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2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction (HFpEF)

HFpEF Diagnosis

Summary by EUNBEE CHO MD

Diagnosing HFpEF requires a comprehensive analysis of signs, symptoms, lab, echocardiogram, exclusion of mimics, and the likelihood based on the scoring system (Figure 1).

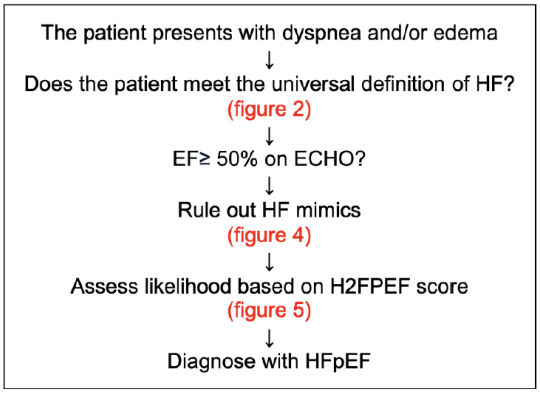

Figure 1. Simplified Algorithm for Diagnosis of HFpEF

Universal definition

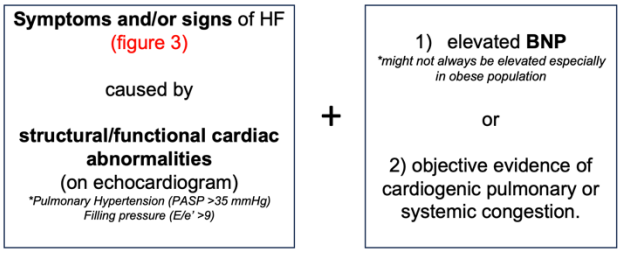

Figure 2. The Universal Definition of HF

Figure 3. Framingham HF Diagnostic Criteria
Positive when [1 major + 2 minor] or [2 major] met.

Major Criteria	Minor Criteria
Acute pulmonary edema	Ankle edema
Cardiomegaly	Dyspnea on exertion
Hepatojugular reflex	hepatomegaly
Neck vein distension	Nocturnal cough
Paroxysmal nocturnal dyspnea or orthopnea	Pleural effusion
Rales	Tachycardia (>120bpm)
Third heart sound gallop	

Figure 4. HF Mimics

Noncardiac	Cardiac
Kidney (renal failure, nephrosis)	Infiltrative cardiomyopathy
Liver (portal hypertension, cirrhosis)	Hypertrophic cardiomyopathy
Chronic venous insufficiency	Pericardial disease
Pregnancy	Valvular heart disease
Medications (CCB, NSAIDS, steroids)	High-output heart failure
Malnutrition	

Figure 5. H2FPEF score system
Likely if the sum ≥ 6

	Clinical Variable	Values	Points
H2	Heavy	BMI > 30 kg/m^2	2
	Hypertensive	2 or more antihypertensives	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
p	Pulmonary Hypertension	Doppler echocardiographic estimated Pulmonary Artery Systolic Pressure > 35mmHg	1
E	Elder	Age > 60	1
F	Filling Pressure	Doppler echocardiographic E/e' > 9	1
	H2PEF score		Sum (0-9)

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Nonpharmacological therapies

Summary by JIAN GARCIA-CRUZ MD

Nonpharmacological therapies are attractive strategies to improve HFpEF patients' quality of life and clinical outcomes.
Some non-pharmacological treatment that we could recommend as physician are:

I. **Aerobic exercise of >150 minutes/week or >30 minutes/day.** To improve cardiac function and the capacity of the circulatory and respiratory systems to supply oxygen to skeletal muscle.
II. Comprehensive lifestyle intervention consisting of a structured program to encourage *weight loss*, with **self-monitoring** of food intake, and weight.
III. **Cardiac rehabilitation programs** should be implemented before discharge. It has been shown that these programs *improve quality of life and functional capacity of the individual.* Although there is benefit, lack of insurance coverage makes it difficult to arrange.
IV. **Pulmonary Artery Pressure Monitoring devices / sensors,** to analyze changes in pulmonary artery pressure measurements. Class 2B recommendation. Conflicting evidence between CHAMPION-HF and GUIDED-HF trials has emerged. The former showing reductions in hospitalization versus latter trial that was blinded did not reveal any difference in outcomes.
V. **Treat comorbidities** especially *atrial fibrillation, hypertension, coronary artery disease, obstructive sleep apnea, diabetes, chronic kidney disease and obesity*. In general, there is no evidence for HFpEF specific management of these conditions.

