Heart Failure

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Terms Related to Cardiac Performance

Preload	The ventricular wall tension at the end of diastole. In clinical terms, it is the stretch on the ventricular fibers just before contraction, often approximated by the end diastolic volume or end diastolic pressure.
Afterload	The ventricular wall tension during contraction; the resistance that must be overcome for the ventricle to eject its content. Often approximated by the systolic ventricular (or arterial) pressure
Contractility (Inotropic state)	Property of heart muscle that accounts for changes in the strength of contraction, independent of the preload and afterload. Reflects chemical or hormonal influences (e.g., catecholamines) on the force of contraction.
Stroke volume (SV)	Volume of blood ejected from the ventricle during systole. **SV = End diastolic volume - End systolic volume**
Ejection fraction (EF)	The fraction of end-diastolic volume ejected from the ventricle during each systolic contraction (normal range 55% to 75%). **EF = Stroke volume : End diastolic volume**
Cardiac Output (CO)	Volume of blood ejected from the ventricle per minute. **CO = SV x Heart rate**
Compliance	Intrinsic property of a chamber that describes its pressure–volume relationship during filling. Reflects the ease or difficulty with which the chamber can be filled. **Compliance = Δ Volume : Δ Pressure**

Leonard S Lily ,2011

HEART FAILURE

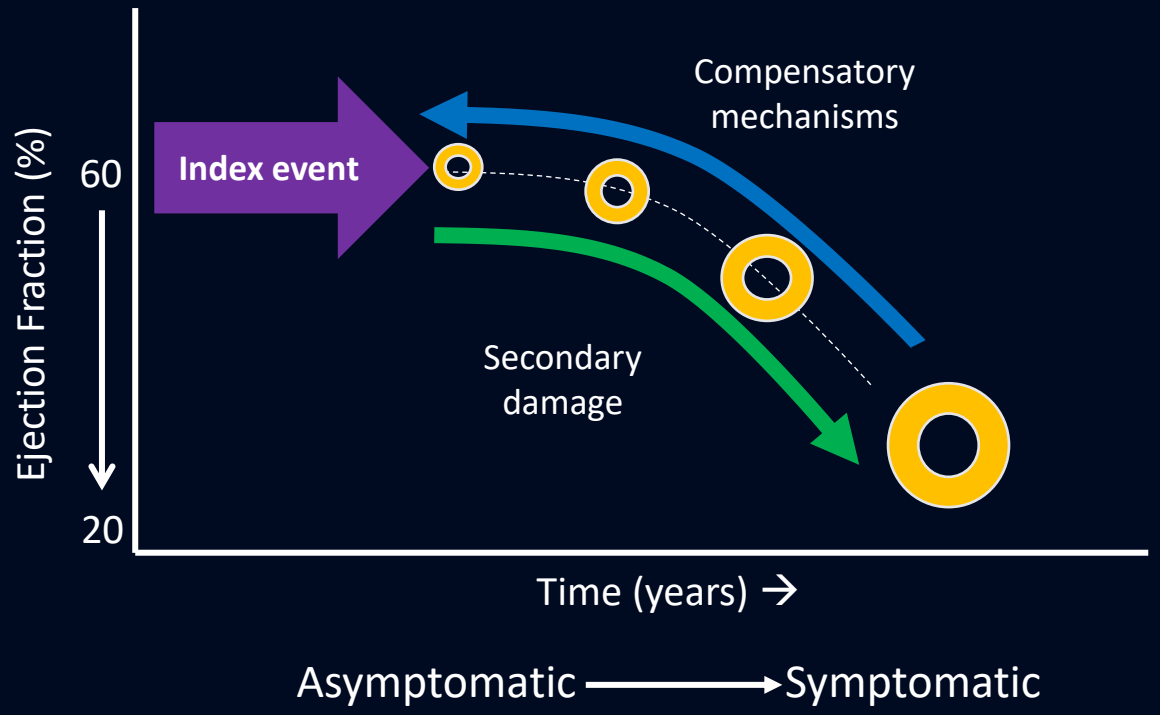
The heart is unable to pump blood forward at a sufficient rate to meet the metabolic demands of the body (forward failure), or is able to do so only if the cardiac filling pressures are abnormally high (backward failure), or both.

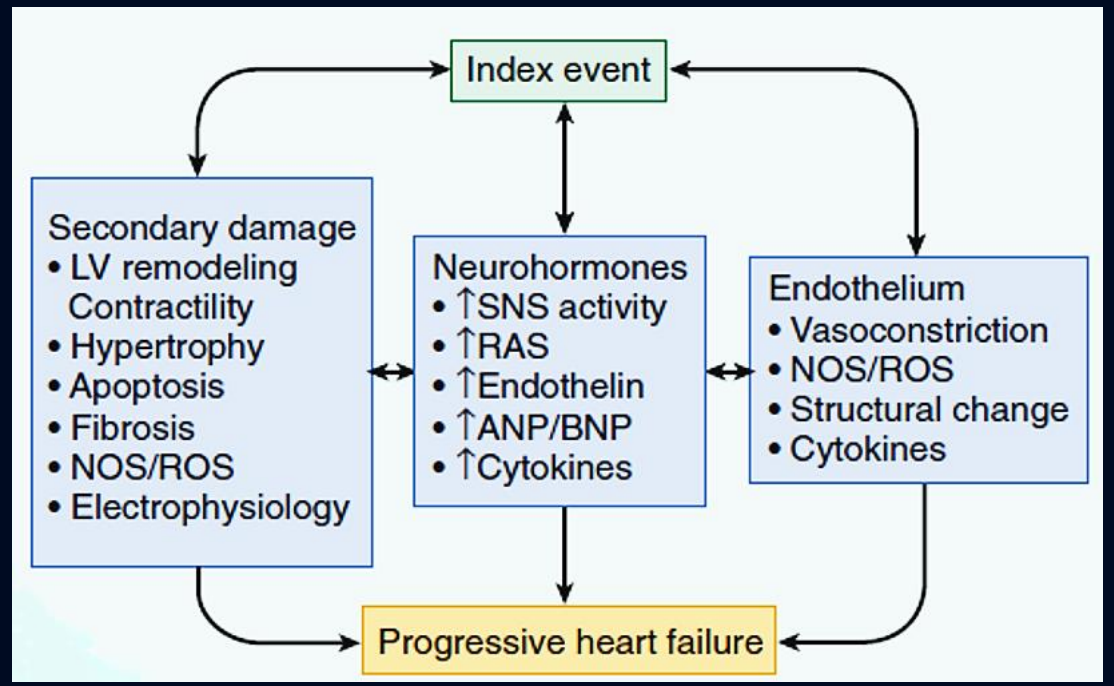
McMurray et al,2012

Epidemiology

- 1–2% of the adult population in developed countries has HF
- The prevalence rising to ≥10% among persons 70 years of age or older
- Before 1990, 60–70% of patients died within 5 years of diagnosis, and admission to hospital with worsening symptoms was frequent and recurrent.
- Effective treatment has improved these outcomes, with a relative reduction in hospitalization in recent years of 30–50% and smaller but significant decreases in mortality.

