Heart Failure

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Disclosures

None

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 83, NO. 15, 2024

PUBLISHED BY ELSEVIER

EXPERT CONSENSUS DECISION PATHWAY

2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction

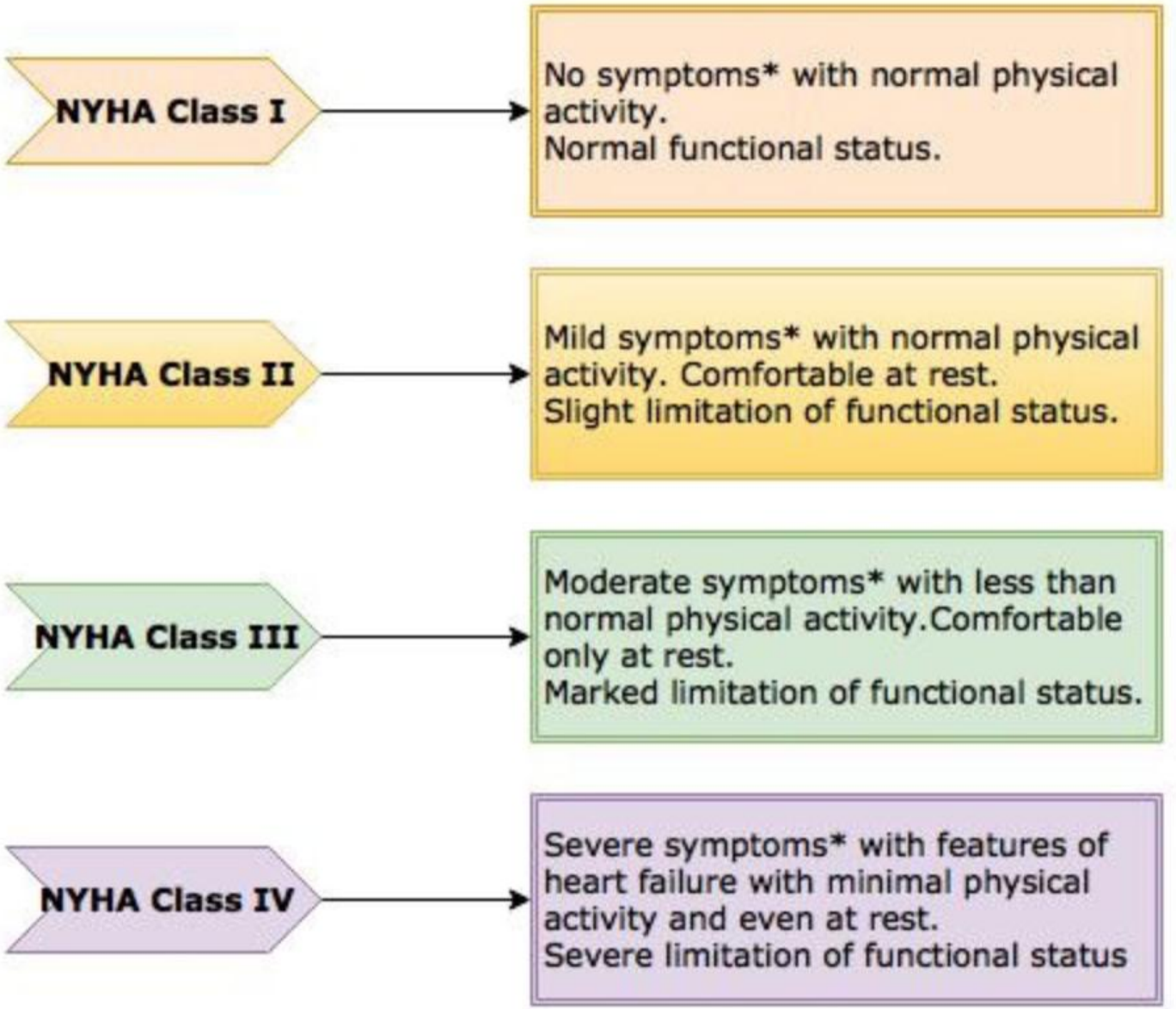
A Report of the American College of Cardiology Solution Set Oversight Committee

