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Friday, April 25, 2025
CMDA's 30th Annual Conference
Honoring Our Why:
Colorado's Collective Purpose in PALTC Medicine
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Summary of the 2022 ACC/AHA Heart Failure Guidelines.

HFrEF

HFpEF

CMDA Journal Club
3/6/25
David Shepherd

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Developed in partnership with the Heart Failure Society of America

Definition of HF

Universal Definition of HF

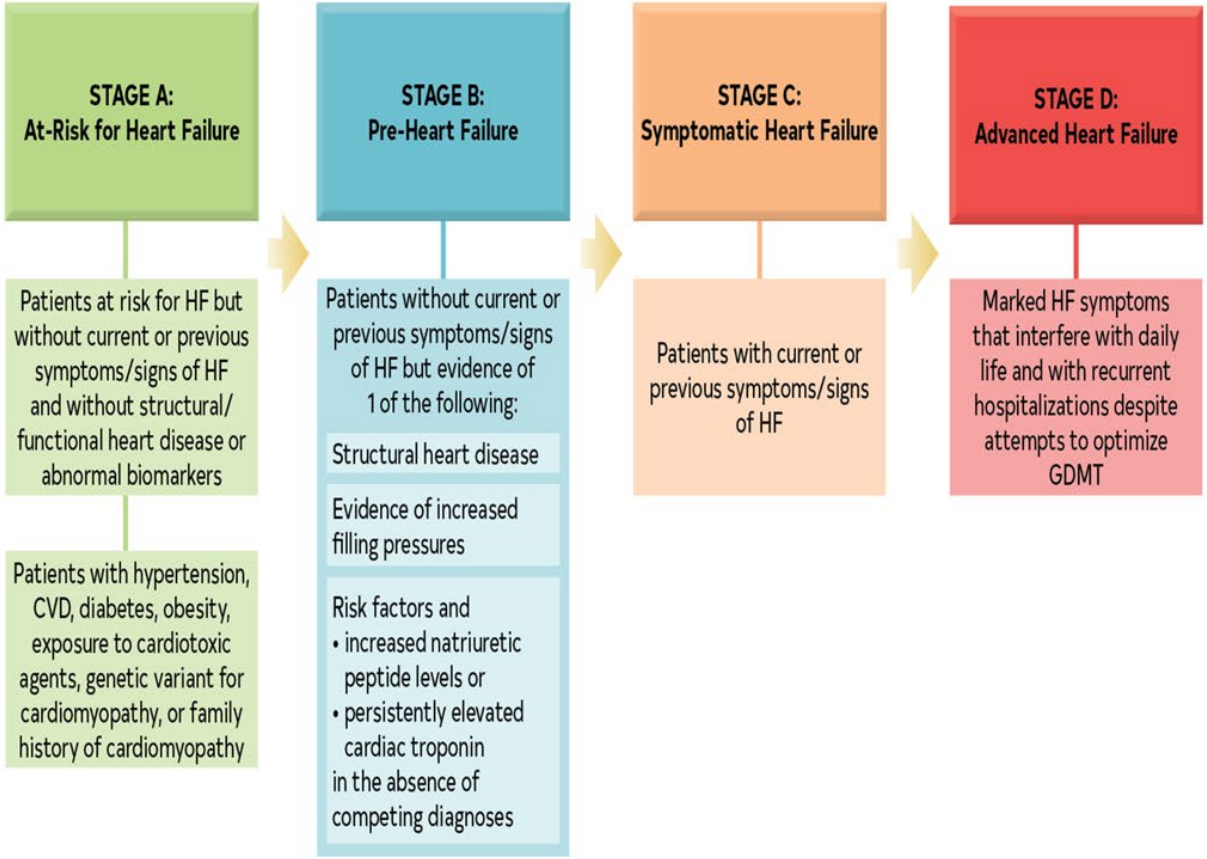
The Universal Definition of HF requires symptoms and/or signs of HF caused by structural/functional cardiac abnormalities *and* at least 1 of the following:

1) elevated natriuretic peptides;

2) objective evidence of cardiogenic pulmonary or systemic congestion.

Universal Definition and Classification of Heart Failure - Journal of Cardiac Failure