Pathophysiology



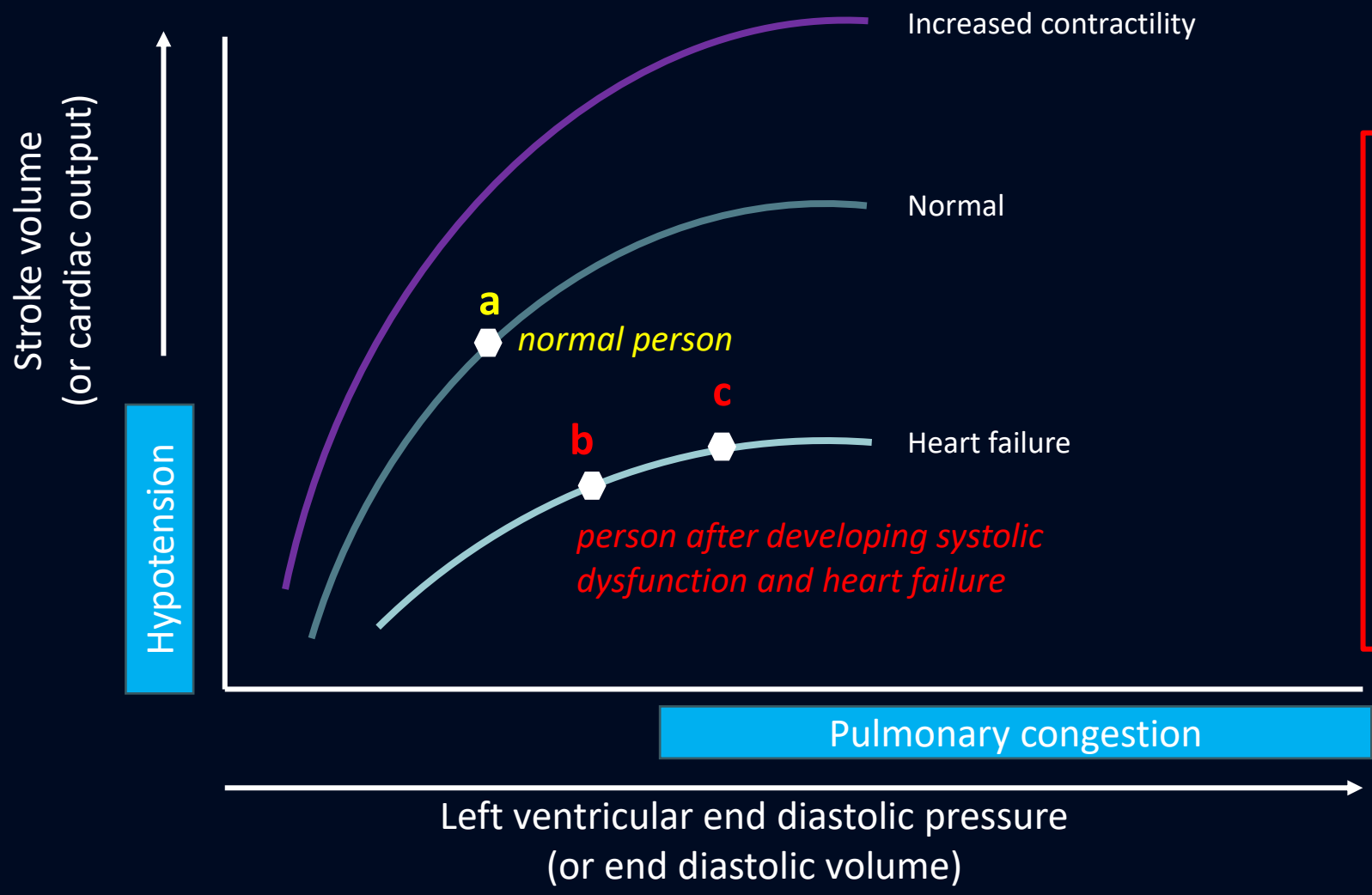


Compensatory Mechanism

- The Frank–Starling mechanism
- Neurohormonal alterations
- Ventricular hypertrophy and remodeling

Leonard S Lily ,2011

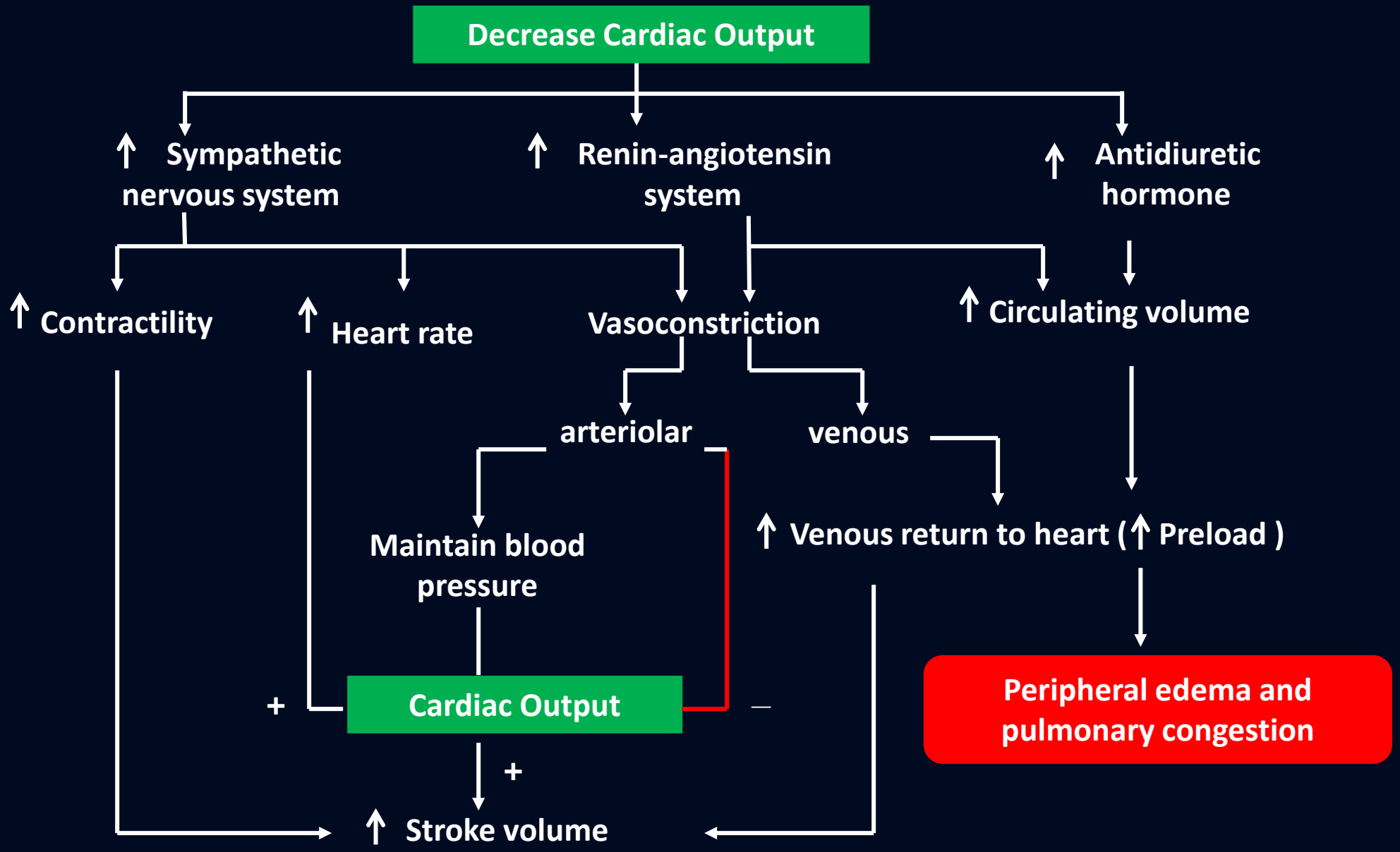
Frank–Starling Mechanism



Further augmentation of LV filling (e.g., increased circulating volume) in the heart failure patient is represented by point c, which resides on the relatively flat part of the curve: stroke volume is only slightly augmented, but the signifcantly increased EDP results in pulmonary congestion.

