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Hypertensive Heart Disease and HFpEF

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Outline

- Definitions
- Cardiac Manifestations
- Hypertension prevalence
- HFpEF

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Hypertensive Heart Disease

~~Hypertrophic cardiomyopathy due to non-hypertensive disease~~

Cardiac manifestations of hypertension

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Hypertensive Heart Disease

- HHD refers to the cardiac manifestations of chronic uncontrolled hypertension
- Initially affects the left ventricle (heart failure), left atrium (atrial arrhythmias) and coronary arteries (CAD)
- Mechanical stress from elevated BP, neurohormones, growth factors, and cytokines

Drazner, MH. *Circ 2011;123:327-334*

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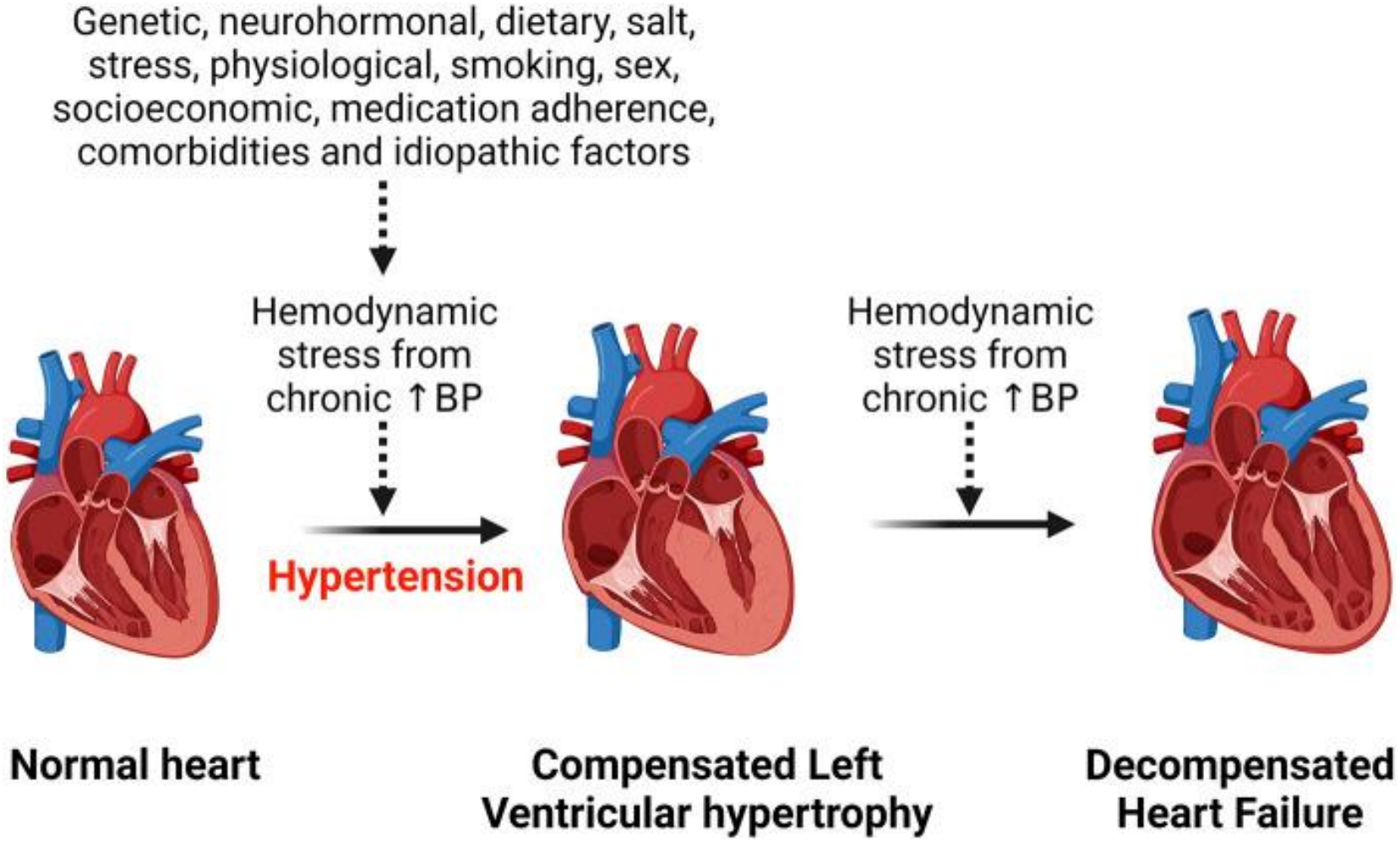
Pathophysiology and Risk Factors



- Hypertension
- Age
- Race
- Obesity
- Smoking
- EtOH intake
- High salt diet
- Diabetes
- Genetics

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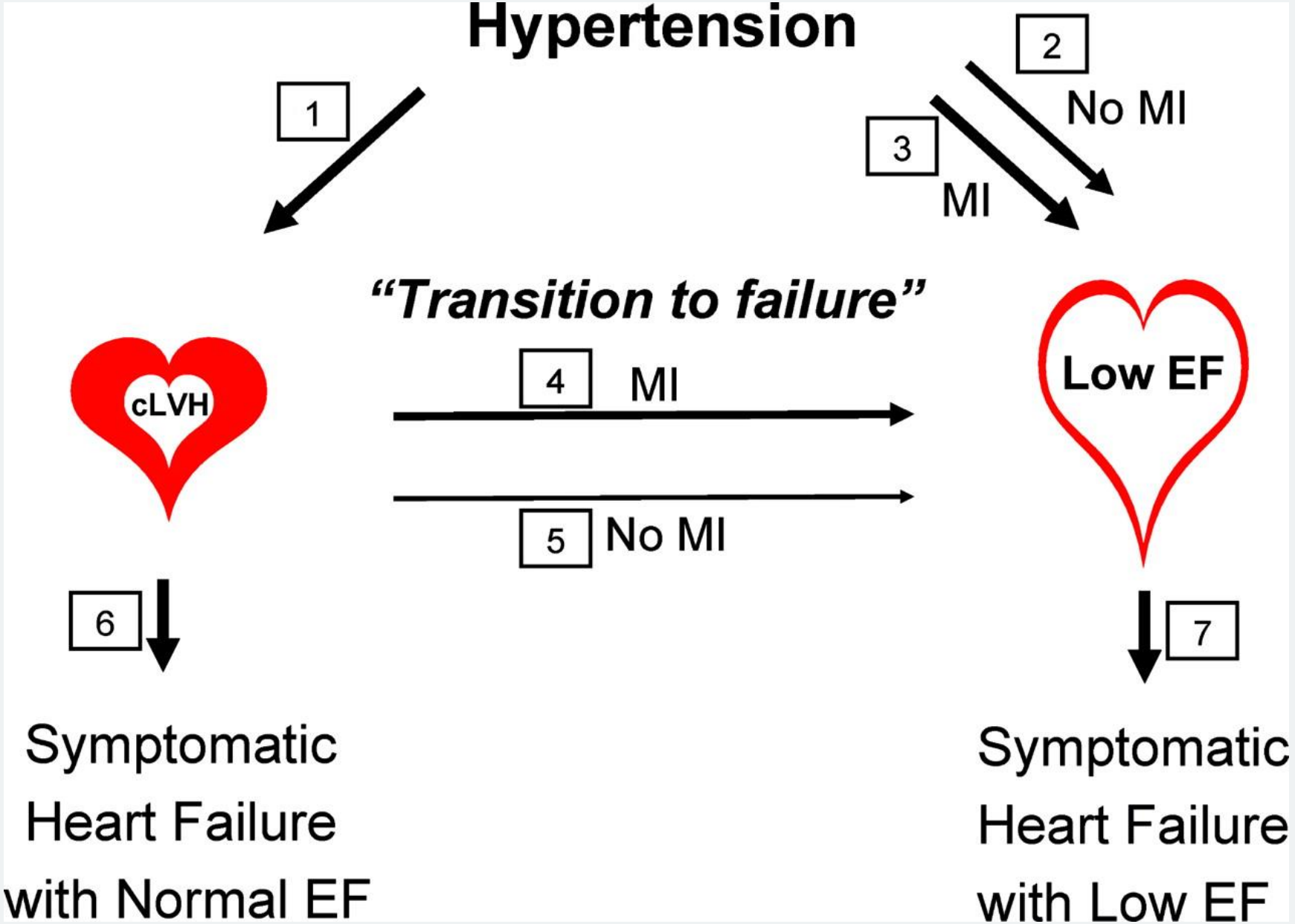
Masenga SK, Kirabo A. *Front Cardiovasc Med* 2023;10:1205475