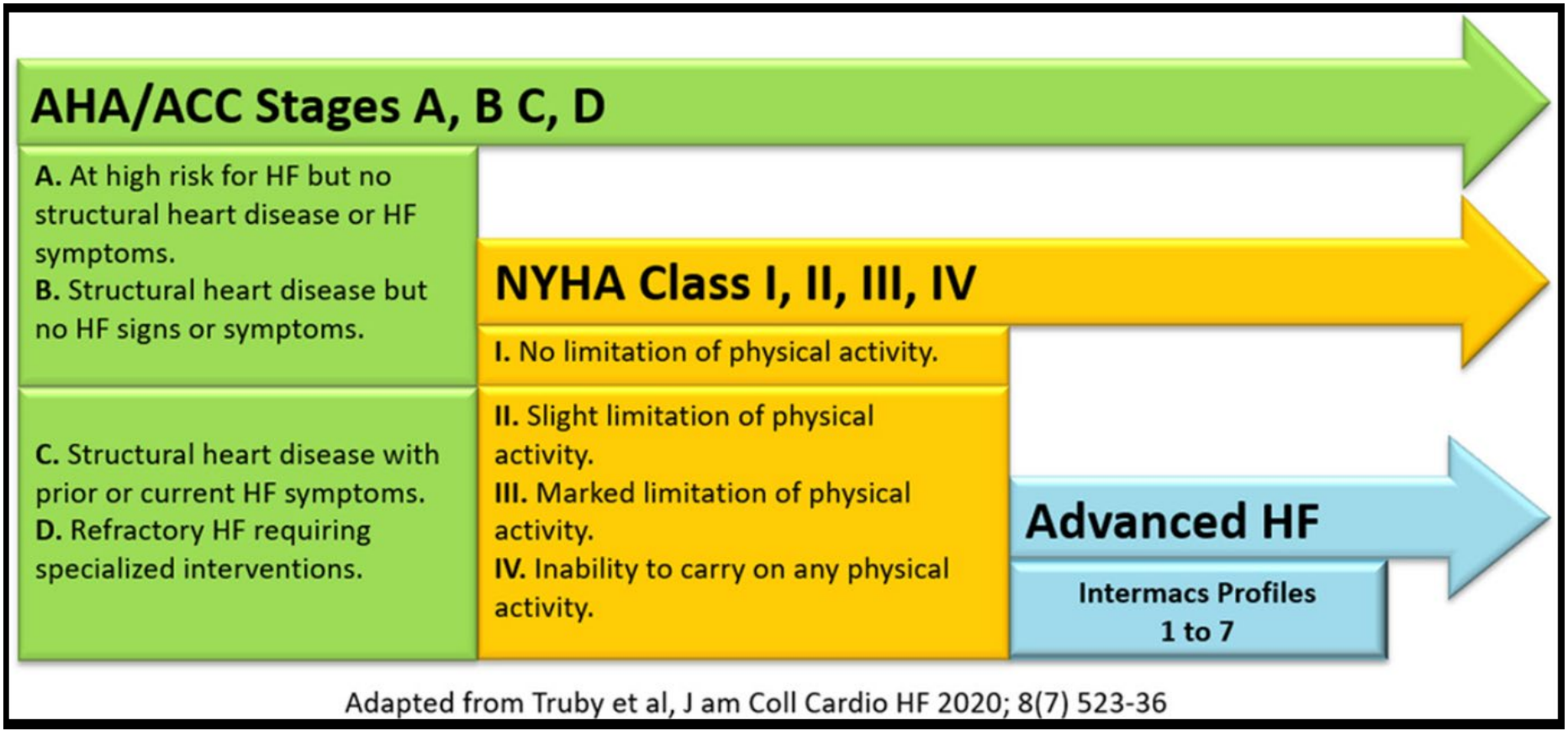
Figure 1. ACC/AHA Stages of HF



The ACC/AHA stages of HF are shown.

ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.

Stages and Classes of Heart Failure



Epidemiology of Heart Failure | Circulation Research

Figure 3. Classification and Trajectories of HF Based on LVEF

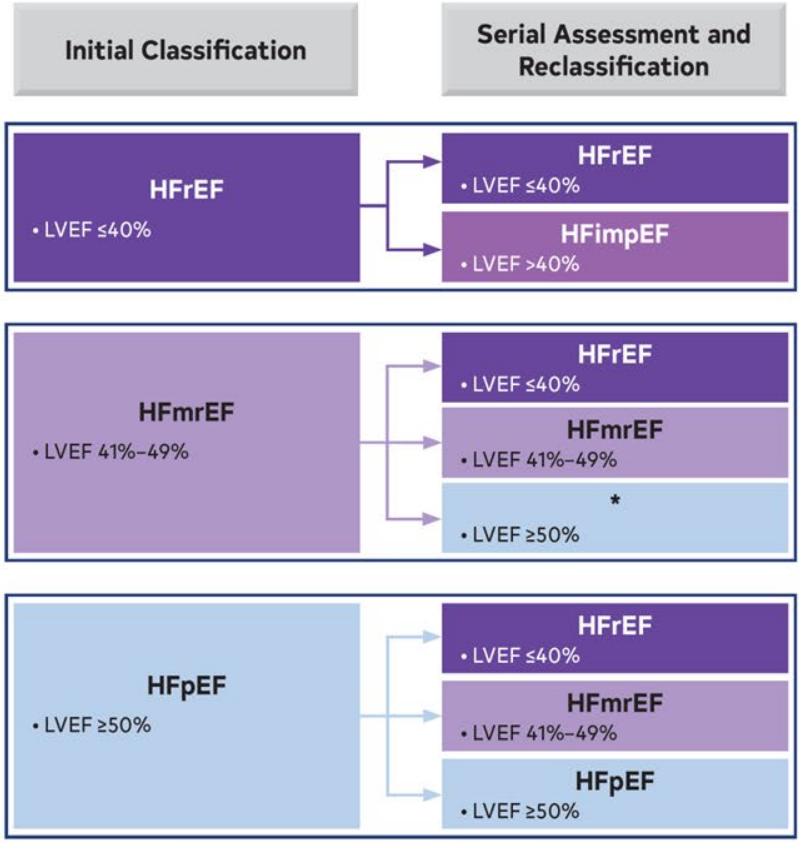
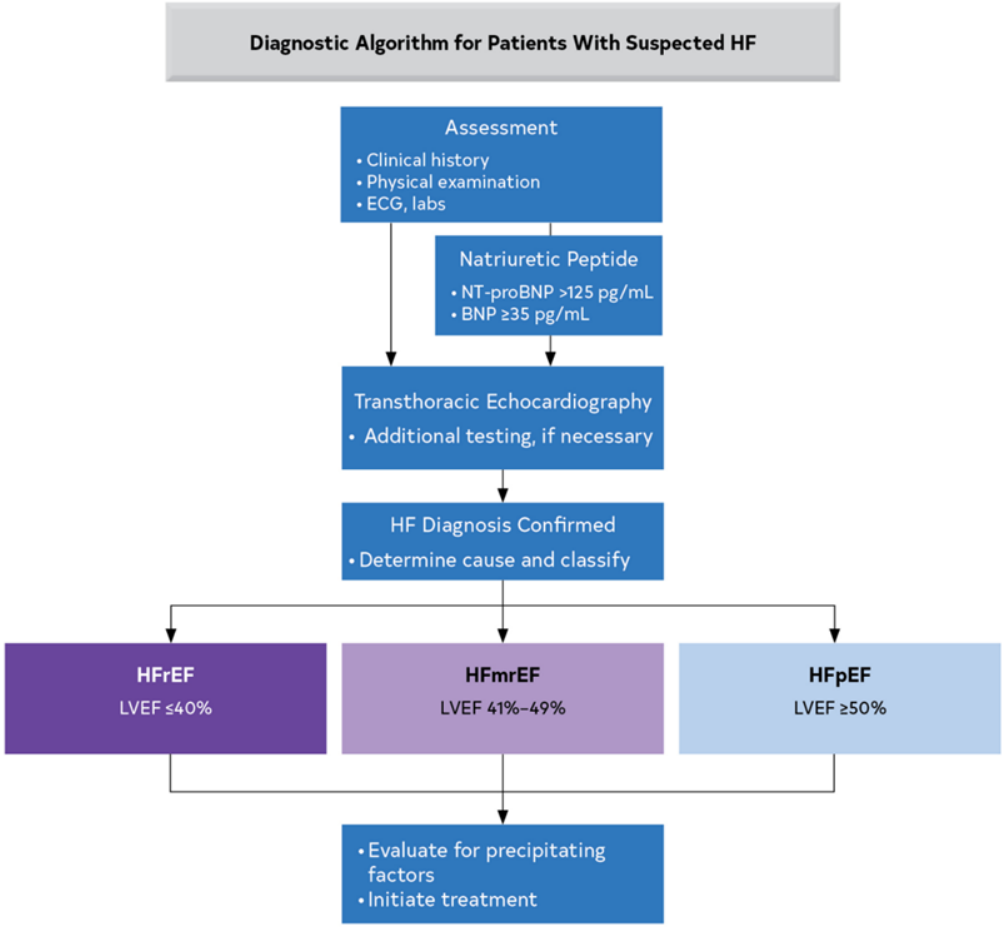