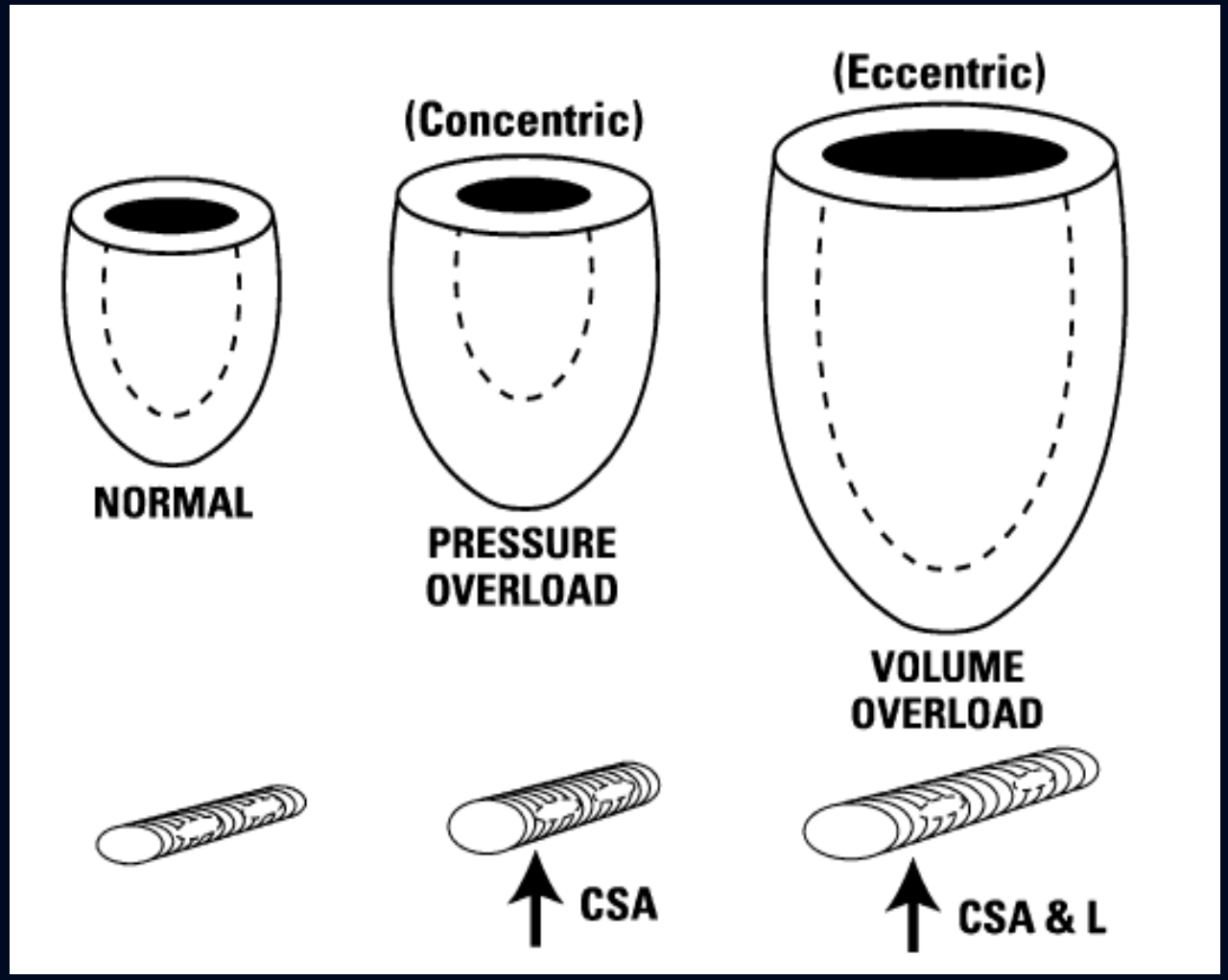
Leonard S Lily ,2011

Neurohormonal Alterations



Leonard S Lily ,2011

Ventricular Hypertrophy and Remodeling



Schematic representation of myocyte change in left ventricular concentric and eccentric hypertension. In pressure overload hypertrophy, the myocyte cross-sectional area increases and the ventricular wall becomes thicker during the compensatory phase. In volume overload hypertrophy, ventricular volume and wall thickness increase proportionally; this is associated with a corresponding proportional increase in both myocyte length and cross sectional area

Jay N Cohn et al,2006

Terminology of Heart Failure

- **Left/right sided heart failure**
- Systolic/diastolic heart failure
- Backward/forward heart failure
- Acute/chronic heart failure
- Congestive heart failure
- **Reduce/mid-range/preserved ejection fraction heart failure**

Leonard S Lily ,2011

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

Ponikowski et al,2016

Left Sided Heart Failure

Impaired Contractility

1. Coronary artery disease
   - Myocardial infarction
   - Transient myocardial ischemia
2. Chronic volume overload
   - Mitral regurgitation
   - Aortic regurgitation
3. Dilated cardiomyopathies