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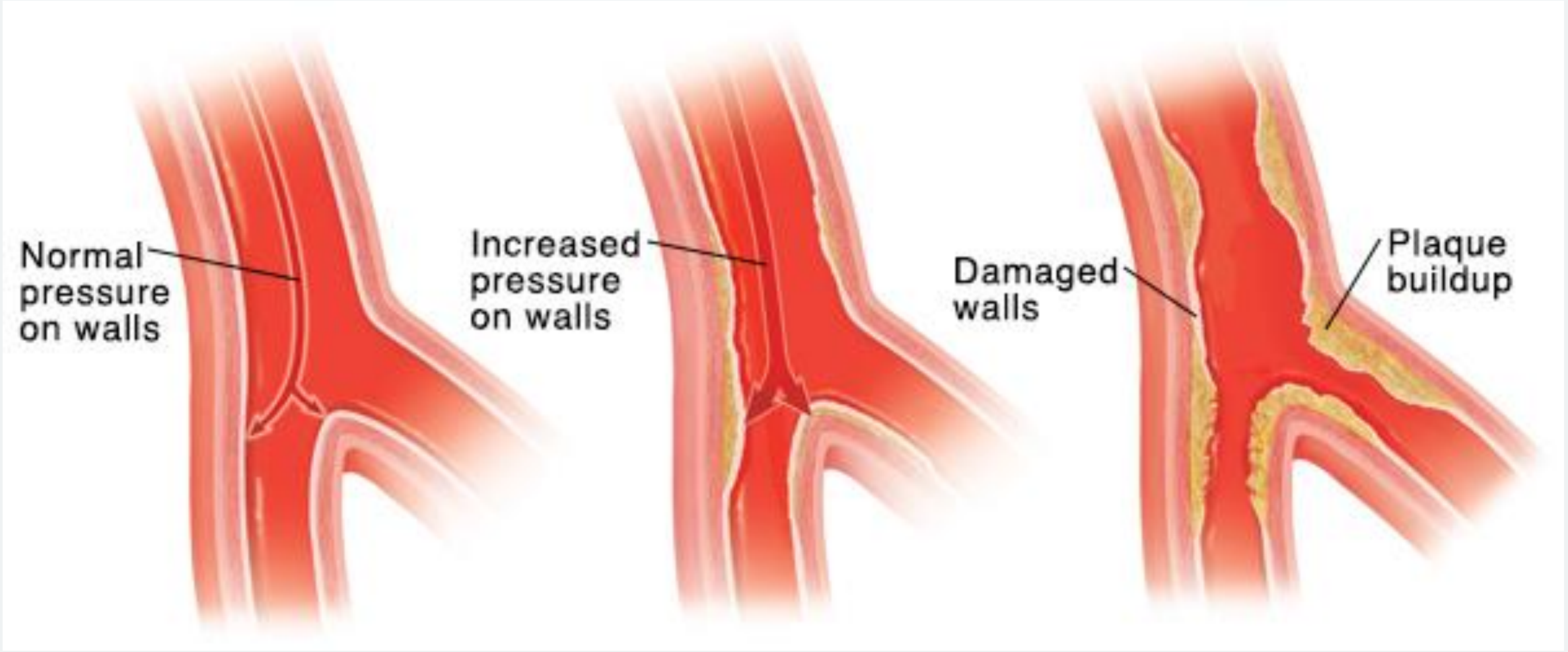
Drazner, MH. *Circ 2011;123:327-334*



https://www.saintlukeskc.org/health-library/understanding-high-blood-pressure

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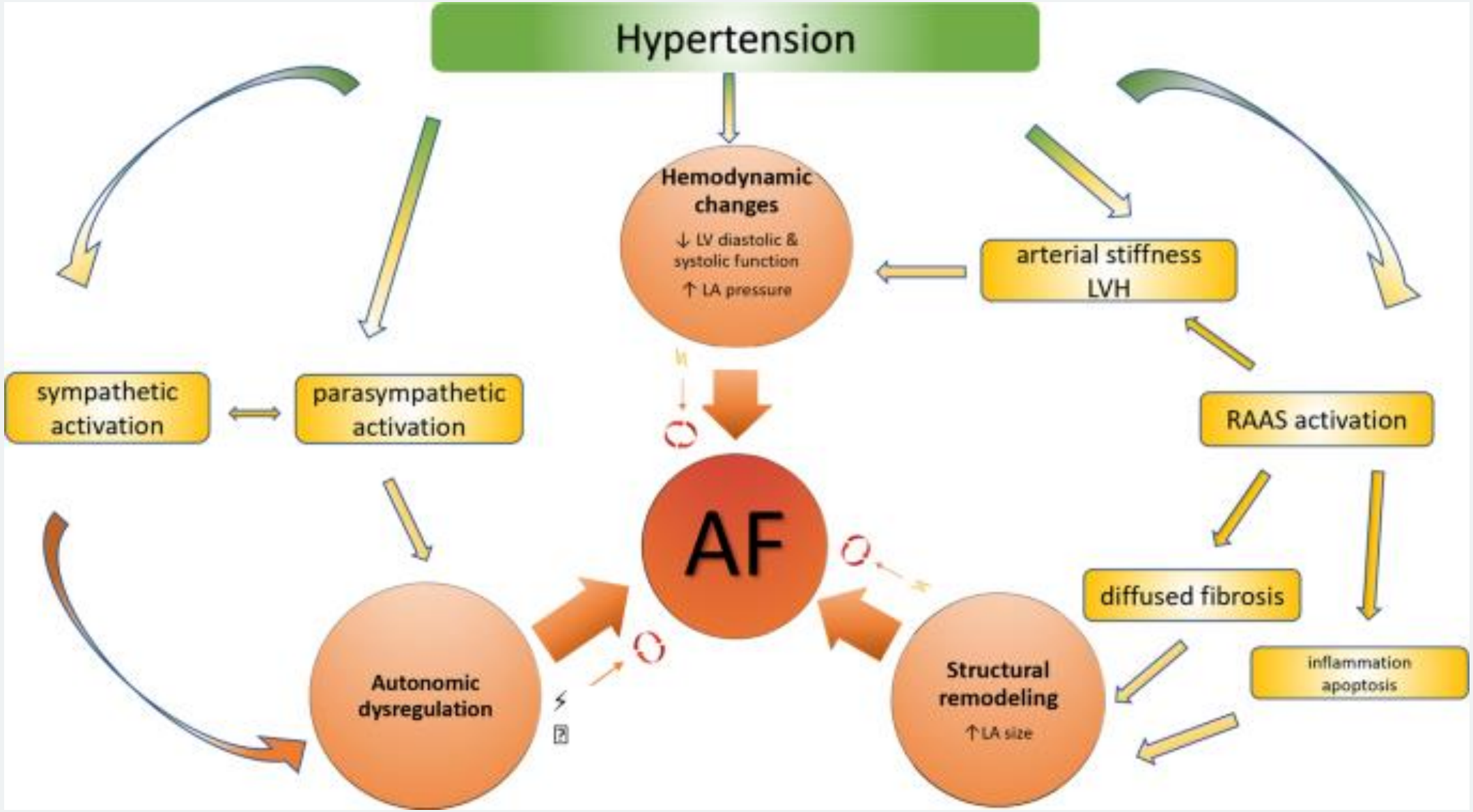

Gumprecht, J et al. *J Hum Hypertens* 33, 824-836 (2019)

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Summary

- HHD refers to the cardiac manifestations of hypertension and is driven by mechanical stress, neurohormonal effect and inflammation
- Common cardiac manifestation: HF, Afib, CAD

