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Heart Failure Updates

Washington 2023 American College of Physicians

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Reflection

Our Objectives

1. Review definitions and key terms related to heart failure.
2. Review four pillars of comprehensive guideline directed medical therapy for heart failure.
3. Discuss updates in the management of Hypertrophic Cardiomyopathy and Cardiac Amyloidosis.

Disclosures

Clinical trial work

- Site investigator for trials with NovoNordisc (ASCVD), Cytokinetics (HCM), Pfizer (Amyloid), BridgeBio Pharma (Amyloid), Medtronic (TAVR).

American College of Cardiology

- Question writing SAP
- WA ACC State Board

Amyloidosis Support Group

- PNW Physician leader

Pfizer Speaker Bureau for Cardiac Amyloidosis

Definition of Heart Failure

Heart failure (HF) is a complex clinical syndrome with symptoms and signs that result from any structural or functional impairment of ventricular filling or ejection of blood.

Bozkurt B, et al. J Card Fail. 2021.

Heidenreich PA, et al. Circulation. 2022.

Question 1

A 21yr old man sees you in clinic for follow up of screening tests ordered after his father was diagnosed with hypertrophic cardiomyopathy.

He denies difficulty keeping up with friends playing pick up basketball or soccer. He ran track in high school. His pediatrician had no concerns about cardiopulmonary issues. Physical exam is unremarkable.

ECG shows sinus rhythm with left ventricular hypertrophy and repolarization abnormalities.

Echocardiogram shows mildly increased concentric wall thickness with moderate septal hypertrophy at 14mm and normal left and right ventricular function with average GLS -22%. There is no LV gradient at rest or with valsalva.

NT pro BNP is 31. CBC and CMP are within normal limits.

What is an appropriate diagnosis for the student?

- Stage A heart failure
- Stage B heart failure
- Stage C heart failure
- Stage D heart failure
- None of the above

Question 1 answer

Patients with Pre-Heart Failure (stage B), are patients who do not have current or prior symptoms or signs of heart failure, but have evidence of structural heart disease, abnormal cardiac function, and/or elevated natriuretic peptide levels.

What is an appropriate diagnosis for the student?

- Stage A heart failure
- Stage B heart failure
- Stage C heart failure
- Stage D heart failure
- None of the above

Definition of Heart Failure

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

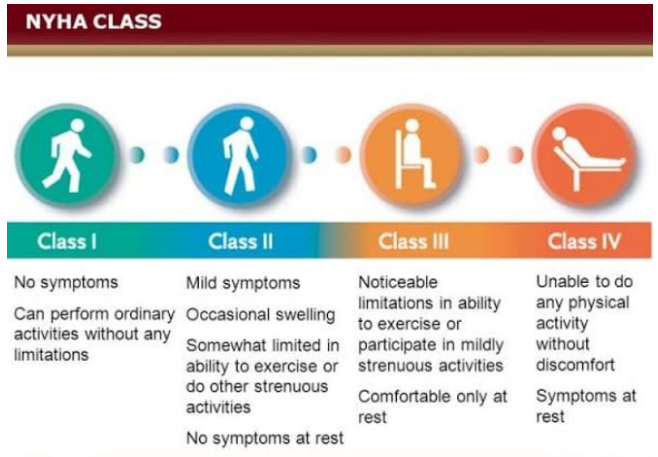
in the absence of competing diagnoses

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



Profile	Title	Description
1	Critical cardiogenic shock	Life-threatening hypotension refractory to IV inotropes. "*crash and burn*"
2	Progressive decline	IV inotropes required with worsening end-organ function. "sliding on inotropes"
3	Inotrope dependent	Stable blood pressure and end-organ function but failure to wean from IV inotropes. "dependent stability"
4	Resting symptoms	Daily symptoms of congestion at rest or with ADLs. High doses of diuretics
5	Exertion intolerant	Unable to engage in any activity above ADLs
6	Exertion limited	Can participate in minor activities but quickly fatigues. "walking wounded"
7	Advanced NYHA III	Comfortable with meaningful activity, limited to mild exertion

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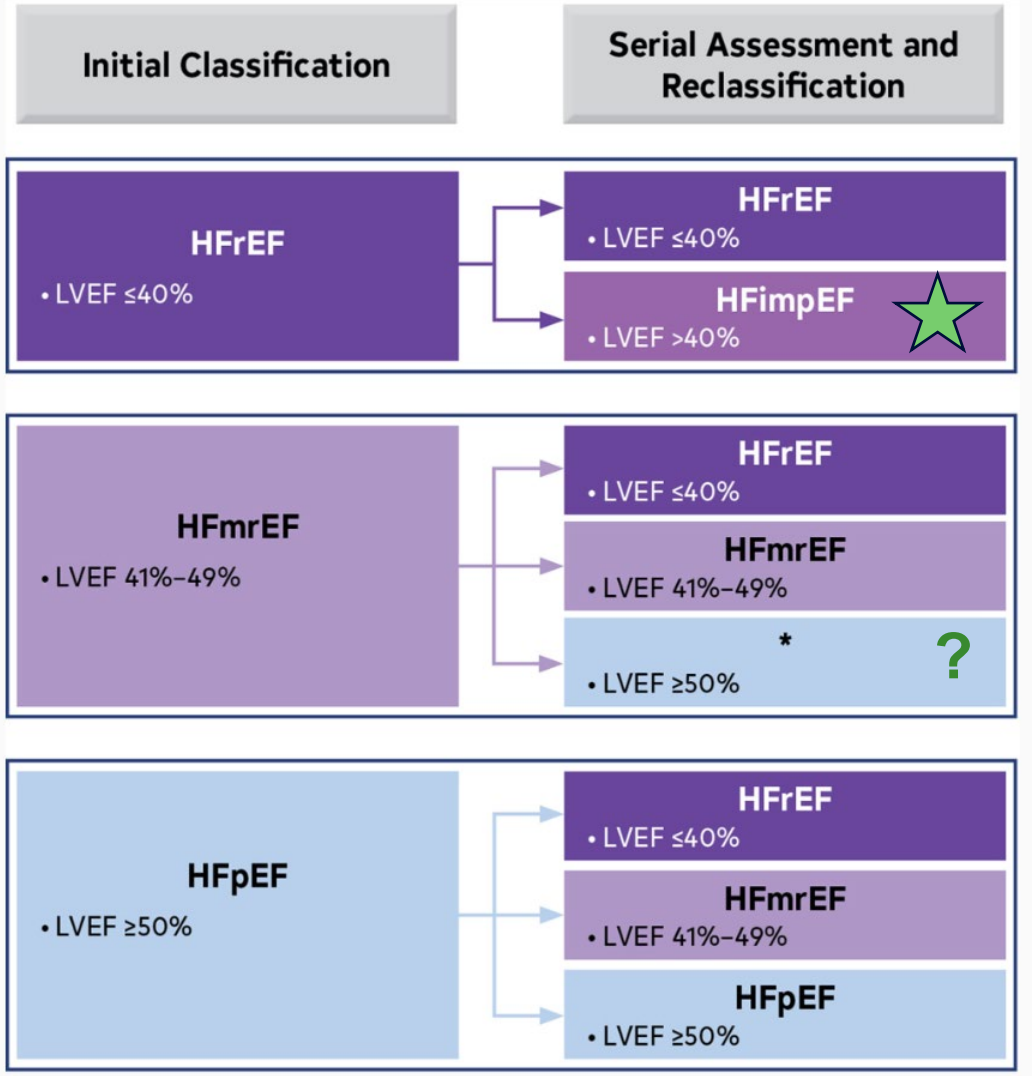
Bozkurt B, et al. J Card Fail. 2021. Heidenreich PA, et al. Circulation. 2022.

Definitions and Classification of Heart Failure 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 (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)



Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022 May 3;145(18):e895-e1032.

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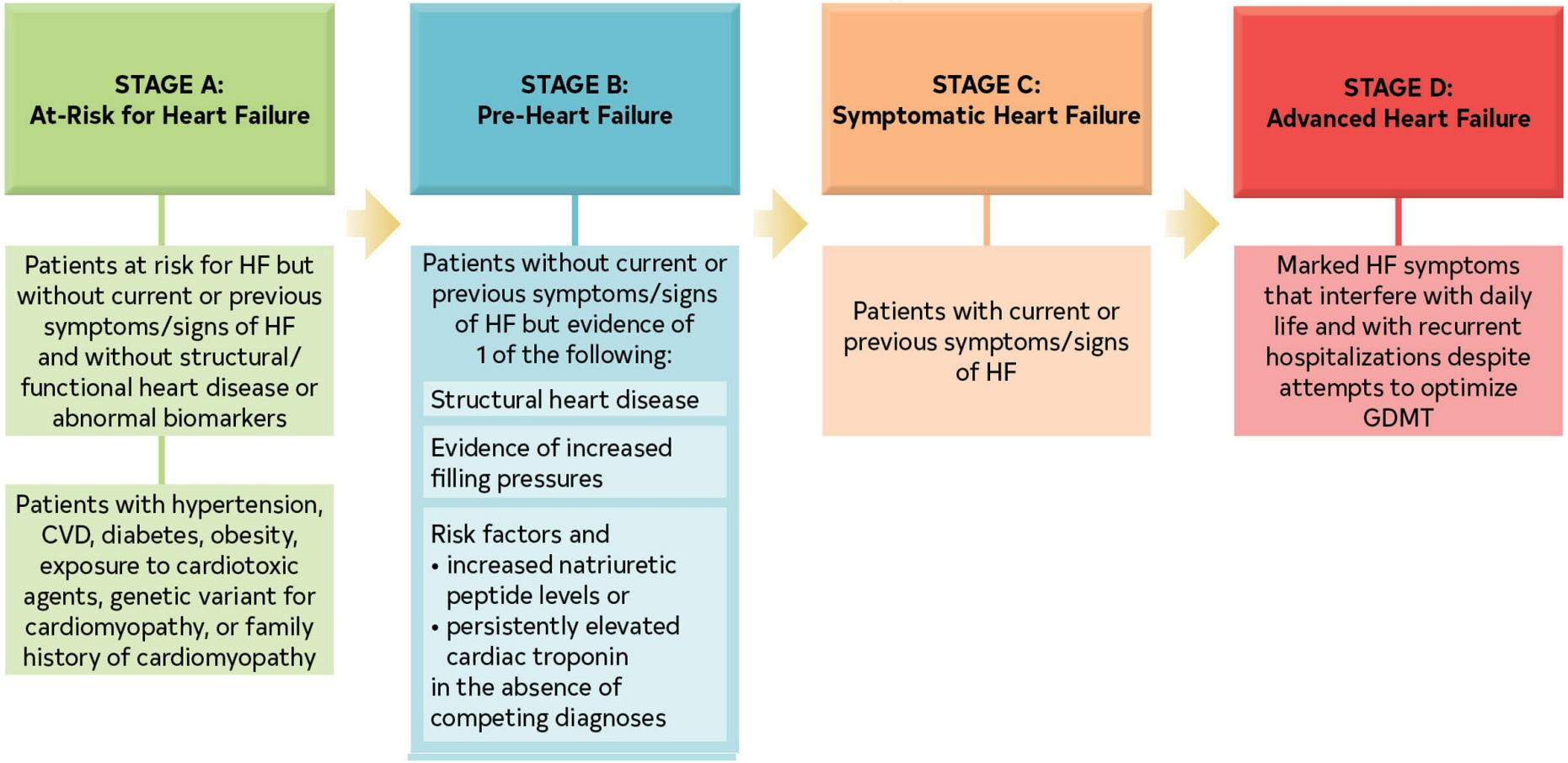
Heart Failure Trajectory



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Heart Failure with Preserved Ejection fraction

The diagnosis of HFpEF is often challenging!

If the LVEF is >40%, evidence supporting increased filling pressures is important for the diagnosis. Examples include:

- Natriuretic peptide levels
- Orthopnea, Jugular venous distension, Bendopnea, Edema
- Diastolic function at rest or exercise (stress echo)
- Invasive testing (eg, hemodynamic measurements in cath lab).

In patients with unexplained exertional dyspnea, composite clinical scores such as H2PEF may help to facilitate discrimination from noncardiac causes of dyspnea and can assist in determination of the need for further diagnostic testing.