Reduced Ejection Fraction *(Systolic Dysfunction)*

Heart Failure

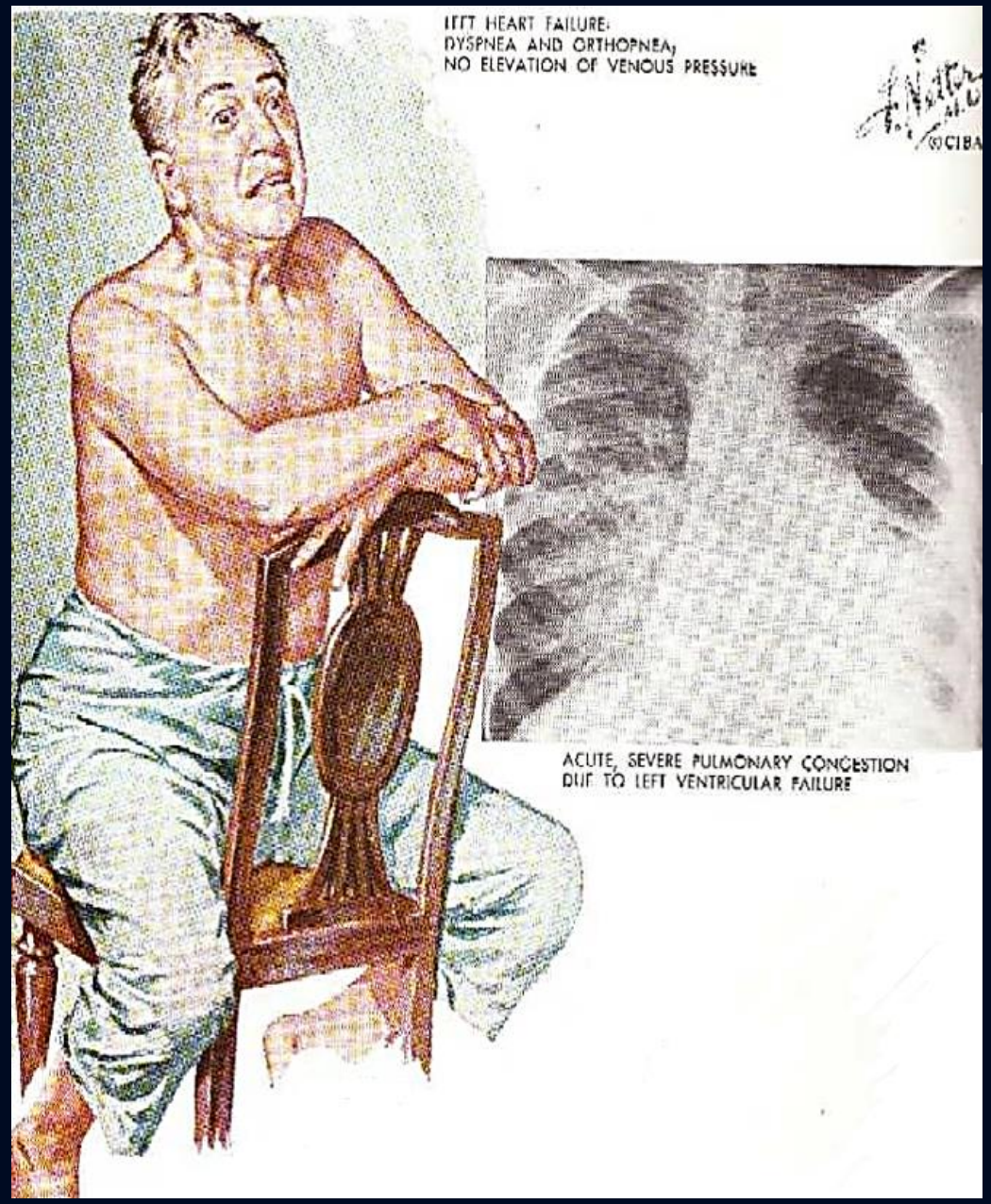
Preserved Ejection Fraction *(Diastolic Dysfunction)*

↑↑Afterload (Chronic Pressure Overload[a])

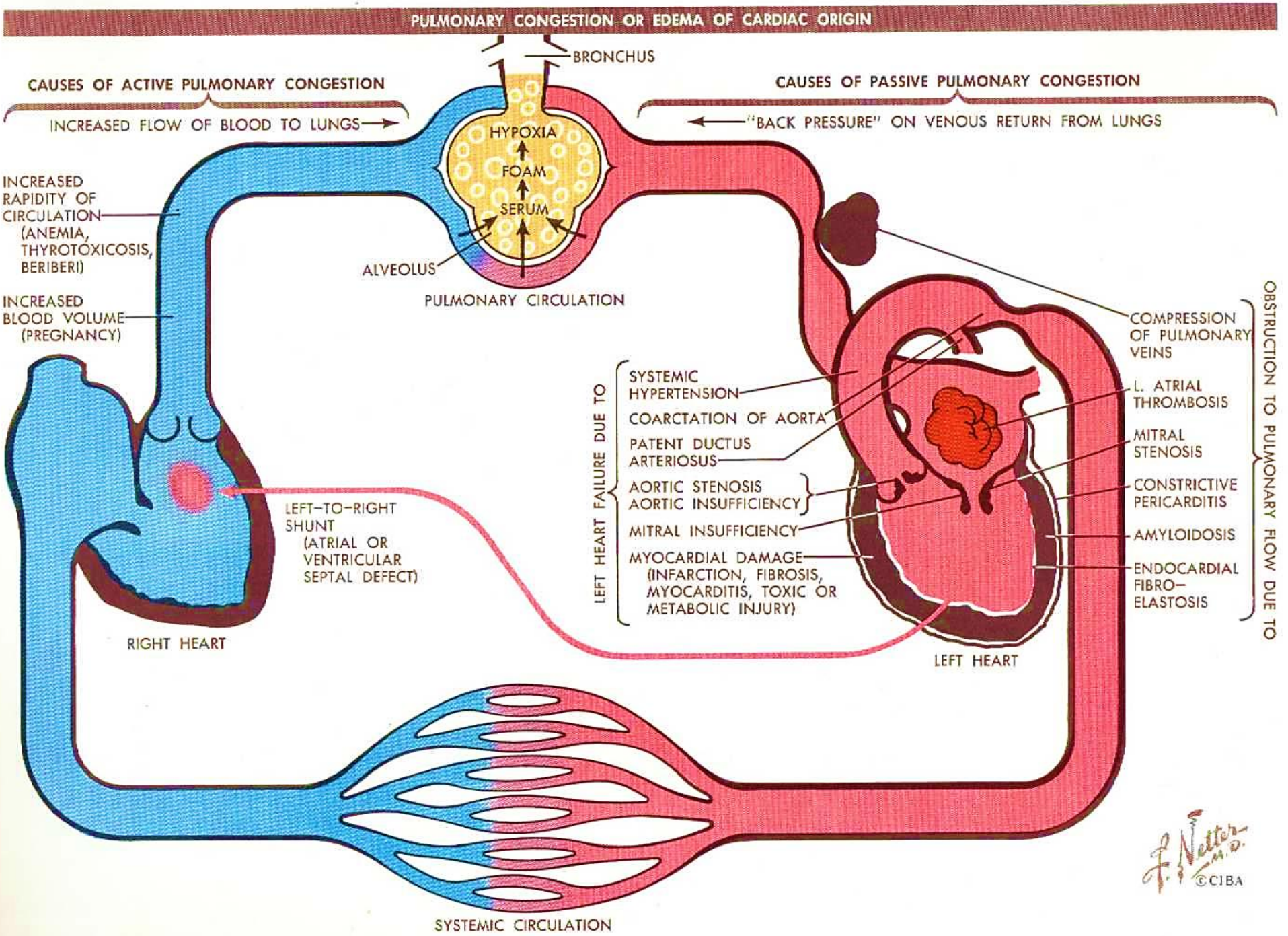
1. Advanced aortic stenosis
2. Uncontrolled severe hypertension

Impaired Diastolic Filling

1. Left ventricular hypertrophy
2. Restrictive cardiomyopathy
3. Myocardial fibrosis
4. Transient myocardial ischemia
5. Pericardial constriction or tamponade