Table 4. Classification of HF by LVEF

Type of HF According to LVEF	Criteria
HFrEF (HF with reduced EF)	• LVEF ≤40%
HFimpEF (HF with improved EF)	• Previous LVEF ≤40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	• LVEF 41%–49% • Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	• LVEF ≥50% • Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)

HF indicates heart failure; LV, left ventricular; and LVEF, left ventricular ejection fraction.

Figure 4. Diagnostic Algorithm for HF and EF-Based Classification



The algorithm for a diagnosis of HF and EF-based classification is shown.

BNP indicates B-type natriuretic peptide; ECG, electrocardiogram; EF, ejection fraction; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; LV, left ventricular; NP, natriuretic peptides; and NT-proBNP, N-terminal pro-B type natriuretic peptide.

Treatment of HFrEF

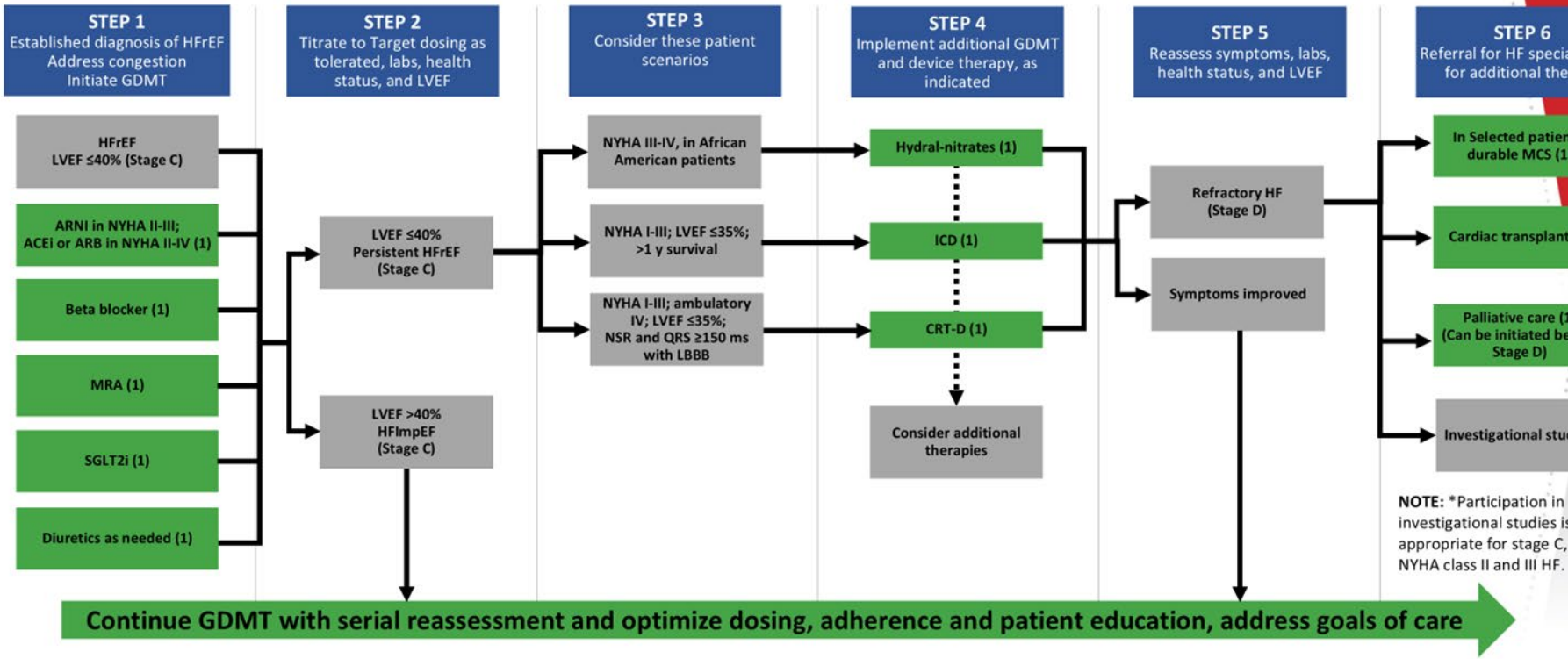
Treatment of HFrEF

Guideline-directed medical therapy (GDMT) for HF with reduced ejection fraction (HFrEF) now includes 4 medication classes that include SGLT2i. In symptomatic HFrEF, the following therapies reduce morbidity and mortality

- **Renin angiotensin inhibition -** ARNi (angiotensin receptor-neprilysin inhibitors), ACEi, ARB
- **Beta blockers** - carvedilol, metoprolol succinate, bisoprolol
- **MRA** - spironolactone, eplerenone
  - Recommended if eGFR >30 mL/min/1.73 m2 and serum potassium is <5.0 mEq/L.
- **SGLT2i** - dapagliflozin (HFref), empagliflozin (HFref, HFpEF)
  - SGLT-2i is recommended to reduce hospitalizations and CV mortality REGARDLESS of diabetes status and regardless of HF class.
  - Gliflozins in the Management of Cardiovascular Disease | New England Journal of Medicine
- **Loop Diuretics** - utilized AS NEEDED. Only use when fluid status needs to be optimized. Stop them if possible.

