



The Future for CHF

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Epidemiology of Heart Failure in the United States

Increase in HF hospitalizations from 2013 to 2017.

Increase in HF related deaths from 2009 to 2014.

Decline in overall HF incidence from 2011 to 2014 with declining incidence of HF_rEF but increasing incidence of HF_pEF.

Racial and ethnic disparities in death resulting from HF persist.

Age-adjusted mortality rates for HF:
92/100,000 for non-Hispanic Black patients
87/100,000 for non-Hispanic White patients
53/100,000 for Hispanic patients



Causes of Heart Failure

- ISCHEMIC
- Chemotherapy, cardiotoxic medications, meth, Etoh
- Rheumatologic or autoimmune, Endocrine or metabolic
- Familial, inherited or genetic heart disease
- Heart rhythm-related (*tachycardia-mediated, PVCs, RV pacing*)
- HTN
- Infiltrative cardiac disease (*amyloid, sarcoid, hemochromatosis*)
- Myocarditis
- Peripartum cardiomyopathy
- Stress cardiomyopathy (*Takotsubo*)

Stages of HF

Stages	Definition and Criteria
Stage A: At Risk for HF	At risk for HF but without symptoms, structural heart disease, or cardiac biomarkers of stretch or injury (e.g., patients with hypertension, atherosclerotic CVD, diabetes, metabolic syndrome and obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or positive family history of cardiomyopathy).
Stage B: Pre-HF	<p>No symptoms or signs of HF and 1 of the following:</p> <p><i>Structural heart disease*</i></p> <ul style="list-style-type: none"> • Reduced left or right ventricular systolic function <ul style="list-style-type: none"> ○ Reduced ejection fraction, reduced strain • Ventricular hypertrophy or enlargement • Wall motion abnormalities <p><i>Evidence for increased filling pressures*</i></p> <ul style="list-style-type: none"> • By invasive hemodynamic measurements • By noninvasive imaging suggesting elevated filling pressures (e.g., Doppler echocardiography) <p><i>Patients with risk factors and</i></p> <ul style="list-style-type: none"> • <i>Increased levels of BNP*s* or</i> • <i>Persistently elevated cardiac troponin</i> <p>in the absence of competing</p>