Leonard S Lily ,2011



Marshall,2005

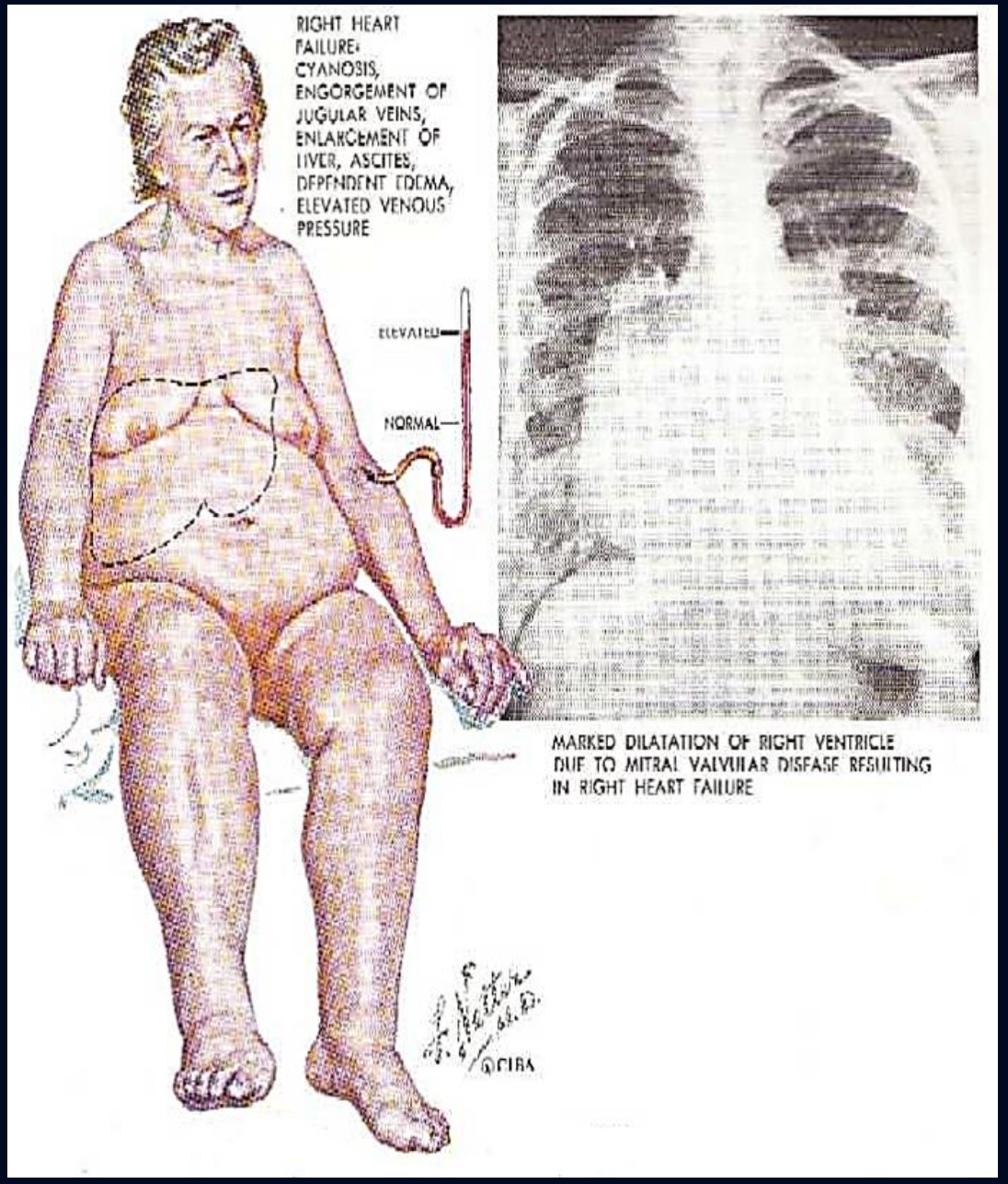
Right Sided Heart Failure

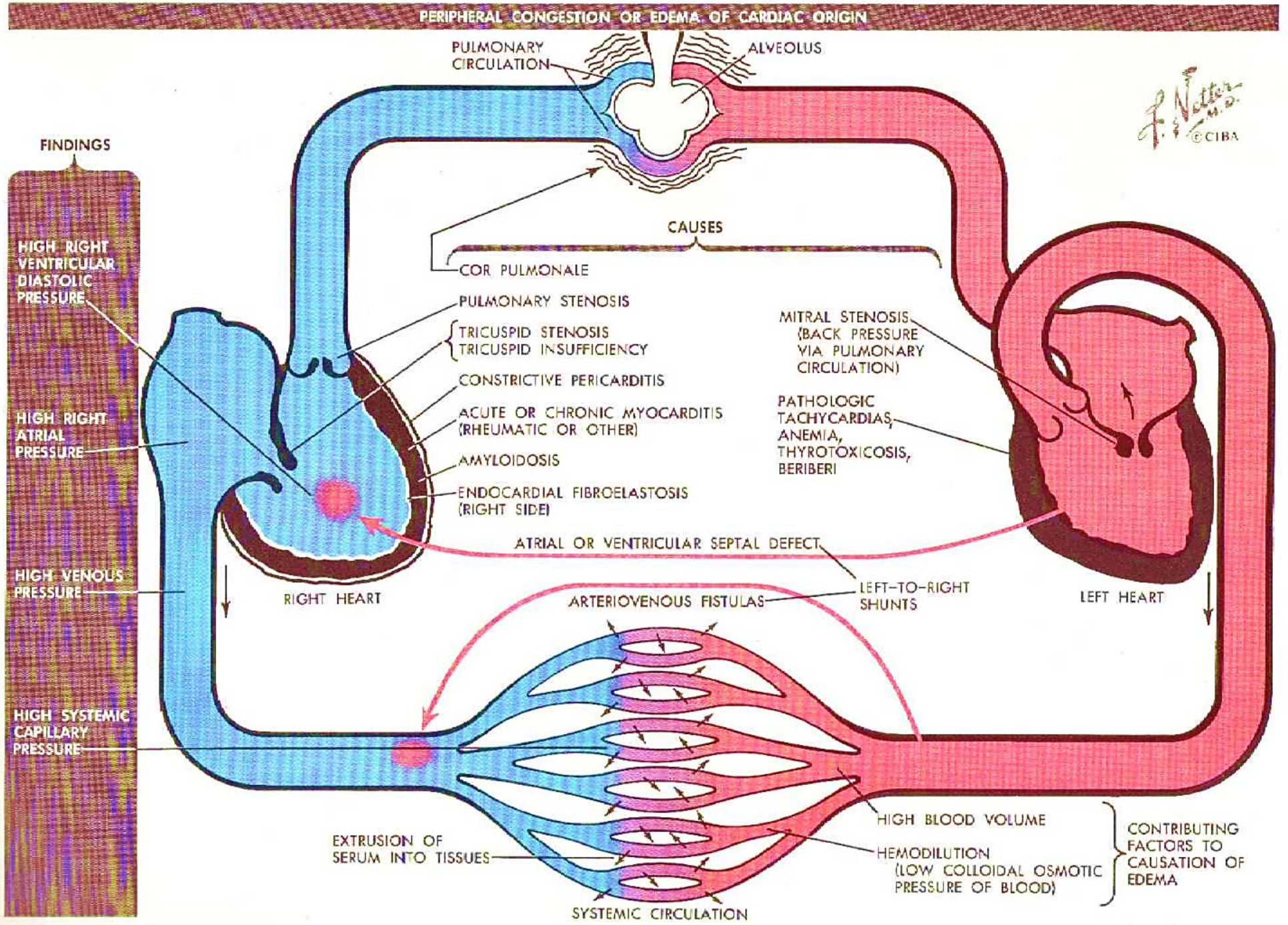
- **Cardiac causes** : Left-sided heart failure, Pulmonic valve stenosis, Right ventricular infarction

- **Pulmonary parenchymal disease** : Chronic obstructive pulmonary disease, Interstitial lung disease (e.g., sarcoidosis), Adult respiratory distress syndrome, Chronic lung infection or bronchiectasis

- **Pulmonary vascular disease** : Pulmonary embolism, Primary pulmonary hypertension

Leonard S Lily ,2011





Marshall,2005

Stages of Chronic Heart Failure

Stage A — Patient who is at risk of developing heart failure but has not yet developed structural cardiac dysfunction (e.g., patient with coronary artery disease, hypertension, or family history of cardiomyopathy).