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines | JACC

Treatment of HFrEF Stages C and D



Abbreviations: ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; hydral-nitrates, hydralazine and isosorbide dinitrate; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; MRA, mineralocorticoid receptor antagonist; NSR, normal sinus rhythm; NYHA, New York Heart Association; SCD, sudden cardiac death; and SGLT2i, sodium-glucose cotransporter 2 inhibitor.

American Heart Association.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.

HFmrEF

LVEF 41%–49%

Treatment of HFmrEF

Treatment of HFmrEF

HFmrEF
LVEF 41%–49%

If previously or currently symptomatic, 4 drug GDMT should be continued or considered.

- **Renin angiotensin inhibition -** ARNi (angiotensin receptor-neprilysin inhibitors), ACEi, ARB
- **Beta blockers** - carvedilol, metoprolol succinate, bisoprolol
- **MRA** spironolactone, eplerenone
  - Recommended if eGFR >30 mL/min/1.73 m2 and serum potassium is <5.0 mEq/L.
- **SGLT2i** dapagliflozin (HFref), empagliflozin (HFref, HFpEF)
  - SGLT-2i is recommended to reduce hospitalizations and CV mortality REGARDLESS of diabetes status and regardless of HF class.
  - Gliflozins in the Management of Cardiovascular Disease | New England Journal of Medicine
- **Loop Diuretics** - utilized AS NEEDED. Only use when fluid status needs to be optimized. Stop them if possible.

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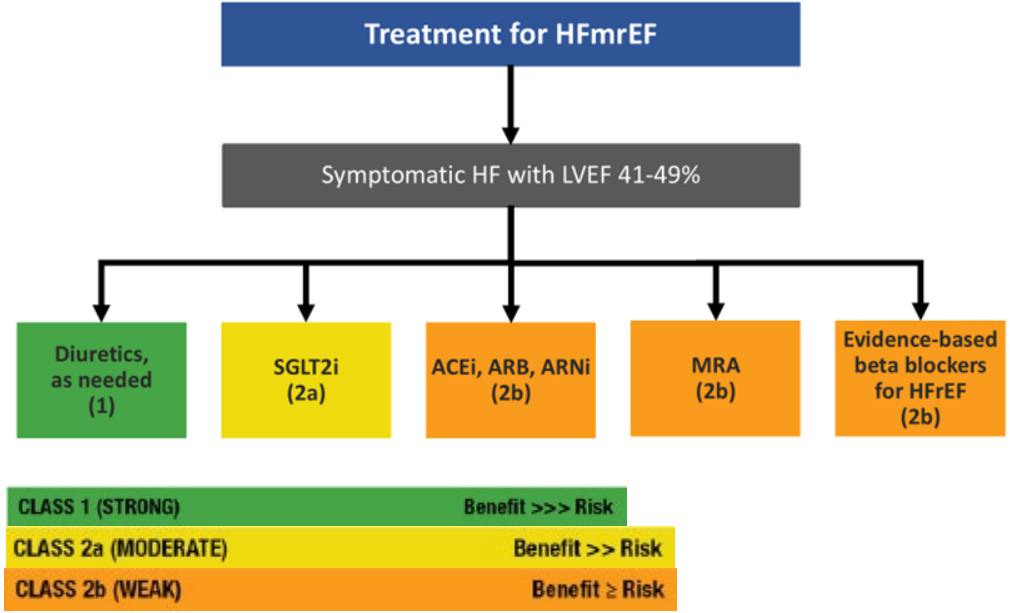
Recommendations for Patients with Mildly Reduced LVEF



Patients With HFimpEF

COR	RECOMMENDATIONS
1	1. In patients with HFimpEF after treatment, GDMT should be continued to prevent relapse of HF and LV dysfunction, even in patients who may become asymptomatic. (1)

Recommendations for HFmrEF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
2a	B-R	1. In patients with HFmrEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.[33]
2b	B-NR	2. Among patients with current or previous symptomatic HFmrEF (LVEF, 41%–49%), use of evidence-based beta blockers for HFrEF, ARNi, ACEi, or ARB, and MRAs may be considered, to reduce the risk of HF hospitalization and cardiovascular mortality, particularly among patients with LVEF on the lower end of this spectrum.[34–41]

Abbreviations: ARB indicates angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; LV, left ventricle; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium-glucose cotransporter-2 inhibitor.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.

HFpEF
LVEF ≥50%

Treatment of HFpEF

What is HFpEF?

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

- HFpEF is underrecognized
- 50% of HF is HPpEF
- Outcomes comparable to HFrEF
- May be more common in women.
  - Pre-eclampsia increases risk.
- Obesity is a risk factor.
- BNP issues
  - Obesity can lower BNP levels
  - BNP levels generally lower in HFpEF
  - Renal disease can raise BNP
- Risk factors:
  - Dyspnea
  - Edema
  - Older age
  - Obesity
  - Diabetes
  - HTN
  - Afib
- Mimics: renal dz, infiltrative cardiomyopathy, liver dz, ...etc

H2FPEF Score for Heart Failure with Preserved Ejection Fraction

A H_2FPEF

H_2	**H**eavy (BMI >30 kg/m²)	2
	On ≥2 anti**H**ypertensives	1
F	Atrial **F**ibrilllation	3
P	**P**ulmonary hypertension (PASP >35 mm Hg on Doppler echocardiography	1
E	**E**lder (age >60 years)	1
F	**F**illing pressure (E/e' >9 on Doppler echocardiography)	1