COR	LOE	Recommendations
1	A	1. In patients presenting with dyspnea, measurement of B-type natriuretic peptide (BNP) or N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) is useful to support a diagnosis or exclusion of HF.[1–12]
1	A	2. In patients with chronic HF, measurements of BNP or NT-proBNP levels are recommended for risk stratification.[11,13–29]
1	A	3. In patients hospitalized for HF, measurement of BNP or NT-proBNP levels at admission is recommended to establish prognosis.[11,13–19]
2a	B-R	4. In patients at risk of developing HF, BNP or NT-proBNP–based screening followed by team-based care, including a cardiovascular specialist, can be useful to prevent the development of LV dysfunction or new-onset HF.[30,31]
2a	B-NR	5. In patients hospitalized for HF, a predischarge BNP or NT-proBNP level can be useful to inform the trajectory of the patient and establish a postdischarge prognosis.[14,17,20–29]

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Heart Failure with Preserved Ejection fraction

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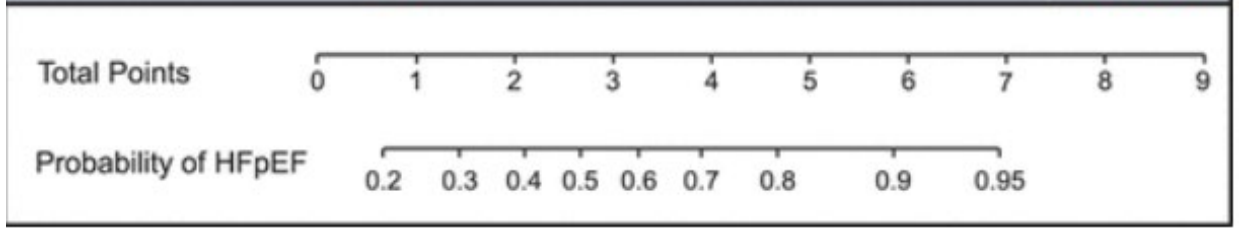
	Clinical Variable	Values	Points
H_2	Heavy	Body mass index > 30 kg/m²	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	Elder	Age > 60 years	1
F	Filling Pressure	Doppler Echocardiographic E/e' > 9	1
	H_2FPEF score		Sum (0-9)



Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022 May 3;145(18):e895-e1032.

Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction. Circulation. 2018 Aug 28;138(9):861-870.

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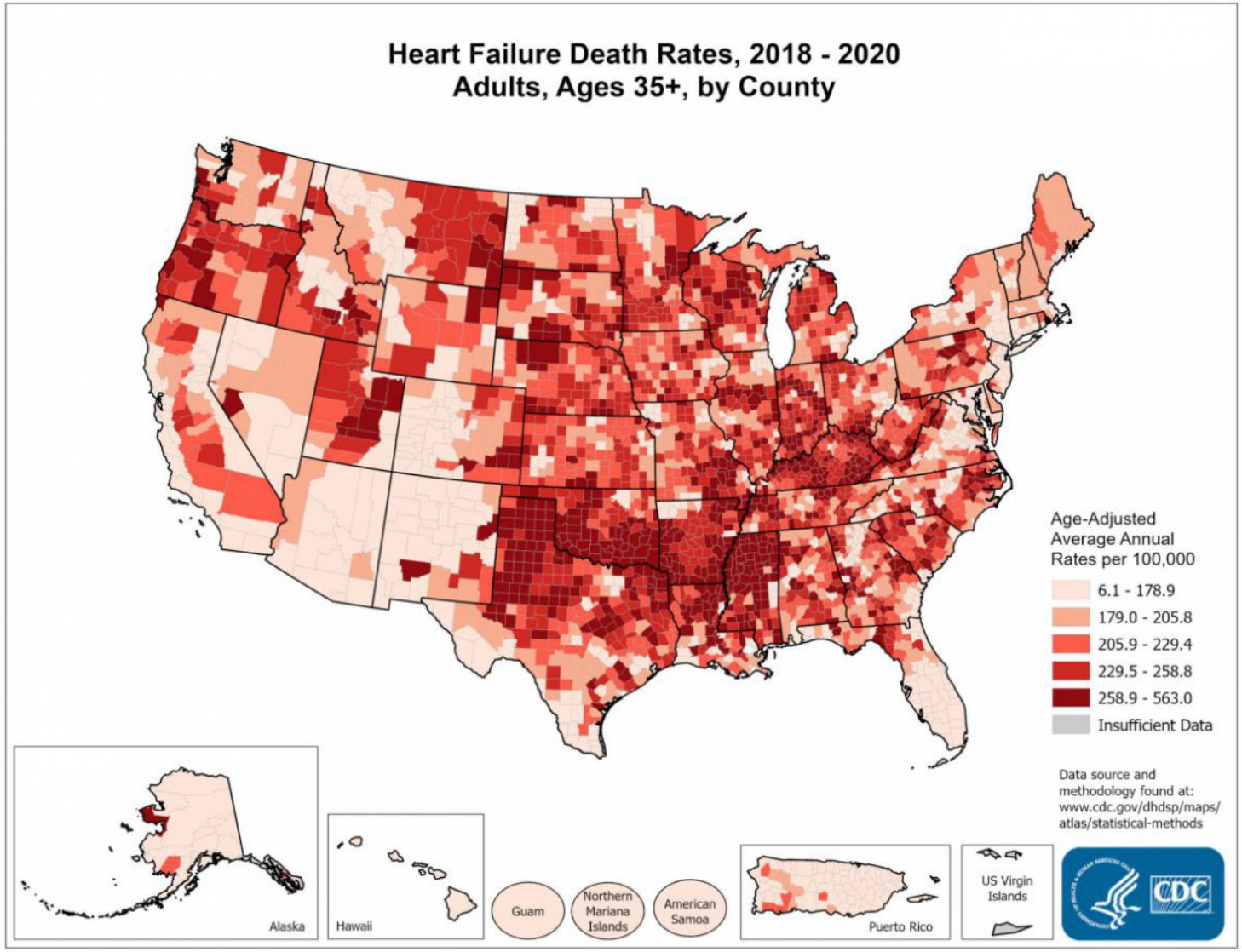
Epidemiology

About 6.2 million adults in the United States have heart failure.

In 2017, there were **1.2 million** HF hospitalizations (HFH) in the United States among 924 000 patients with HF.

This represents a 26% increase in HFH and number of patients hospitalized with HF.

Racial and ethnic disparities in death resulting from HF persist, with non-Hispanic Black patients having the highest death rate per capita.



Dexit NM, et al. JACC HF 2023.

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022 .

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Comprehensive guideline directed medical therapy for heart failure

Question 2

Which of the following does **NOT** describe the mechanism of action of a pharmaceutical class with a class 1 recommendation for heart failure with reduced ejection fraction?

1. Beta-1-adrenergic receptor inhibitor
2. Sodium-glucose cotransporter-2 inhibitors
3. Soluble guanylate cyclase stimulation
4. Angiotensin receptor/neprilysin inhibitor
5. Mineralocorticoid receptor agonist

Question 2 Answer

Which of the following does not describe the mechanism of action of a pharmaceutical class with a class 1 recommendation for heart failure with reduced ejection fraction?

1. Beta-1-adrenergic receptor inhibition = Beta blockers
2. Sodium-glucose cotransporter-2 inhibition = SGLT2 inhibitors
3. Soluble guanylate cyclase stimulation = Vericiguat
4. Angiotensin receptor/neprilysin inhibition = ARNI
5. Mineralocorticoid receptor agonism = MRAs

Comprehensive guideline directed medical therapy for heart failure reduced EF

Step 1: Establish the diagnosis

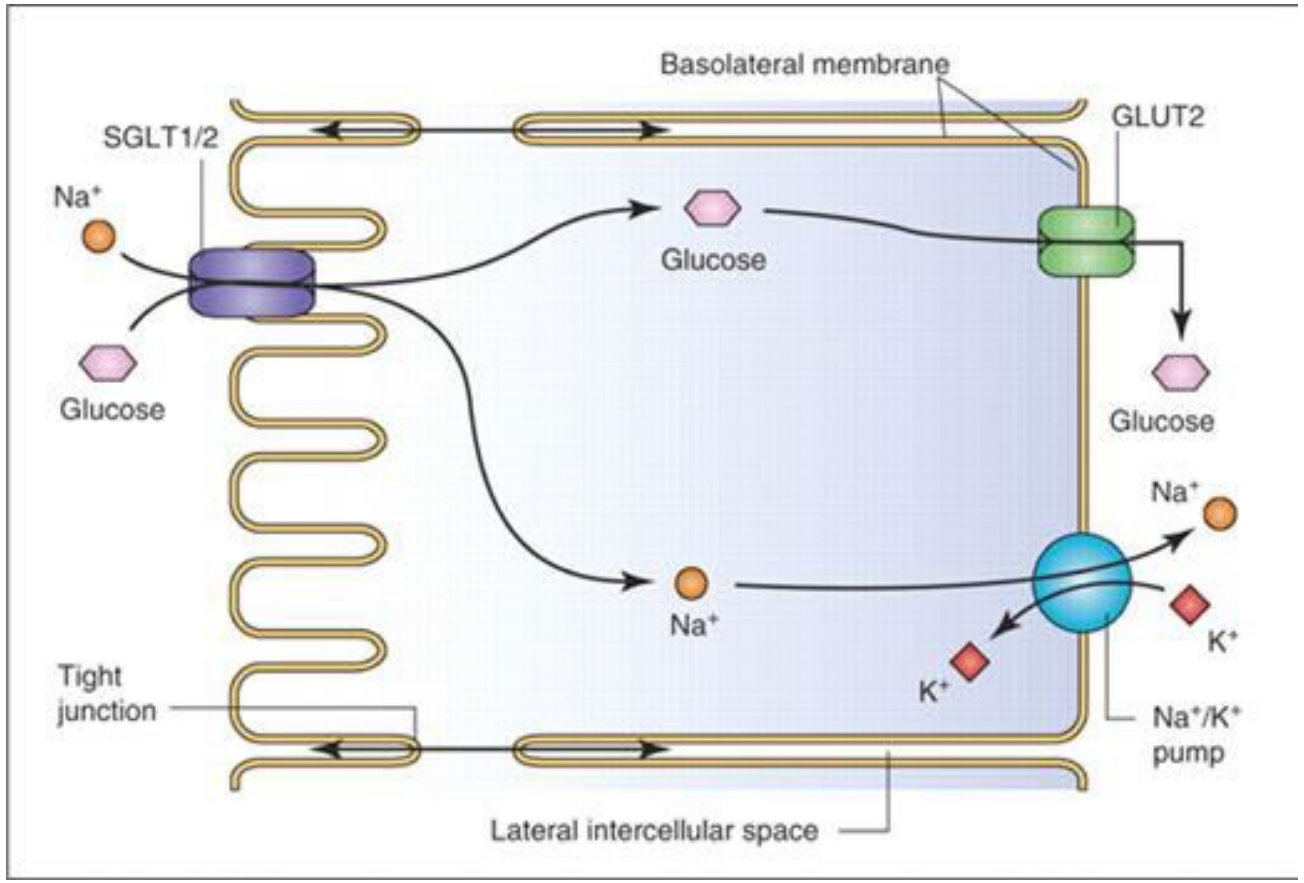
Step 2: Address congestion and Initiate GDMT

Step 3: Address co-morbidities and lifestyle

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

Sodium-Glucose Cotransporter 2 Inhibitors

"*SGLT2 inhibitors: the statins of the 21st century.*" - Dr Braunwald



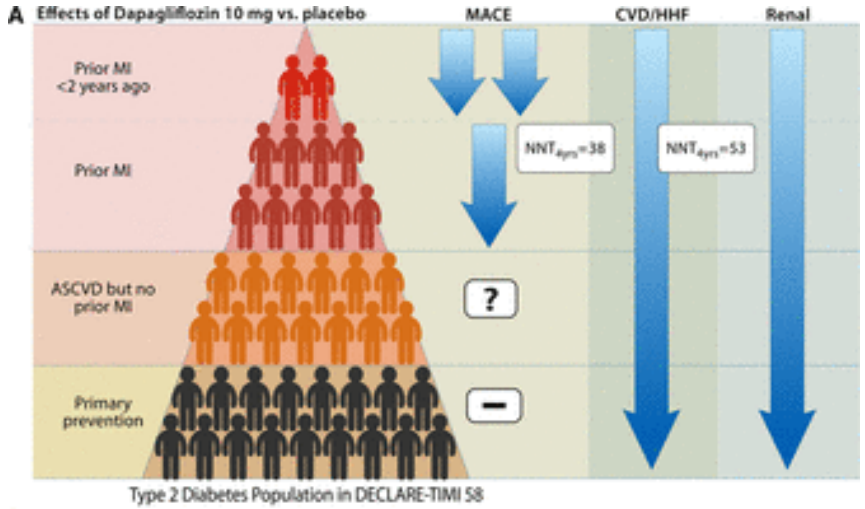
Braunwald E. Eur Heart J 2022. Zelniker TA, Braunwald E. JACC 2020. Bakris GL, et al. Kidney Int 2009. Heidenreich PA, et al. Circ 2022.

