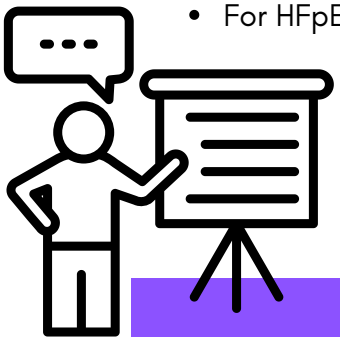
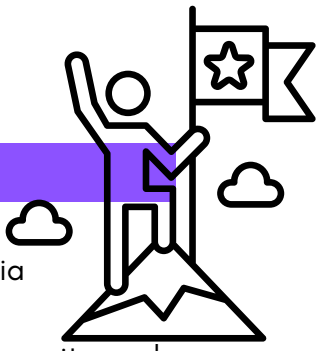
HFPEF FAQ

DEFINITION

- Previous definition of heart failure with preserved ejection fraction (HFpEF): no consensus definition across various society guidelines and clinical trials. Often considered a diagnosis of exclusion.
- Differential Clinical Profiles, Exercise Responses, and Outcomes Associated With Existing HFpEF Definitions | Circulation
- Current: Current or prior signs and symptoms with structural or functional cardiac causes corroborated by elevated natriuretic peptide levels and/or evidence of cardiogenic pulmonary or systemic congestion
- For HFpEF classified by EF: HF with EF > 50%





GOALS OF THERAPY

- Prevention of disease progression, hospitalization, and symptom management via decongestion
- Exercise/cardiac rehab for all patients to improve functional status, exercise capacity, and quality of life
- Optimization of medication therapy:
  - SGLT2 inhibitors for all those without contraindications
  - MRAs for select patients with EF 50-60%
  - ARNI or ARB for select patients with EF 50-60%
  - Loop diuretics for symptom management alone
- Evidence emerging for incretin therapies, but not yet considered Guideline-Directed Medical Therapy (GDMT) due to lack of complete evidence
- Management of all concomitant comorbidities
  - How to Manage Heart Failure With Preserved Ejection Fraction: Practical Guidance for Clinicians | JACC: Heart Failure

GUIDANCE

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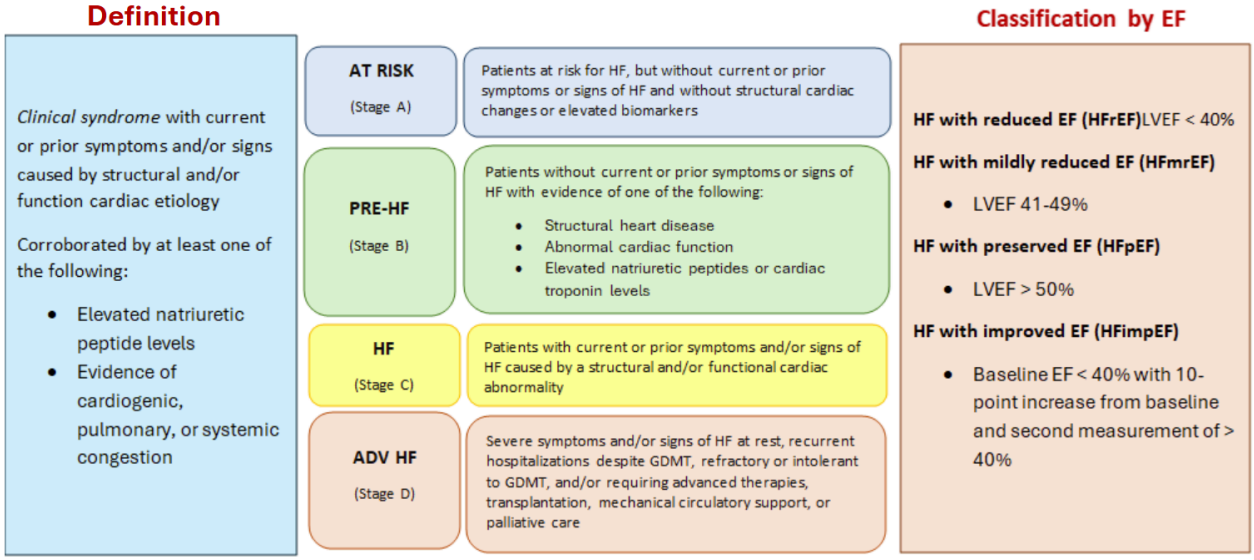
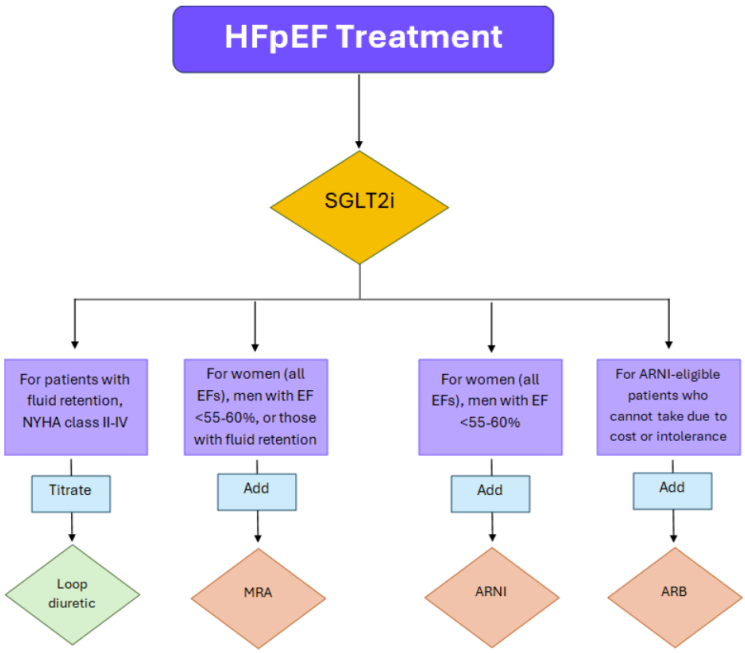