Maddox et al., 2024 JACC

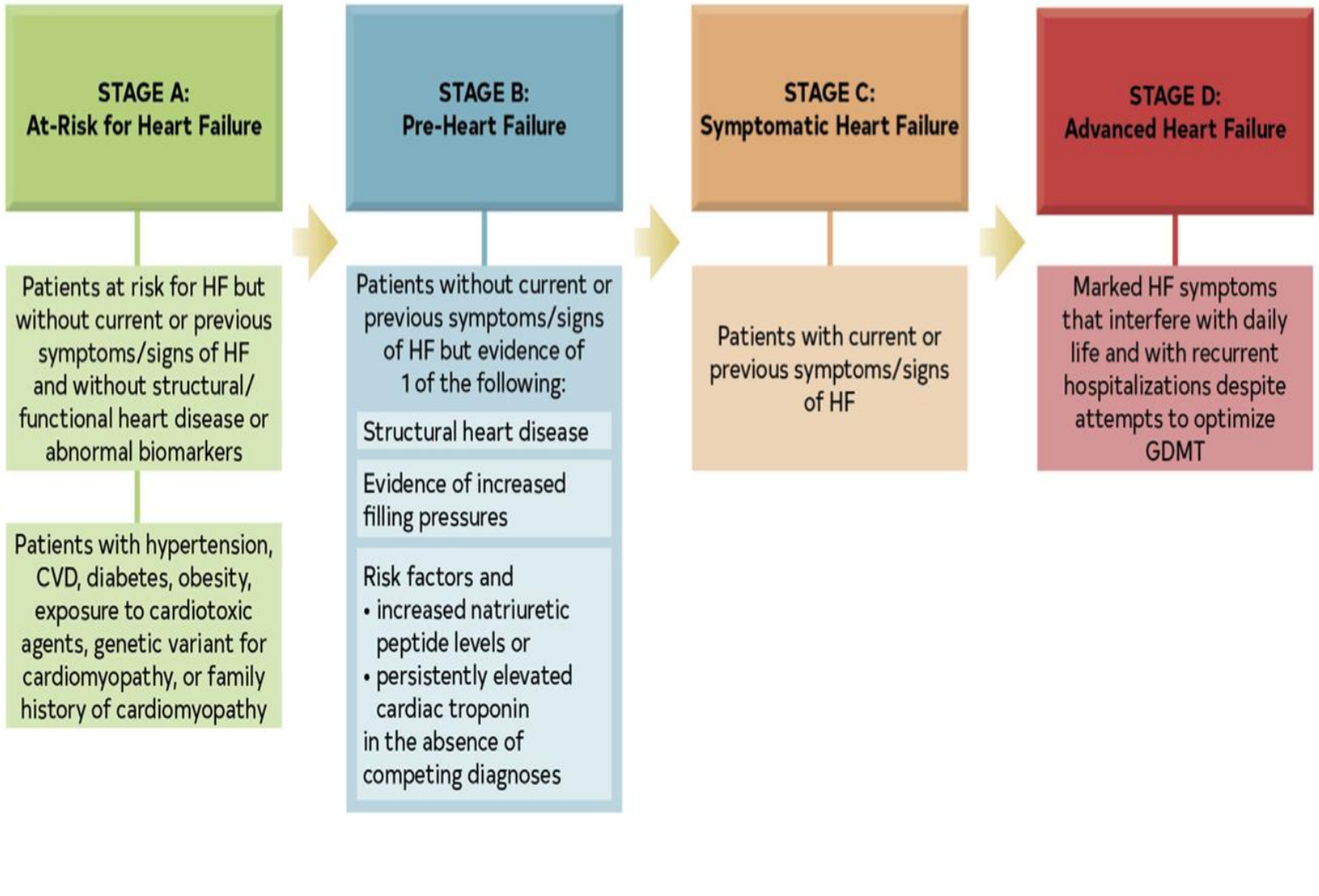
Outline - Ten How-tos in Heart Failure

1. How to initiate, add, or switch therapies with consideration of newer evidence-based guideline- directed treatments for HFrEF.
2. How to achieve optimal therapy given multiple drugs for HF, including augmented clinical assessment that may trigger modifications in guideline-directed therapy.
3. How to know when to refer to an HF specialist.
4. How to enhance care coordination.
5. How to improve medication adherence.
6. How to tailor treatment in specific patient cohorts: African-American patients, older adults, and patients with frailty.
7. How to manage patients' costs and increase access to HF medications.
8. How to manage common comorbidities.
9. How to manage the increasing complexity of HF.
10. How to integrate palliative care and the transition to hospice care.