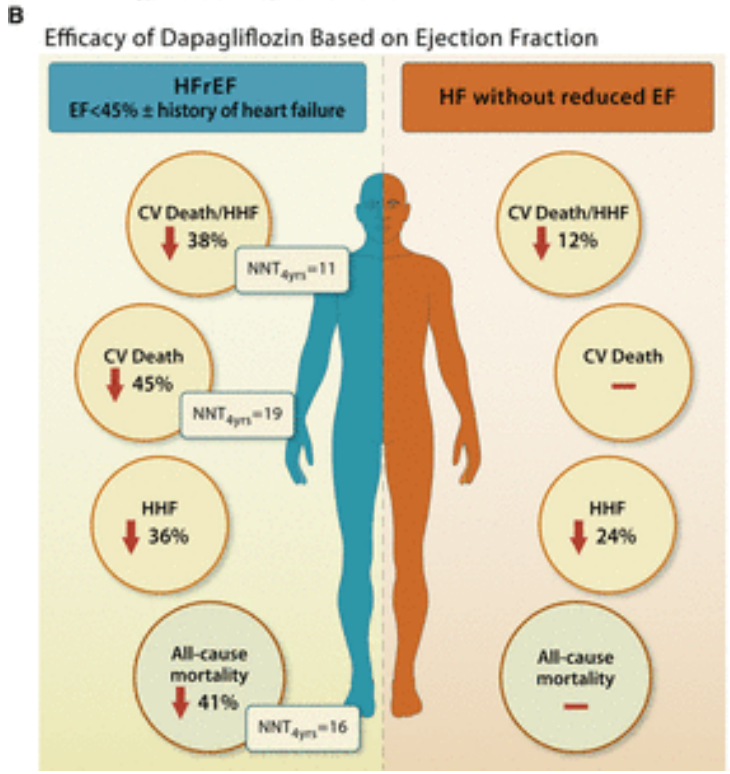
Sodium-Glucose Cotransporter 2 Inhibitors

SGLT2 inhibitors have been serially demonstrated to:

1. Reduce the development and progression of HF, and prolong life in patients with T2DM and reduced LVEF.
2. Improve outcomes in patients with HFrEF irrespective of presence or absence of T2DM
   - In the DAPA-HF and EMPEROR-Reduced trials, SGLT2i compared with placebo reduced composite of CV death or HF hospitalization ~ 25%!
3. Be beneficial in patients with chronic HF over a wide range of EF
4. Be renoprotective and slow the development of end-stage kidney disease in patients with chronic kidney disease.

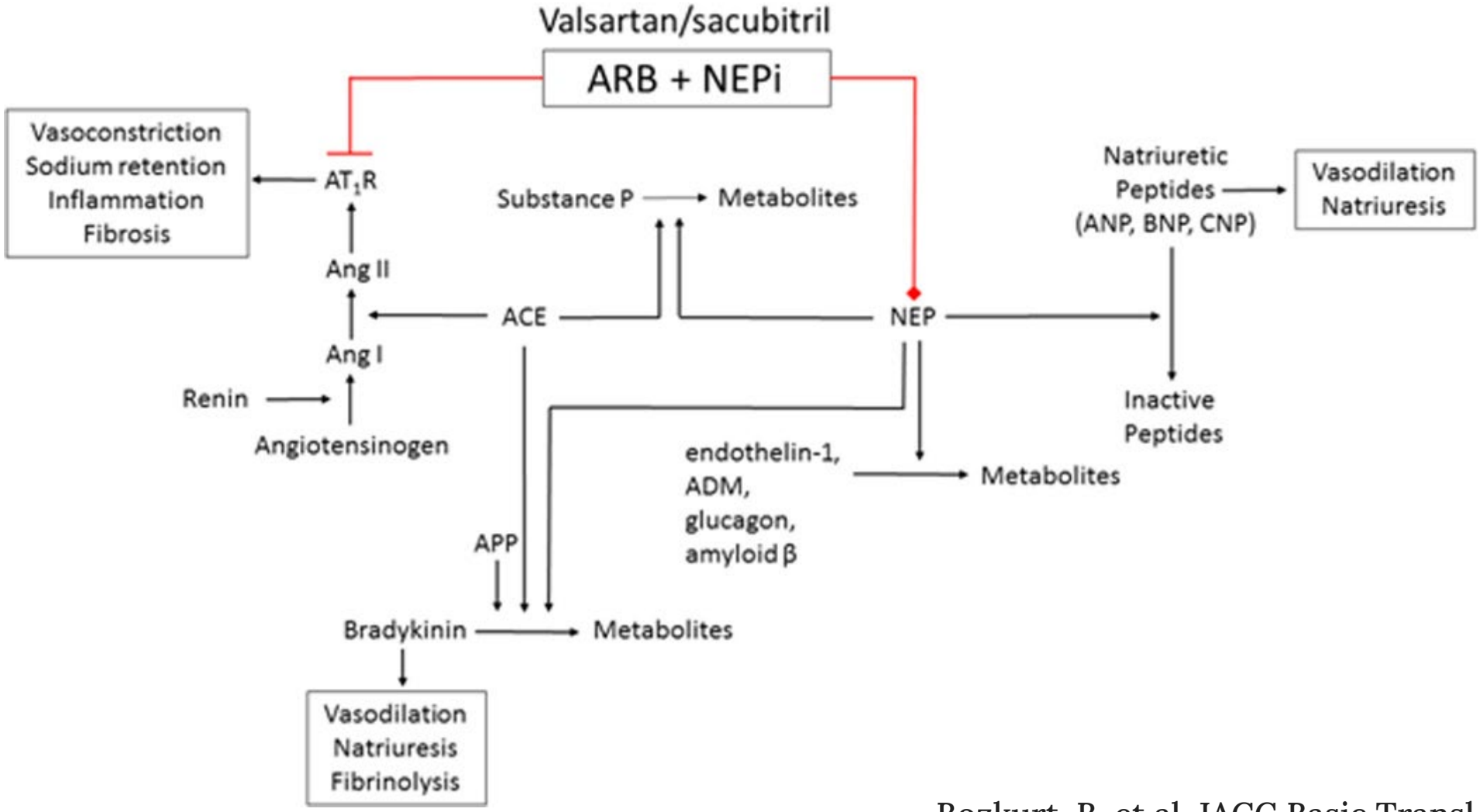
COR	LOE	Recommendation
1	A	1. In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.[1,2]
Value Statement: Intermediate Value (A)		2. In patients with symptomatic chronic HFrEF, SGLT2i therapy provides intermediate economic value.[3,4]





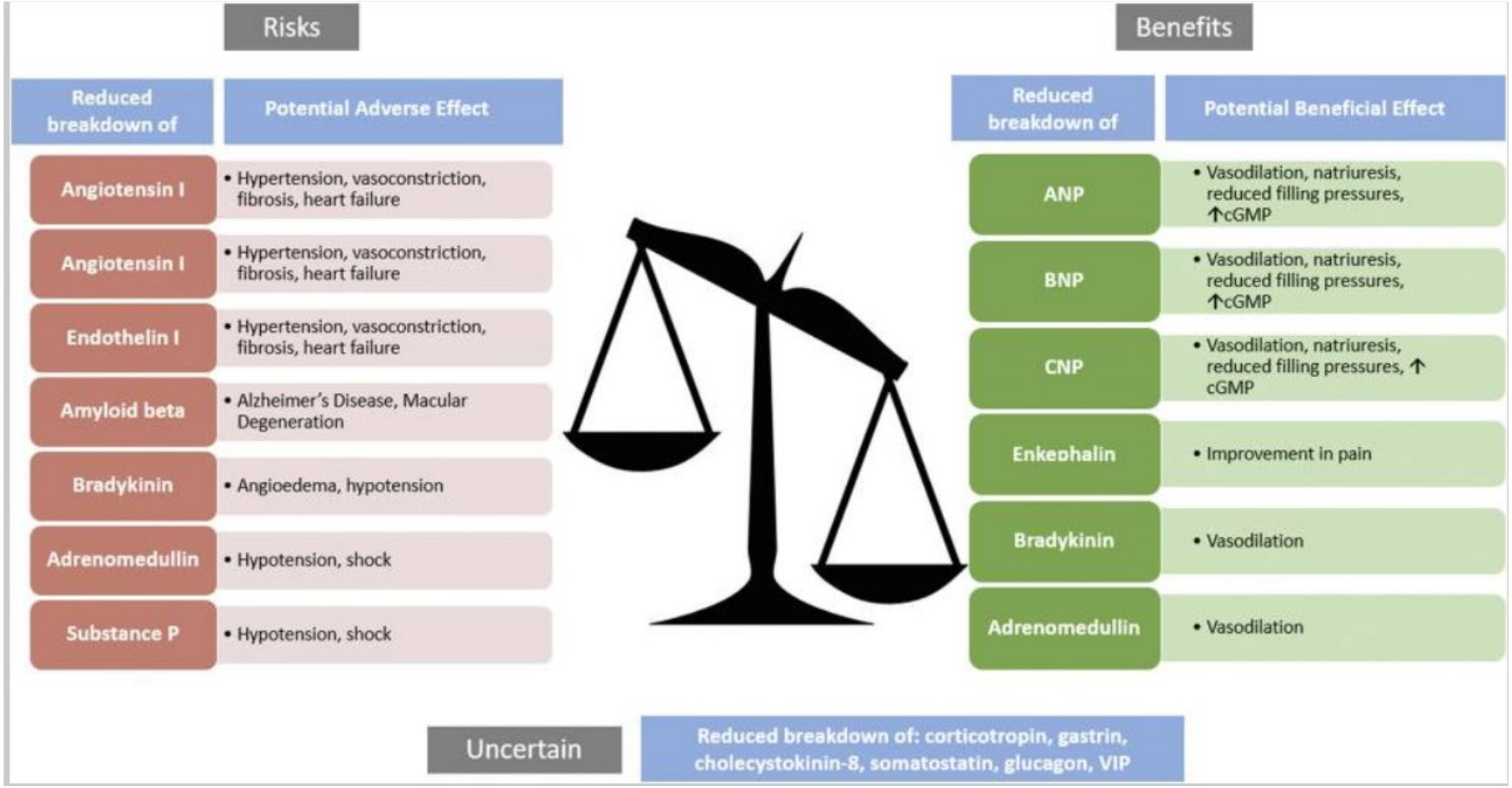
Braunwald E. Eur Heart J 2022. Zelniker TA, Braunwald E. JACC 2020. Bakris GL, et al. Kidney Int 2009. Heidenreich PA, et al. Circ 2022.