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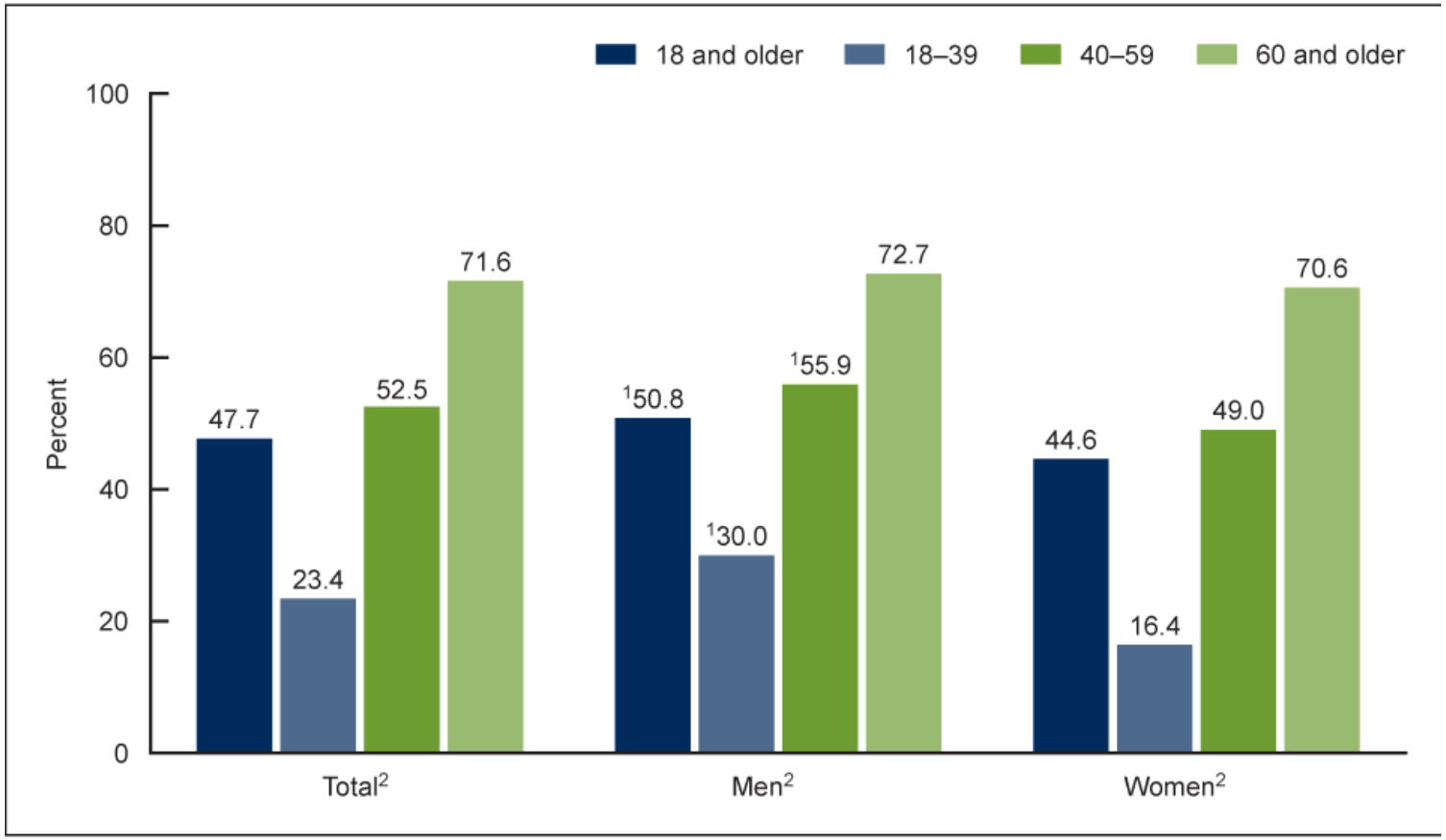
Hypertension Prevalence: USA

Figure 1. Prevalence of hypertension in adults age 18 and older, by sex and age: United States, August 2021–August 2023



https://www.cdc.gov/nchs/products/databriefs/db511.htm

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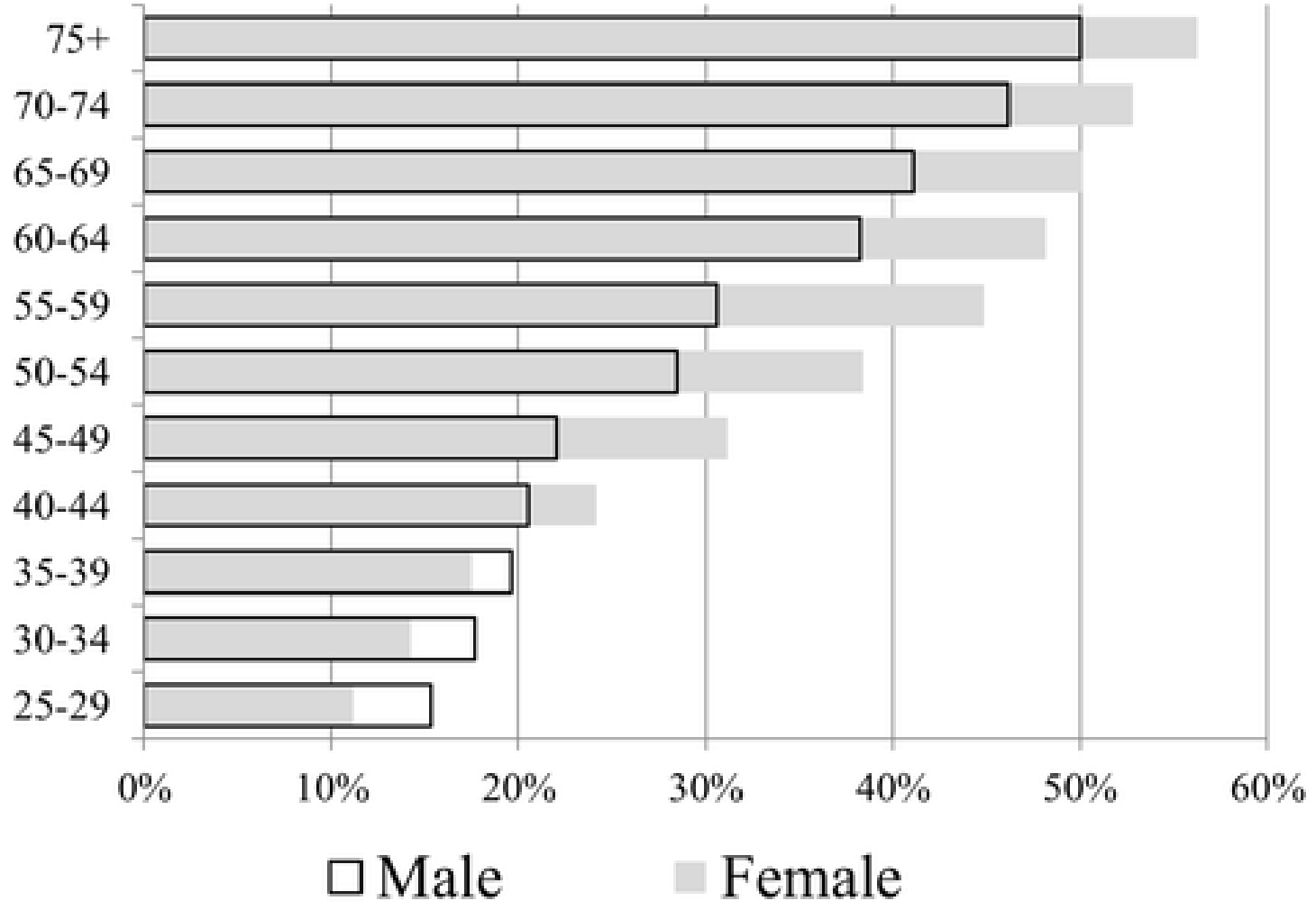
Hypertension Prevalence: Zambia



Yan, L.D. et al. *BMC Public Health* 15, 933 (2015)

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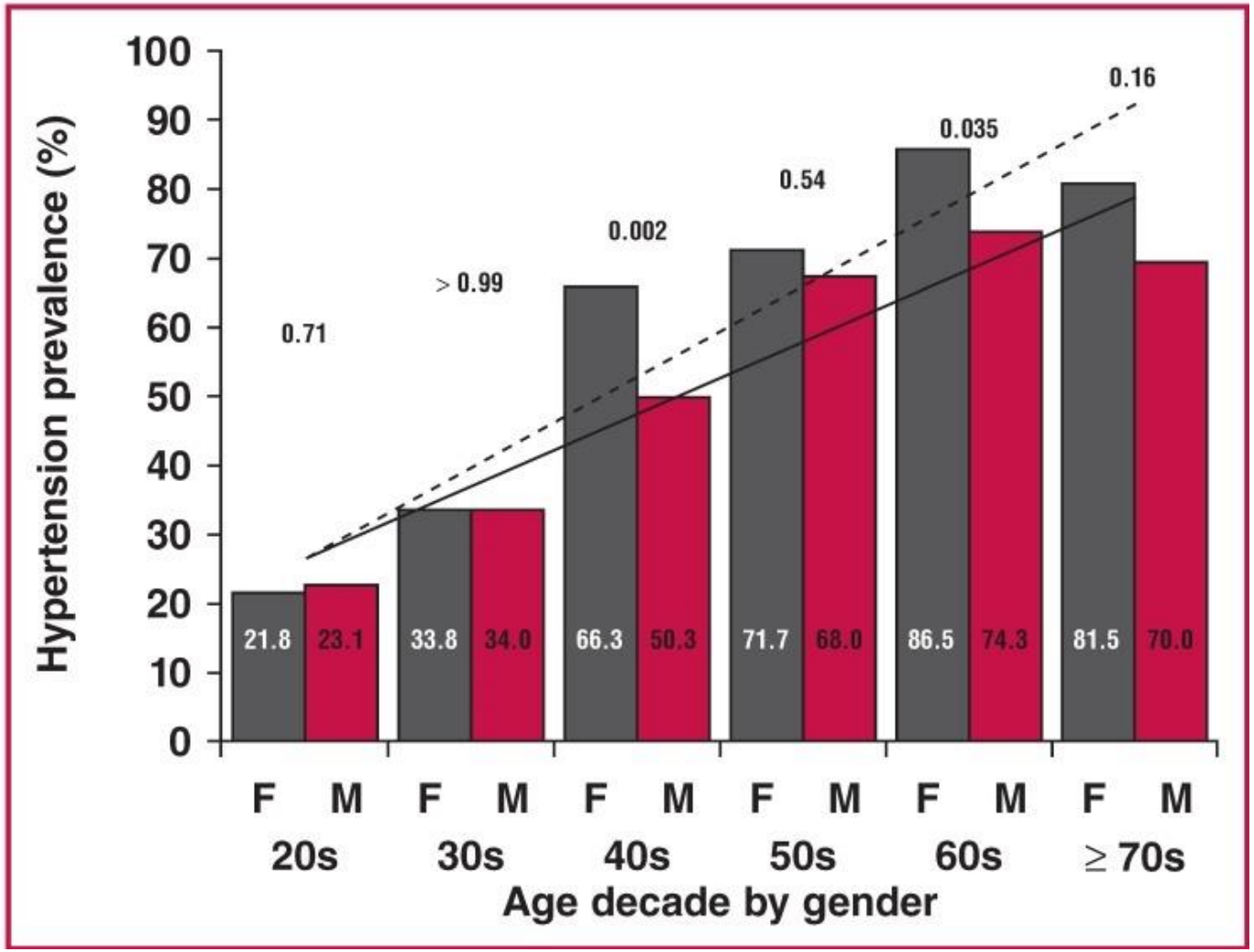
Hypertension Prevalence: Sierra Leone and The Gambia