Multidisciplinary considerations:
Several specialists play essential roles in managing HFpEF.
<u>Some referrals that need to be considered as primary care physicians:</u>

a. **Cardiologist**: Are the ones that primarily focus on the heart function, diagnosis, and treatment of HFpEF, including medication management and potential interventions. Patient with multiple challenging comorbidities, high risk features as RV dysfunction and HF hospitalization, cardiorenal syndrome, vascular disease, HCM, amyloidosis, pericardial disease, increased needs of diuretics or NYHA Class III and IV needs to be refered to cardiovascular specialist.
b. **Heart failure specialist:** Patient with HFpEF should have a cardiovascular specialist if lack of convertional HFpEF risk factors, exercise intolerance, non-responsive to diuretics or medical treatment, extremely high brain natriuretic peptides, recurrence hospitalization (2 or more in a year), worsening kidney or liver function, systolic BP <100, management of cardiomyopathy or individuals with high risk of disease progression.
c. **Palliative Care**: Consider referral as soon as patient is diagnosed with HF. Palliative care uses a patient- and family-centered focus to optimize health-related quality of life by anticipating, preventing, and treating suffering.
d. **Pulmonologist**: Manages respiratory aspects, addressing any pulmonary conditions that may contribute to HFpEF symptoms and optimizing oxygenation. If patient has Obstructive sleep apnea or features of this condition pulmonologist referral needs to be done.
e. **Nephrologist**: Monitors and manages renal function, addressing any kidney-related issues that can impact HFpEF progression and treatment. If renal function worsens even on diuretics and decreases urine output, the patient needs to be seen by nephrologist.
f. **Geriatrician**: Especially important in the elderly population, a geriatrician considers age-related factors, polypharmacy, and overall well-being in HFpEF management.
g. **Nutritionist/Dietitian**: Consider if you need help optimizing dietary choices to manage conditions like hypertension, diabetes, or obesity, which can contribute to HFpEF.
h. **Physical Therapist**: Develops exercise programs tailored to the patient's capabilities, promoting physical activity within the limits of their condition. Consider in patient with great mobility.
i. **Hospice**: Typically considered when patient has a limited life expectancy. Offer support for patients and families, including emotional and spiritual care.

Collaboration among these specialists ensures a well-rounded and effective approach to HFpEF, considering its multifaceted nature.

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Pharmacological Therapy

Summary by DIANA OTHÓN-MARTÍNEZ MD

Clinical Trials in HFpEF – decreased HF hospitalization and CV death.

Significant findings in DELIVER and EMPEROR-PRESERVED, *non-clinical significant in the rest*.

DELIVER / EMPEROR-PRESERVED / TOPCAT / PARAGON-HF / CHARM-PRESERVED

Results included >23k patients; average age 70.6; 46.6% female; total follow-up 2.2 – 3.3 years; mean LVEF 55%; 39.8% of patients with T2DM.

- Diuretic use (all, except EMPEROR-PRESERVED. Ranging from 75-95%)
- ACE inhibitor / ARB (Ranging from 75-95%, except CHARM-PRESERVED)
- ARNI (only 5% deliver, 2% emperor preserved)
- Beta-blocker (Ranging from 56-86%)

MRA (Ranging from 12-43%, except TOPCAT).

GDMT Contraindications

GDMT for HFpEF is *contraindicated or to be used with caution* in **pregnancy, during lactation**, and if **hypersensitivities** present.

GDMT	SGLT2 (Dapagliflozin / Empagliflozin)
Contraindications	• T1DM • Hemodialysis
Precautions	• CKD – (D – eGFR < 25; E – eGFR <30) • Poorly controled DM (Ketoacidosis) • Increased risk for mycotic and genital infections • Necrotizing fasciitis of perineum (Fournier's Gangrene) • Hypovolemia
Clinical trials	**DELIVER** (dapa) and **EMPEROR** (empa), included patients with HF >40% LVEF → significant decrease in HF hospitalization and all CV death. Also improved health status and QoL demonstrated in **PRESEVED HF** (dapa). Benefit is additive if concomitant use with MRA & ARNI Promising data from other clinical trials, that also included patients w/ HFrEF: **SOLOIST – WHF** (sotagliflozin – SGLT1 & SGLT2 inhibitor) → decreased HF hospitalization and CV death. (pending FDA approval) **EMPULSE** (empa) → significant improvement in 2ndary outcomes in patients with acute HF exacerbation. <decreased CV death, HF events, and improved health status). Should be started in all HFpEF patients if no contraindications! OK to use when **inpatient** for acute decompensation of HF, but once clinically STABLE!