≥6 points: highly diagnostic of HFpEF

Treatment of HFpEF

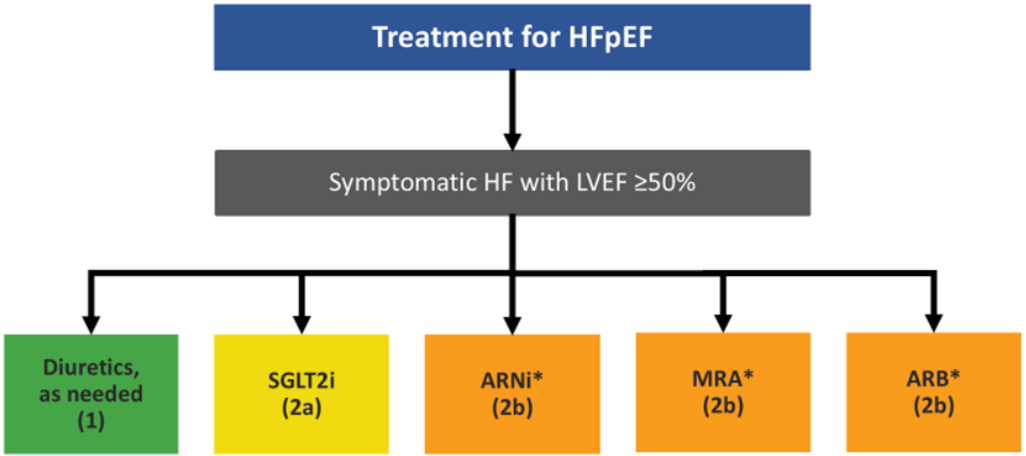
HFpEF
LVEF ≥50%

- **SGLT2i** - dapagliflozin (HFref), empagliflozin (HFref, HFpEF)
  - Reduce hospitalizations and CV mortality REGARDLESS of diabetes status and regardless of HF class.
  - 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 - ScienceDirect
  - Gliflozins in the Management of Cardiovascular Disease | New England Journal of Medicine
- **Loop Diuretics** - utilized AS NEEDED.
- **Renin angiotensin inhibition -** ARNi (angiotensin receptor-neprilysin inhibitors), ACEi, ARB
- **MRA -** spironolactone, eplerenone
- ~~**Beta blockers** - carvedilol, metoprolol succinate, bisoprolol~~

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines | JACC

Recommendations for Patients with Preserved LVEF

HFpEF
LVEF ≥50%



NOTE: *Greater benefit in patients with LVEF closer to 50%

CLASS 1 (STRONG)	Benefit >>> Risk
CLASS 2a (MODERATE)	Benefit >> Risk
CLASS 2b (WEAK)	Benefit ≥ Risk

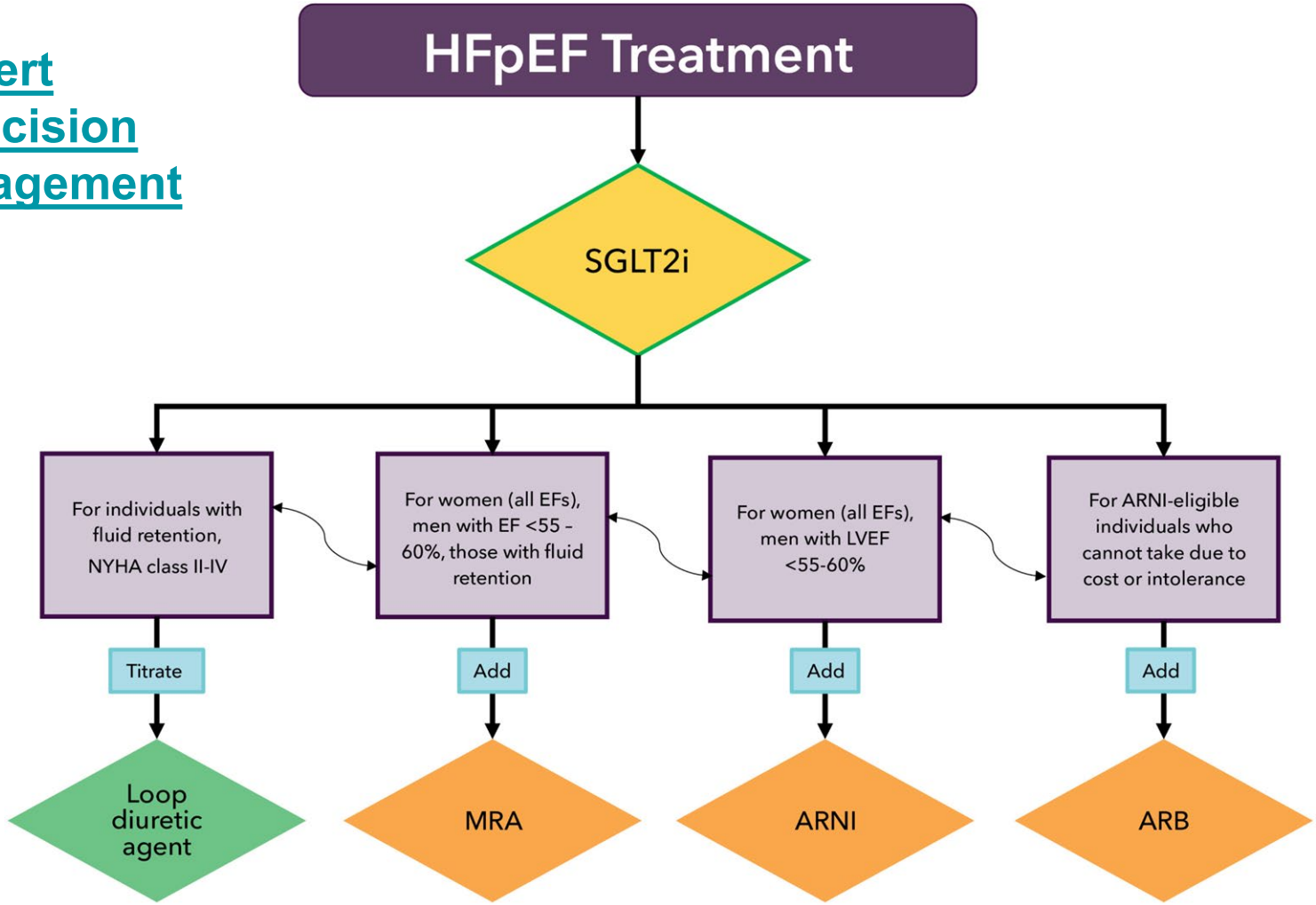
New Recommendations for HFpEF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
2a	B-R	1. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.[33]
2b	B-R	2. In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[38,42,43]
2b	B-R	3. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[35,40]

Renewed Recommendations for HFpEF
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	C-LD	1. Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity.[44–46]
2a	C-EO	2. In patients with HFpEF, management of AF can be useful to improve symptoms.
2b	B-R	3. In selected patients with HFpEF, the use of ARB may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[47,48]
3: No Benefit	B-R	4. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life is ineffective.[49,50]