Angiotensin receptor– Neprilysin Inhibitor (ARNI)



Bozkurt, B, et al. JACC Basic Transl Sci. 2022

Neprilysin Inhibition



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Bozkurt, B, et al. JACC Basic Transl Sci. 2022

Angiotensin receptor– Neprilysin Inhibitor (ARNI)

COR	LOE	Recommendations
1	A	1. In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality.[1–5]
1	A	2. In patients with previous or current symptoms of chronic HFrEF, the use of ACEi is beneficial to reduce morbidity and mortality when the use of ARNi is not feasible.[6–13]
1	A	3. In patients with previous or current symptoms of chronic HFrEF who are intolerant to ACEi because of cough or angioedema and when the use of ARNi is not feasible, the use of ARB is recommended to reduce morbidity and mortality.[14–18]
Value Statement: High Value (A)		4. In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value.[19–25]
1	B-R	5. In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNi is recommended to further reduce morbidity and mortality.[1–5]
Value Statement: High Value (A)		6. In patients with chronic symptomatic HFrEF, treatment with an ARNi instead of an ACEi provides high economic value.[26–29]

3: Harm	**B-R**	7. ARNi should not be administered concomitantly with ACEi or within 36 hours of the last dose of an ACEi.[30,31]
3: Harm	**C-LD**	8. ARNi should not be administered to patients with any history of angioedema.[32–35]
3: Harm	**C-LD**	9. ACEi should not be administered to patients with any history of angioedema.[36–39]

**A washout period is NOT necessary transitioning from ARB to ARNI.*

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

Beta Blockers & Mineralocorticoid Receptor Antagonists

COR	LOE	Recommendation
1	A	1. In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality (eg, bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations.[1–3]
Value Statement: High Value (A)		2. In patients with HFrEF, with current or previous symptoms, beta-blocker therapy provides high economic value.[4–8]

COR	LOE	Recommendations
1	A	1. In patients with HFrEF and NYHA class II to IV symptoms, an MRA (spironolactone or eplerenone) is recommended to reduce morbidity and mortality, if eGFR is >30 mL/min/1.73 m² and serum potassium is <5.0 mEq/L. Careful monitoring of potassium, renal function, and diuretic dosing should be performed at initiation and closely monitored thereafter to minimize risk of hyperkalemia and renal insufficiency.[1–3]
Value Statement: High Value (A)		2. In patients with HFrEF and NYHA class II to IV symptoms, MRA therapy provides high economic value.[4–7]
3: Harm	**B-NR**	3. In patients taking MRA whose serum potassium cannot be maintained at <5.5 mEq/L, MRA should be discontinued to avoid life-threatening hyperkalemia.[8,9]

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

Comparative and collective benefits of GDMT

Combined use of comprehensive GDMT (ARNI, BB, MRA + SGLT2) vs prior conventional therapy (ACEI/ARB + BB) is estimated to:

- Further reduce cardiovascular mortality in HFrEF by 50%
- Improve life expectancy by 1.4 - 6.3 years
- Afford 2.7 - 8.3 additional years free from cardiovascular death or HF hospitalization.

Table 15. Benefits of Evidence-Based Therapies for Patients With HFrEF[3–6,8,10–14,23,31–42]

Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal RCTs, %	NNT to Prevent All-Cause Mortality Over Time*	NNT for All-Cause Mortality (Standardized to 12 mo)	NNT for All-Cause Mortality (Standardized to 36 mo)
ACEi or ARB	17	22 over 42 mo	77	26
ARNi†	16	36 over 27 mo	80	27
Beta blocker	34	28 over 12 mo	28	9
Mineralocorticoid receptor antagonist	30	9 over 24 mo	18	6
SGLT2i	17	43 over 18 mo	63	22
Hydralazine or nitrate‡	43	25 over 10 mo	21	7
CRT	36	12 over 24 mo	24	8
ICD	23	14 over 60 mo	70	23

Vaduganathan M, et al. Lancet 2020.

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

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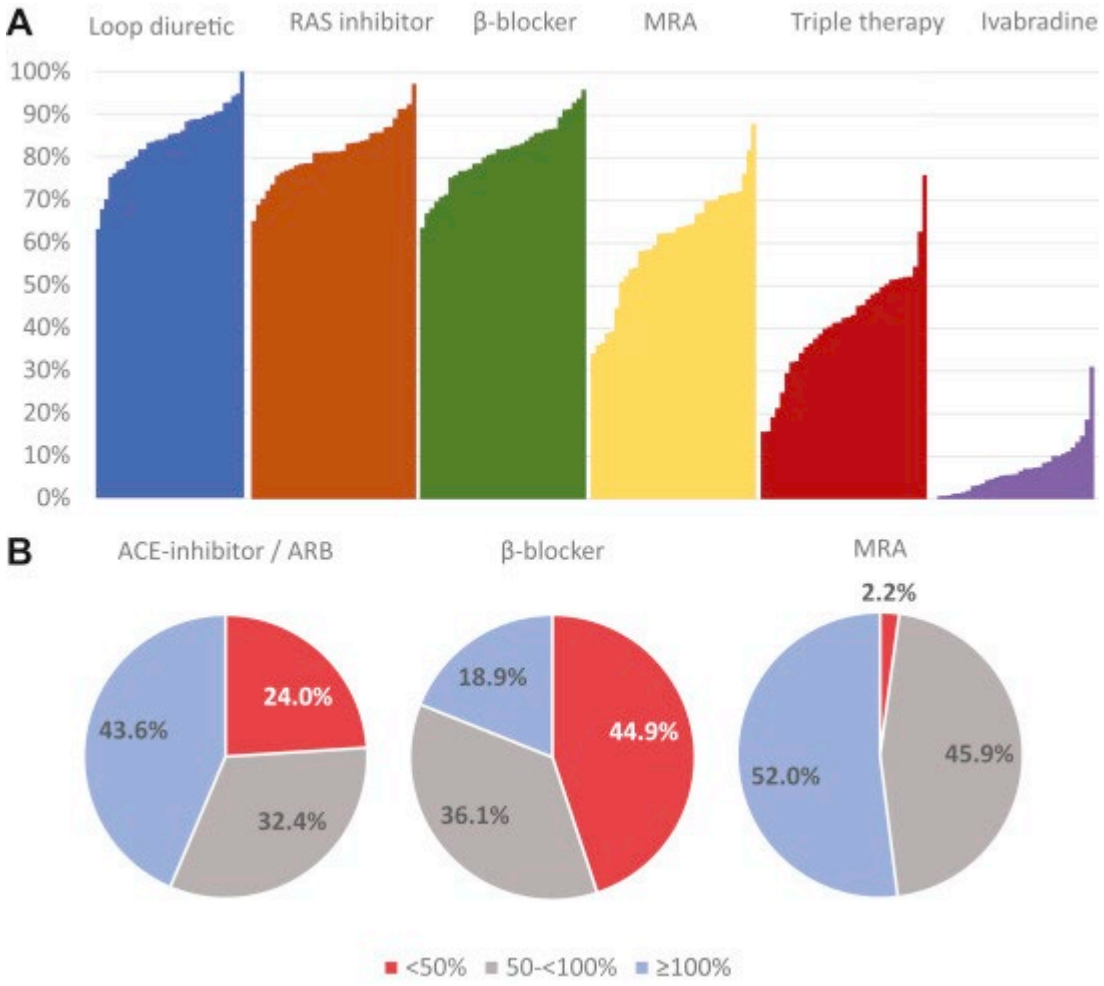
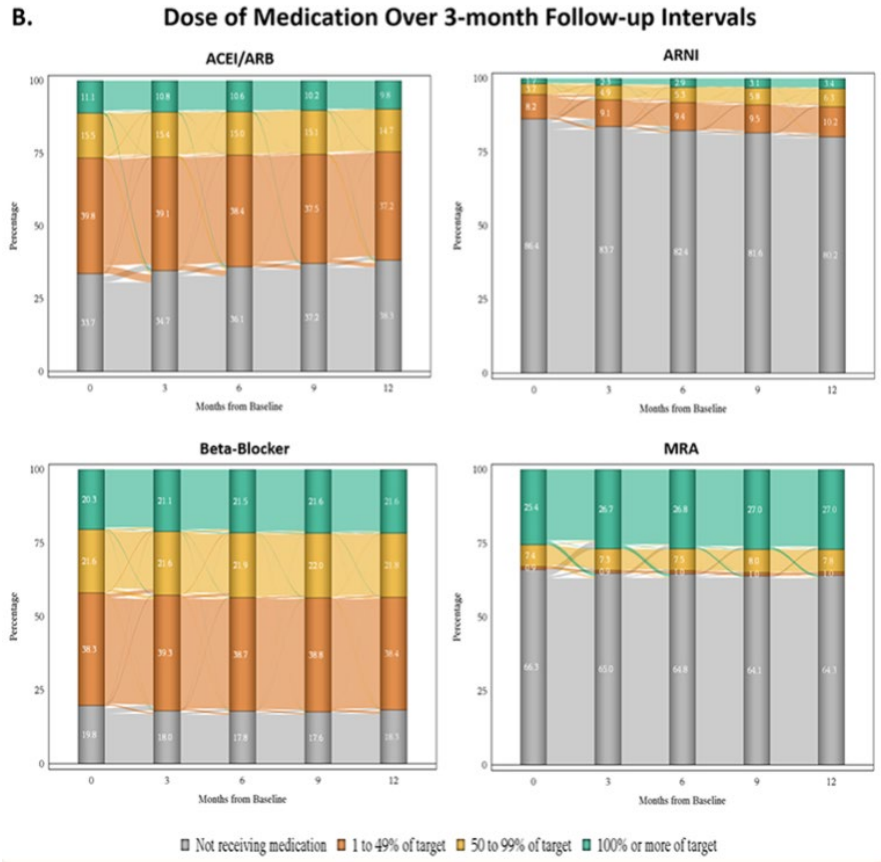
Implementation of GDMT



We are not doing it.

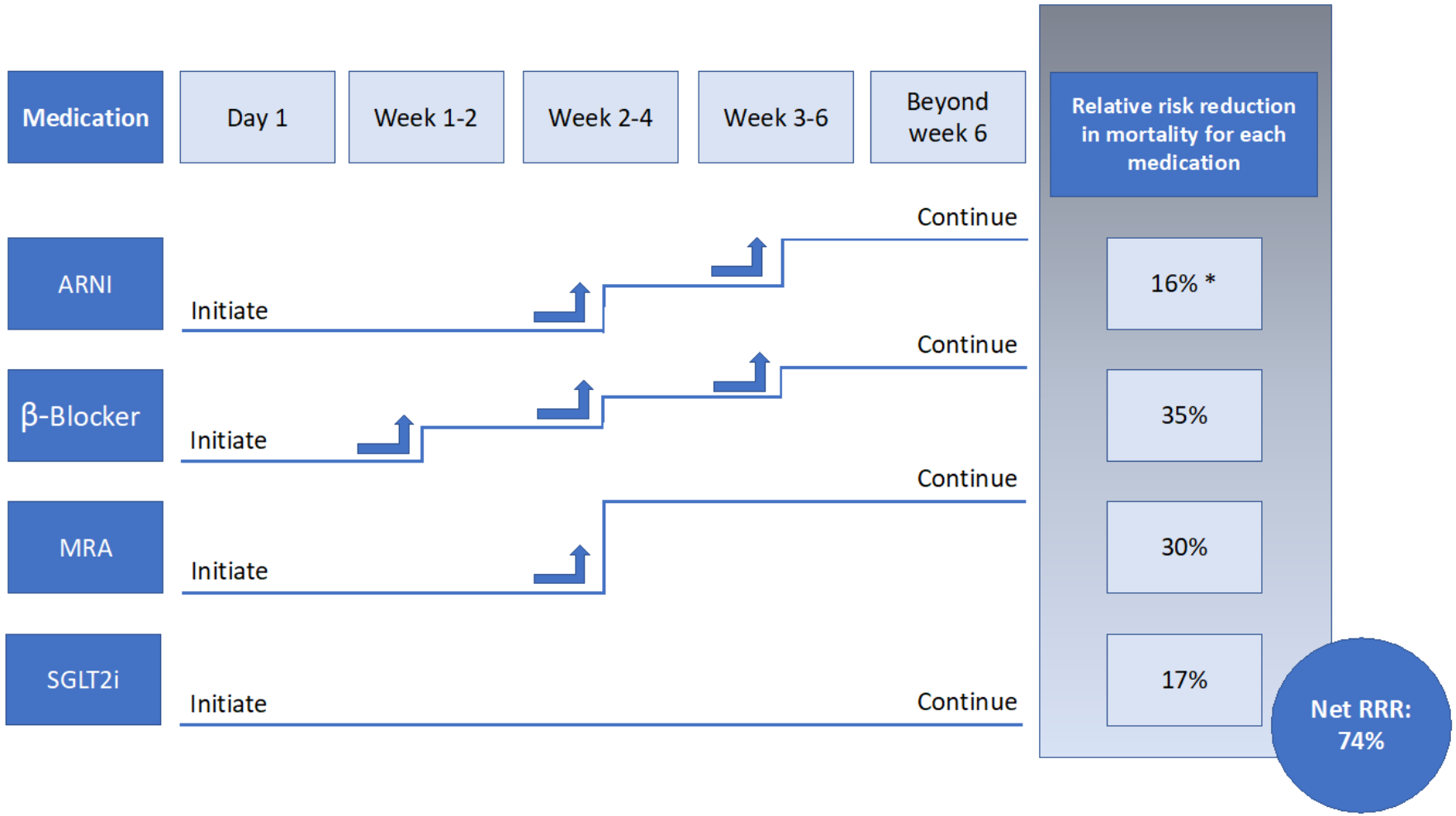
Most eligible HFrEF patients do not receive target doses of even one agent!