Stage B — Patient who has structural heart disease associated with heart failure but has not yet developed symptoms.

Stage C — Patient who has current or prior symptoms of heart failure associated with structural heart disease.

Stage D — Patient who has structural heart disease and *marked* heart failure symptoms despite maximal medical therapy and requires advanced interventions (e.g., cardiac transplantation).

McMurray et al,2012

New York Heart Association (NYHA) Functional Classification

based on severity of symptoms and physical activity

Class I

No limitation of physical activity.
Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.

Class II

Slight limitation of physical activity.
Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.

Class III

Marked limitation of physical activity.
Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.

Class IV

Unable to carry on any physical activity without discomfort.
Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

McMurray et al,2012

Criteria for diagnosis of HF: Framingham Criteria

Major Criteria	Minor Criteria
• Paroxysmal nocturnal dyspnea or orthopnea • Neck-vein distention • Rales • Cardiomegaly • Acute pulmonary edema • Protodiastolic gallop (S3 gallop) • Increased venous pressure (≥16 cm H_2O at right atrium) • Increased circulation time (≥25 sec) • Hepatojugular reflux	• Ankle edema • Nocturnal cough • Dyspnea on ordinary exertion • Hepatomegaly • Pleural effusion • Decrease in vital capacity by one third from maximum recorded • Tachycardia (heart rate ≥120 bpm)

Izumi et al ,2012

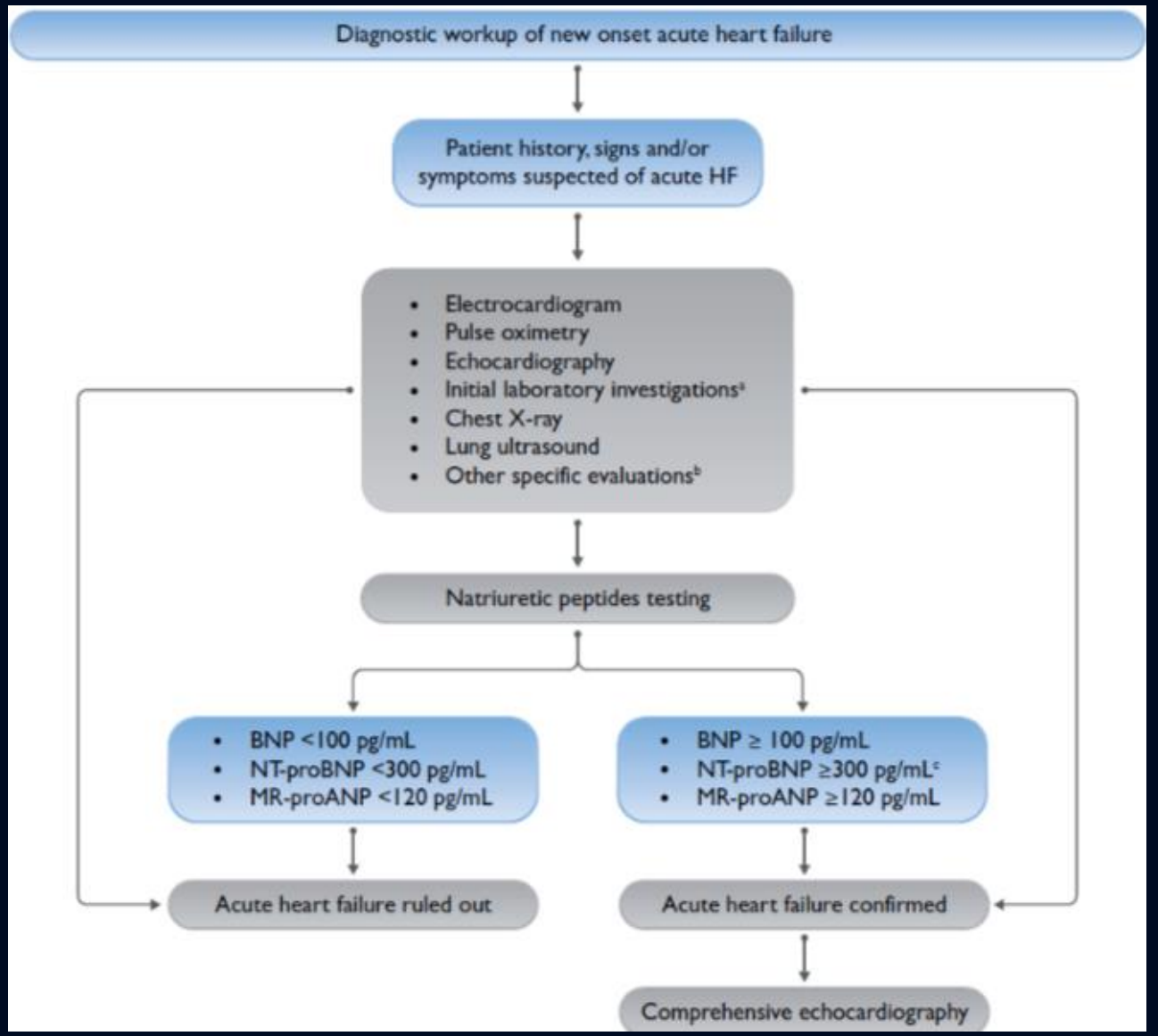
Major or Minor Criteria

Weight loss of 4.5 kg or more in 5 days in response to treatment. When the weight loss is attributable to the treatment of heart failure, it is considered 1 major criterion. Otherwise it is considered a minor criterion.

Diagnosis of heart failure requires the simultaneous presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria.