2023 ACC Expert Consensus Decision Pathway: Management of HFpEF



Fluid and Sodium Restriction

Non-pharmacological Management in Advanced HF

Meta-analysis[1] of 6 RCTs comparing liberal and restricted fluid intake

⊖

- No difference in mortality or HF hospitalization
- No difference in serum Na+ or Cr
- No difference in duration of IV diuretics

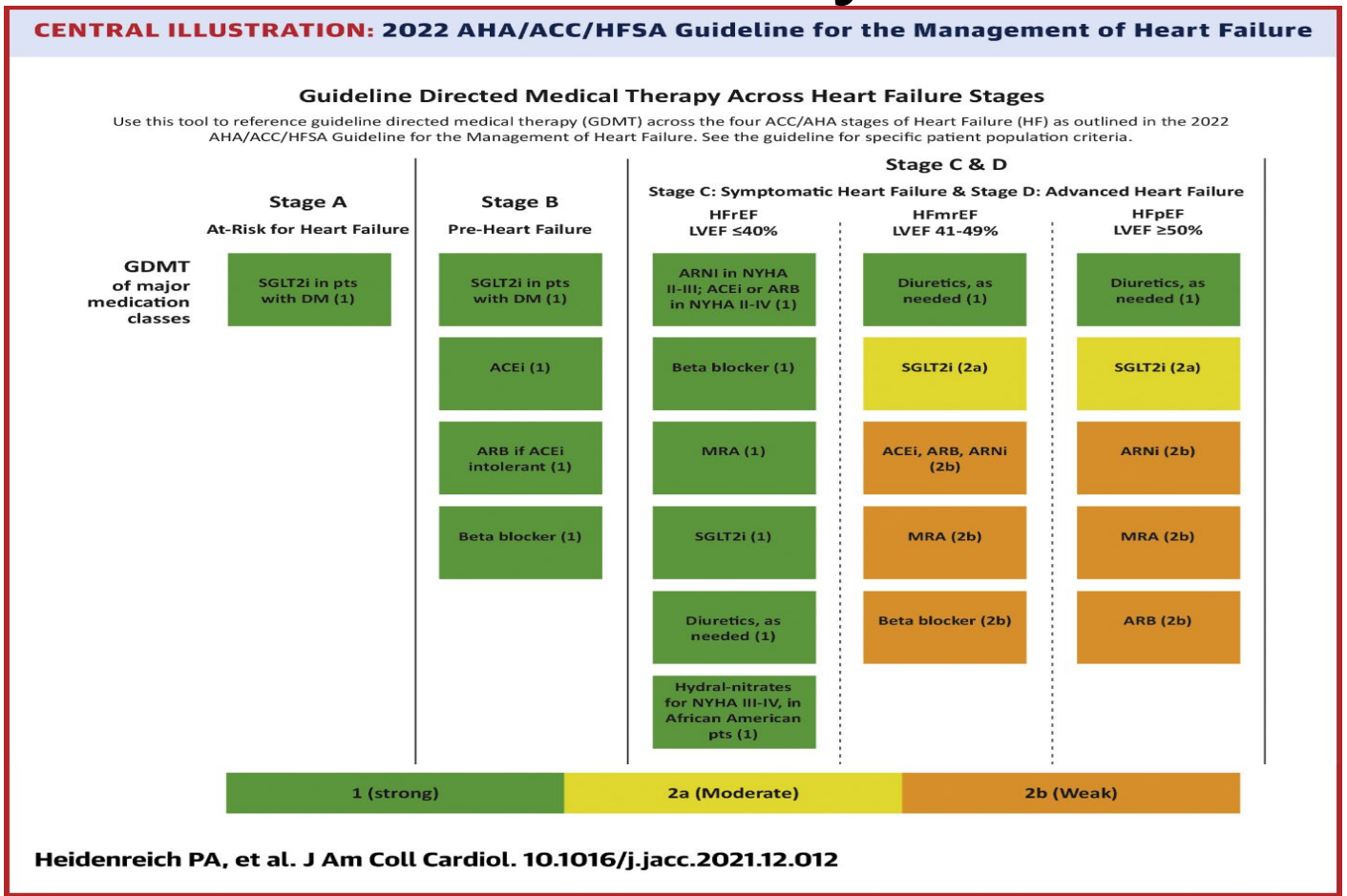
COR	RECOMMENDATIONS
2b	1. For patients with advanced HF and hyponatremia, the benefit of fluid restriction to reduce congestive symptoms is uncertain

Abbreviations: Cr indicates creatinine; HF, heart failure; IV, intravenous; Na^+, sodium; and RCT, randomized clinical trial.

American Heart Association.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.

Summary


CENTRAL ILLUSTRATION: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure
Guideline Directed Medical Therapy Across Heart Failure Stages
Use this tool to reference guideline directed medical therapy (GDMT) across the four ACC/AHA stages of Heart Failure (HF) as outlined in the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. See the guideline for specific patient population criteria.
Stage A
At-Risk for Heart Failure
Stage B
Pre-Heart Failure
Stage C & D
Stage C: Symptomatic Heart Failure & Stage D: Advanced Heart Failure
HFrEF
LVEF ≤40%
HFmrEF
LVEF 41-49%
HFpEF
LVEF ≥50%
GDMT of major medication classes
SGLT2i in pts with DM (1)
SGLT2i in pts with DM (1)
ACEi (1)
ARB if ACEi intolerant (1)
Beta blocker (1)
ARNI in NYHA II-III; ACEi or ARB in NYHA II-IV (1)
Beta blocker (1)
MRA (1)
SGLT2i (1)
Diuretics, as needed (1)
Hydral-nitrates for NYHA III-IV, in African American pts (1)
Diuretics, as needed (1)
SGLT2i (2a)
ACEi, ARB, ARNi (2b)
MRA (2b)
Beta blocker (2b)
Diuretics, as needed (1)
SGLT2i (2a)
ARNi (2b)
MRA (2b)
ARB (2b)
1 (strong)
2a (Moderate)
2b (Weak)
Heidenreich PA, et al. J Am Coll Cardiol. 10.1016/j.jacc.2021.12.012

Supplementary Slides

Evidence of Elevated LV Pressures

Clinical Evidence

- **Dyspnea on exertion or at rest** (due to pulmonary congestion)
- **Orthopnea and paroxysmal nocturnal dyspnea** (suggesting elevated pulmonary venous pressure)
- **Peripheral edema**
- **S3 heart sound** (suggests increased LV filling pressure and volume overload)
- **Jugular venous distension (JVD)** and **hepatojugular reflux** (if right heart involvement)

Biomarkers

- **Brain Natriuretic Peptide (BNP) or NT-proBNP**
  - Elevated levels indicate increased ventricular wall stress, which correlates with high LVFP.