Awad, M et al. *Cardiovasc J Afr*. 2014; 25(6):269-78

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Hypertension Prevalence: Ghana

Bosu *BMC Public Health* 2010, **10**:418
http://www.biomedcentral.com/1471-2458/10/418

BMC
Public Health

RESEARCH ARTICLE Open Access

Epidemic of hypertension in Ghana: a systematic review

William K Bosu[1,2]

Prevalence: 19% to 48%
Minimal sex differences
Urban> rural

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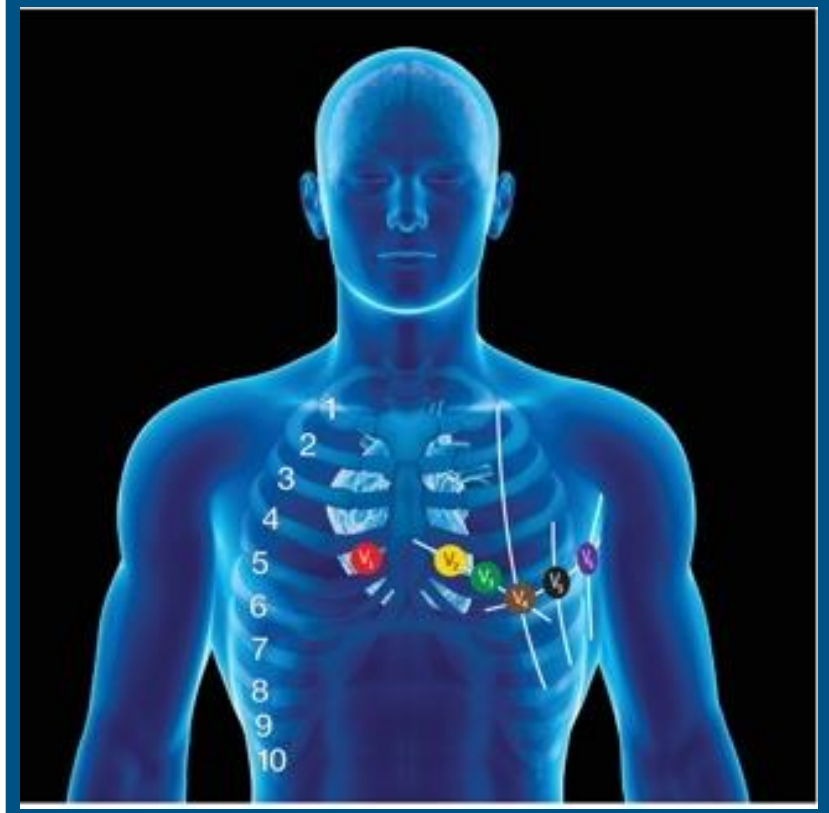
Electrocardiogram

Left ventricular hypertrophy criteria

- Underlying theme: increased R-wave in leads overlying the LV and increased S-wave in RV leads
- Sokolov-Lyon: S-wave in V1 + R-wave in V5 or V6 > 35mm
- Cornell: R-wave in aVL + S-wave in V3 >28mm in men and 20mm in women
- R in aVL > 11 mm



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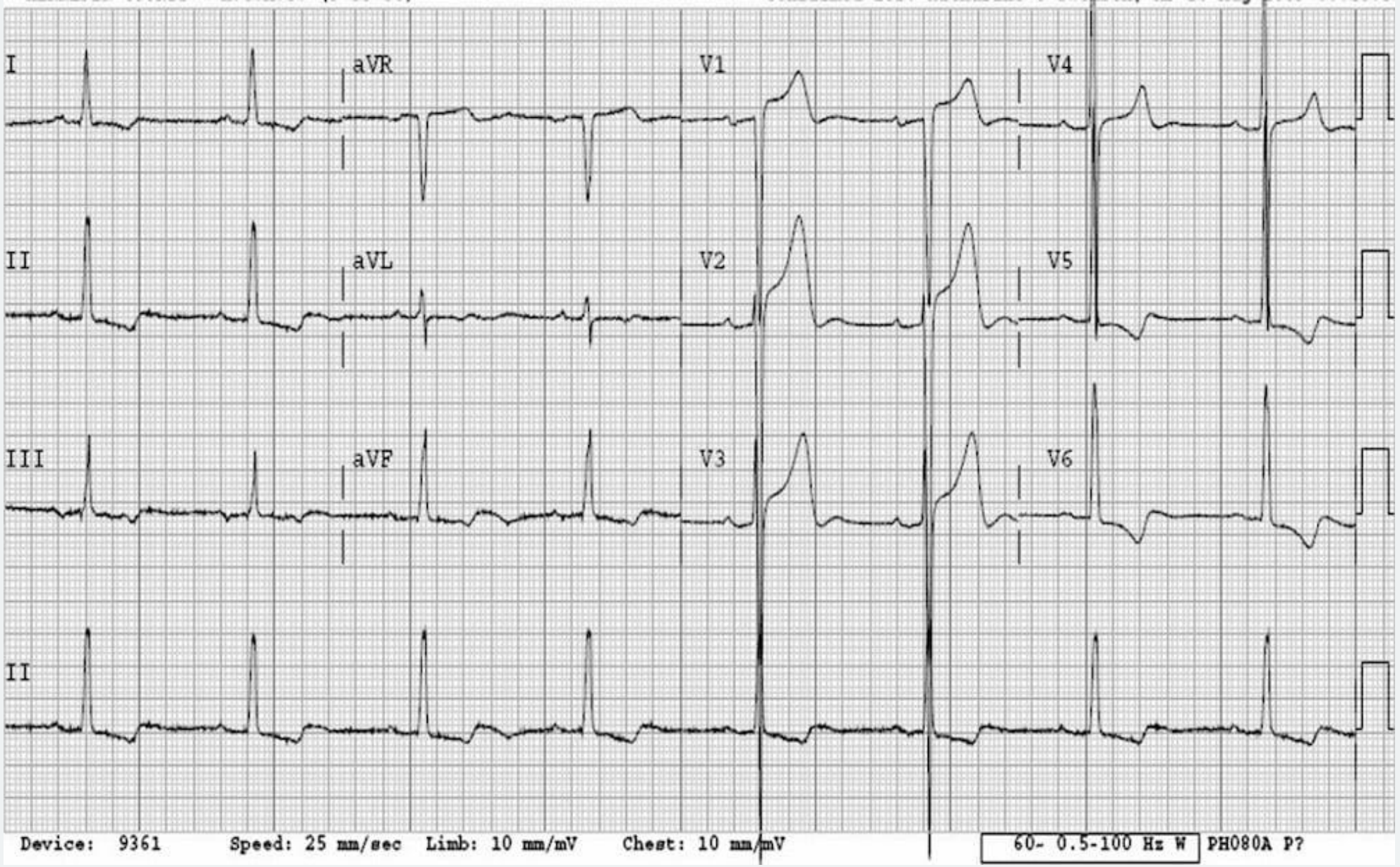