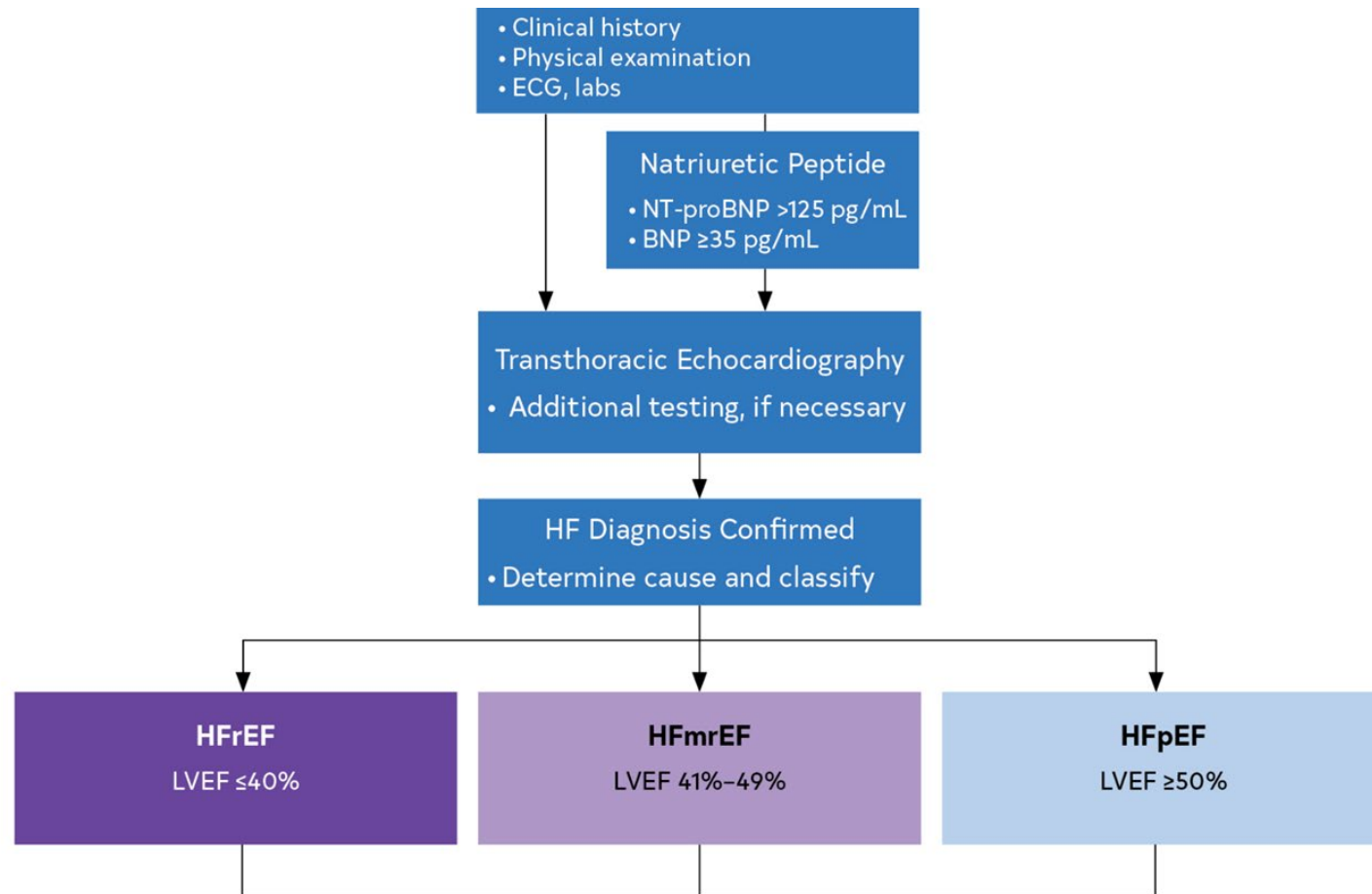
Stages of HF

Stage C: Symptomatic HF	Structural heart disease with current or previous symptoms of HF.
Stage D: Advanced HF	Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT.

Classification of HF by LVEF

Type of HF According to LVEF	Criteria
HFrEF (HF with reduced EF)	<ul style="list-style-type: none">• LVEF $\leq 40\%$
HFimpEF (HF with improved EF)	<ul style="list-style-type: none">• Previous LVEF $\leq 40\%$ and a follow-up measurement of LVEF $> 40\%$
HFmrEF (HF with mildly reduced EF)	<ul style="list-style-type: none">• LVEF 41%–49%• Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive/ invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	<ul style="list-style-type: none">• LVEF $\geq 50\%$• Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, noninvasive/invasive hemodynamic measurement)

