

2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

ד"ר בן שדה- רופא בכיר, היחידה לאי ספיקת לב ויתר לחץ דם ריאתי המרכז הרפואי תל אביב (איכילוב)

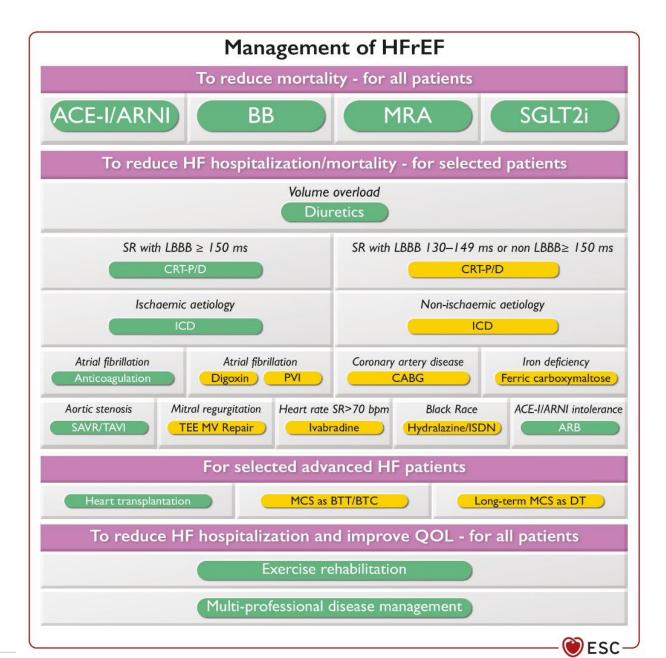
Definition of heart failure with reduced ejection fraction, mildly reduced **ESC** ejection fraction and preserved ejection fraction



Тур	e of HF	HFrEF	HFmrEF	HFpEF
	1	Symptoms ± Signs ^a	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	2	LVEF ≤40%	LVEF 41-49%b	LVEF ≥50%
CRITERIA	3	-	_	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides ^c

- Considering changing HFmrEF and HFpEF to HfrEF and HFnEF
- No consensus (71% vs 75% needed)