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https://litfl.com/wp-content/uploads/2018/08/ECG-LVH-ST-elevation-not-MI.jpg

Heart Failure with Preserved Ejection Fraction (HFpEF)

- Normal EF with increased LV filling pressures
  - Dyspnea
  - Edema
- Affects 1% to 3% globally
- Accounts for 50% of all HF diagnoses
- Similar prognosis to HFrEF

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Golla MSG, et al. *StatPearls*

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VOL. 81, NO. 18, 2023

PUBLISHED BY ELSEVIER

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

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3627–3639
https://doi.org/10.1093/eurheartj/ehad195

ESC GUIDELINES

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

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Definitions

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 measurement of LVEF >4
HFmrEF (HF with mildly reduced EF)	LVEF 41%–49% Evidence of spontaneous increased LV filling press natriuretic peptide, noni hemodynamic measurem
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous increased LV filling press natriuretic peptide, noninvasive and invasive hemodynamic measurement)

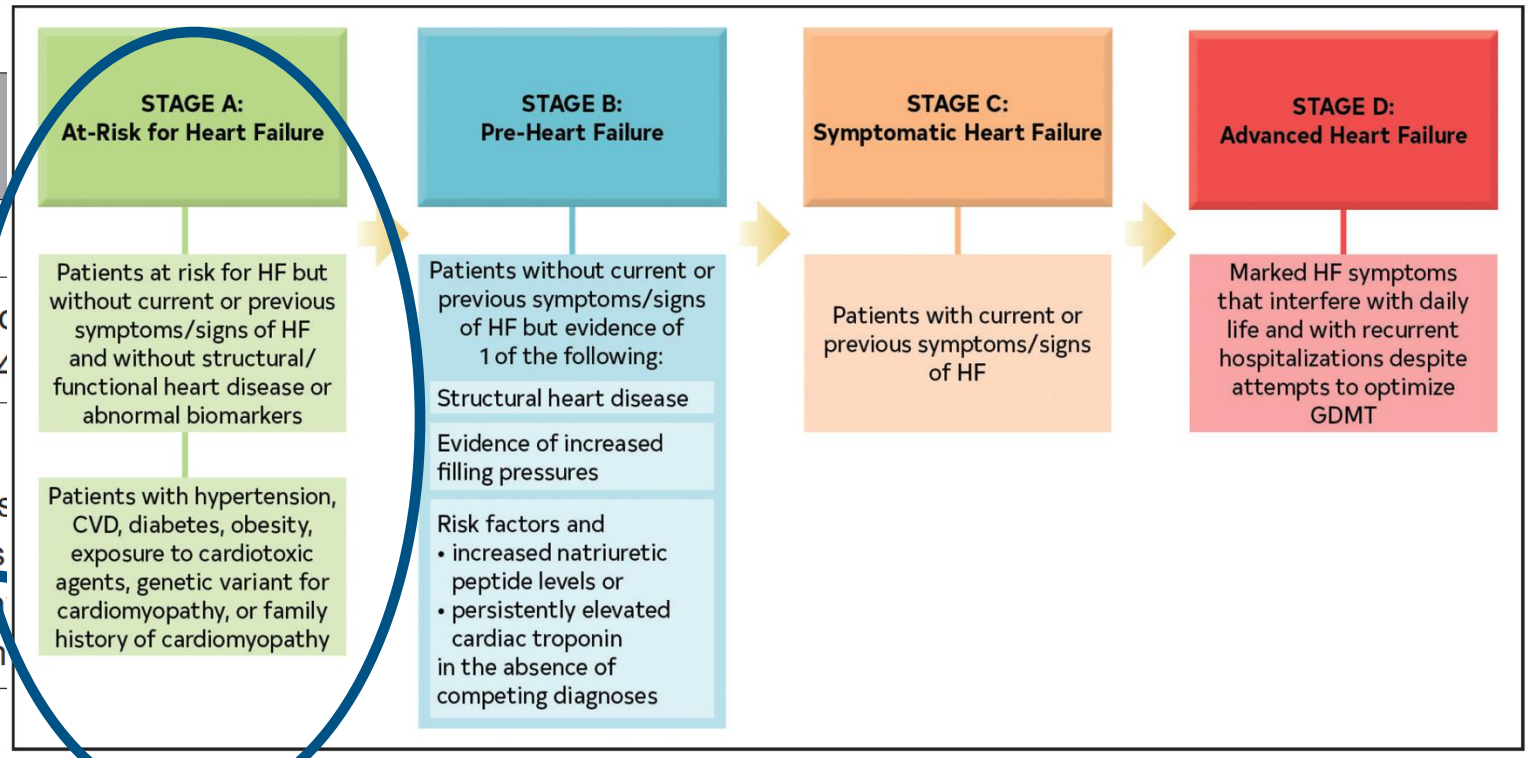

Figure 1. ACC/AHA Stages of HF.
The ACC/AHA stages of HF are shown. ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.

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Paul A. Heidenreich et al. *Circ* 2022; 145: e892-e1032

Some Risk Factors

Risk factors for heart failure	Preventive strategies
Sedentary habit	Regular physical activity
Cigarette smoking	Cigarette smoking cessation
Obesity	Physical activity and healthy diet
Excessive alcohol intake[286]	General population: no/light alcohol intake is beneficial Patients with alcohol-induced CMP should abstain from alcohol
Influenza	Influenza vaccination
Microbes (e.g. *Trypanosoma cruzi*, Streptococci)	Early diagnosis, specific antimicrobial therapy for either prevention and/or treatment
Cardiotoxic drugs (e.g., anthracyclines)	Cardiac function and side effect monitoring, dose adaptation, change of chemotherapy
Chest radiation	Cardiac function and side effect monitoring, dose adaptation
Hypertension	Lifestyle changes, antihypertensive therapy
Dyslipidaemia	Healthy diet, statins
Diabetes mellitus	Physical activity and healthy diet, SGLT2 inhibitors
CAD	Lifestyle changes, statin therapy

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Theresa A. McDonagh et al. *EHJ* 2021; 42:3599-3726