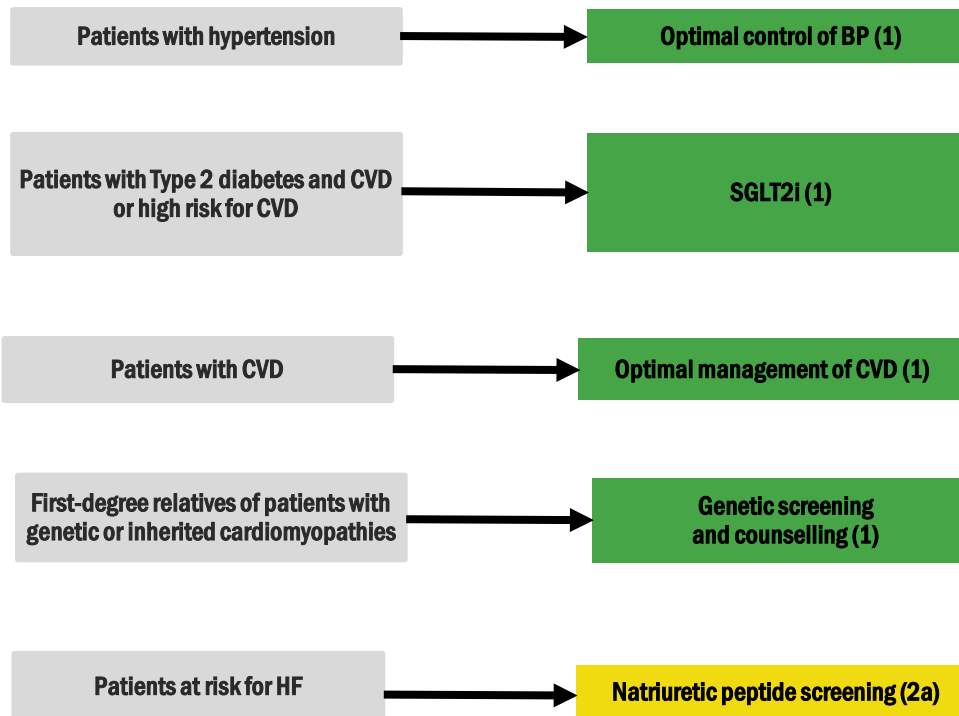
Diagnostic Algorithm for HF and EF-Based Classification



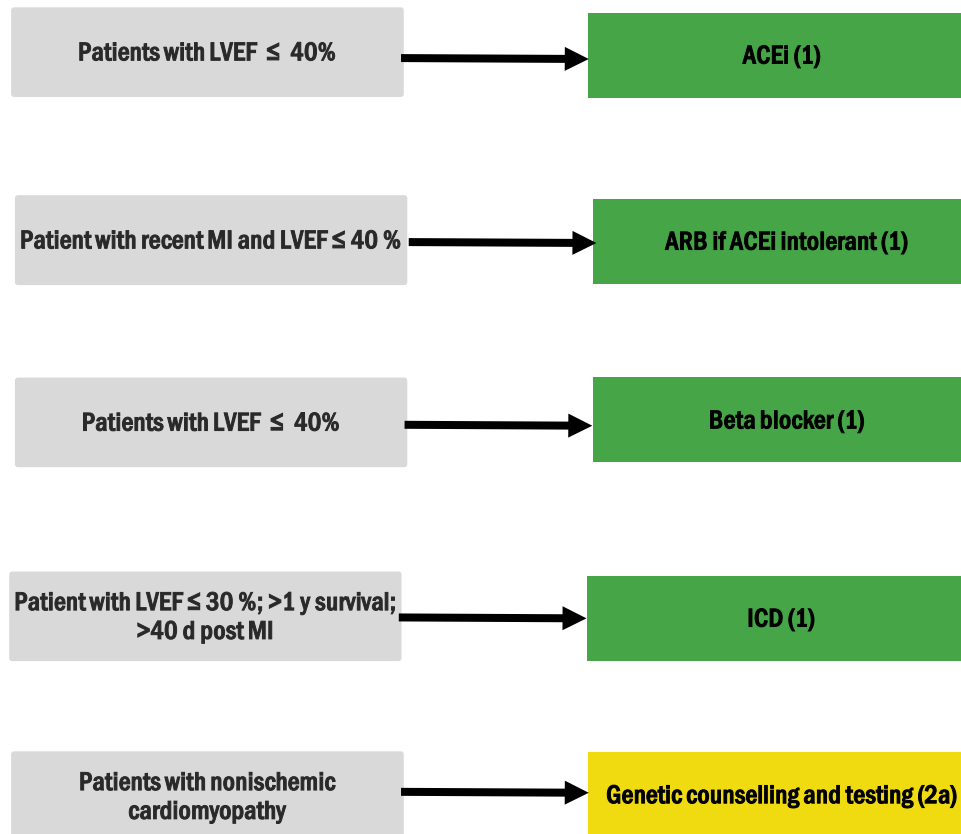
Potential Causes of Elevated Natriuretic Peptide Levels