Chronic heart failure



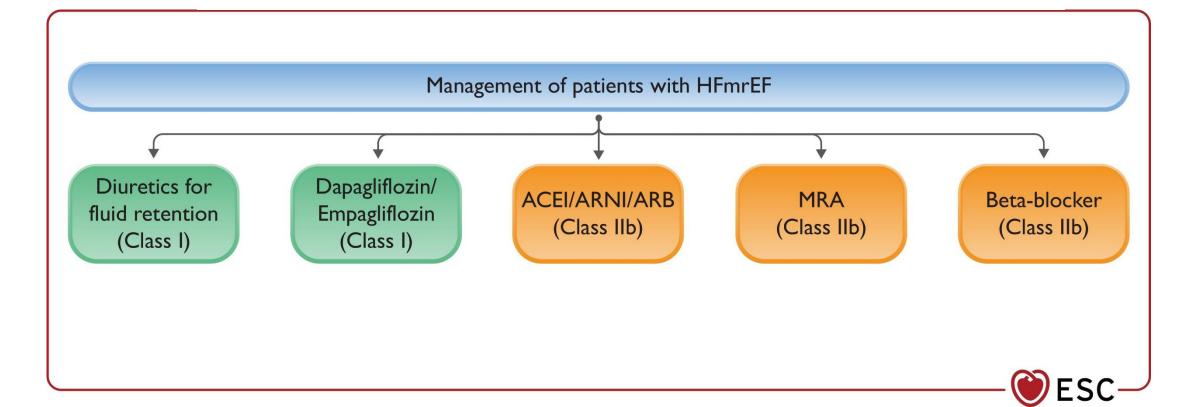
HFpEF and HFmrEF

SGLT2i for everyone with heart failure - Regardless of LVEF



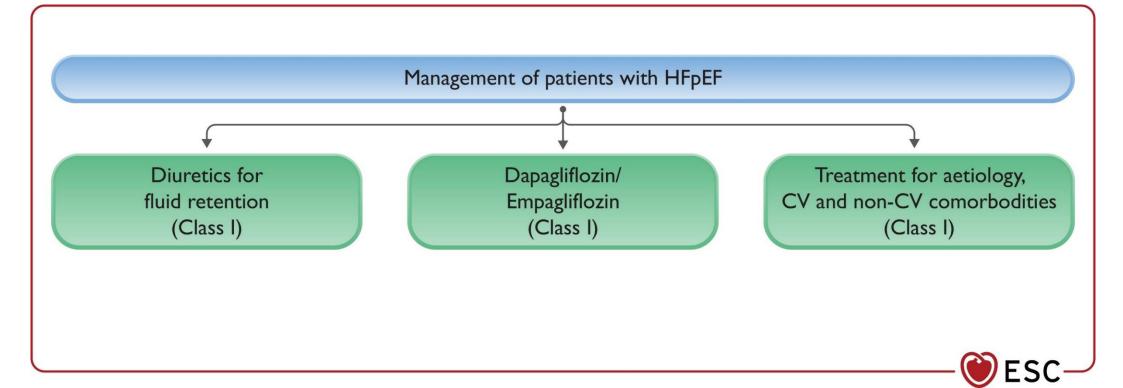
HFmrEF

Recommendation	Class ^a	Level ^b	
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is			2023
recommended in patients with HFmrEF to reduce	1	Α	ESC 2
the risk of HF hospitalization or CV death. ^c 6,8			<u>О</u>

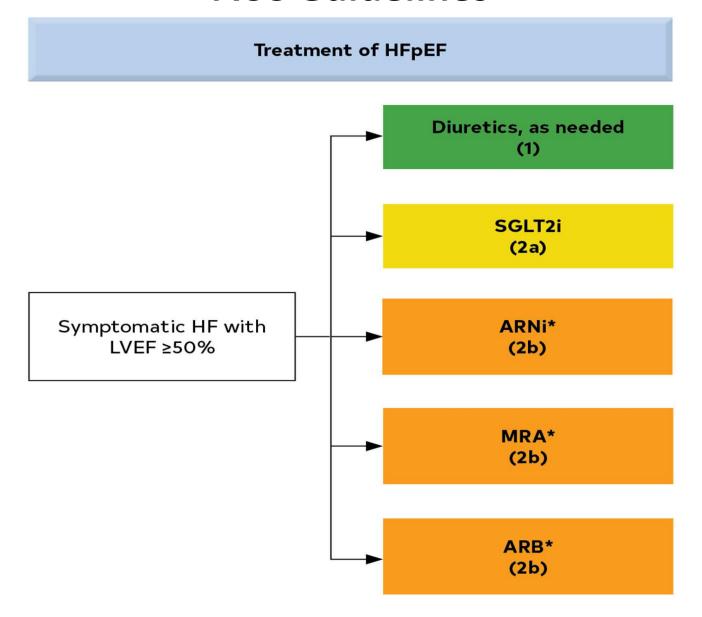


HFpEF

Recommendation	Class ^a	Level ^b	
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recommended in patients with HFpEF to reduce the	1	Α	SC
risk of HF hospitalization or CV death. ^c 6,8			() ()



ACC Guidelines



VOL. 81, NO. 18, 2023

EXPERT CONSENSUS DECISION PATHWAY

2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction



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

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THE PRESENT AND FUTURE

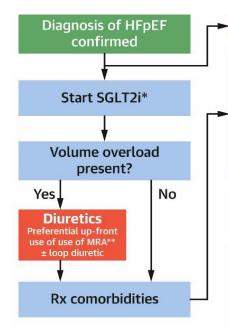
JACC SCIENTIFIC STATEMENT

Heart Failure With Preserved Ejection Fraction

JACC Scientific Statement

Barry A. Borlaug, MD, a Kavita Sharma, MD, Sanjiv J. Shah, MD, Jennifer E. Ho, MD





*SGLT2i should be considered in all patients except those with type 1 diabetes, orthostatic hypotension, eGFR <20-25 mL/min/1.73 m², or very frequent yeast infections (or history of severe genitourinary infections, including Fournier's gangrene). Yeast infections on therapy are readily treatable (eg, fluconazole 150 mg PO x 1, unless contraindicated). Instruct patients to hold SGLT2i therapy for a few days during active yeast infection and on "sick days" (GI illness, dehydrated, active infections that predispose to dehydration). High HgbAIc levels are not a contraindication to SGLT2i. Slight elevation in serum creatinine (and slight reduction in eGFR) is normal and expected on SGLT2i therapy.

**MRA should be considered in all patients except those with K+ >5.0 or eGFR <30 mL/min/1.73 m². Replace potassium supplementation with MRA whenever possible. Use eplerenone in patients with gynecomastia due to spironolactone. Eplerenone is ½ as potent as spironolactone. Recheck K+ and renal function 1 week and 1 month after initiation, and q3-6 months thereafter.