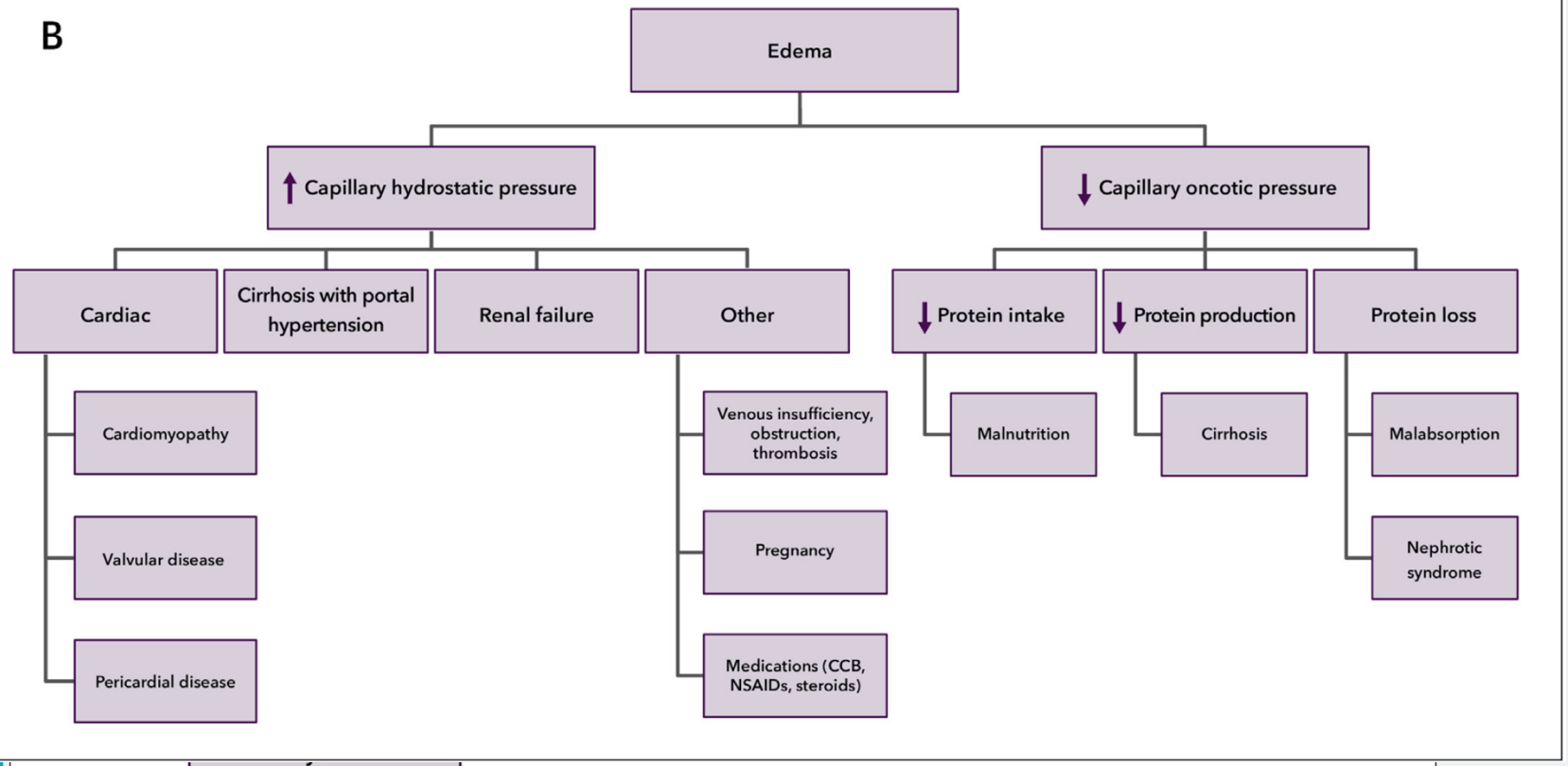
Diagnostic Challenges

FIGURE 3 Differential Diagnosis of Dyspnea and Edema*

A

Dyspnea

FIGURE 3 Continued



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Michelle M. Kittleson et al. *JACC* 2023; 81:1835-1878.

Diagnostic Scoring Systems

- Derived and validated using invasive exercise hemodynamics
- Readily available information
- Score of ≥6 highly suggestive of HFpEF
- Does not include natriuretic peptide levels

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

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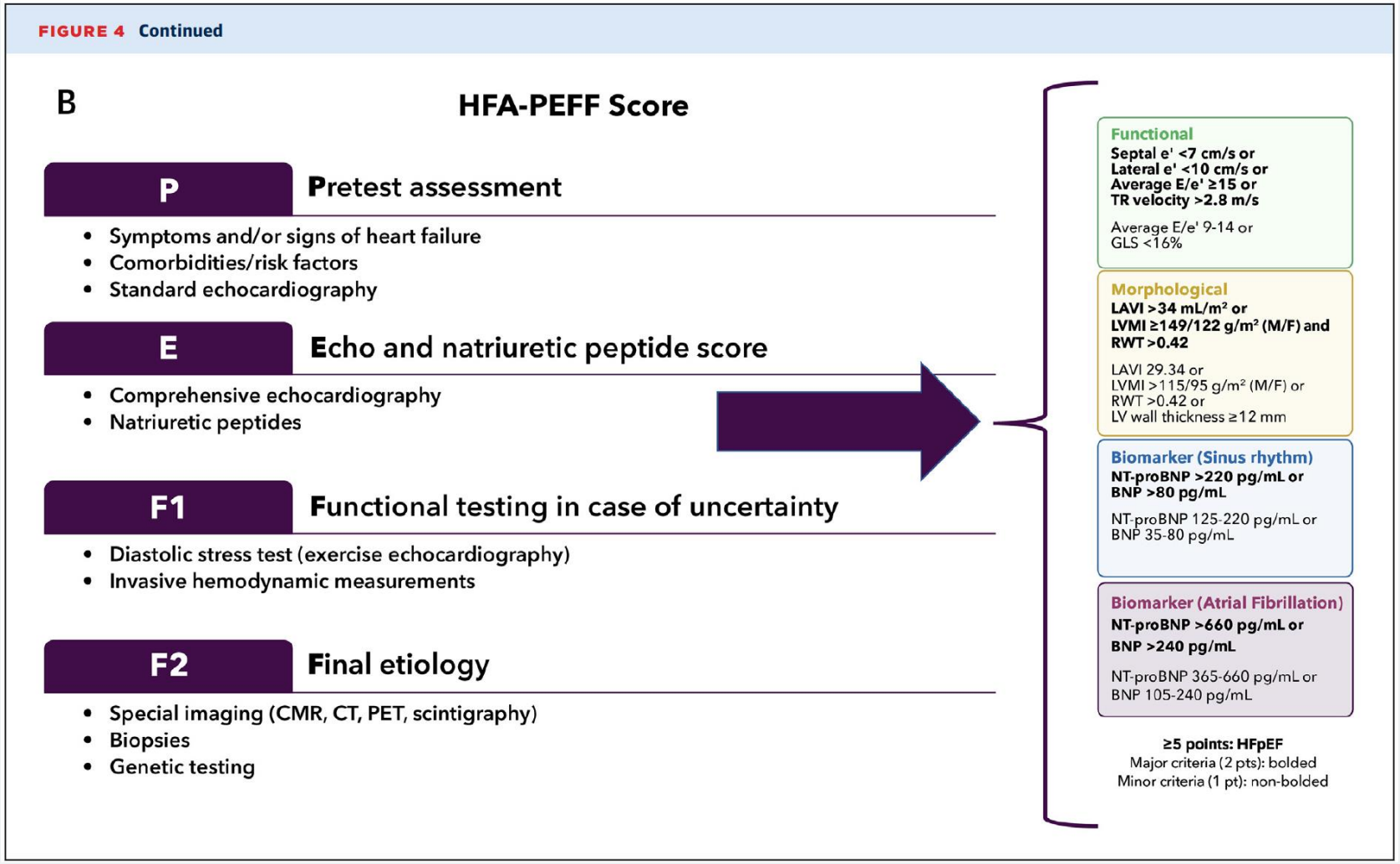
Diagnostic Scoring Systems



- Developed based on expert consensus
- May need invasive hemodynamic testing

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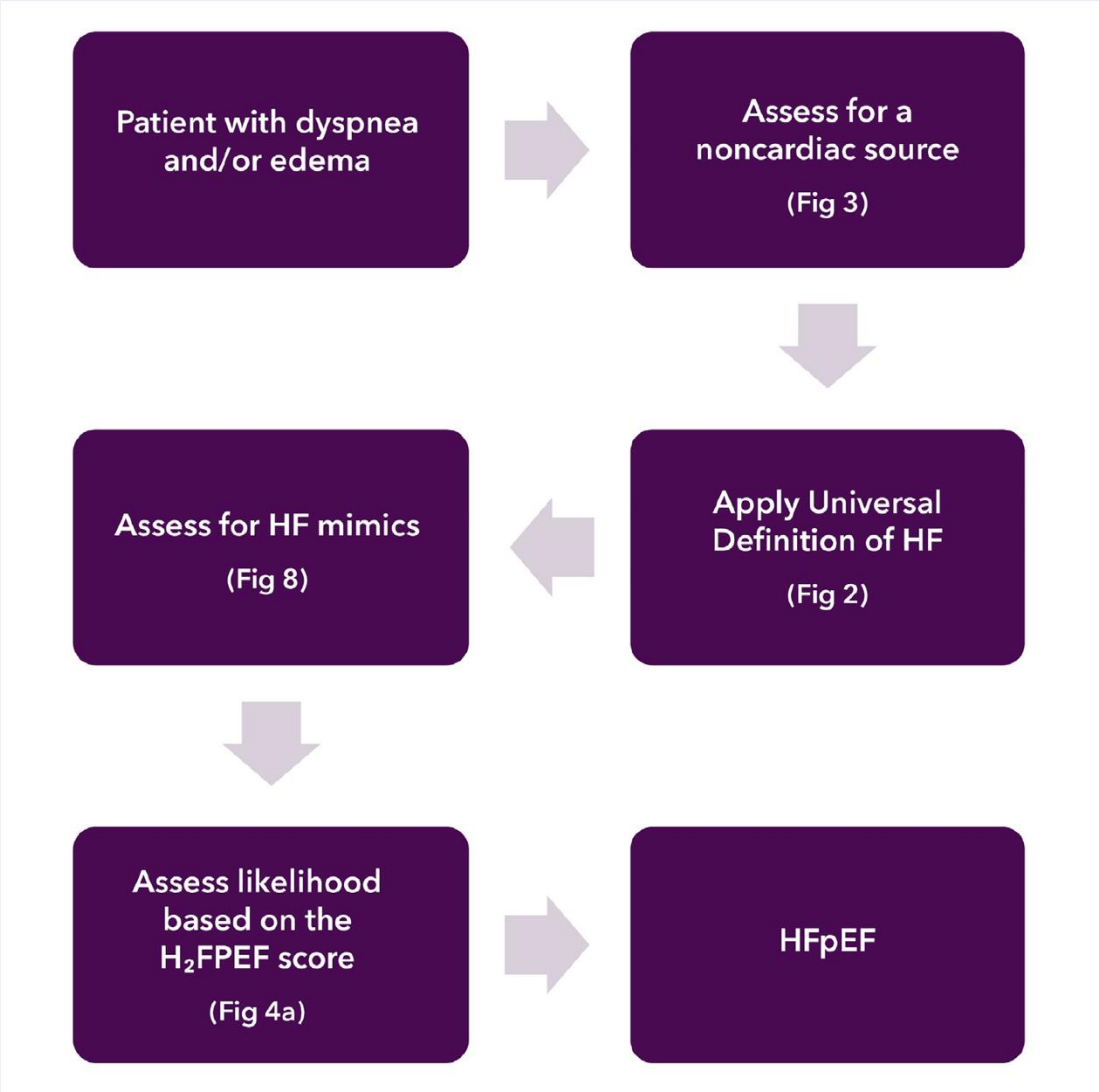
A Diagnostic Approach