Cardiac
HF, including RV HF syndromes
ACS
Heart muscle disease, including LVH
VHD
Pericardial disease
AF
Myocarditis
Cardiac surgery
CRF
Toxic-metabolic myocardial insults, including cancer chemotherapy

At Risk for HF (Stage A)

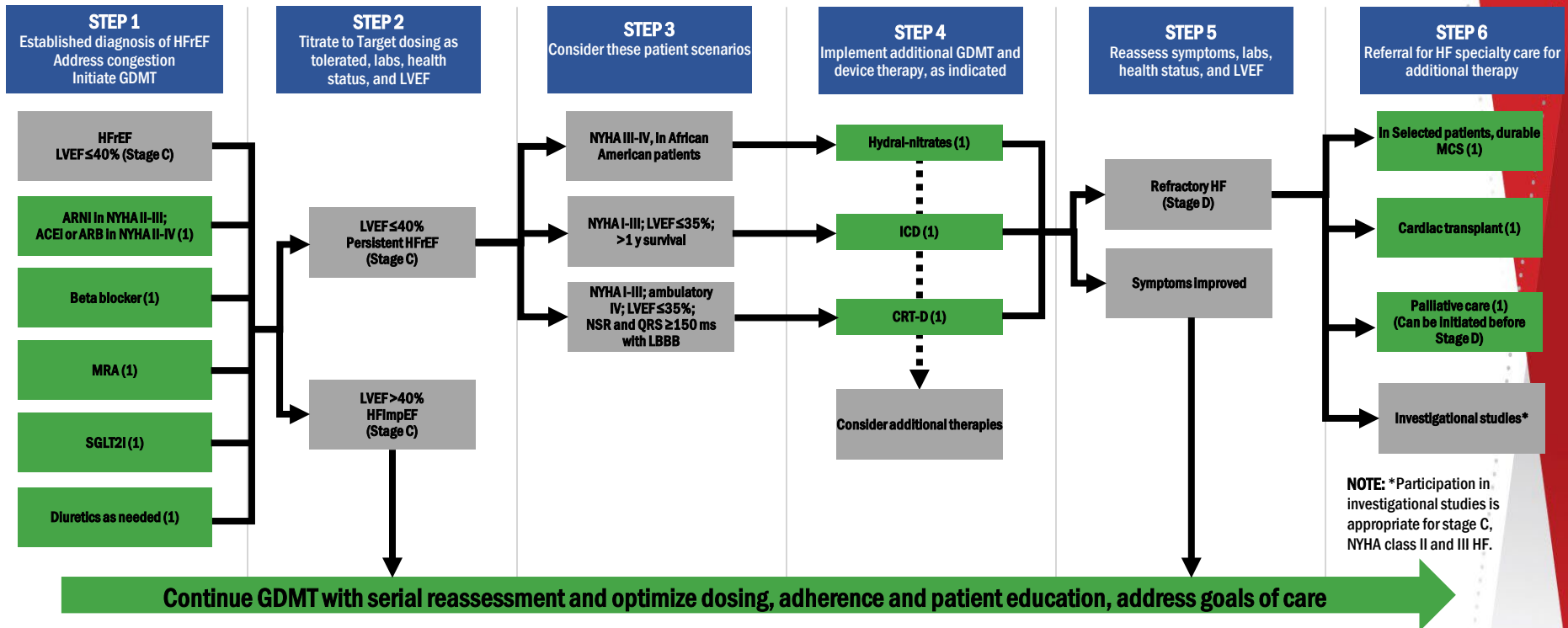


Pre-HF (Stage B)





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.