***ARNI most effective if EF <55%-60% or frequent HF hospitalizations (congested phenotype): avoid

***ARNI most effective if EF <55%-60% or frequent HF hospitalizations (congested phenotype); avoid in patients with history of angioedema, low BP, orthostatic hypotension, restrictive cardiomyopathy, pulmonary arterial hypertension, constrictive pericarditis, cardiac amyloidosis.

[†]AF patients often have low stroke volume and inability to augment stroke volume during exertion due to LA dysfunction. Avoid excessive rate control in these patients.

[‡]Caloric restriction, aerobic training, and resistance training protocols per Brubaker PH, et al. *Circ Heart Fail* 2022.

Rule out alternate etiologies ("masqueraders") of HFpEF (see Table 2)

- Hypertension: Diuresis first (SGLT2i*/MRA**), ARNI*** or ACE inhibitor, or ARB, other medications according to comorbidities. Goal BP <130/80 mm Hg.
- Iron deficiency: Treat with IV iron if anemic and transferrin saturation <20%.
- Diabetes: Preferential use of SGLT2i followed by GLP1 receptor agonist.
- CAD: Statins, aspirin, consider revascularization.
- AF: Anticoagulation, consider rhythm control, rate control to HR ~80 beats/min.[†]
- Obesity: Caloric restriction,[‡] weight loss drugs/surgery.
- CKD: ACE inhibitor/ARB and/or SGLT2i, especially if +microalbuminuria; avoid nephrotoxins.
- Lung disease and OSA: Treat per guidelines but also make sure euvolemic.

Still symptomatic + EF <55%-60% or multiple HF hospitalizations and SBP >110-120 mm Hg?

· Start ARNI and uptitrate to maximum dose as tolerated.

Ask 6 questions in all patients:

- 1. Is the patient on an SGLT2i? If not, why not?
- 2. Is the patient on an MRA? If not, why not?
- 3. Is the patient on an ARNI? If not, why not?
- 4. Is the patient on potassium supplementation? If yes, replace with MRA if possible.
- 5. Is the patient on **nitrates** or a **PDE5 inhibitor** (or other pulmonary vasodilator)? If possible, discontinue these drugs to see if symptoms improve
- 6. Is the patient on a **beta-blocker?** Unless using for AF, angina, or history of MI, try discontinuing to see if symptoms improve. For HTN, vasodilating beta-blocker (eg, carvedilol) preferred.

Implement in all patients:

- **HF** education: record daily weights, BP, HR; establish "dry weight" for volumeoverloaded patients to guide diuretic dosing (especially loop diuretics).
- Exercise training regimen: aerobic training + resistance training preferred[‡]; consider cardiac rehabilitation referral.

Persistent symptoms and/or HF hospitalizations?

- Refer to HF clinic (or HFpEF clinic, if available).
- Reevaluate for "masqueraders" (atypical etiologies, eg, cardiac amyloidosis).
- Evaluate for worsening comorbidities (eg, worsening renal function, CAD progression, poor control of diabetes).
- If persistent fluid overload: Start HCTZ, even if eGFR is low. Sequential nephron blockade can augment diuresis, and low-potency thiazide often sufficient.
- Implantable hemodynamic-guided management (especially if frequently hospitalized for HF or cardiorenal syndrome).
- Evaluate for chronotropic incompetence: If present, stop rate-controlling agents, such as beta-blockers, if possible.
- ENROLL IN AN HFPEF CLINICAL TRIAL

Borlaug BA, Sharma K, Shah SJ, Ho JE. Heart Failure With Preserved Ejection Fraction: JACC Scientific Statement. J Am Coll Cardiol. 2023 May.

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- 1. Is the patient on an **SGLT2i?** If not, why not?
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Acute Heart Failure

Recommendation	Classa	Level ^b	
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death. ^{c,d,e 16}	1	В	© ESC 2023

Acute Heart Failure





Safety, Tolerability and Efficacy of Rapid Optimization, Helped by NT-proBNP Testing, of **Heart Failure Therapies**

Mebazaa et al. Nov 7 2022, The Lancet



Question: Is rapid up-titration of guideline directed medical therapy (GDMT) before discharge from an acute heart failure admission effective and safe compared to usual care?