Evidence of Elevated LV Pressures

Echocardiographic Evidence (Doppler and Tissue Doppler Imaging)

- **E/A Ratio on Mitral Inflow Doppler**:
  - **E/A > 2** suggests restrictive filling and high LVFP.
  - **E/A < 0.8 with increased E-wave deceleration time** can indicate impaired relaxation but may still have elevated LVFP if left atrial pressure is high.
- **Mitral E/e' Ratio (Tissue Doppler Imaging)**
  - **E/e' > 14** suggests elevated LVFP.
- **Left Atrial Volume Index (LAVI)**
  - **>34 mL/m²** suggests chronically increased LVFP.
- **Tricuspid Regurgitation (TR) Velocity**
  - **>2.8-3.0 m/s** suggests increased pulmonary artery pressures, indirectly indicating increased LVFP.
- **Pulmonary Venous Flow Pattern** (assessed via Doppler)
  - **Decreased systolic fraction and increased diastolic flow** suggest elevated left atrial pressure.

Invasive Hemodynamic Measurements (Gold Standard)

- **Pulmonary Capillary Wedge Pressure (PCWP)**
  - **>15 mmHg** (normal is 8-12 mmHg) is indicative of increased LVFP.
- **Left Ventricular End-Diastolic Pressure (LVEDP)**
  - **>16 mmHg** suggests elevated LV filling pressures.
- **Right Heart Catheterization**
  - Can confirm elevated **PCWP** and **mean left atrial pressure** in heart failure patients.

BNP and NT-proBNP Cutoff Values in Chronic Kidney Disease (CKD) for Heart Failure Diagnosis

Since renal failure can independently elevate **BNP** and **NT-proBNP**, different cutoff values are recommended to distinguish **heart failure (HF)** from elevations due to kidney dysfunction. **BNP and NT-proBNP rise with worsening kidney function**, even without heart failure.

General BNP and NT-proBNP Cutoff Values for Heart Failure

Marker	Heart Failure Unlikely	Heart Failure Possible	Heart Failure Likely
BNP (pg/mL)	<100	100–400	>400
NT-proBNP (pg/mL)	<300	300–1800	>1800

Adjusted BNP and NT-proBNP Cutoffs in CKD

CKD Stage	BNP Cutoff for Heart Failure	NT-proBNP Cutoff for Heart Failure
Stage 3 (eGFR 30–59)	>200 pg/mL	>1200 pg/mL
Stage 4 (eGFR 15–29)	>300 pg/mL	>3000 pg/mL
Stage 5 (eGFR <15, incl. dialysis)	>400 pg/mL	>6000 pg/mL