Drugs Commonly Used for HFrEF (Stage C HF)

Drug	Initial Daily Dose(s)	Target Doses(s)	Mean Doses Achieved in Clinical Trials	
ACEi				
Captopril	6.25 mg 3 times daily	50 mg 3 times daily	122.7 mg total daily	
Enalapril	2.5 mg twice daily	10–20 mg twice daily	16.6 mg total daily	
Fosinopril	5–10 mg once daily	40 mg once daily	NA	
Lisinopril	2.5–5 mg once daily	20–40 mg once daily	32.5–35.0 mg total daily	
Perindopril	2 mg once daily	8–16 mg once daily	NA	
Quinapril	5 mg twice daily	20 mg twice daily	NA	
Ramipril	1.25–2.5 mg once daily	10 mg once daily	NA	
Trandolapril	1 mg once daily	4 mg once daily	NA	

Drugs Commonly Used for HFrEF (Stage C HF)

ARB				
Candesartan	4–8 mg once daily	32 mg once daily	24 mg total daily	
Losartan	25–50 mg once daily	50–150 mg once daily	129 mg total daily	
Valsartan	20–40 mg once daily	160 mg twice daily	254 mg total daily	
ARNi				
Sacubitril-valsartan	49 mg sacubitril and 51 mg valsartan twice daily (therapy may be initiated at 24 mg sacubitril and 26 mg valsartan twice daily)	97 mg sacubitril and 103 mg valsartan twice daily	182 mg sacubitril and 193 mg valsartan total daily	

Drugs Commonly Used for HFrEF (Stage C HF)

SGLT2i				
Dapagliflozin	10 mg once daily	10 mg once daily	9.8 mg total daily	
Empagliflozin	10 mg once daily	10 mg once daily	NR	
Isosorbide dinitrate and hydralazine				
Fixed dose combination	20 mg isosorbide dinitrate and 37.5 mg hydralazine 3 times daily	40 mg isosorbide dinitrate and 75 mg hydralazine 3 times daily	90 mg isosorbide dinitrate and ~175 mg hydralazine total daily	
Isosorbide dinitrate and hydralazine	20–30 mg isosorbide dinitrate and 25–50 mg hydralazine 3–4 times daily	120 mg isosorbide dinitrate total daily in divided doses and 300 mg hydralazine total daily in divided doses	NA	

Drugs Commonly Used for HFrEF (Stage C HF)

I_f Channel inhibitor				
Ivabradine	5 mg twice daily	7.5 mg twice daily	12.8 total daily	(25-27)
Soluble guanylate cyclase stimulator				
Vericiguat	2.5 mg once daily	10 mg once daily	9.2 mg total daily	(28)
Digoxin	0.125–0.25 mg daily (modified according to monogram)	Individualized variable dose to achieve serum digoxin concentration 0.5–<0.9 ng/mL	NA	(29, 30)

Take home point

Guideline-directed medical therapy (GDMT) for heart failure (HF) with reduced ejection fraction (HFrEF) now includes 4 medication classes which include sodium-glucose cotransporter-2 inhibitors (SGLT2i).

All have high economic value (SGLT- intermediate economic value)

Value Statements for Device Therapy

NYHA I-III; LVEF \leq 35%;
>1 y survival

A transvenous ICD provides high economic value in the primary prevention of SCD particularly when the patient's risk of death caused by ventricular arrhythmia is deemed high and the risk of nonarrhythmic death (either cardiac or noncardiac) is deemed low based on the patient's burden of comorbidities & functional status.

Value Statement: High Value (A)

NYHA I-III; ambulatory
IV; LVEF \leq 35%;
NSR and QRS \geq 150 ms
with LBBB

For patients who have LVEF \leq 35%, sinus rhythm, LBBB with a QRS duration of \geq 150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT implantation provides high economic value.