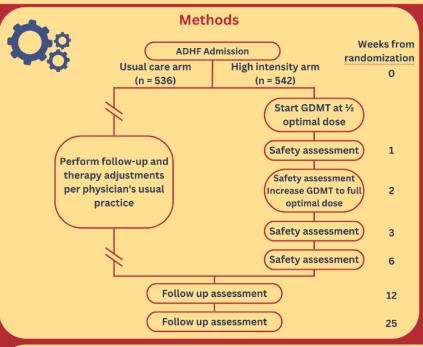
Selection Criteria

Inclusion

- Age 18 85
- HF admission w/in 72 hours
- · Hemodynamically stable
- Serum potassium ≤ 5.0 mEq/L
- NT-proBNP ≥ 2500 pg/mL
- · Not recently on optimal **GDMT**

Exclusion

- Intolerance to BB, ACEi, or ARB
- Need for invasive mechanical ventilation
- · Severe lung, liver, brain, or kidney disease
- Index hospitalization caused by correctable etiology (e.g. arrhythmia, COPD exacerbation, etc)









GDMT

GDMT in this study was defined as ACEi/ARB/ARNi, beta blocker, and mineralocorticoid receptor antagonist. SGLT2 inhibitors were not yet recommended as standard of care!



Conclusion: Rapid up-titration of guideline directed medical therapies with close follow up and monitoring during and soon after discharge from an acute heart failure hospital admission can be done safely and improves patient quality of life, readmission rates, or all-cause mortality

* Although strong HF was based only on triple therapy, current recommendation also include SGLT2i based on recent evidence (EMPULSE, DELIVER – 1/3 patients on SGLT2i within 1 month of admission)

Heart Failure: A Progressive Disease

STAGE A: At-Risk for Heart Failure

Patients at risk for HF but without current or previous symptoms/signs of HF and without structural/functional heart disease or abnormal biomarkers

Patients with hypertension, CVD, diabetes, obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or family history of cardiomyopathy STAGE B: Pre-Heart Failure

Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:

Structural heart disease

Evidence of increased filling pressures

Risk factors and

- increased natriuretic peptide levels or
- persistently elevated cardiac troponin in the absence of competing diagnoses

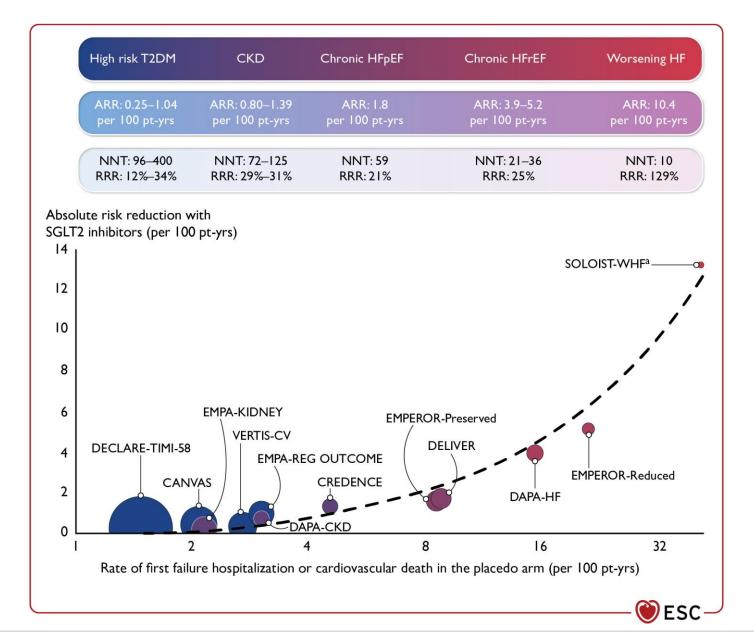
STAGE C: Symptomatic Heart Failure

Patients with current or previous symptoms/signs of HF STAGE D: Advanced Heart Failure

Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT

Figure 15

Absolute risk reduction with sodium-glucose cotransporter-2 inhibitors in relation to patient risk based on rate of heart failure-related endpoints in the placebo arm of the respective trials





Comorbidities Prevention of HF in patients with CKD and T2DM

Recommendations	Class ^a	Level ^b
In patients with T2DM and CKD, ^c SGLT2 inhibitors (dapagliflozin or empagliflozin) are recommended to reduce the risk of HF hospitalization or CV death. ^{5,7,35}	ı	A

Based on DAPA CKD, EMPA KIDENY AND large meta analysis including CREDENCE and SCORED trials

