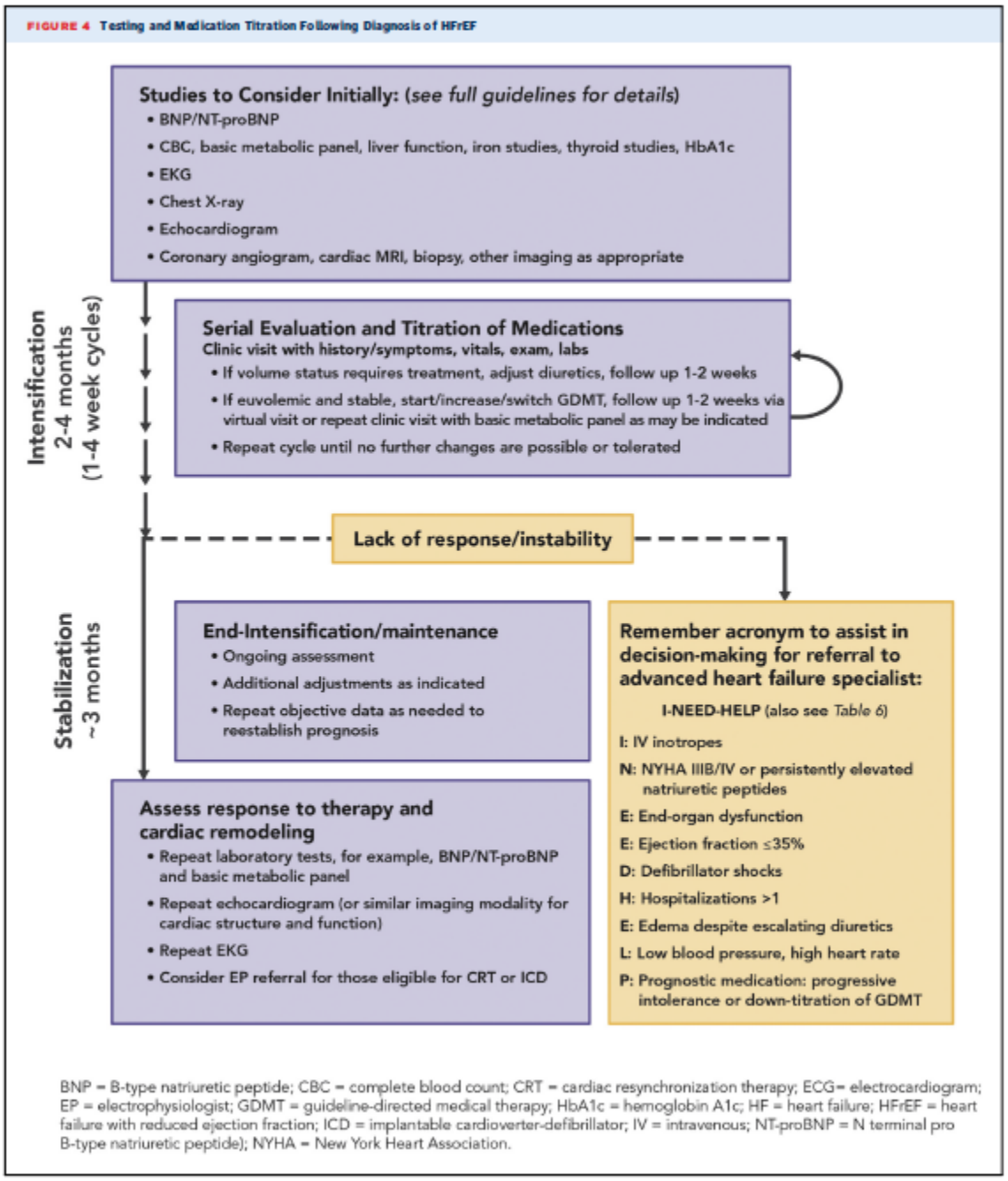


Table 6: Triggers for HF Patient Referral to a Specialist/Program

TABLE 6	Triggers for HF Patient Referral to a Specialist/Program
Clinical Scenario	1. New-onset HF (regardless of EF): Refer for evaluation of etiology, guideline-directed evaluation and management of recommended therapies, and assistance in disease management, including consideration of advanced imaging, endomyocardial biopsy, or genetic testing for primary evaluation of new-onset HF
	2. Chronic HF with high-risk features, such as development or persistence of one or more of the following risk factors: ■ Need for chronic intravenous inotropes ■ Persistent NYHA functional class III–IV symptoms of congestion or profound fatigue ■ Systolic blood pressure ≤90 mm Hg or symptomatic hypotension ■ Creatinine ≥1.8 mg/dL or BUN ≥43 mg/dL ■ Onset of atrial fibrillation, ventricular arrhythmias, or repetitive ICD shocks ■ Two or more emergency department visits or hospitalizations for worsening HF in the prior 12 months ■ Inability to tolerate optimally dosed beta-blockers and/or ACEI/ARB/ARNI and/or aldosterone antagonists ■ Clinical deterioration, as indicated by worsening edema, rising biomarkers (BNP, NT-proBNP, others), worsened exercise testing, decompensated hemodynamics, or evidence of progressive remodeling on imaging ■ High mortality risk using a validated risk model for further assessment and consideration of advanced therapies, such as the Seattle Heart Failure Model
	3. Persistently reduced LVEF ≤35% despite GDMT for ≥3 months: refer for consideration of device therapy in those patients without prior placement of ICD or CRT, unless device therapy is contraindicated or inconsistent with overall goals of care