Value Statement: High Value (B-NR)

Diastolic Heart Failure

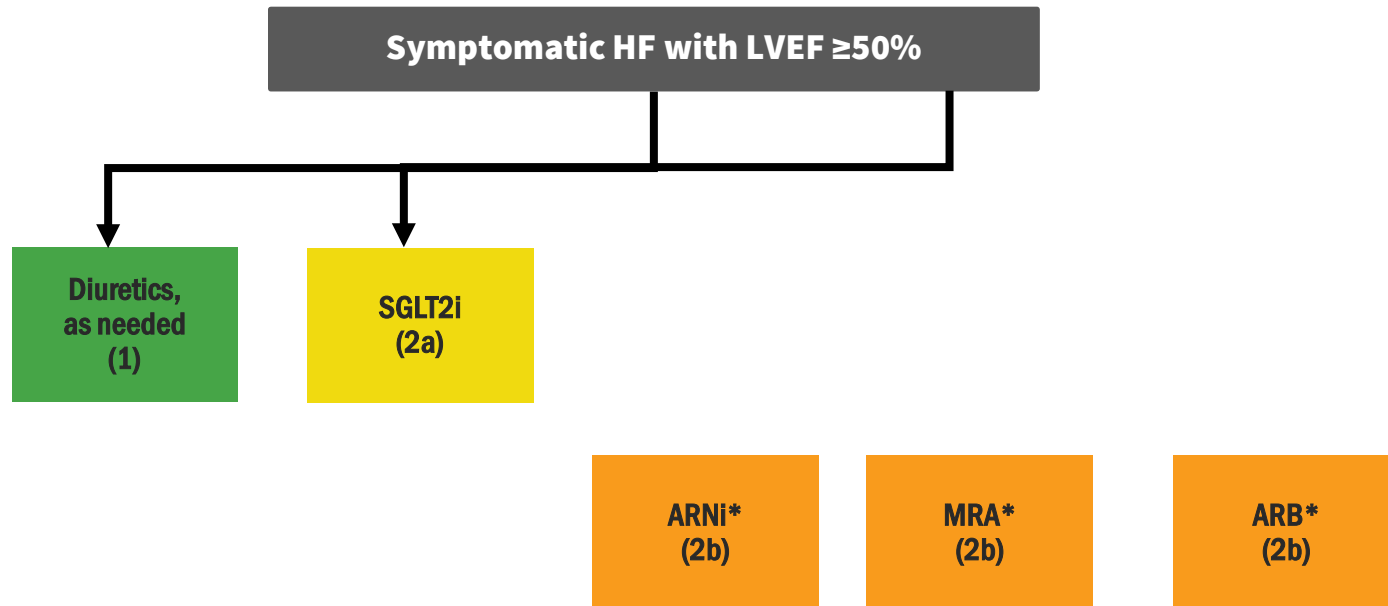
H₂FPEF score

- 414 patients with unexplained dyspnea between 2006-2016 at the Mayo Clinic undergoing invasive exercise testing
- Patients with HFpEF (64%) were identified by elevated pulmonary capillary wedge pressure at rest (≥ 15 mm Hg) or during exercise (≥ 25 mm Hg)
- Robust calibration ($P > 0.1$)
- Validation in 100 patients, AUC 0.89 for points-based score and 0.910 for the continuous variable-based score

	Clinical Variable	Values	Points
H ₂	Heavy	Body mass index > 30 kg/m ²	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
H₂FPEF score			Sum (0-9)

Reddy et al. Circ 2018;138:861

Recommendations for Patients with Preserved LVEF



Additional Therapies in Patients with HF and Comorbidities

IV iron replacement (2a)

**AV nodal ablation and
CRT implantation (2a)**

**Atrial Fibrillation
ablation (2a)**

CPAP (2a)

Treatment for Stage D

In Selected patients, durable MCS (1)

Cardiac transplant (1)

**Palliative care (1)
(Can be initiated before Stage D)**

Diagnosis and Treatment of Transthyretin Cardiac Amyloidosis

History, ECG, echocardiogram, cardiac MRI suggestive of cardiac amyloidosis

Presence of monoclonal light chain?

YES

At 2020 list prices, tafamidis provides low economic value (>\$180,000 per QALY gained) in patients with HF with wild-type or variant transthyretin cardiac amyloidosis.

*Value Statement:
Low Value (B-NR)*

NO

YES

Check Tc-99m-PYP scan (1)

Perform TTR gene sequencing (1)

ATTRwt-CM

ATTRv-CM

Treatment

Tafamidis (1)



Whats on the Horizon for CHF ?