NYHA Functional Classification of Heart Failure



AHA/ACC/HFSA Stages of Heart Failure



Heidenreich et al., 2022 JACC

Class of Recommendation

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) **(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	
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	

Heidenreich et al., 2022 JACC

1. How To Initiate, Add, or Switch To Evidence-Based Guideline-Directed Therapy

Four Pillars of GDMT

Angiotensin II receptor/neprilysin inhibitors (ARNIs)

Angiotensin-converting enzyme (ACE) inhibitors

Angiotensin receptor blockers (ARBs)

Evidence-based beta-blockers

Sodium-glucose cotransporter (SGLT) inhibitors

Mineralocorticoid antagonists

Maddox et al., 2024 JACC

ACE-I, ARB, ARNI

- ARNIs are the preferred renin-angiotensin system inhibitor and should be used as first-line therapy whenever possible
- For patients in whom ARNI administration is not possible, an ACE inhibitor/ARB is recommended
- If previously on an ACE-I, ensure 36 hours off prior to initiation of an ARNI
- Doses can be increased every week to allow time for adjustment to the vasodilatory effects
- Monitor BP, electrolytes, and renal function after initiation & during titration

	Starting Dose	Target Dose
ARNI		
Sacubitril/valsartan	24/26 mg to 49/51 mg twice daily	97/103 mg twice daily
ACE inhibitors		
Captopril	6.25 mg 3× daily	50 mg 3× daily
Enalapril	2.5 mg twice daily	10-20 mg twice daily
Lisinopril	2.5-5 mg daily	20-40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARBs		
Candesartan	4-8 mg daily	32 mg daily
Losartan	25-50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily

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Beta Blockers

- Consider increasing dose of beta-blocker every 2 weeks until maximum tolerated or target dose achieved
- Monitor heart rate, blood pressure and for signs of congestion after initiation and during titration

	Starting Dose	Target Dose
Beta-blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5-25 mg daily	200 mg daily

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Sodium-glucose cotransporter (SGLT) Inhibitors

- Ensure eGFR ≥ 25 mL/min/1.73 m^2 for Dapagliflozin & Sotagliflozin before initiation and eGFR ≥ 20 mL/min/1.73 m^2 for Empagliflozin
- These agents are used in a fixed dose; titration is not required
- Loop diuretic dose may need to be adjusted based on close monitoring of weight and symptoms

SGLT inhibitors	Starting Dose	Target Dose
Dapagliflozin	10 mg daily	10 mg daily
Empagliflozin	10 mg daily	10 mg daily
Sotagliflozin	200 mg daily	400 mg daily

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Mineralocorticoid Antagonists

- Consider increasing dose at least every 2 weeks until maximum tolerated or target dose achieved
- Monitor electrolytes and kidney function at 1-2 weeks following initiation and then 7 days after initiation/titration. Then check monthly for 3 months and every 3 months for 1 year
- Contraindicated in patients with eGFR <30 mL/min/1.73 m2, or Cr >2.5 mg/dL in men or Cr >2 mg/dL in women or with potassium >5.0

	Starting Dose	Target Dose
Mineralocorticoid antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5-25 mg daily	25-50 mg daily