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Some HFpEF Mimics

TABLE 1 Diagnostic Clues and Recommended Testing for HFpEF Mimics

HFpEF Mimic	Clinical Clues	Diagnostic Testing
Cardiac amyloidosis	Increased LV wall thickness Musculoskeletal issues (carpal tunnel syndrome, lumbar spinal stenosis) Neuropathy (sensory or autonomic)	Monoclonal protein screen (serum/urine immunofixation electrophoresis and serum free light chains) Technetium pyrophosphate scan (interpreted in the context of a negative monoclonal protein screen) Endomyocardial biopsy if monoclonal protein screen is positive
Hypertrophic cardiomyopathy	Unexplained LV hypertrophy LV outflow tract obstruction Family history	CMR if diagnosis is uncertain based on echocardiogram
Cardiac sarcoidosis	Extracardiac disease (pulmonary, ocular, dermatologic) High-degree atrioventricular block (especially if age <60 y) Ventricular arrhythmias	CMR FDG-PET scan Tissue biopsy (cardiac or extracardiac)
Hemochromatosis	Family history or history of frequent blood transfusions Diabetes Erectile dysfunction	Ferritin and transferrin *HFE* genetic testing CMR with T2* imaging
Fabry disease	Angiokeratomas Sensory neuropathy Proteinuria X-linked inheritance	Serum alpha-galactosidase level (in men) *GLA* genetic testing Biopsy of affected tissue
High-output HF	Echocardiogram with 4-chamber enlargement and/or increased LV outflow tract VTI	Investigate and treat underlying cause: anemia, arteriovenous malformations, cirrhosis, fistulas, thiamine deficiency
Myocarditis	Antecedent viral infection Elevated troponin in the absence of coronary artery disease Heart block and/or ventricular arrhythmias	CMR Endomyocardial biopsy
Pericardial disease	Prior cardiac surgery, chest radiation, or pericarditis Right-sided HF symptoms	CMR Right and left heart catheterization to demonstrate discordance in LV/RV pressure tracings during inspiration

CMR = cardiac magnetic resonance; FDG-PET = fluorodeoxyglucose-positron emission tomography; HF = heart failure; *HFE* = hereditary hemochromatosis gene; HFpEF = heart failure with preserved ejection fraction; LV = left ventricular; RV = right ventricular; VTI = velocity time integral.

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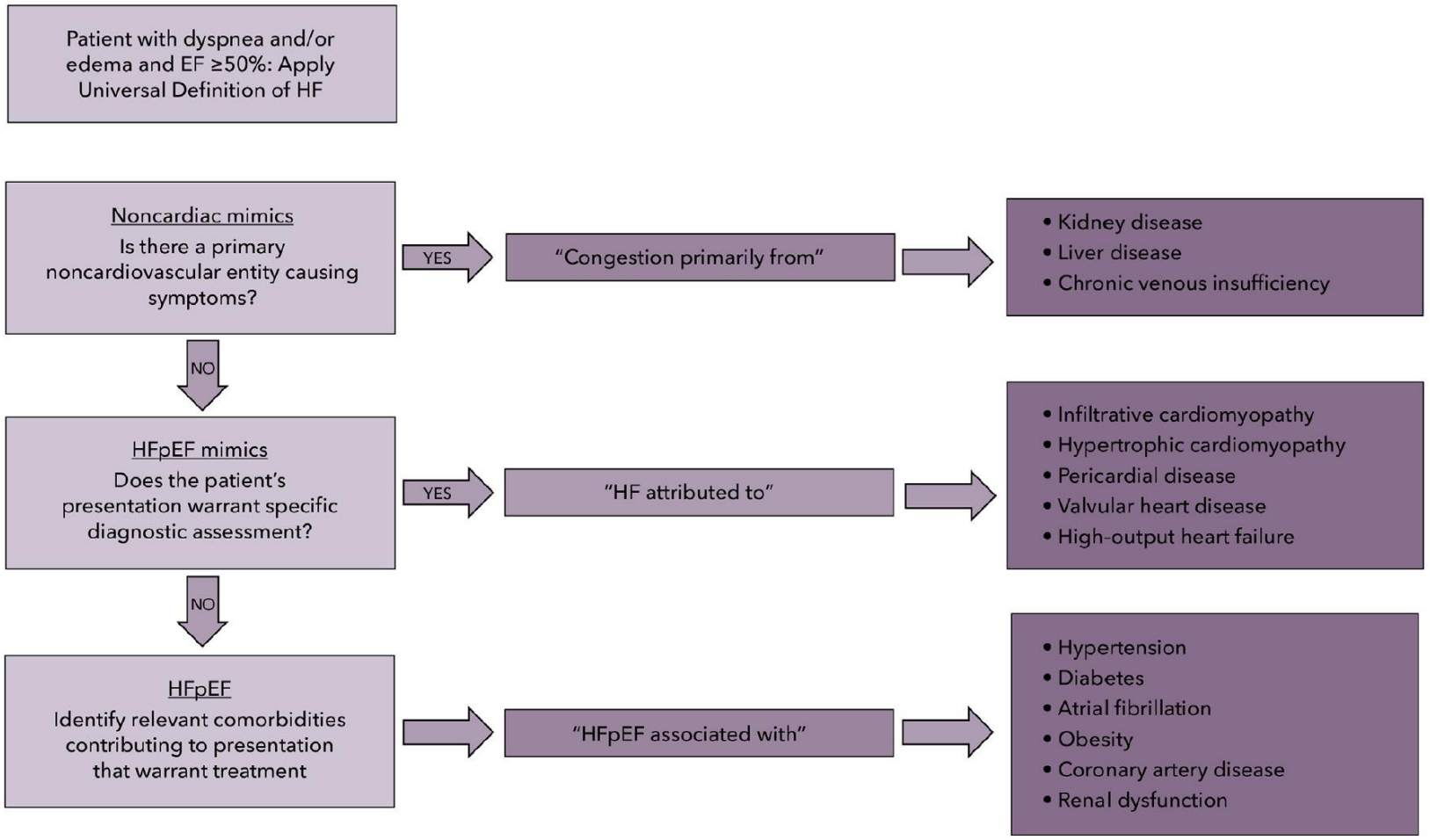
Excluding Mimics of HFpEF

FIGURE 8 Stepwise Approach to Assessment of Individuals With Shortness of Breath and/or Edema



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Management Strategy

- Minimize risk of disease progression in at-risk patients
- Risk stratification and management of comorbidities
- Lifestyle modifications
- Medical management

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HFpEF Clinical Trials

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)

TABLE 3 Starting and Target Doses of Select GDMTs for HFpEF

Drug Class	Starting Dose	Target Dose
SGLT2is		
Dapagliflozin	10 mg daily	10 mg daily
Empagliflozin	10 mg daily	10 mg daily
Aldosterone antagonists		
Spironolactone	25 mg daily	50 mg daily
ARNIs		
Sacubitril/valsartan	24 mg/26 mg twice daily	97 mg/103 mg twice daily
ARBs		
Candesartan	4 mg to 8 mg daily	32 mg daily