	4. Second opinion needed regarding etiology of HF; for example: ■ Coronary ischemia and the possible value of revascularization ■ Valvular heart disease and the possible value of valve repair ■ Suspected myocarditis ■ Established or suspected specific cardiomyopathies (e.g., hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, Chagas disease, restrictive cardiomyopathy, cardiac sarcoidosis, amyloid, aortic stenosis)
	5. Annual review needed for patients with established advanced HF in which patients/caregivers and clinicians discuss current and potential therapies for both anticipated and unanticipated events, possible HF disease trajectory and prognosis, patient preferences, and advanced care planning
	6. Assessment of patient for possible participation in a clinical trial

ACEI = angiotensin converting enzyme inhibitors; ARB = angiotensin receptor blockers; ARNI = angiotensin receptor-neprilysin inhibitor; BNP = B-type natriuretic peptide; BUN = blood, urea, nitrogen; CRT = cardiac resynchronization therapy; EF = ejection fraction; GDMT = guideline-directed medical therapy; HF = heart failure; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; SGLT2 = sodium-glucose cotransporter-2.

The MedStar Health Cardiology Clinical Practice Council recommends that all individuals with new onset HFrEF be referred for a Cardiology Consult. The decision to refer an individual to a heart failure specialist when the clinical scenario outlined in 2 above should be a join decision between the PCP and the cardiologist.