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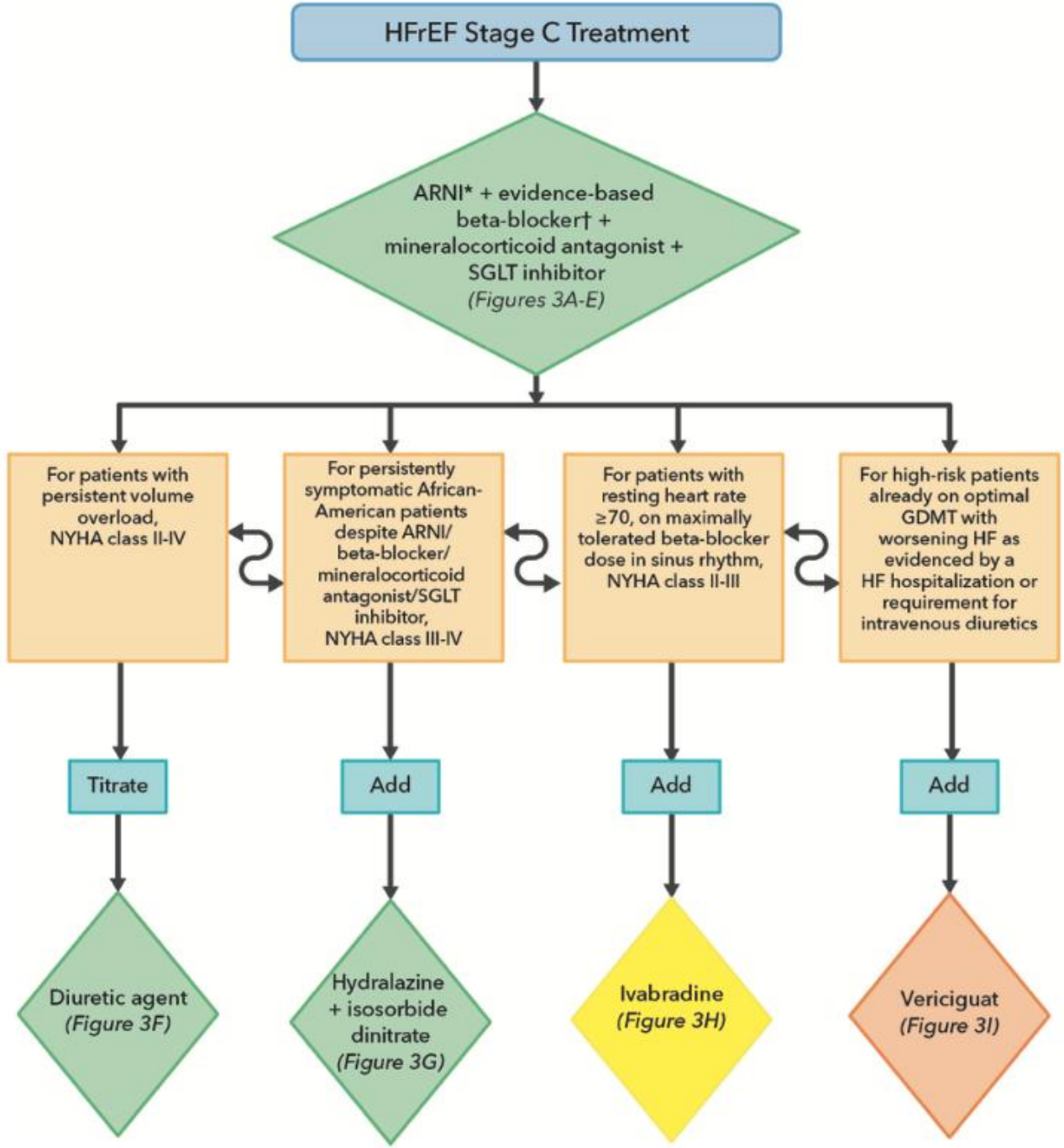
2. How To Achieve Optimal Therapy



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Diuretics

Initial dose depends on multiple factors including kidney function and prior exposure to diuretic therapy

Titrate dose to achieve relief of congestion over days to weeks

Monitor blood pressure, electrolytes, and kidney function after initiation and during titration

If reaching high doses of loop diuretic agents consider changing to a different loop diuretic agent or adding a thiazide diuretic to be taken together with loop diuretic

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Hydralazine + Isosorbide Dinitrate

Vasodilators	Starting Dose	Target Dose
Hydralazine	25 mg 3× daily	75 mg 3× daily
Isosorbide dinitrate†	20 mg 3× daily	40 mg 3× daily
Fixed-dose combination isosorbide dinitrate/hydralazine‡	20 mg/37.5 mg (one tab) 3× daily	2 tabs 3× daily

- Recommended in African-American patients who remain symptomatic with NYHA III to IV symptoms while on maximally tolerated GDMT
- Consider increasing dose of hydralazine and or isosorbide/dinitrate every 2 weeks until max tolerated or target dose achieved
- Titration should proceed with careful blood pressure monitoring and close monitoring of other side effects (headache, dizziness)

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Ivabradine

Ivabradine	Starting Dose	Target Dose
Ivabradine	2.5-5 mg twice daily	Titrate to heart rate 50-60 beats/min. Maximum dose 7.5 mg twice daily

- Recommended in patients with resting heart rate in sinus rhythm >70 bpm on maximally tolerated beta blocker
- Re-assess heart rate in at least 2-4 weeks:
  - If HR <50 bpm, reduce by half or discontinue if already at 2.5 mg BID
  - If HR 50-60 bpm, maintain current dose
  - If HR >60 bpm, increase by 2.5 mg BID until max dose of 7.5 mg BID
- Because of a higher risk of ischemic complications, Ivabradine should not be used in patients with a history of activity-limiting angina