- Class 1, LOE A to achieve target doses from RCT
- Class 2a LOE C-EO Titration and optimization q1-2 weeks



Brunner-La Rocca H-P, et al. JACC Heart Fail 2019.

Simultaneous Vs Sequential Initiation of HFrEF Therapies



Brownell, NB et al. ACC.org. [Simultaneous Versus Sequential Initiation of HFrEF Therapies - American College of Cardiology (acc.org)]

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A salty topic: dietary sodium

Restricting is a common nonpharmacological treatment for patients with HF symptomatic with congestion

Specific recommendations have been based on low-quality evidence with unclear benefit and some concern for harm

The AHA currently recommends a reduction of sodium intake to <2300 mg/d for general cardiovascular health promotion·

COR	LOE	Recommendation
2a	C-LD	1. For patients with stage C HF, avoiding excessive sodium intake is reasonable to reduce congestive symptoms.[1–6]

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

Sequential Nephron Blockade

The treatment goal of diuretic use is to eliminate clinical evidence of fluid retention, using the lowest dose possible to maintain euvolemia.

- With the exception of MRAs, the effects of diuretics on morbidity and mortality are uncertain.
- Maximize GDMT first, including SGLT2 and MRA

Hyponatremia complicates HF management.

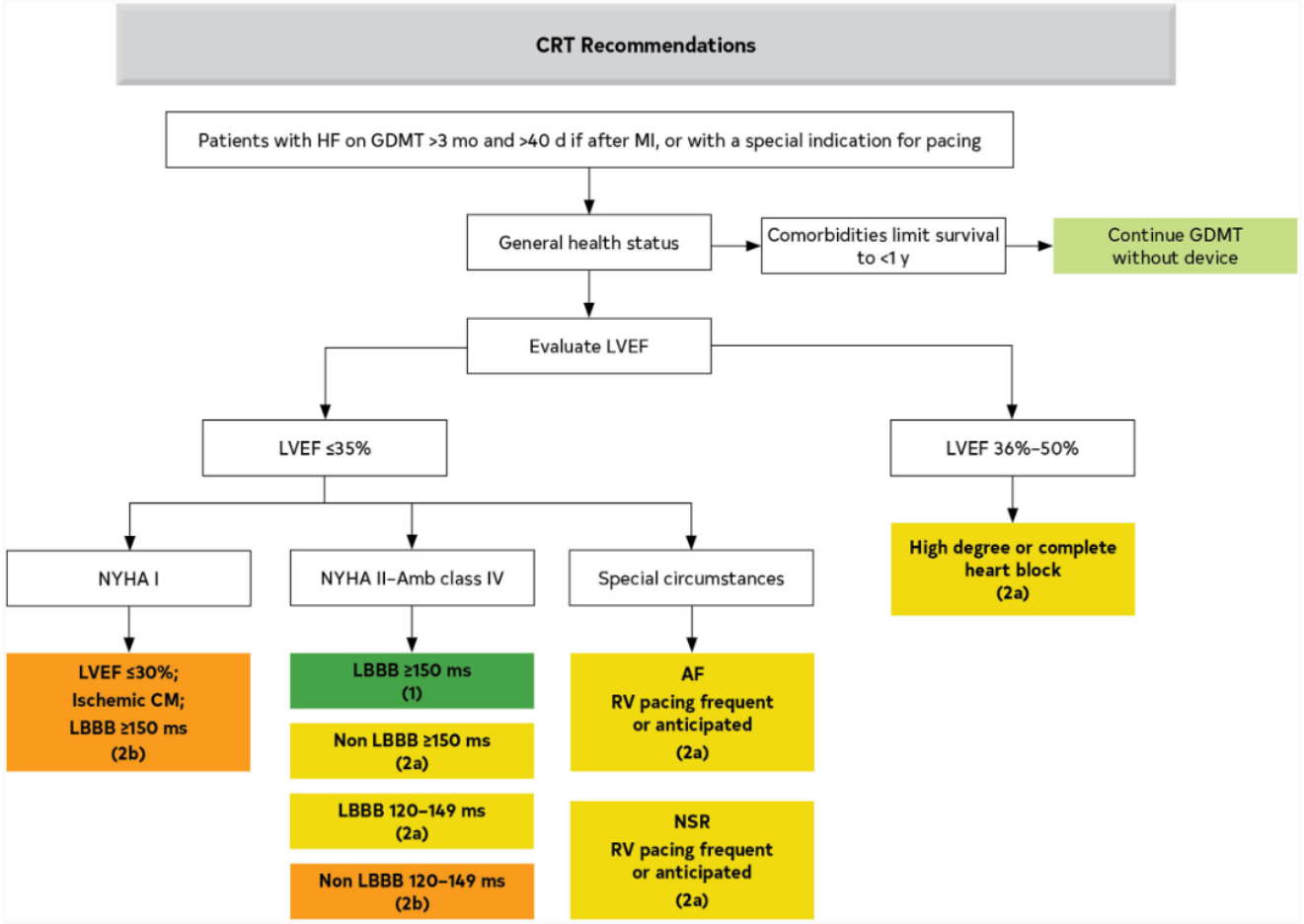
- If reversing potential causes and free water restriction do not improve hyponatremia, vasopressin antagonists may be helpful in the acute management of volume overload to decrease congestion while maintaining serum sodium

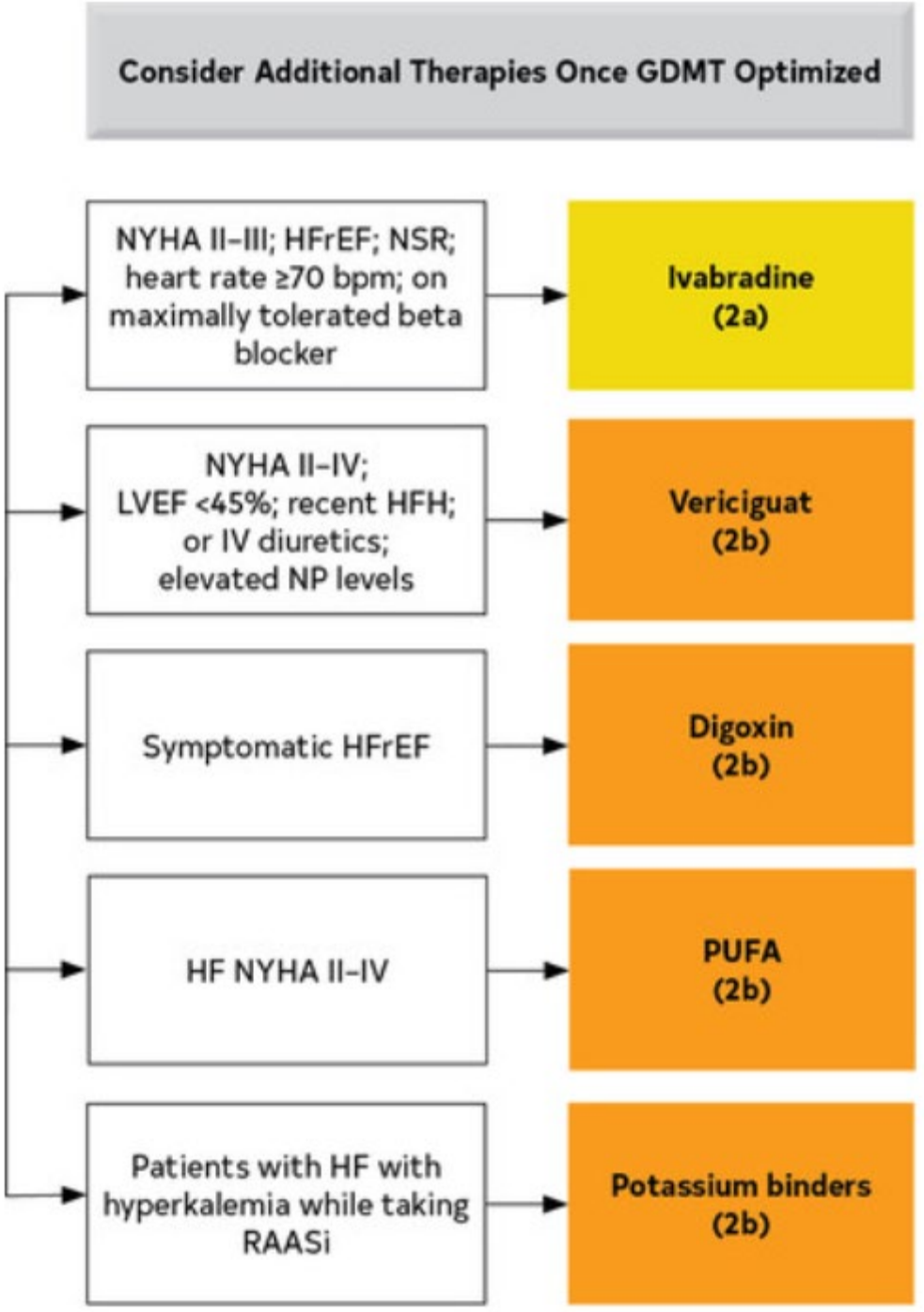
COR	LOE	Recommendations
1	B-NR	1. In patients with HF who have fluid retention, diuretics are recommended to relieve congestion, improve symptoms, and prevent worsening HF.[1–5]
1	B-NR	2. For patients with HF and congestive symptoms, addition of a thiazide (eg, metolazone) to treatment with a loop diuretic should be reserved for patients who do not respond to moderate- or high-dose loop diuretics to minimize electrolyte abnormalities.[6]

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

Additional GDMT

After maximizing the four pillars of comprehensive GDMT, there are additional therapies for patients with HFrEF





Recommendations for Nonpharmacological Interventions

Refer to heart failure teams

Utilize trained multidisciplinary staff

- Dieticians
- Social workers
- PT, OT and SLP
- Home health
- Pharmacists

Vaccination for respiratory illnesses

COR	LOE	Recommendations
1	A	1. Patients with HF should receive care from multidisciplinary teams to facilitate the implementation of GDMT, address potential barriers to self-care, reduce the risk of subsequent rehospitalization for HF, and improve survival.[1–4]
1	B-R	2. Patients with HF should receive specific education and support to facilitate HF self-care in a multidisciplinary manner.[2,5–9]
2a	B-NR	3. In patients with HF, vaccinating against respiratory illnesses is reasonable to reduce mortality.[10–16]
2a	B-NR	4. In adults with HF, screening for depression,[17,18] social isolation,[19–22] frailty,[23,24] and low health literacy[25,26] as risk factors for poor self-care is reasonable to improve management.