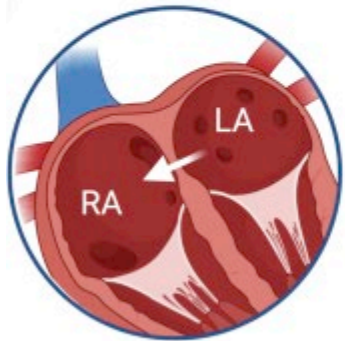
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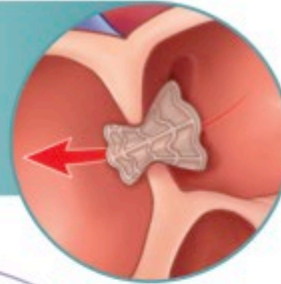


AFR
Occlutech



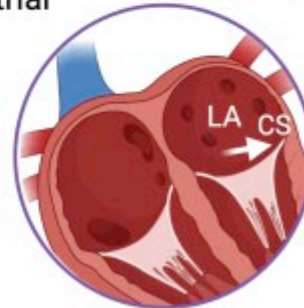
LA-RA shunts

ATRIAL SHUNTS



Transcatheter Atrial Shunt System

Edwards
Lifesciences

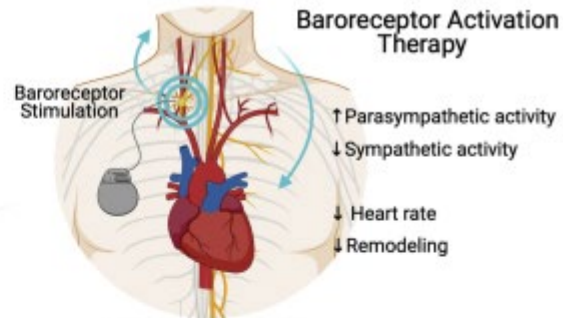
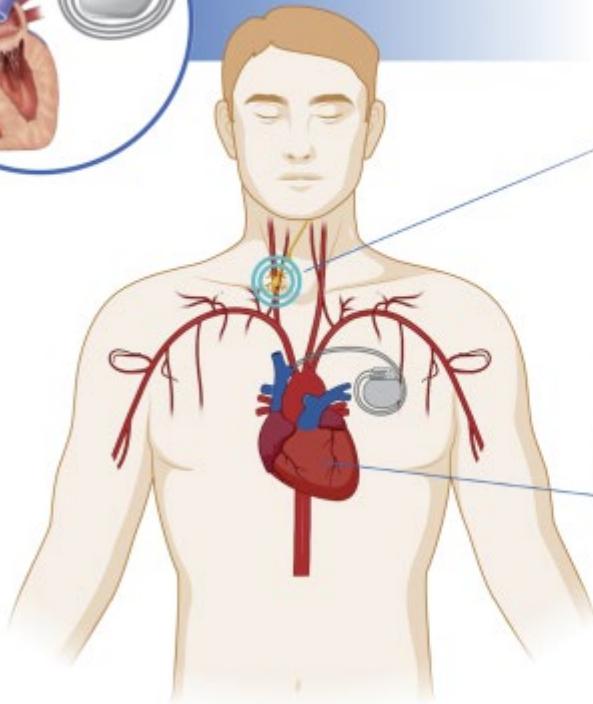


LA-CS shunts

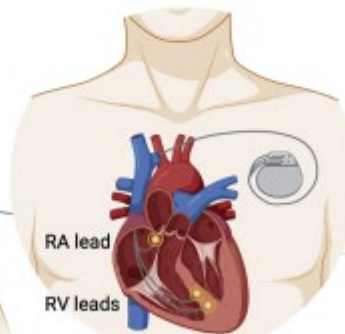




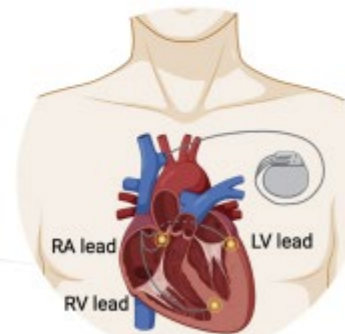
STIMULATION THERAPY



BAROSTIM™ NEO
CRVx Inc.