TABLE 15: Reviews the common comorbidities and potential actions

Comorbidity	Association With Heart Failure Outcomes	Clinical Trial Evidence for Modulating Comorbidity	Suggested Action
Cardiovascular			
Coronary artery disease	Strong	Strong	■ Evaluate and revascularize in appropriate patients
Atrial fibrillation/ flutter	Strong	Intermediate	■ Treat according to the current AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation (158,159)
Mitral regurgitation	Strong	Intermediate	■ Refer to a structural heart disease expert ■ Treat according to the current AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (160,161) and ACC ECDP on the Management of MR (162) ■ Consider transcatheter intervention in carefully selected patients with symptomatic HF and secondary MR (163)
Aortic stenosis	Strong	Strong	■ Refer to a structural heart disease expert ■ Treat according to current AHA/ACC Guidelines for the Management of Patients with Valvular Heart Disease (160,161)
Hypertension	Uncertain	Strong for prevention	■ Treat according to current ACC/AHA Guidelines for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (164)
Dyslipidemia	Uncertain	Strong for prevention	■ Treat according to current AHA/ACC Guidelines on the Management of Blood Cholesterol (165) and the ACC ECDP on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of ASCVD Risk (166)
Peripheral vascular disease	Moderate	None	■ Treat according to current AHA/ACC Guidelines on the Management of Patients With Lower Extremity Peripheral Artery Disease (167)
Cerebrovascular disease	Moderate	Weak	■ Treat according to current ASA/AHA Guidelines for the Early Management of Patients with Acute Ischemic Stroke (168)
Noncardiovascular			
Obesity	Moderate (inverse association)	Weak	■ Further data needed
Chronic lung disease	Strong	Weak	■ Smoking cessation ■ Optimize therapy ■ Consider pulmonary consultation
Diabetes	Strong	Strong	■ Optimize therapy ■ Administer SGLT2 inhibitor ■ Consider consult with endocrinologist ■ Treat according to the ACC ECDP on Novel Therapies for CV Risk Reduction in Patients with T2D (31) and ADA Standards of Medical Care in Diabetes (169)
Chronic kidney disease	Strong	Strong	■ Optimize RAAS inhibitor therapy ■ Use hydralazine/ISDN if an ARNI/ACEI/ARB cannot be used ■ Administer SGLT2 inhibitor ■ Consider nephrology consult
Anemia	Moderate	Weak	■ Evaluate secondary causes ■ Consider transfusion in severe cases
Iron deficiency	Strong	Intermediate	■ Consider intravenous iron replacement for symptom improvement
Thyroid disorder (hypo or hyper)	Strong	Weak	■ Evaluate and initiate treatment ■ Consider referral to endocrinologist
Sleep disordered breathing	Strong	Intermediate; note that in patients with symptomatic HFrEF and central sleep apnea, adaptive servo-ventilation is harmful (170)	■ Refer for sleep study ■ Treat severe obstructive sleep apnea ■ Consider referral to sleep medicine specialist
Hyperkalemia	Uncertain; may limit initiation and titration of GDMT	Weak	■ Recommend dietary modifications ■ Consider treating with patiromer (note: data regarding clinical outcomes are pending [NCT03888066]) or sodium zirconium cyclosilicate

Patient Education and Resources

Patient Self Care Education (Outpatient Setting)
Source: https://www.acc.org/tools-and-practice-support/clinical-toolkits/heart-failure-practice-solutions/patient-self-care-education-outpatient-setting

https://www.cardiosmart.org/topics/heart-failure

https://www.cardiosmart.org/

Providing Self-Care Education

Patients at high risk for developing heart failure should be counseled to:

- **implement those behaviors that facilitate self-care, e.g.,**
  - monitor symptoms and weight fluctuations
  - take medications as prescribed
  - stay physically active
  - seek social support
  - change to a healthier lifestyle with an improved diet and exercise
- **avoid behaviors that may increase the risk of heart failure, e.g.,**
  - smoking
  - excessive alcohol consumption and illicit drug use
  - use of non-steroidal anti-inflammatory drugs
  - noncompliance with medical regimen
  - high salt and/or processed food binges

Sodium Restriction

Sodium restriction is a reasonable recommendation to improve symptoms in patients with symptomatic HF. Exact restriction levels are unclear, with recommendations differing across organizations. Overall, however, patients should be counseled to reduce sodium in their diets, especially from processed foods.

References:

1) Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJV,Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WHW, Tsai EJ, Wilkoff BL. **2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines.** J Am Coll Cardiol 2013;62:e147–239.
2) Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, Drazner MH, Filippatos GS, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masoudi FA, McBride PE, Peterson PN, Stevenson LW, Westlake C.**2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America.** J Am Coll Cardiol.2017;70:776–803.
3) Maddox TM, Januzzi JL Jr., Allen LA, Breathett K, Butler J, Davis LL, Fonarow GC, Ibrahim NE, Lindenfeld J, Masoudi FA, Motiwala SR, Oliveros E, Patterson JH, Walsh MN, Wasserman A, Yancy CW, Youmans QR**. 2021update to the 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee**. J Am Coll Cardiol 2021;77:772–810
4) Shore, Supriya. **2021 Expert Decision Pathway for HFrEF Treatment Optimization- key points**. https://www.acc.org/Latest-in-Cardiology/ten-points-to remember/2021/01/2021/21/56/2021-Update-Expert-Consensus-for-HFrEF (accessed 2/14/21)