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

HFrEF: What **NOT** to do

Avoid:

- Calcium channel blockers – nondihydropyridine
- Thiazolidinediones
- DPP-4 inhibitors saxagliptin + alogliptin
- NSAIDS
- Doxazosin
- Class IC antiarrhythmics (Propafenone, flecainide) and dronedarone

Unclear benefit:

- Calcium channel blockers - dihydropyridine
- Vitamins, supplements, hormonal therapy unless there is a specific deficiency

COR	LOE	Recommendations
3: No Benefit	A	1. In patients with HFrEF, dihydropyridine calcium channel-blocking drugs are not recommended treatment for HF.[1,2]
3: No Benefit	B-R	2. In patients with HFrEF, vitamins, nutritional supplements, and hormonal therapy are not recommended other than to correct specific deficiencies.[3–9]
3: Harm	A	3. In patients with HFrEF, nondihydropyridine calcium channel-blocking drugs are not recommended.[10–13]
3: Harm	A	4. In patients with HFrEF, class IC antiarrhythmic medications and dronedarone may increase the risk of mortality.[14–16]
3: Harm	A	5. In patients with HFrEF, thiazolidinediones increase the risk of worsening HF symptoms and hospitalizations.[17–21]
3: Harm	B-R	6. In patients with type 2 diabetes and high cardiovascular risk, the dipeptidyl peptidase-4 (DPP-4) inhibitors saxagliptin and alogliptin increase the risk of HF hospitalization and should be avoided in patients with HF.[22–24]
3: Harm	B-NR	7. In patients with HFrEF, NSAIDs worsen HF symptoms and should be avoided or withdrawn whenever possible.[25–28]

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circ. 2022.

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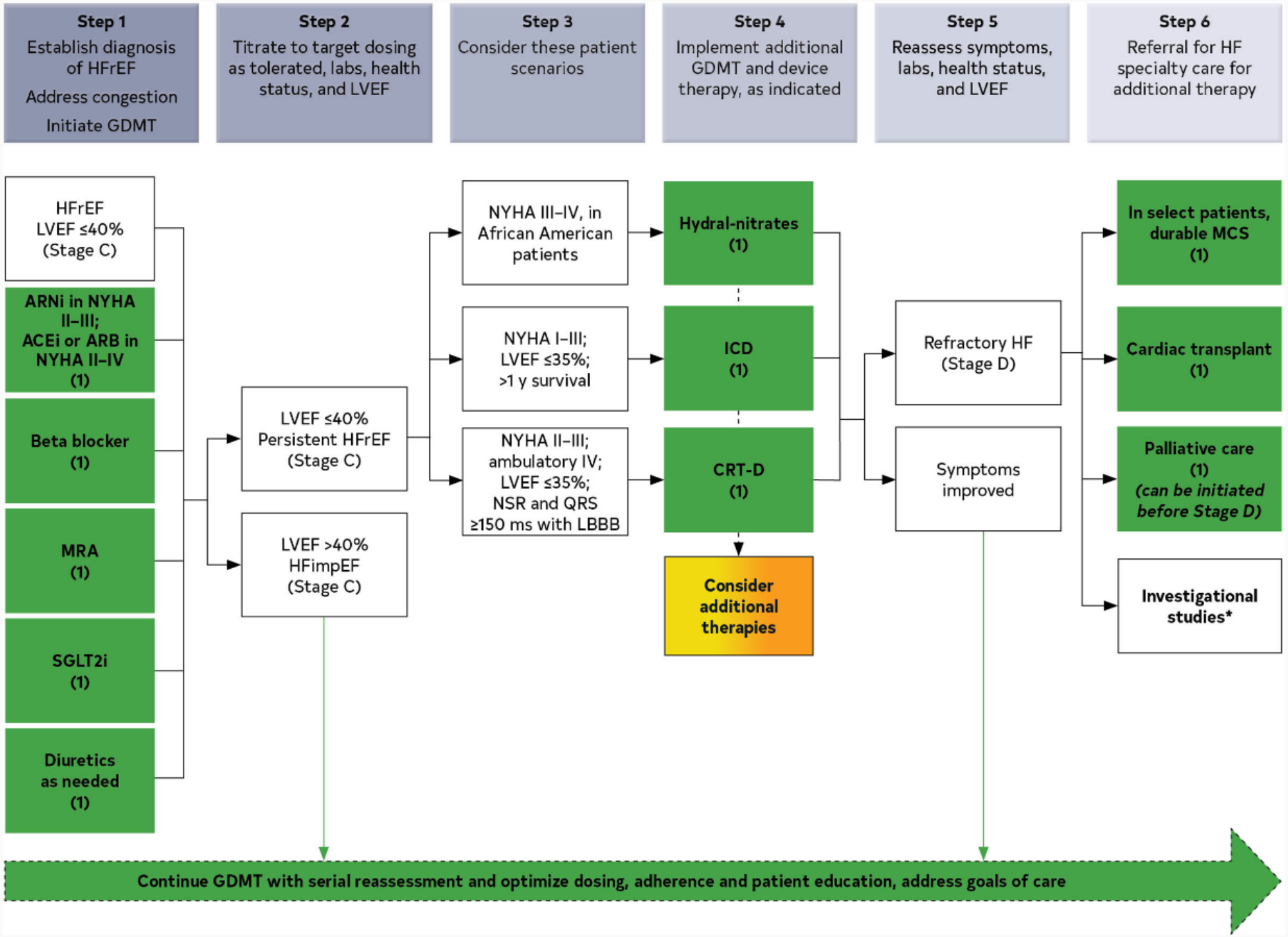

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

GDMT: HF with mildly reduced ejection fraction (HFmrEF)

In general, we apply HFREF principles with weaker class of recommendations (COR) based on limited evidence:

- SGLT2i: 2a
- ARNi, ACEi, ARB, MRA, and BB: 2b

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Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

GDMT: HFPEF – We have recommendations!

SGLT2i: Class of Recommendation 2a

MRAs: Class of Recommendation 2b

ARNi or ARB: Class of Recommendation 2b

Avoidance of routine use of nitrates or phosphodiesterase-5 inhibitors:
Class of Recommendation 3: No Benefit

Treatment of hypertension: Class of Recommendation 1

Treatment of atrial fibrillation: Class of Recommendation 2a

Future directions for GDMT for HF?

- Finerenone
  - FIGARO-DKD trial
- Anti-inflammatory therapy
  - Colchicine
  - IL-6 inhibition
- Device therapies
  - Vagus nerve modulation
  - Calcium modulation
  - Percutaneous valve interventions
  - Percutaneous ventricular interventions

Updates on Cardiac Amyloidosis and Hypertrophic Cardiomyopathy

Etiology matters

Certain conditions that cause HF require disease-specific therapies.

Expeditious and accurate diagnosis of such conditions is important. Examples include:

- Ischemic heart disease
- Amyloidosis, sarcoidosis, hypertrophic CMY
- Hypothyroidism, hyperthyroidism
- Connective tissue disease, hemochromatosis
- Tachycardia-induced cardiomyopathy, alcohol heart disease, or high-output HF from an arteriovenous fistula

Maintaining up to date noncardiac medical history and a family history is relevant

COR	LOE	Recommendations
1	B-NR	1. For patients presenting with HF, the specific cause of HF should be explored using additional laboratory testing for appropriate management.[1–8]
1	C-EO	2. For patients who are diagnosed with HF, laboratory evaluation should include complete blood count, urinalysis, serum electrolytes, blood urea nitrogen, serum creatinine, glucose, lipid profile, liver function tests, iron studies, and thyroid-stimulating hormone to optimize management.
1	C-EO	3. For all patients presenting with HF, a 12-lead ECG should be performed at the initial encounter to optimize management.

Heidenreich PA, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. Circulation. 2022.

Question 3

What is the mechanism of action for recently approved targeted therapy for hypertrophic cardiomyopathy?

- Inhibition of cardiac myosin ATPase
- Stimulation of catalytic S1 domain of cardiac myosin
- Myocardial sodium (f) channel blockade
- Prevention of dissociation and monomer misfolding of TTR

Question 3

What is the mechanism of action for recently approved targeted therapy for hypertrophic cardiomyopathy?

- Inhibition of cardiac myosin ATPase:
  Mavacamten / Camzyos is approved for oHCM

- Stimulation of catalytic S1 domain of cardiac myosin
  Omecamtiv mecarbil is in trials for HFrEF

- Myocardial sodium (f) channel blockade
  Ivabridine / Corlanor is approved for HFrEF

- Prevention of dissociation and monomer misfolding of TTR
  Tafamidis / Vyndaquel/Vyndamax for ATTR cardiac amyloidosis

Hypertrophic Cardiomyopathy

Optimal care for patients with HCM

- Accurate diagnosis
- Risk stratification for sudden cardiac death (SCD), syncope, outflow tract obstruction, and arrythmias
- Co-morbidity management: heart failure, atrial fibrillation, chest pain
- Family counseling

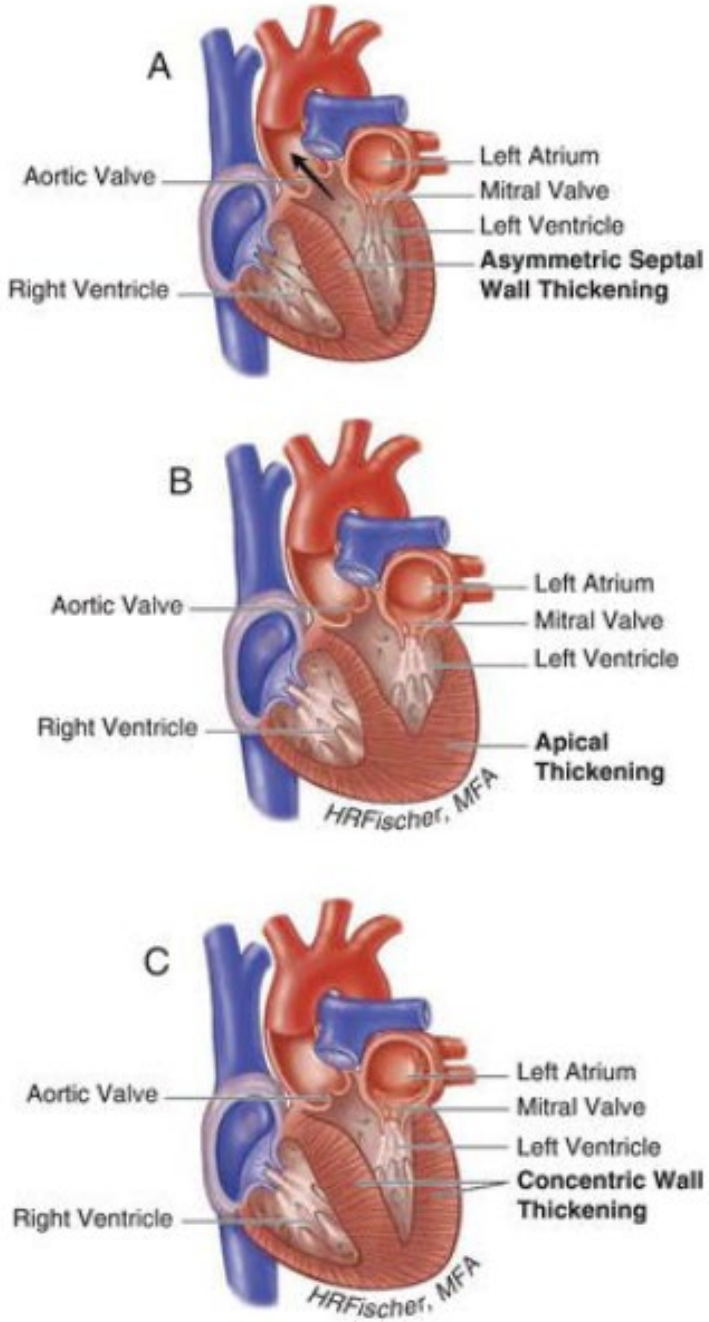
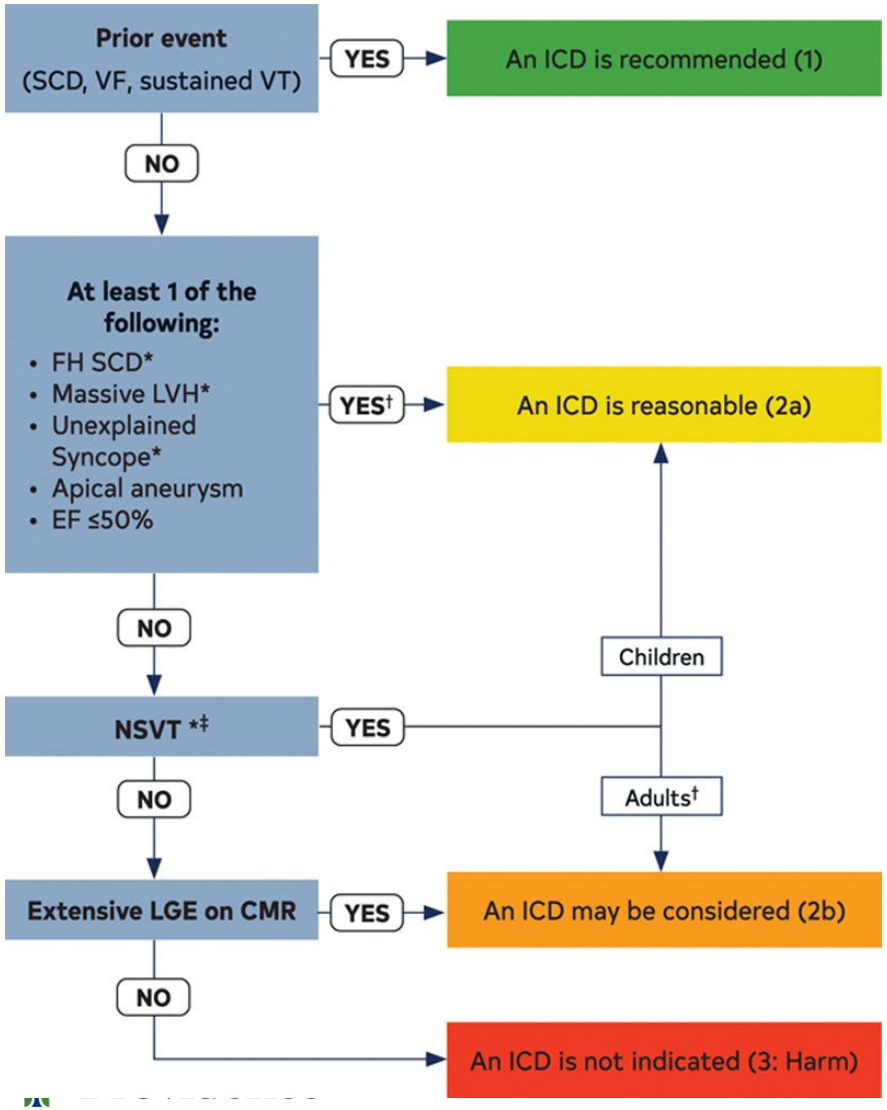