- 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction
- 2022 AHA/ACC/HFSA Guideline for the for Management of Heart Failure



AGENTS

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Drug Class	Clinical Trial	Most Benefit	Contraindications / Cautions	Dosing
SGLT2i Class 2a	EMPEROR- Preserved Empagliflozin Hospitalization for HF, HR: 0.71 (0.60-0.83)	All patients	Contraindications: breastfeeding Type 1 diabetes mellitus Hemodialysis Cautions: eGFR <20 mL/min (empagliflozin) eGFR <25 mL/min (dapagliflozin) Pregnant SBP ≤100 mm Hg (excluded from trials, however low impact on BP) History or at risk for ketoacidosis Acute kidney injury Necrotizing fasciitis of the perineum (Fournier's gangrene) Increased risk of mycotic genital	10 mg daily (no need to titrate)
	DELIVER Dapagliflozin Hospitalization for HF, HR: 0.77 (0.67-0.89)			10 mg daily (no need to titrate)
ARB/ARNi Class 2b Use of ARBs might be considered to decrease the number of hospitalizations for patients with HFpEF.	CHARM-Preserved Trial Candesartan Hospitalization for HF, HR: 0.84 (0.70-1.00)	ARNi ineligible due to cost or intolerance	Contraindications: History of angioedema Pregnancy or breastfeeding Renal artery Stenosis sacubitril-valsartan: Hepatic impairment (Child-Pugh C), History of angioedema Cautions: Hyperkalemia Hypotension Acute kidney injury History of angioedema	Start 4-8 mg daily, target dose 32 mg daily
	PARAGON-HF sacubitril-valsartan Hospitalization for HF, Rate ratio: 0.85 (0.72-1.00)	Women (all EFs) Men LVEF <55-60%		Wash out of >36h of ACEi use Start 24-26 mg BID, target dose 97-103 mg BID
MRA Class 2b - In appropriately selected patients with HFpEF (with an ejection fraction of 45% or greater, elevated BNP levels or an HF admission within 1 year, eGFR >30 mL/min, creatinine <2.5 mg/dL, potassium <5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease the number of hospitalizations.	TOPCAT Clincal Trial Spironolactone Hospitalization for HF, HR: 0.83 (0.69-0.99)	Women (all EFs) Men LVEF <55-60% Fluid retention	Contraindications: Severe renal impairment (eGFR <30 ml/min or SCr ≥ 2.5 mg/dL) Hyperkalemia (Potassium ≥5.0 mmol/L) Addison's disease Cautions: Other medications that can cause increase risk for hyperkalemia or AKI (ACEi, ARB, ARNis, NSAIDs, trimethoprim) Breastfeeding	Start 25 mg daily, target 50 mg daily Initiate at half dose if eGFR 30 to 50 mL/min
	FINEARTS-HF finerenone			

HFPEF SYMPTOM RELIEF

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We currently have two major drug classes to assist with symptom relief. The goal of symptom relief is to reduce fluid and weight for patients to regain activities of daily living.

DIURETICS/FLUID OVERLOAD

Loop Diuretics - first line
SGLT2i - (2a)
Mineralocorticoid Receptor Antagonists (MRAs) (2b)
Thiazides/Thiazide Like Diuretics

GLP-1/GIP AGONISTS

Semaglutide - labeled indication in HF
Tirzepatide - labeled indication in obesity

CURRENT GUIDANCE

Diuretics and Fluid Overload/Congestion

- Class I Recommendation: Loop diuretics are the preferred diuretics for patients with these symptoms. Torsemide and bumetanide are preferred over furosemide due to higher bioavailability
- Use the lowest effective dose to avoid excessive pre-load reduction. Monitor for renal function, blood pressure, weight and electrolytes
- Emperor-Preserved: showed significant benefit in symptomatic patients

GLPs and Obesity

- ADA 2026: Recommendation 9.9b for the glycemic treatment plan for people with type 2 diabetes and symptomatic heart failure with preserved ejection fraction (HFpEF), include a GLP-1 RA with demonstrated benefits in heart failure-related symptoms and/or reduction in heart failure events.