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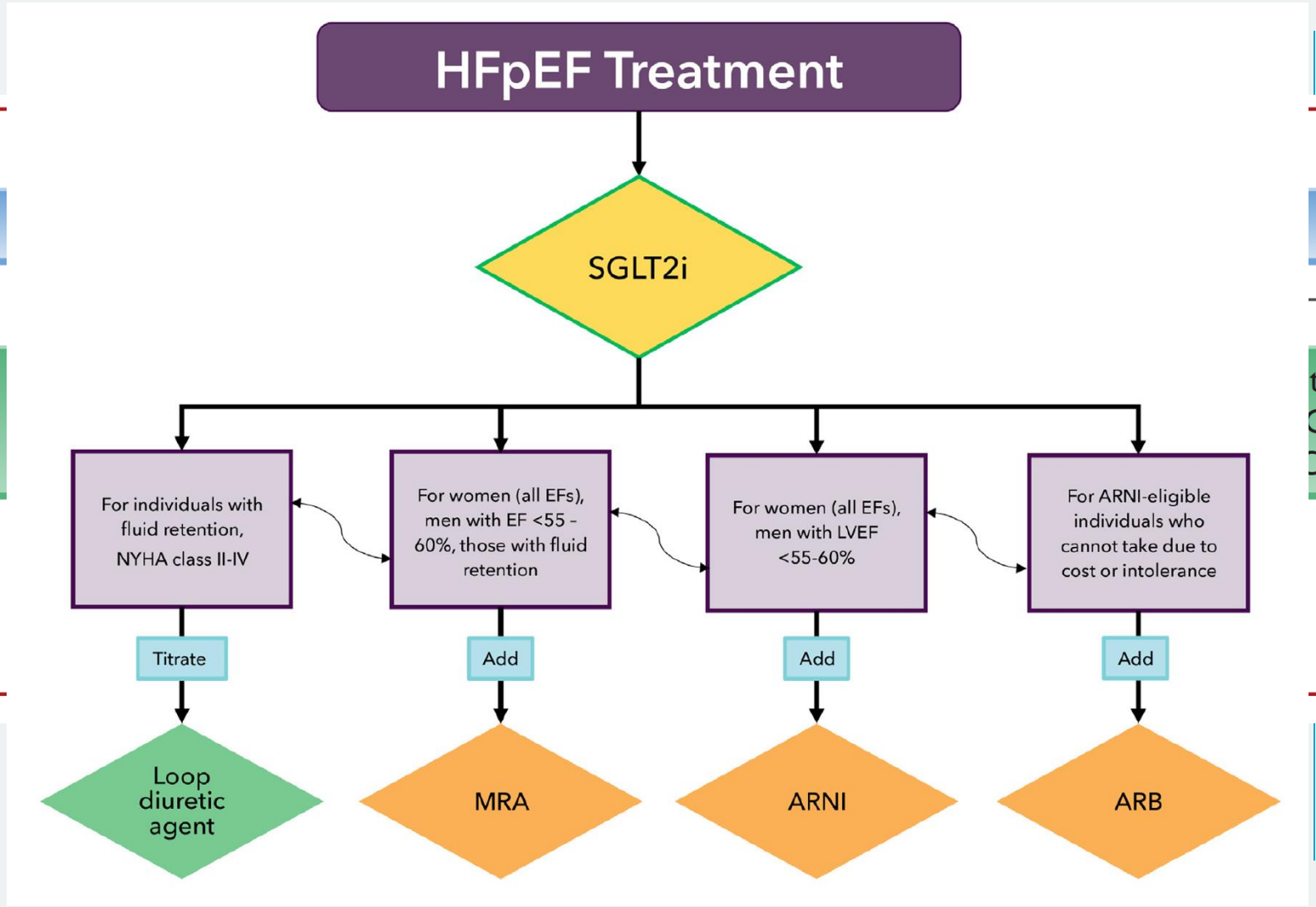
Medical Management



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Nonpharmacological Management

TABLE 5 Nonpharmacological Interventions in HFpEF

Study	Sample Size (HFpEF only)	Intervention	Outcome
WEIGHT LOSS AND/OR EXERCISE TRAINING			
Edelmann et al[84]	64	3 months of endurance/resistance training	■ Peak Vo_2 increased by 3.3 mL/kg/min ■ Improved quality of life ■ Improvement in E/e' and left atrial volume index
Mueller et al[85]	176	12 weeks of high-intensity interval training and moderate continuous training	■ Improved peak Vo_2 at 3 months
Kitzman et al[86]	63	16 weeks of exercise training	■ Peak Vo_2 increased by 2 mL/kg/min ■ Improved quality of life
Kitzman et al[87]	100	20 weeks of caloric restriction, aerobic exercise, or both	Increase in peak Vo_2 by: ■ Exercise: 1.2 mL/kg/min ■ Diet: 1.3 mL/kg/min ■ Both (additive): 2.5 mL/kg/min
Brubaker et al[88]	88	20 weeks of (caloric restriction and aerobic exercise) ± resistance training	Addition of resistance training to caloric restriction and aerobic exercise ■ increase in leg strength and muscle quality ■ no additive increase in peak Vo_2 or QOL
Mikhalkova et al[89]	12 (all women)	Gastric bypass	■ Improvement in Minnesota Living with Heart Failure score ■ Improved diastolic relaxation on echocardiogram
DEVICE THERAPIES			
Adamson et al[90,91]	119	Implantable pulmonary artery monitor	50% reduction in HF hospitalization with mean follow-up of 17.6 months
Lindenfeld et al[92]	795	Implantable pulmonary artery monitor	No reduction in all-cause mortality, HF hospitalizations, and urgent HF visits.

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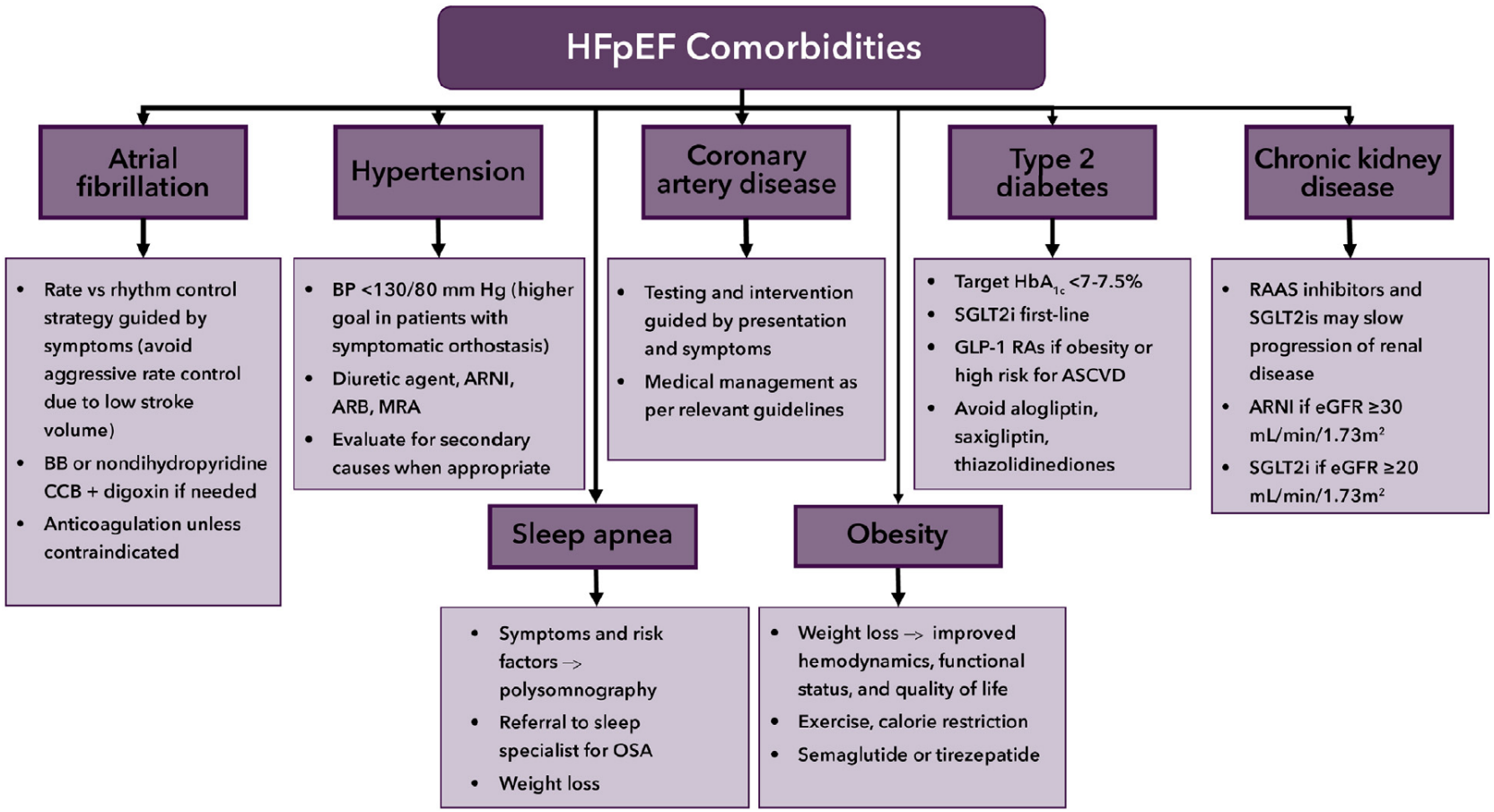
Managing Comorbidities

FIGURE 11 Management of Comorbidities Associated With HFpEF



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Future Therapies

- GLP1 agonist
- Vaccines to target inflammatory markers leading to reverse remodeling

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Questions

Thank you for your attention

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