Image credit: https://thoracickey.com/hypertrophic-cardiomyopathy-10/

Hypertrophic Cardiomyopathy & Sudden Cardiac Death



AHA HCM SCD Calculator

Hypertrophic Cardiomyopathy - Sudden Cardiac Death Risk Calculator

Age
16-80 years

MLVWT
10-35 mm

LA Size
28-67 mm

Max LVOT Gradient
2-154 mmHg

FH SCD	No	Yes
NSVT	No	Yes
Unexplained Syncope	No	Yes
EF ≤ 50%	No	Yes
Apical Aneurysm	No	Yes
Extensive LGE	No	Yes

Risk of SCD at 5 years(%)

Recommendation

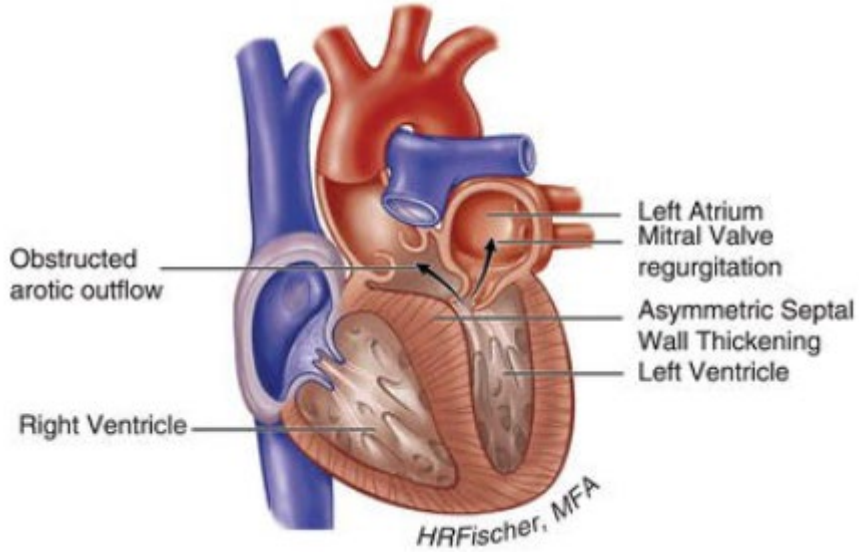
Hypertrophic Cardiomyopathy LV outflow tract obstruction

Treatment of symptomatic peak resting or provoked doppler LV outflow tract (LVOT) gradient consists of:

- Avoiding dehydration, excess alcohol, obesity
- Avoiding arterial and venous dilators (nitrates, PDE5i)
- Rate or rhythm control for AF
- Beta blockade and/or Calcium channel blockers

Mavacamten is a novel first-in-class targeted inhibitor of cardiac myosin

- Shown to reduce LV outflow tract obstruction
- Improve exercise capacity
- Relieve symptoms of oHCM in PIONEER-HCM phase 2 study and EXPORER-HCM trial
- Reduce the need for septal reduction therapy based on Phase III VALOR-HCM clinical study



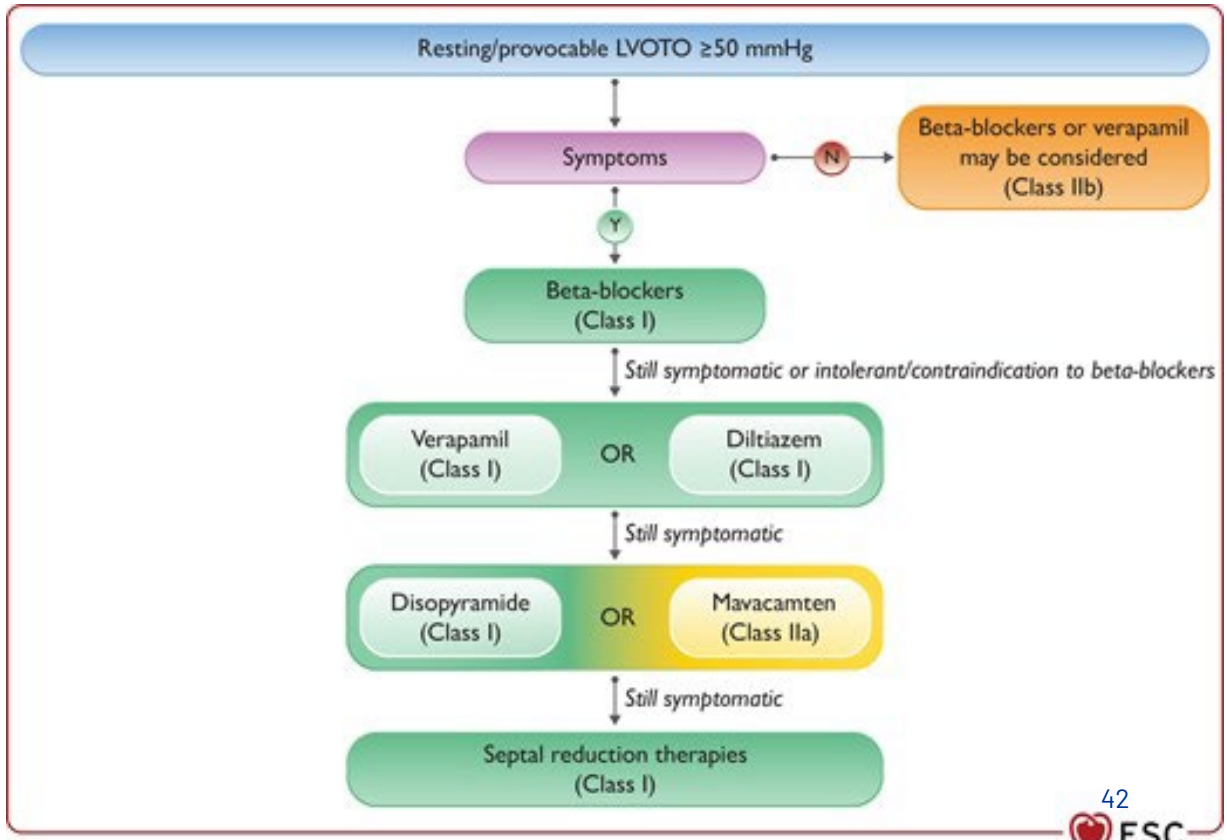


Image credit: https://thoracickey.com/hypertrophic-cardiomyopathy-10/

Reference:

Question 4

Which of the following is NOT a classic symptom of cardiac amyloidosis?

1. History of bilateral carpal tunnel surgery 7-10 years prior
2. Rate controlled atrial fibrillation
3. Painful numbness and tingling in the feet
4. Escalating antihypertensive needs
5. Irritable bowel syndrome

Question 4 Answer

Which of the following is NOT a classic symptom of cardiac amyloidosis?

1. History of bilateral carpal tunnel surgery 7-10 years prior
2. Rate controlled atrial fibrillation
3. Painful numbness and tingling in the feet
4. Escalating antihypertensive needs
5. Irritable bowel syndrome

Patients with cardiac amyloid often develop “improved blood pressure control” out of proportion to lifestyle.

The remainder of the options are all classic signs or symptoms of cardiac amyloidosis.

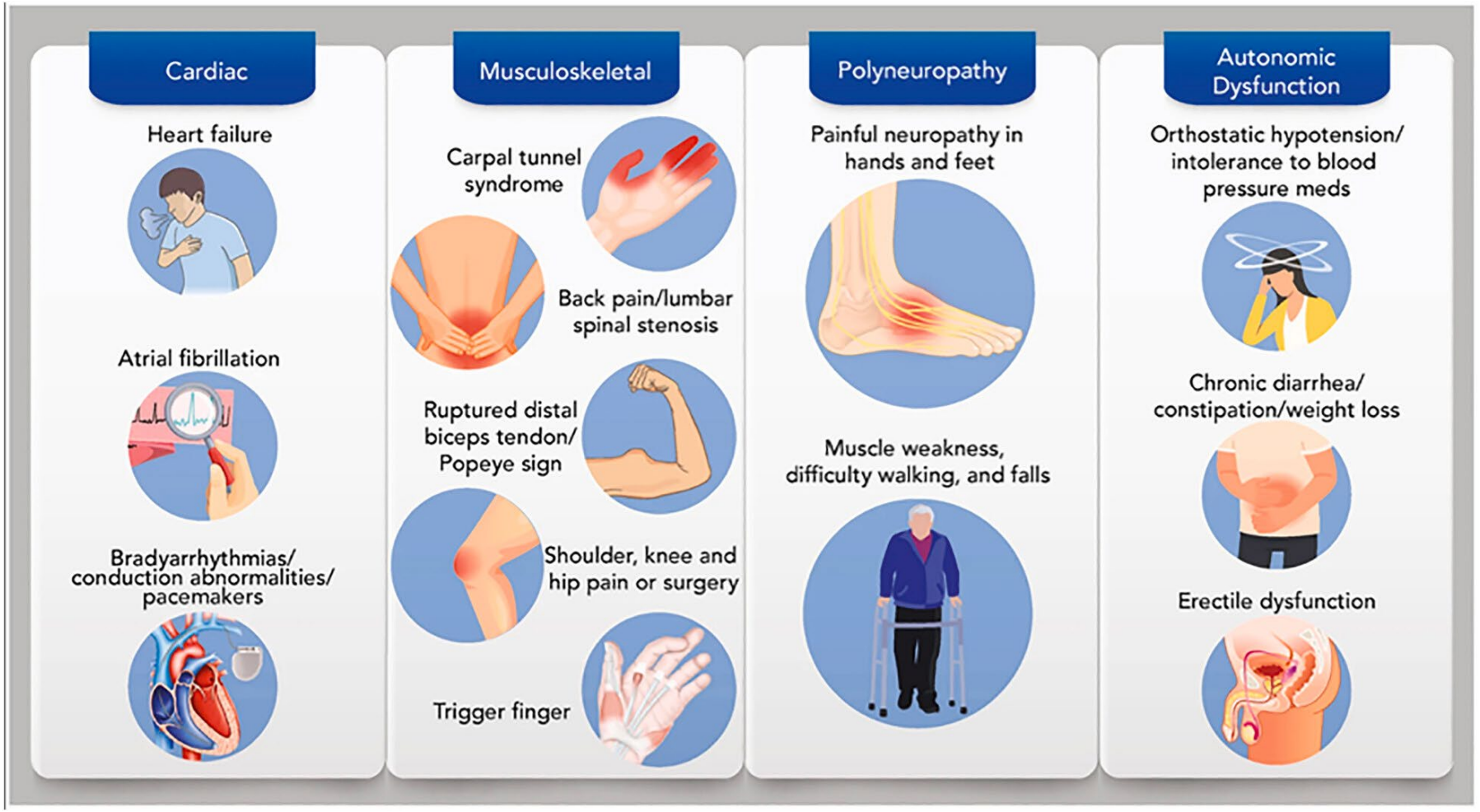
Cardiac Amyloidosis

Restrictive cardiomyopathy

- Extracellular myocardial protein deposition

Previously believed to be rare

- ~10-15% patients presenting for TAVR or new HF at 65/70+yrs
- ~25% patients 80+ years had cardiac amyloid deposition on autopsy