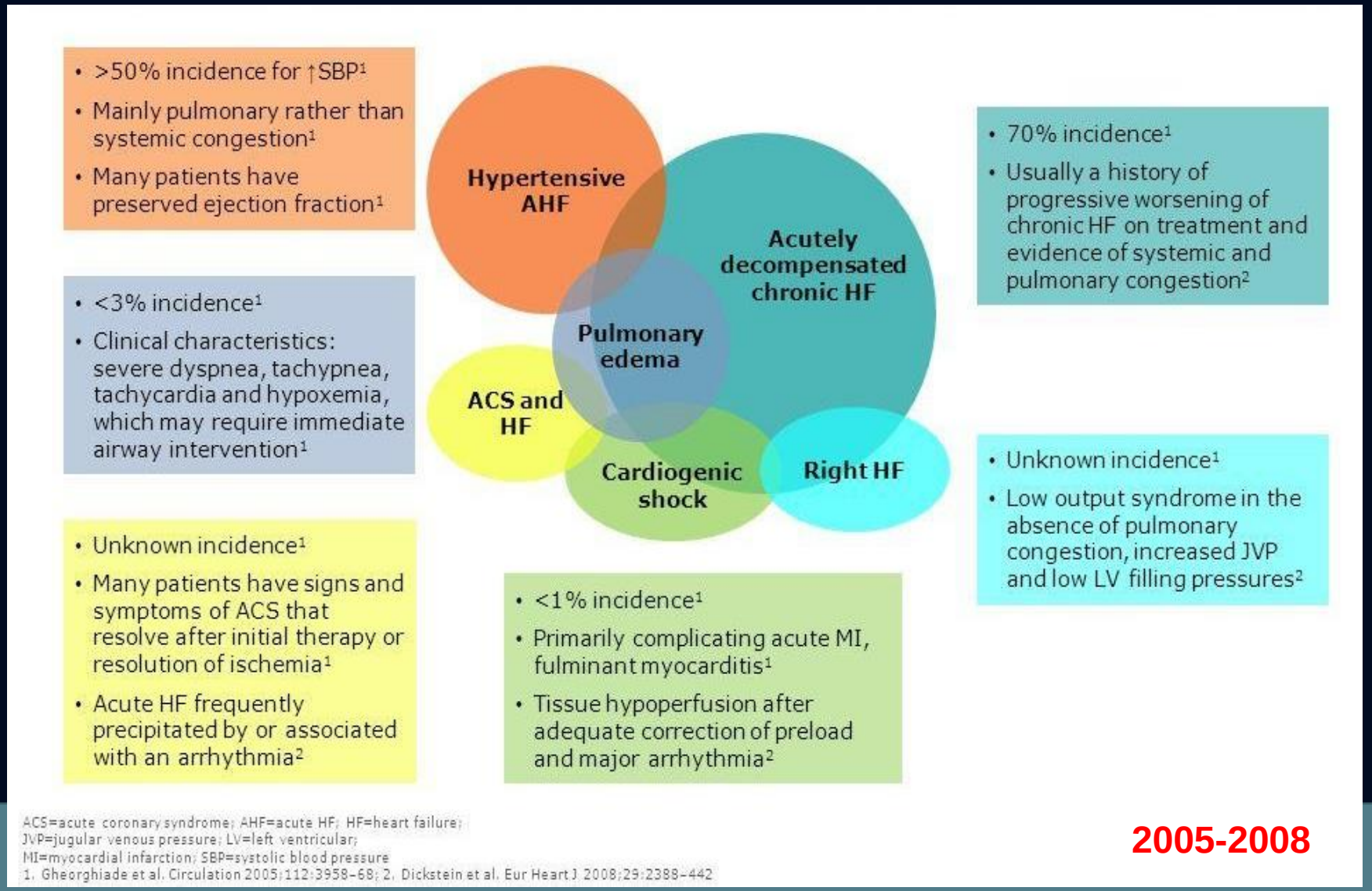
GAGAL JANTUNG AKUT

DIAGNOSIS



McDonagh TA, et al. 2021 ESC guidelines for the diagnosis and management of the chronic and acute heart failure. Eur Heart J. 2021;00:1-128

Gagal Jantung Akut: istilah untuk kejadian atau perubahan yang cepat dari tanda dan gejala gagal jantung.



2005-2008

Precipitating Factors for ADHF

- **Increased metabolic demands :** Fever, Infection, Anemia, Tachycardia, Hyperthyroidism, Pregnancy
- **Increased circulating volume (increased preload) :** Excessive sodium content in diet, Excessive fluid administration, Renal failure
- **Conditions that increase afterload :** Uncontrolled hypertension, Pulmonary embolism (increased right ventricular afterload)
- **Conditions that impair contractility :** Negative inotropic medications, Myocardial ischemia or infarction, Excessive ethanol ingestion
- **Failure to take prescribed heart failure medications**
- **Excessively slow heart rate**

McMurray et al,2012

Clinical presentations of acute heart failure

	Acutely decompensated heart failure (ADHF)	Acute pulmonary oedema	Isolated right ventricular failure	Cardiogenic Shock
Main mechanisms	LV dysfunction Sodium and water renal retention	Increased afterload and/or predominant LV diastolic dysfunction Valvular heart disease	RV dysfunction and/or pulmonary hypertension	Severe cardiac dysfunction
Main cause of symptoms	Fluid accumulation, increased intraventricular pressure	Fluid redistribution to the lungs and acute respiratory failure	Increased central venous pressure and often systemic hypoperfusion	Systemic hypoperfusion
Onset	Gradual (days)	Rapid (hours)	Gradual or rapid	Gradual or rapid
Main haemodynamic abnormalities	Increased LVEDP and PCWP[a] Low or normal cardiac output Normal to low SBP	Increased LVEDP and PCWP[a] Normal cardiac output Normal to high SBP	Increased RVEDP Low cardiac output Low SBP	Increased LVEDP and PCWP[a] Low cardiac output Low SBP
Main clinical presentations	Wet and warm OR Dry and cold	Wet and warm[b]	Dry and cold OR Wet and cold	Wet and cold
Main treatment	Diuretics Inotropic agents/vasopressors (if peripheral hypoperfusion/ hypotension) Short-term MCS if needed	Diuretics Vasodilators[b]	Diuretics for peripheral congestion Inotropic agents/vasopressors (if peripheral hypoperfusion/ hypotension) Short-term MCS if needed	Inotropic agents/ vasopressors Short-term MCS

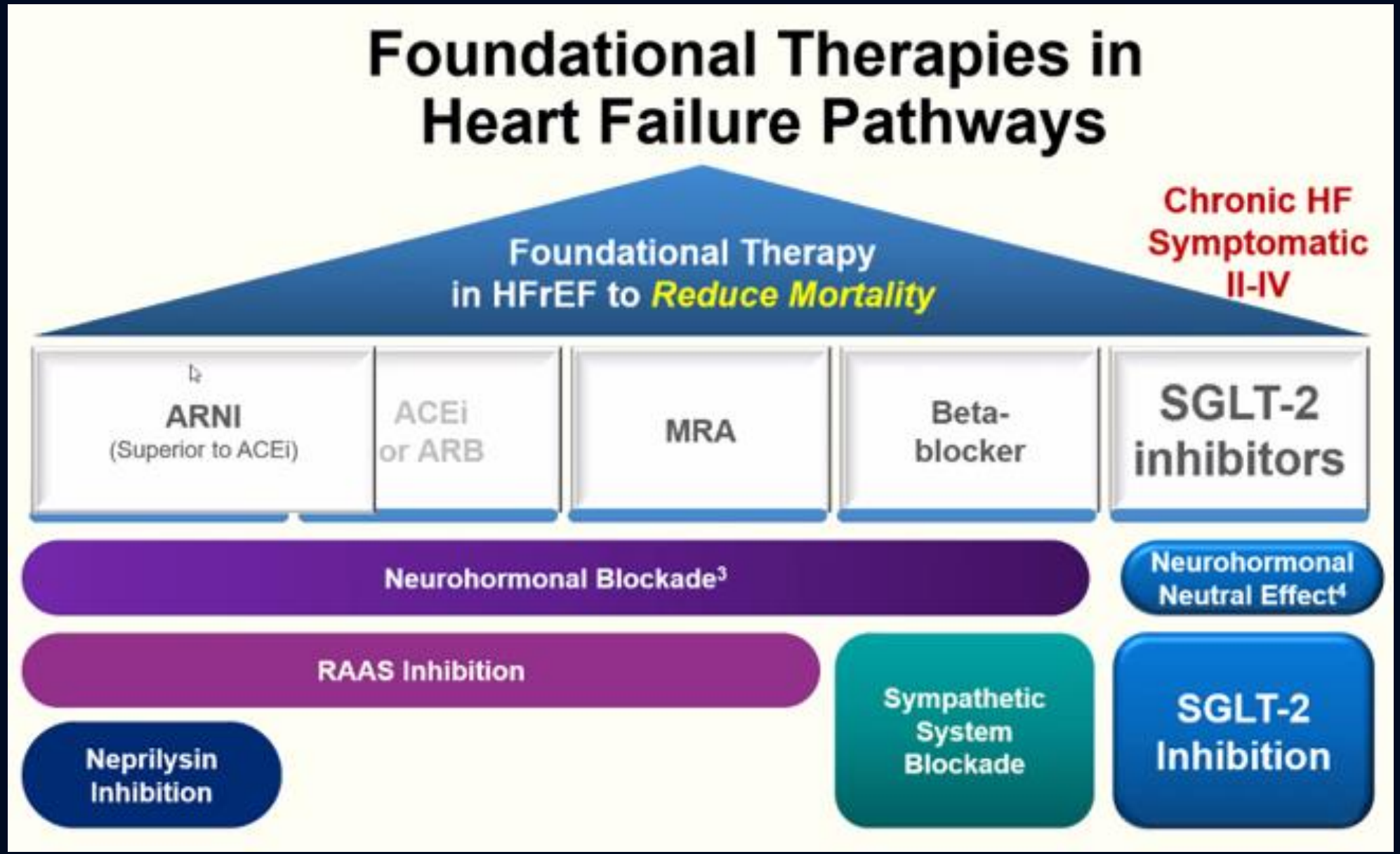
LV = left ventricular; LVEDP = left ventricular end-diastolic pressure; MCS = mechanical circulatory support; PCWP = pulmonary capillary wedge pressure; RV = right ventricular; RVEDP = right ventricular end-diastolic pressure; RRT = renal replacement therapy; SBP = systolic blood pressure. [a]May be normal with low cardiac output. [b]Wet and cold profile with need of inotropes and/or vasopressors may rarely occur.