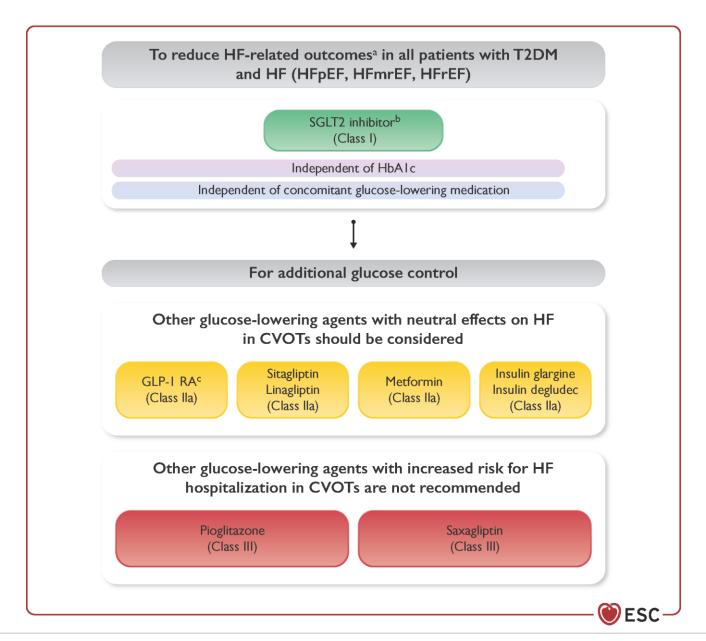
Comorbidities - Iron deficiency

Recommendations	Class ^a	Level ^b	
Intravenous iron supplementation is recommended in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to alleviate HF symptoms and improve quality of life. ^c 12,41,47–49	ı	A	
Intravenous iron supplementation with ferric carboxymaltose or ferric derisomaltose should be considered in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to reduce the risk of HF hospitalization. ^c 12,41,43–46	lla	A	© ESC 2023

- Based on the IRONMAN study (sensitivity analysis) and meta analysis
- Is it going to change? HEART-FID study

Figure 16

Glucose-lowering treatment of patients with heart failure and type 2 diabetes





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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C Petrie, for the STEP-HFpEF Trial Committees and Investigators*



תודה רבה!

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UNMET NEED Advanced heart failure Valvular disease Iron in HFPEF SGLT2i in HFPEF and NORMAL BNP Should we switch from Aldactone to Finerenone patients with DM and CKD – HF patients were

not included in the Finerenone studies

ACC Guidelines

TABLE 2 Selected Randomized Controlled Trials in Individuals With HFPEF					
	DELIVER ⁶	EMPEROR-PRESERVED ⁷	TOPCAT*16	PARAGON-HF ¹⁹	CHARM-PRESERVED ²⁴
Size	N = 6,263	N = 5,988	N = 3,445	N = 4,822	N = 3,023
Agent	Dapagliflozin	Empagliflozin	Spironolactone	Sacubitril/valsartan	Candesartan
Median age, y	72	72	69†	73	67
Female sex	44%	45%	52%	52%	40%
Median follow-up, y	2.3	2.2	3.3	2.9	3.1
EF entry criteria	>40%	>40%	≥45%	≥45%	>40%
Mean baseline LVEF	54%	54%	56%†	58%	54%
Proportion with T2DM	45%	49%	33%	43%	29%
HF medical therapy					
Diuretic agent	77%	NR	82%	95%	75%
ACE inhibitor or ARB	73%	81%	84%	86%	19%‡
ARNI	5%	2%	N/A	N/A	N/A
Beta-blocker	83%	86%	78%	80%	56%
MRA	43%	37%	N/A	26%	12%
Primary composite outcome, HR or rate ratio (95% CI)	Worsening HF and CV death: HR: 0.82 (0.73-0.92)	Hospitalization for HF and CV death: HR: 0.79 (0.69-0.90)	Hospitalization for HF, aborted cardiac arrest, CV death: HR: 0.89 (0.77-1.04)	Total hospitalizations for HF and CV death: Rate ratio: 0.87 (0.75-1.01)	Hospitalization for HF and CV death: HR: 0.86 (0.74-1.00)
Hospitalization for HF, HR or rate ratio (95% CI)	HR: 0.77 (0.67- 0.89)	HR: 0.71 (0.60-0.83)	HR: 0.83 (0.69-0.99)	Rate ratio: 0.85 (0.72-1.00)	HR: 0.84 (0.70-1.00)
Urgent visit for HF, HR (95% CI)	0.76 (0.55-1.07)	NR	NR	NR	NR
CV death, HR (95% CI)	0.88 (0.74-1.05)	0.91 (0.76-1.09)	0.90 (0.73-1.12)	0.95 (0.79-1.16)	0.95 (0.76-1.18)

ARTS-HF Study

Mortality/morbidity outcomes in patients with worsening chronic heart failure with reduced ejection fraction