GDMT	MRA (Spironolactone)
Contraindications	• Hyperkalemia (>5) • Addisson's disease
Precautions	• CKD – (eGFR <30 or Cr. >2.5– avoid use); eGFR 30 – 50 use ½ dose) • Concomitant hyperkalemic drugs (ACE/ARB/ARNI/NSAID/TMP) • If gynecomastia → use EPLERENONE!
Clinical trials	**TOPCAT** (spironolactone 15-45mg vs pbo) → significant reduction in HF hospitalization. More evident in North American patients with BNP <166, pro-BNP <682; LVEF <60%; women. Improves diastolic function in HFpEF. Benefit by balancing diuresis, control of hypertension, and decreased HF hospitalization.

GDMT	ARNI (Sacubitril/valsartan)
Contraindications	• Severe hepatic impairment (Child Pugh C) • Angioedema • ACE administration 36h • Aliskiren (direct renin inhibitor)
Precautions	• Moderate hepatic impairment (Child Pugh B) • Renal artery stenosis • Hypotension
Clinical trials	**PARAGON-HF** (sacubitril/valsartan vs valsartan alone) in patients with LVEF 45-57% → decreased HF hospitalization & CV death & risk reduction while in therapy with ARNI, during in hospitalization (non-significant). Goal of inhibiting neprilysin is to decrease disease progression!

GDMT	ARB (Candesartan)
Contraindications	• Renal artery stenosis • Concomitant ACE, ARNI, or Aliskiren
Precautions	• Angioedema • Hyperkalemia • Hypotension • AKI
Clinical trials	**CHARM** (Candesartan) in patients with LVEF 40% → decreased HF hospitalization and CV death. (borderline significant). **I-PRESERVE** (Irbersartan vs pbo) in patients with LVEF 45% → no benefit demonstrated, likely secondary to 34% drug discontinuation rate and 40% utilized ACE concomitantly. OK to use when ARNI is contra-indicated (ex. angioedema, not affordable)

Pharmacological Therapy Flowchart

Summary by EDGAR G. DORSEY-TREVIÑO MD MMSc

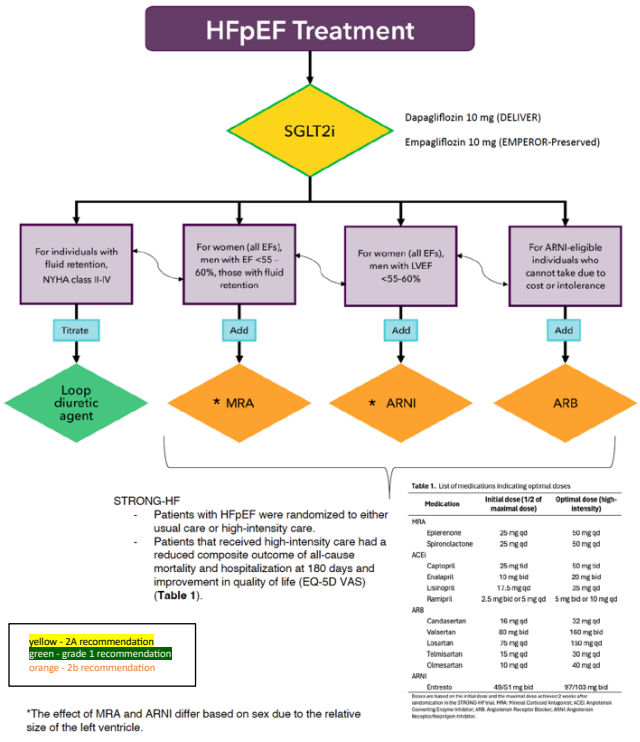

Table 1. List of medications indicating optimal doses

Medication	Initial dose (1/2 of maximal dose)	Optimal dose (high-intensity)
MRA		
Eplerenone	25 mg qd	50 mg qd
Spironolactone	25 mg qd	50 mg qd
ACEi		
Captopril	25 mg tid	50 mg tid
Enalapril	10 mg bid	20 mg bid
Lisinopril	17.5 mg qd	35 mg qd
Ramipril	2.5 mg bid or 5 mg qd	5 mg bid or 10 mg qd
ARB		
Candesartan	16 mg qd	32 mg qd
Valsartan	80 mg bid	160 mg bid
Losartan	75 mg qd	150 mg qd
Telmisartan	15 mg qd	30 mg qd
Olmesartan	10 mg qd	40 mg qd
ARNI		
Entresto	49/51 mg bid	97/103 mg bid

Doses are based on the initial dose and the maximal dose achieved 2 weeks after randomization in the STRONG-HF trial. MRA, Mineral Corticoid Antagonist; ACEi, Angiotensin Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blocker; ARNI Angiotensin Receptor/Neprilysin Inhibitor.

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