Maddox et al., 2024 JACC

Vericiguat

Oral soluble guanylyl cyclase stimulator	Starting Dose	Target Dose
Vericiguat	2.5 mg daily	10 mg daily

- May be considered in select high-risk patients with HFrEF and recent worsening HF to reduce HF hospitalization and CV death
- Double the dose every 2 weeks until target dose of 10 mg daily as tolerated
- Monitor blood pressure and CBC for anemia

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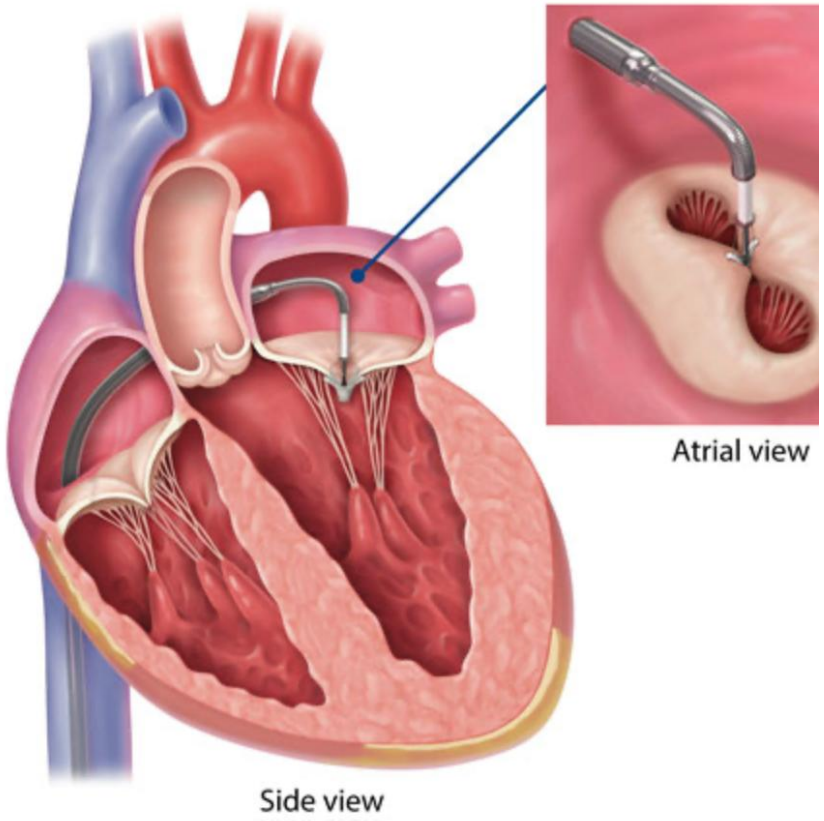
Transcatheter Mitral Valve Repair

- Surgical treatment should be considered as first-line therapy in cases of severe primary (structural) chronic MR resulting in HFrEF

- For severe secondary (functional) MR, the rise of transcatheter edge-to-edge repair of the mitral valve has demonstrated benefit

- It is essential that GDMT is optimized before referral for the procedure to ensure the greatest likelihood that patients will receive the combined benefits both therapies



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Barriers to Medication Titration

- Abnormal kidney function and/or hyperkalemia
- Older age and multiple comorbidities
- Socioeconomic barriers to care
- Limited ability to attend frequent office visits for GDMT optimization

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When To Consider an Echocardiogram

- During the initial evaluation of the patient with signs/symptoms of HF to assess LVEF, diastolic function, chamber size, ventricular wall thickness, valvular abnormalities, and hemodynamic parameters
- Reassessment of ventricular function should occur 3 to 6 months after target (or maximally tolerated) doses of GDMT are achieved
- Can be considered during changes in clinical status
- Routine surveillance echocardiograms in the absence of change in clinical status or some other signal of risk are not recommended

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Can GDMT Be Discontinued If LVEF Recovers?