- 2025 AAC Scientific Statement on Management of Obesity in Adults with HF: in people with BMI >30kg/m2 and HF with EF >45% (semaglutide) and EF >50% (tirzepatide), weight loss is associated with improvements in symptoms and functional capacity. (STEP-HFpEF and SUMMIT)

- STEP-HFpEF: semaglutide improved functional capacity, reduced symptoms, and promoted significant weight loss, regardless of diabetes status.
- SUMMIT: tirzepatide significant decrease in CV death/worsening HF

COMORBIDITIES MANAGEMENT

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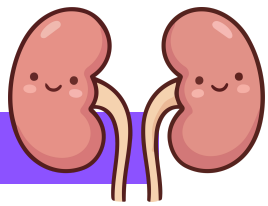
DIABETES

- Target HbA1c <7–7.5% for patients with fewer comorbidities or milder HF, and <8–8.5% for patients with advanced HF, higher comorbidity burden, or older age (2023 ACC Guidelines).
- First-line options in HFpEF with T2DM:
  - SGLT2 inhibitors (empagliflozin, dapagliflozin).
- For patients with obesity and high CV risk, dual GIP/GLP-1 receptor agonists are an additional option.
- Avoid TZDs, saxagliptin, and alogliptin, as these may worsen HF (2023 ACC Guidelines).

OBESITY

- Obesity is a major risk factor for HFpEF. Calorie restriction and aerobic exercise improve functional status and quality of life.
- The STEP-HFpEF trial demonstrated that semaglutide 2.4 mg significantly improved symptoms, physical limitations, exercise capacity, and weight compared with placebo.



CHRONIC KIDNEY DISEASE (CKD)

CKD is defined as ⩾3 months of renal dysfunction with eGFR <60 mL/min/1.73 m^2, albumin-to-creatinine ratio ⩾30 mg/g, or other markers of kidney damage (2023 ACC Guidelines). Management should follow KDIGO guidelines in collaboration with nephrology. CKD contributes to adverse cardiac remodeling and more severe HF symptoms.

Therapies that reduce CKD progression and cardiovascular events in HFpEF with CKD include:

- SGLT2 inhibitors (dapagliflozin, empagliflozin) for eGFR ⩾20 mL/min/1.73 m^2, regardless of diabetes status.
- ACE inhibitors or ARBs for eGFR ⩾30 mL/min/1.73 m^2.
- Finerenone for eGFR ⩾25 mL/min/1.73 m^2 in diabetic kidney disease (2023 ACC Guidelines).

SLEEP APNEA

Obstructive sleep apnea (OSA) is the most common sleep-disordered breathing pattern in HFpEF (2023 ACC Guidelines). Small studies have shown symptom improvement, and treating OSA in resistant hypertension may reduce BP. Patients with AF should be evaluated for OSA, as treatment may reduce AF recurrence.

COMORBIDITIES MANAGEMENT

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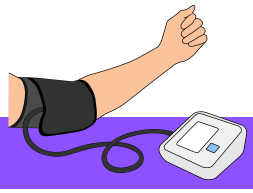
HYPERTENSION

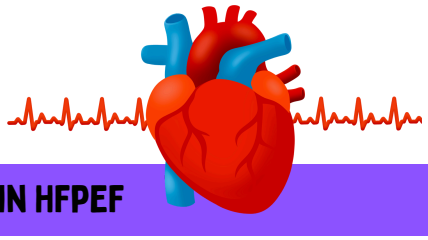
- Aim for a systolic blood pressure <130 mm Hg, unless limited by orthostasis or worsening renal function (2023 ACC Guidelines).
- The 2025 AHA/ACC Hypertension Guidelines recommend RAAS-inhibiting therapies as preferred agents: MRAs, ARNIs, or ARBs when ARNI is not feasible.
- Beta-blockers are not recommended for blood pressure control in HFpEF due to negative chronotropic effects and should be reserved for patients with other indications (e.g., arrhythmias).



ATRIAL FIBRILLATION (AF)

AF is common in HFpEF and associated with more advanced disease and higher mortality. Management should be individualized:

- Rate vs. rhythm control should be guided by symptoms; avoid aggressive rate control due to impaired left atrial function and reduced stroke volume (2023 ACC Guidelines).
- Options include beta-blockers, nondihydropyridine calcium channel blockers, and digoxin (if needed).
- Provide anticoagulation when indicated.



PHYSICAL ACTIVITY IN HFPEF

Regular physical activity has a Class I, Level A recommendation to improve functional status, exercise performance, and quality of life in HFpEF (2022 AHA/ACC HF Management). Physical inactivity and obesity are strongly associated with poorer outcomes (2023 ACC Guidelines). Exercise improves multiple physiologic mechanisms underlying HFpEF.
Follow the 2019 ACC/AHA Primary Prevention Guidelines:

- ⩾150 minutes/week moderate-intensity aerobic activity, or
- ⩾75 minutes/week vigorous-intensity activity.

Even lower amounts of moderate or vigorous activity are beneficial for ASCVD risk reduction.

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