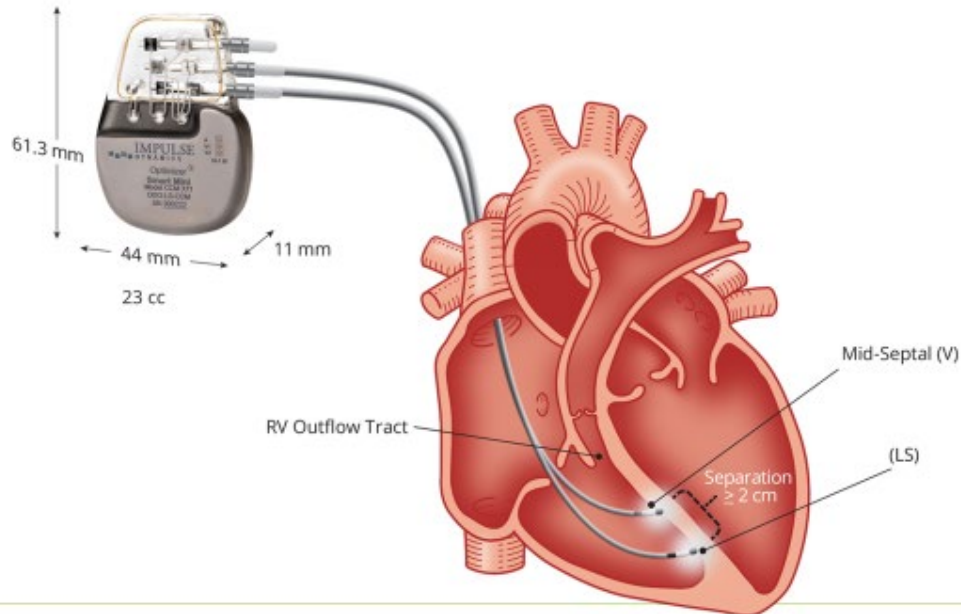
Cardiac Contractility Modulation

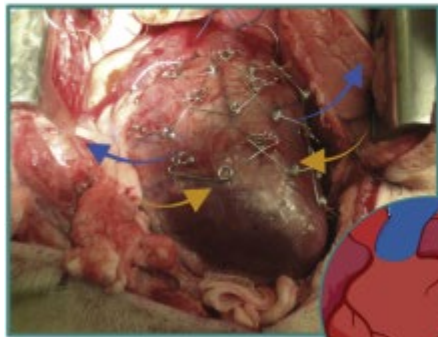


Cardiac Resynchronization Therapy

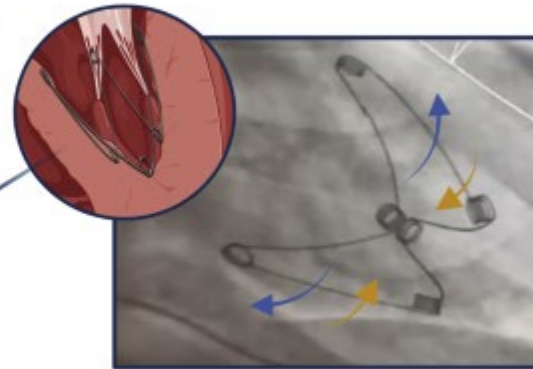
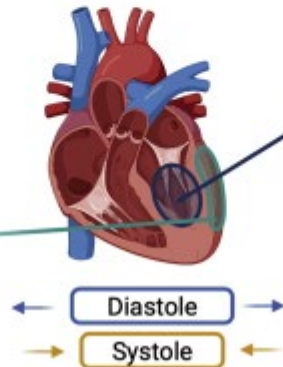


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Questions?