- The TRED-HF (Withdrawal of Pharmacological Treatment for Heart Failure in Patients With Recovered Dilated Cardiomyopathy) found that nearly 50% of subjects withdrawn from GDMT had a relapse of their cardiomyopathy within 6 months

- Ongoing titration of GDMT to target doses is always advised even for those with evidence of recovering or recovered LVEF

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Biomarkers

- Current clinical practice guidelines give a Class I recommendation to measure BNP or NT-proBNP to support a clinical diagnosis of HF, assess disease severity, and/or establish prognosis

- In the GUIDE-IT (Guiding Evidence Based Therapy Using Biomarker Intensified Treatment in HF) trial, among patients with HFrEF, lowering NT- proBNP to <1,000 was associated with significant reverse remodeling and improved outcomes

- Patients whose natriuretic peptide concentrations do not fall with use of GDMT have a worse prognosis, more congestion, and more deleterious LV remodeling

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Invasive Hemodynamics

- Invasive hemodynamic and filling pressure assessment via pulmonary artery catheterization may occasionally be useful to support decision-making

- Implantable sensors that monitor filling pressures in ambulatory patients with NYHA Functional class III HF, such as the CardioMEMS device, may help guide clinical decision making in well-selected patients

- Another approach to monitor heart failure is through monitoring intrathoracic impedance via cardiac implantable electronic devices

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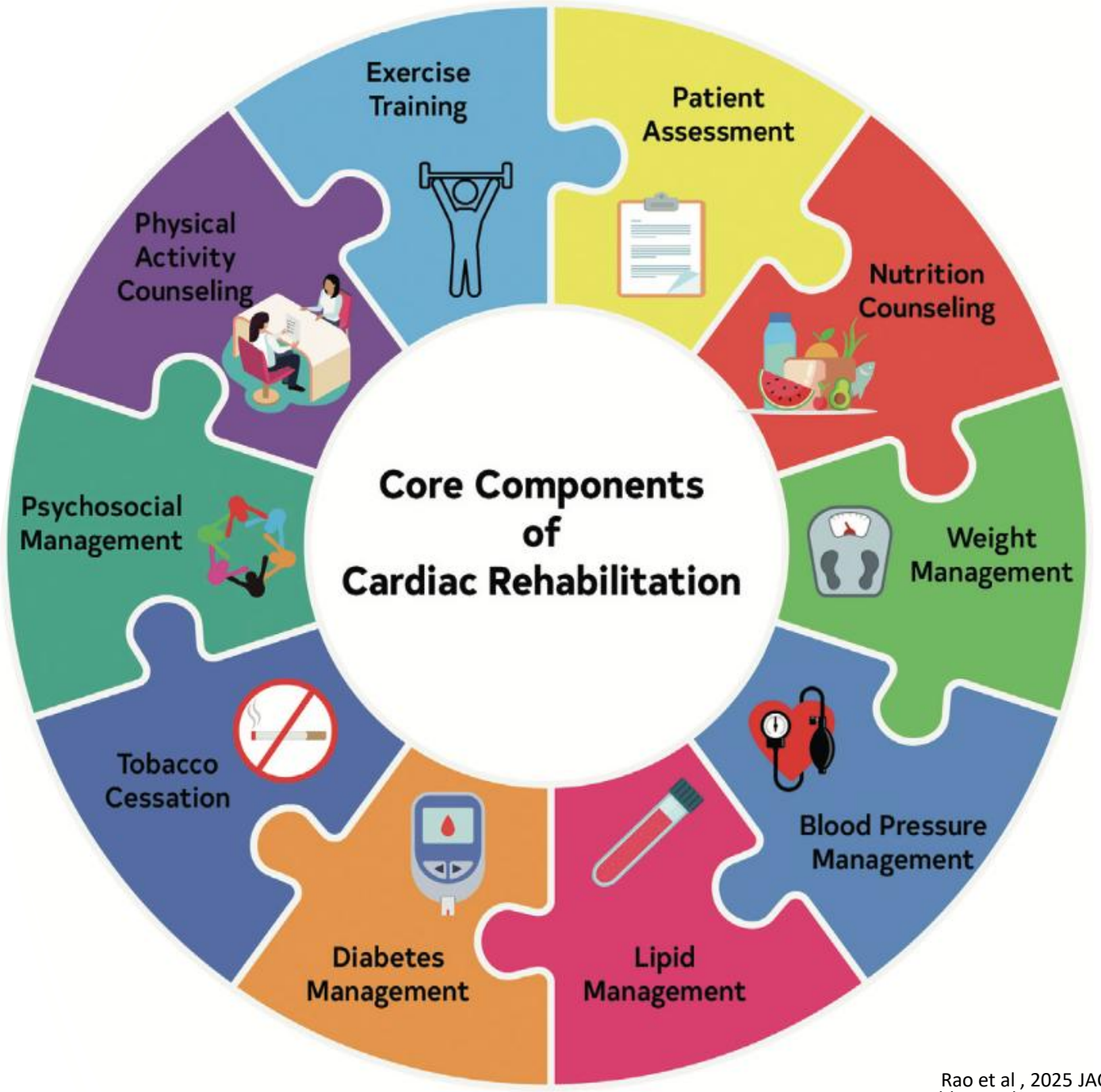
Cardiac Rehabilitation