BNP Interpretation

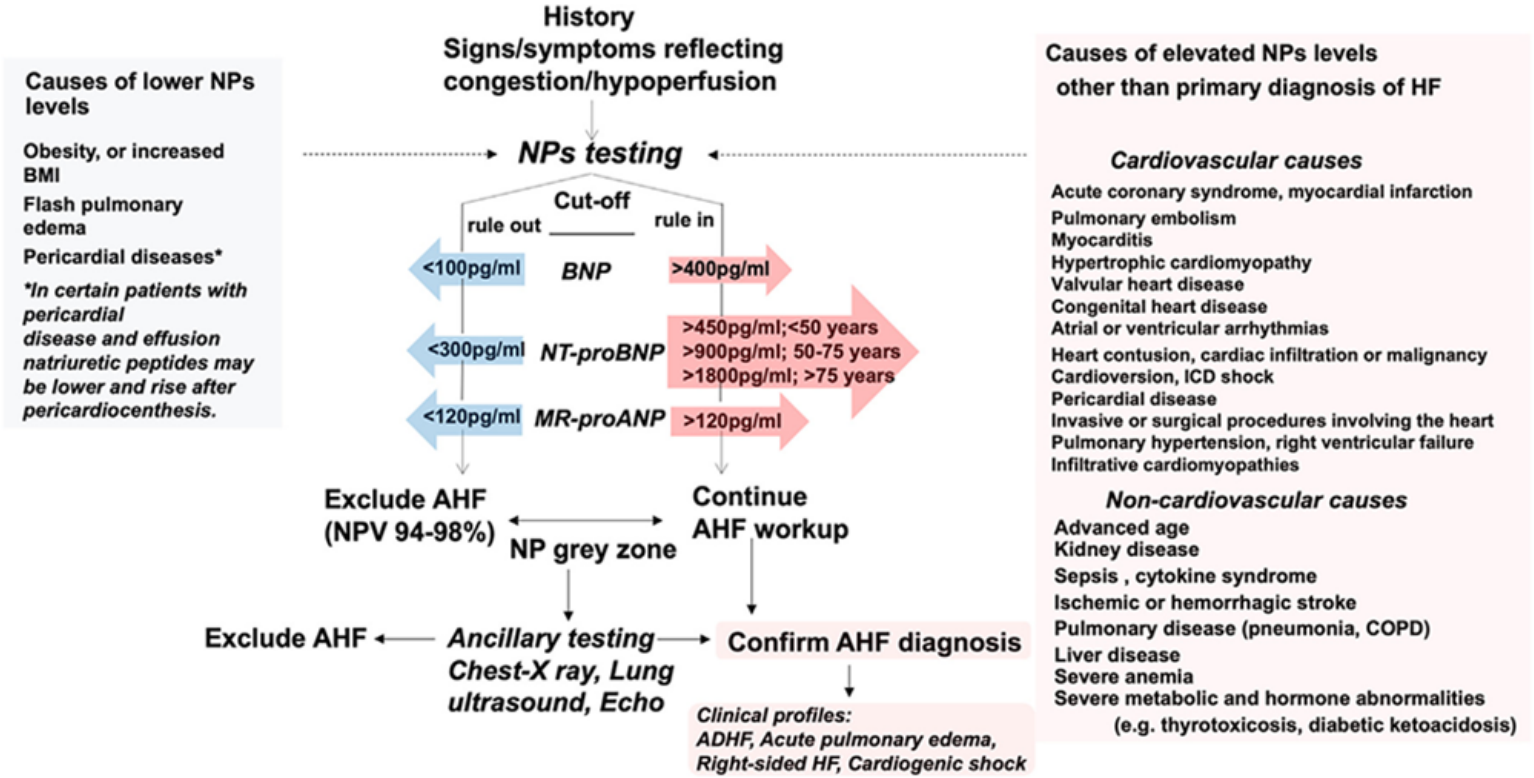


Fig. 5. Use of natriuretic peptide testing for diagnosis of acute heart failure. In patients with suspected acute HF, a BNP cut off concentration of 100 pg/mL provides an excellent NPV to exclude the presence of HF, while higher values (>400 pg/mL) deliver excellent positive predictive value (PPV). For NT-proBNP, age-dependent rule-in cut-offs are preferred (450/900/ 1800 pg/mL). However, independent of age, an NT-proBNP concentration <300 pg/mL provides a very high NPV for HF.

Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement From the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society

References

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines | Circulation

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines | Circulation

2022 AHA/ACC/HFSA Heart Failure Guideline: Key Perspectives - American College of Cardiology

Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement From the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society - Journal of Cardiac Failure

Good HFpEF Review – 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 - ScienceDirect

Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement From the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society

Podcast References

- #458 Heart Failure with Reduced Ejection Fraction – The Curbsiders
- #460 Heart Failure with Preserved Ejection Fraction – The Curbsiders
- Cardio Nerds: Decipher the Guidelines: 2022 AHA / ACC / HFSA Guideline for The Management of Heart Failur
- 412: The Biology of Transthyretin amyloid cardiomyopathy (ATTR-CM) with Dr. Daniel Judge

Supplementary Slides

ACC/AHA Class and Level of Evidence

Table 1. Applying American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

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	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

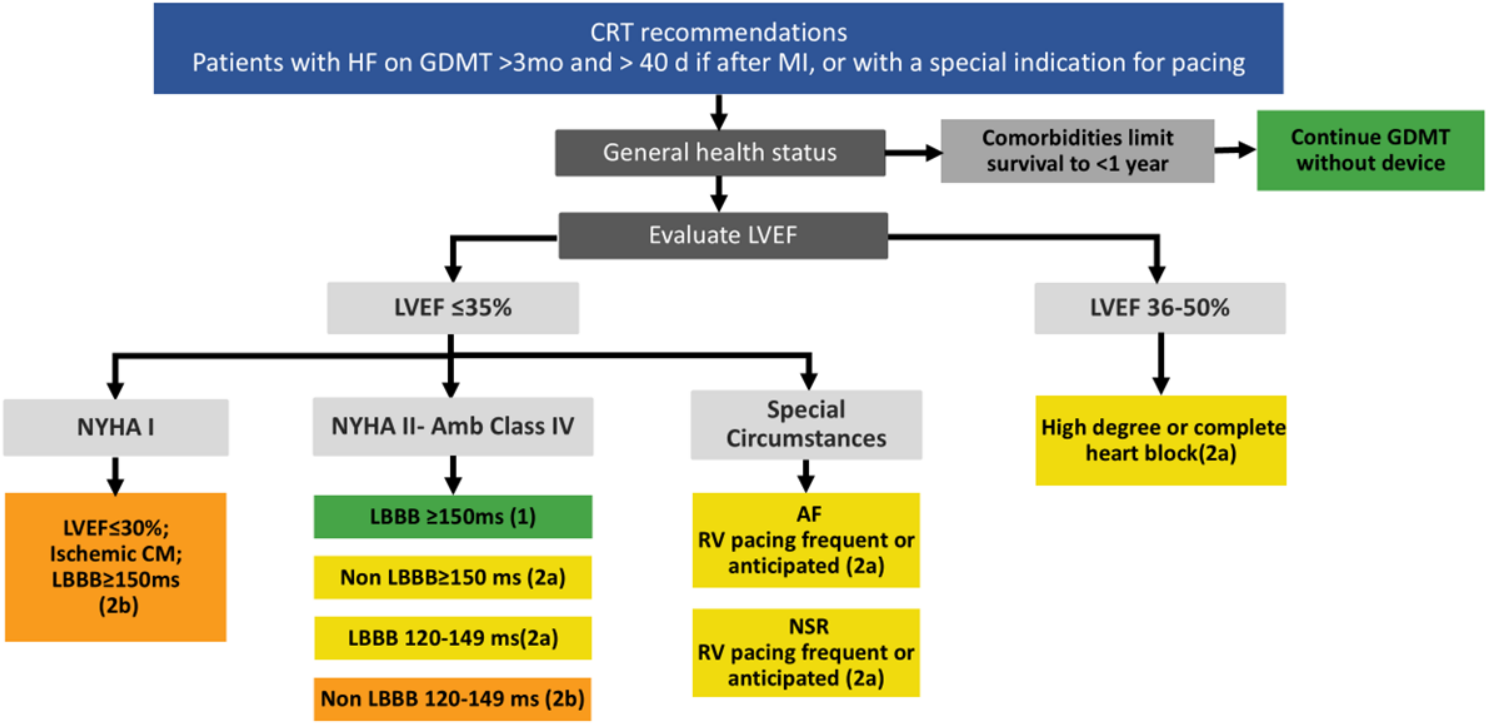
* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Algorithm for CRT Indications in Patients with Cardiomyopathy or HFrEF



Abbreviations: AF indicates atrial fibrillation; Amb, ambulatory; CM, cardiomyopathy; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; HB, heart block; HF, Heart Failure; HFH, heart failure hospitalization; HFrEF, heart failure with reduced ejection fraction; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NSR, normal sinus rhythm; NYHA, New York Heart Association; and RV, right ventricle.

Heidenreich, P. A. et al. (2022). 2022 AHA/ACC/HFSA Guideline for Heart Failure. *Circulation*.

American Heart Association.