Adapted from Nativi-Nicolau et al for Kittleson MM, et al. JACC 2023

Cardiac Amyloidosis

Screening is easier than ever

- Serum and urine monoclonal protein electrophoresis and IFE
- Serum free light chains
- Bone scintigraphy (eg PYP)

Kittleson MM, et al. JACC 2023

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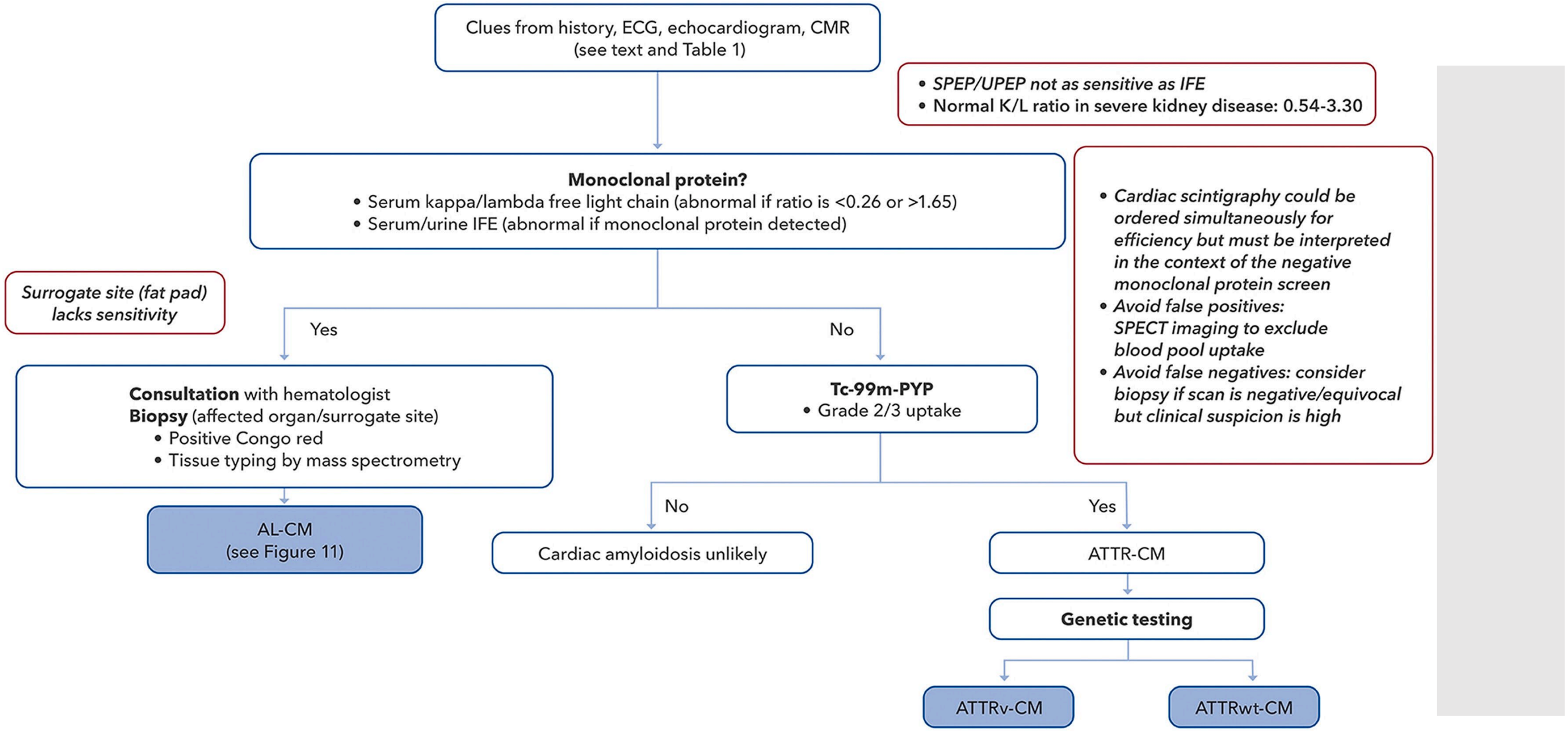
Recommendations for Diagnosis of Cardiac Amyloidosis

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

COR	LOE	Recommendations
1	B-NR	1. Patients for whom there is a clinical suspicion for cardiac amyloidosis*[1-5] should have screening for serum and urine monoclonal light chains with serum and urine immunofixation electrophoresis and serum free light chains.[6]
1	B-NR	2. In patients with high clinical suspicion for cardiac amyloidosis, without evidence of serum or urine monoclonal light chains, bone scintigraphy should be performed to confirm the presence of transthyretin cardiac amyloidosis.[7]
1	B-NR	3. In patients for whom a diagnosis of transthyretin cardiac amyloidosis is made, genetic testing with *TTR* gene sequencing is recommended to differentiate hereditary variant from wild-type transthyretin cardiac amyloidosis.[8]

*LV wall thickness ≥14 mm in conjunction with fatigue, dyspnea, or edema, especially in the context of discordance between wall thickness on echocardiogram and QRS voltage on ECG, and in the context of aortic stenosis, HFpEF, carpal tunnel syndrome, spinal stenosis, and autonomic or sensory polyneuropathy.

Cardiac Amyloidosis



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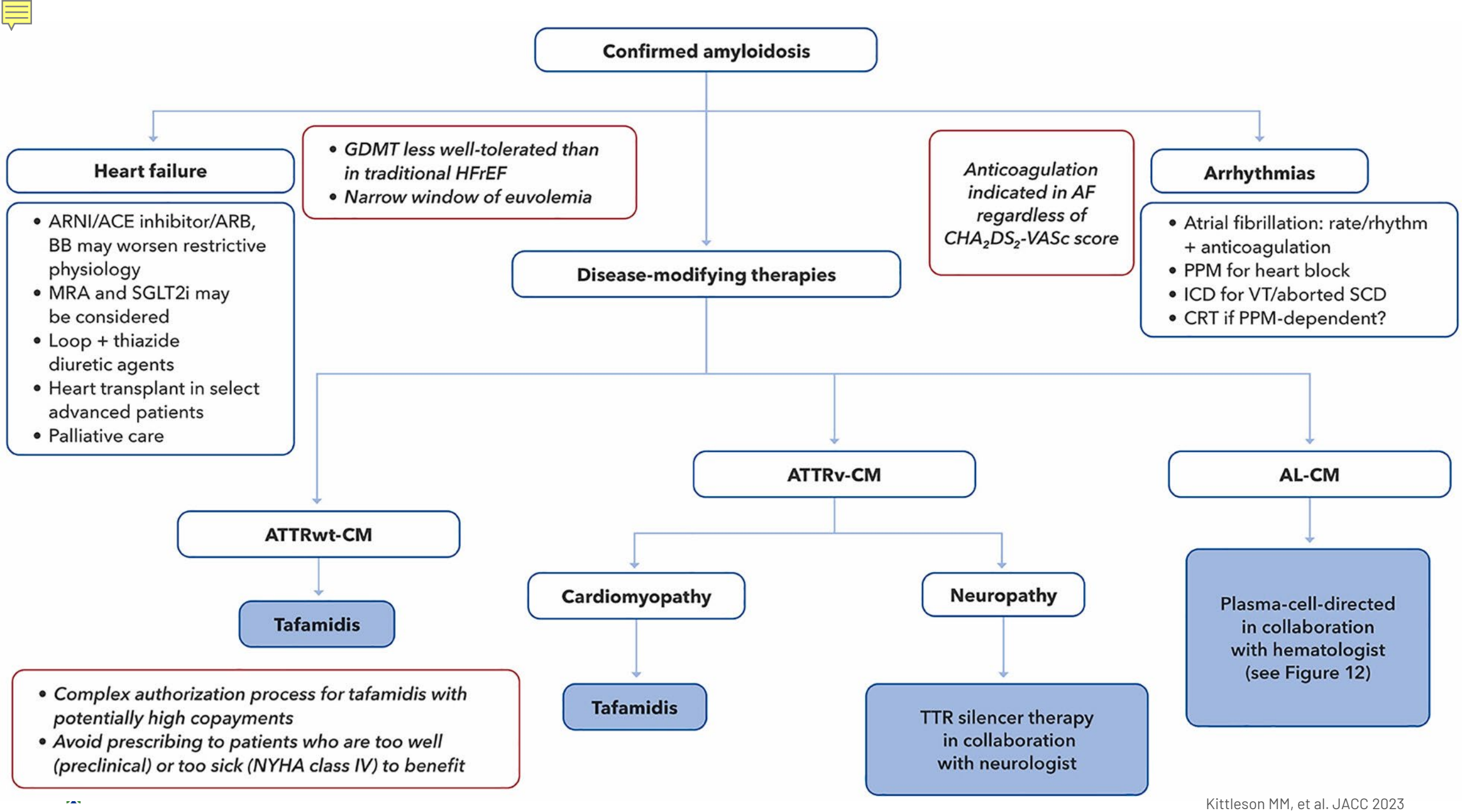

Kittleson MM, et al. JACC 2023

Amyloid Nephropathy

Proteinuria
Reduced GFR
Anasarca

Amyloid Cardiomyopathy

Restrictive cardiomyopathy
Atrial and ventricular arrhythmias
Conduction disturbances

Amyloid Autonomic Neuropathy

Orthostatic hypotension
Diarrhea
Altered heart rate variability

- *Nephrotic syndrome is common in AL but rare in ATTR disease*
- *Due to reduced muscle mass, serum creatinine may overestimate eGFR; Cystatin C-based estimating equations or measurement of creatinine clearance are alternatives*

- Decreased cardiac output
- Venous hypertension
- Decreased effective circulatory volume
- RAAS and SNS activation, reduced nitric oxide
- Low GFR, acute kidney injury
- Sodium and water retention
- Diuretic resistance or intolerance

Diuretic agents to treat anasarca may be poorly tolerated due to autonomic dysfunction and restrictive physiology

Management Strategies

- Amyloid disease-modifying therapies
- Sodium restriction
- Diuretics
- Albumin infusions
- Compression stockings
- Dialysis
- Kidney transplantation

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Kittleson MM, et al. JACC 2023

Our Objectives

1. Review updated definitions of key terms in heart failure management
    - Stage A-D Heart failure
    - HFrEF, HFimpEF, HFmrEF, HFpEF
2. Review four pillars of comprehensive guideline directed medical therapy for heart failure
    - ARNIs - class I for initiation for HFrEF (over ACE/ARB)
    - SGLT2s – class I indication for HFrEF
    - Start early and uptitrate
3. Discuss updates in management of hypertrophic cardiomyopathy and cardiac amyloidosis
    - Screen for amyloid - especially new HF diagnosis in older patients!
    - PYP scan, SPEP/SIFE, UPEP/UIFE, SFLC
    - Refer patients with HCM to HF specialists – but don't promise specific therapies

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Thank you for your time and attention reviewing Heart Failure Updates for 2023

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