- Cardiac rehabilitation is helpful to support drug titration, monitor symptoms, improve health status, and increase exercise tolerance, but remains underused in terms of both prescription and access



Rao et al , 2025 JACC
Maddox et al., 2024 JACC

3. When To Refer To A HF Specialist

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 1 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 • 2 or more emergency department visits or hospitalizations for worsening HF in the prior 12 months • Inability to tolerate optimally dosed beta-blockers and/or ARNI/ACE inhibitors/ARBs and/or mineralocorticoid antagonists • Clinical deterioration, as indicated by worsening edema, worsening symptoms, rising biomarkers (BNP, NT-proBNP, others), worsened exercise testing, decompensated hemodynamic status, or evidence of progressive remodeling on imaging • High mortality risk using a validated risk model, such as the Seattle Heart Failure Model, for further assessment and consideration of advanced therapies
	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 (eg, 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

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I NEED HELP

I: Intravenous inotropes

N: NYHA IIIB/IV or persistently elevated natriuretic peptides

E: End-organ dysfunction

E: Ejection fraction ≤35%

D: Defibrillator shocks

H: Hospitalizations >1

E: Edema despite escalating diuretic agents

L: Low blood pressure, high heart rate

P: Prognostic medication – progressive intolerance or down-titration of GDMT

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4. How To Enhance Care Coordination

Team Based Care

- Team-based HF care is recommended in the most recent HF guidelines
- In a team approach, an interprofessional, multi disciplinary group of clinicians consider novel therapies collectively

TABLE 7 Essential Skills for an HF Team

- HF diagnosis and monitoring for progression
- Treatment prescription, titration, and monitoring
- Patient and caregiver education on disease and treatments
- Lifestyle prescription (eg, diet, exercise), education, and monitoring
- Access to genetic testing and counseling programs
- Psychological and social support assessment, treatment, and monitoring
- Palliative and end-of-life counseling and care
- Coordination of care for concomitant comorbidities
- Nutritional counselling

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5. How To Improve Adherence

Nonadherence

- Patient adherence is fundamental to the therapeutic effectiveness of GDMT
- It is the responsibility of the clinician to assess reasons for reduced adherence and attempt to meet the needs of the patient

Reasons for Nonadherence (World Health Organization)	
Patient	■ Perceived lack of effect ■ Poor health literacy ■ Disabilities without affording appropriate accommodations ■ Mental health disorders (depression, anxiety) ■ Social isolation ■ Cognitive impairment (eg, dementia)
Medical condition	■ High HF regimen complexity ■ Impact of comorbidities (eg, depression) ■ Polypharmacy due to multiple comorbidities
Therapy	■ Frequency of dosing (eg, hydralazine, nitrates) ■ Polypharmacy ■ Side effects
Socioeconomic	■ Difficult access to pharmacy ■ Lack of social support ■ Homelessness
Health system	■ Poor communication ■ Silos of care ■ No automatic refills ■ Difficulty navigating patient assistance programs ■ Unaffordable cost of care, including medication costs

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Ten Considerations to Improve Adherence

1. Capitalize on opportunities when patients are most predisposed to adherence
2. Consider the patient's perspective
3. Simplify medication regimens whenever possible
4. Consider costs and access
5. Communicate with other clinicians involved in care
6. Educate using practical, patient-friendly information
7. Recommend tools that support adherence in real time
8. Consider behavioral supports
9. Anticipate problems
10. Monitor adherence and target patients at risk

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6. How To Tailor Treatment In Specific Patient Cohorts

Efficacy of New HF Medications in African-American Patients

Limited Representation in Trials:

ARNIs, SGLT inhibitors, ivabradine, and vericiguat have been tested in clinical trials with few African-American participants

Efficacy Findings:

No significant race-based differences observed in the effectiveness of these medications

Recommendation:

These newer medications should be included in the treatment of African-American patients with HFrEF, based on their proven benefits in the general population

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Treatment of Heart Failure in Older Patients

Limited Data in the Elderly:

Clinical trials for HF treatments typically exclude patients older than 75 years, and there's limited data for those over 80

Efficacy of GDMT:

Four main classes of GDMT therapies generally show consistent efficacy in older adults based on subgroup analyses

Dosing Considerations:

Target doses of GDMT should be attempted in older patients with close monitoring for adverse reactions

Lower doses may be necessary due to age-related pharmacokinetic changes

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7. How To Manage Patients' Costs and Access To HF Medications

Economic Burden of Heart Failure

Rising Costs:

- Direct medical costs for HF are projected to increase from $21 billion in 2012 to $53 billion in 2030

Medication Costs:

- CV medications account for 15.6% of direct costs for HF patients

Financial Barriers:

- High medication costs and multiple comorbidities create significant financial challenges for patients with HF, impacting adherence to treatment

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Cost Reduction Measures

Strategies to Reduce Patients' Cost of Care
■ Coordinate care (including labs and imaging) among clinicians to minimize unnecessary duplication
■ Consider limitations of medication coverage (insurance, Medicaid, etc.) when prescribing
■ Use generic equivalents for GDMT whenever possible
■ Work with a pharmacist, social worker, or patient navigator to identify and navigate Patient Assistance Programs
■ Request price matching if a drug is found at a lower cost at another pharmacy
■ Determine eligibility for health system participation in 340B Drug Pricing Program to reduce medication-related costs for targeted vulnerable patient populations

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8. How To Manage Common Comorbidities

Key Comorbidities and Management Approaches

Diabetes:

- Strongly linked to HF risk and outcomes
- SGLT inhibitors improve glycemic control and reduce HF events
- In patients with CKD, SGLT inhibitors also decrease the risk of kidney disease progression

Anemia/Iron Deficiency:

- Anemia independently increases mortality
- EPO has been shown to offer no benefit with increased risk of thromboembolic events
- Iron deficiency in HF (ferritin <100 or 100 to 300 with transferrin saturation <20%) improves with IV iron supplementation, showing benefits in exercise capacity and reduced hospitalizations
- Oral iron not effective due to poor absorption

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9. How To Manage The Increasing Complexity of HF Management

Assessing Social Determinants of Health (SDOH) in Heart Failure

Importance of SDOH:

Increasing recognition of SDOH as key drivers of health outcomes in HFrEF

Key SDOH Factors:

Education access and quality, economic stability, access to healthcare, neighborhood and built environment, and social support

AHA/ACC/HFSA 2022 Guidelines:

Class 1 recommendation to target SDOH to reduce health disparities in HFrEF

Maddox et al., 2024 JACC

Methods for Addressing SDOH in Clinical Practice

Data Capture:

Regularly document SDOH during patient encounters (e.g., income, education, insurance status)

Reassess & Update:

SDOH can change over time; confirm and update factors at each visit

Resource Allocation:

Develop resources (e.g., cost-mitigation, nutritional support, educational tools) for patients based on identified needs

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10. How To Integrate Palliative Care and Transition To Hospice Care

Palliative & Hospice Care in Heart Failure

Advances in care have delayed disease progression in HF, but have not provided a cure

Palliative care needs for patients, caregivers, and healthcare systems remain significant

Non-specialist clinicians play a key role in coordinating end-of-life plans aligned with patient and family goals

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Palliative & Hospice Care

- Strive to reduce suffering through pain and symptom relief, integrating psychological and spiritual care
    - Focus on quality of life throughout the disease process, especially as it progresses
    - Effective management of HF therapies (particularly diuretics) remains crucial, even at end-of-life stages

- Support patients in making informed treatment decisions, weighing benefits and burdens
    - Regular (annual) discussions about clinical status, prognosis, values, and care directives

- Calibrate expectations based on clinical trajectory and unpredictability
    - Milestone events such as recurrent hospitalizations & progressive medication intolerance due to hypotension and/or renal dysfunction should trigger heightened preparation with patients and families

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Principles of Heart Failure Management

- Start and titrate GDMT early, focusing on high-benefit therapies, and titrate during each encounter
- Address clinical, social, and financial barriers to medication adherence
- Diligently manage volume status to reduce symptoms
- Primary prevention ICDs and CRT should be considered after consistent use of optimal doses of all GDMTs for at least 3 to 6 m.o.
- Transcatheter mitral valve repair may be considered in symptomatic patients with chronic, moderate-severe to severe MR despite optimal doses of all GDMT
- Use multidisciplinary teams to manage complex patient needs and optimize care

Maddox et al., 2024 JACC

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Questions?