2021

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)

GAGAL JANTUNG KRONIK

Foundational Therapies in Heart Failure Pathways



Drugs recommended in all patients with HFrEF

ESC, 2021

1. Angiotensin-converting enzyme inhibitors
2. Beta-blockers
3. Mineralocorticoid receptor antagonists
4. **Angiotensin receptor-neprilysin inhibitor**
5. **Sodium-glucose co-transporter 2 inhibitors**

ESC, 2016

1. Angiotensin-converting enzyme inhibitors
2. Beta-blockers
3. Mineralocorticoid receptor antagonists

Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

Guidelines Recommended Target Doses

CDMMT	Starting Dose	Typical Titration Dose(s)	Final Dose	Monitoring Parameters
ACEI or ARB				
Captopril	6.25 mg three-times daily	12.5 mg three-times daily; 25 mg three-times daily	50 mg three-times daily	Monitor blood pressure, electrolytes and renal function Can titrate every 1–2 weeks in outpatients and every 1–2 days in hospitalised patients
Enalapril	2.5 mg twice daily	5 mg twice daily; 10 mg twice daily	10–20 mg twice daily	
Lisinopril	2.5–5 mg daily	10 mg daily; 20 mg daily	20–40 mg daily	
Ramipril	1.25 mg daily	2.5 mg daily; 5 mg daily	10 mg daily	
Candesartan	4-8 mg daily	16 mg daily	32 mg daily	
Losartan	25–50 mg daily	100 mg daily	150 mg daily	
Valsartan	40 mg twice daily	80 mg twice daily	160 mg twice daily	
ARNI				
Sacubitril/valsartan	24/26 mg twice daily	49/51 mg twice daily	97/103 mg twice daily	Monitoring same as ACEI or ARB Starting dose based on daily equivalent of ACEI
β-blocker				
Bisoprolol	1.25 mg daily	2.5 mg daily; 5 mg daily	10 mg daily	Initiate only in stable patients Monitor blood pressure, heart rate and for signs of congestion Can titrate every 2 weeks
Carvedilol	3.125 mg twice daily	6.25 mg twice daily; 12.5 mg twice daily	25 mg twice daily*	
Metoprolol succinate	12.5–25 mg daily	50 mg daily; 100 mg daily	200 mg daily	
MRA				
Eplerenone	25 mg daily	NA	50 mg daily	Monitor electrolytes and renal function. Avoid in eGFR ≥30 ml/min/1.73 m^2 or K^+ >5 mEq/l
Spironolactone	12.5–25 mg daily	NA	25–50 mg daily	
SGLT2i				
Dapagliflozin	10 mg daily	NA	10 mg daily	Dapagliflozin: Only if eGFR ≥30 ml/min/1.73 m^2
Empagliflozin	10 mg daily	NA	10 mg daily	Empagliflozin: Only if eGFR ≥20 ml/min/1.73 m^2

**Maximum dose of carvedilol is 50 mg twice daily for weight ≥85 kg. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; MRA = mineralocorticoid receptor antagonist; eGFR = estimated glomerular filtration rate; K+ = potassium; SGLT2i = sodium glucose cotransporter 2 inhibitor. Source: Fonarow et al. 2021[37,39]*

Nicholas K Brownell, Boback Ziaeian, Gregg C Fonarow. Cardiac Failure Review 2021;7:e18.

Management of HFrEF

To reduce mortality - for all patients

ACE-I/ARNI | BB | MRA | SGLT2i

To reduce HF hospitalization/mortality - for selected patients

Volume overload

Diuretics

SR with LBBB ≥ 150 ms	*SR with LBBB 130–149 ms or non LBBB≥ 150 ms*
CRT-P/D	CRT-P/D
Ischaemic aetiology	*Non-ischaemic aetiology*
ICD	ICD

Atrial fibrillation	*Atrial fibrillation*	*Coronary artery disease*	*Iron deficiency*
Anticoagulation	Digoxin / PVI	CABG	Ferric carboxymaltose

Aortic stenosis	*Mitral regurgitation*	*Heart rate SR>70 bpm*	*Black Race*	*ACE-I/ARNI intolerance*
SAVR/TAVI	TEE MV Repair	Ivabradine	Hydralazine/ISDN	ARB

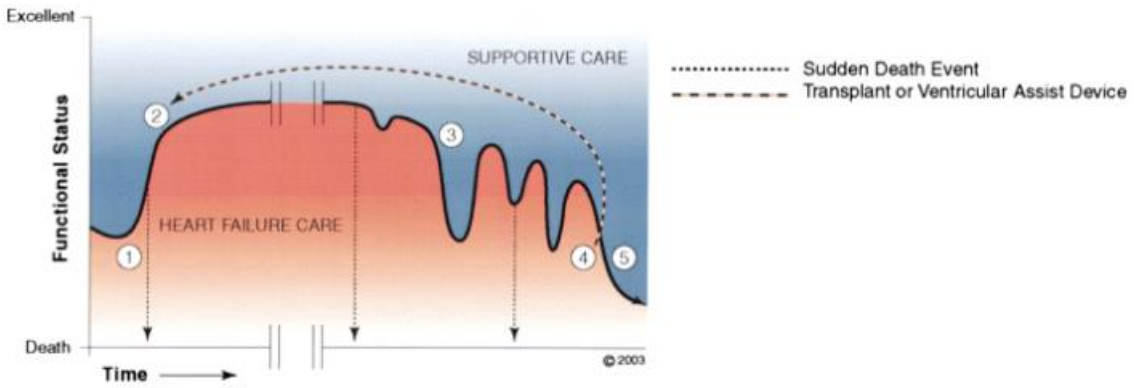
For selected advanced HF patients

Heart transplantation | MCS as BTT/BTC | Long-term MCS as DT

To reduce HF hospitalization and improve QOL - for all patients

Exercise rehabilitation

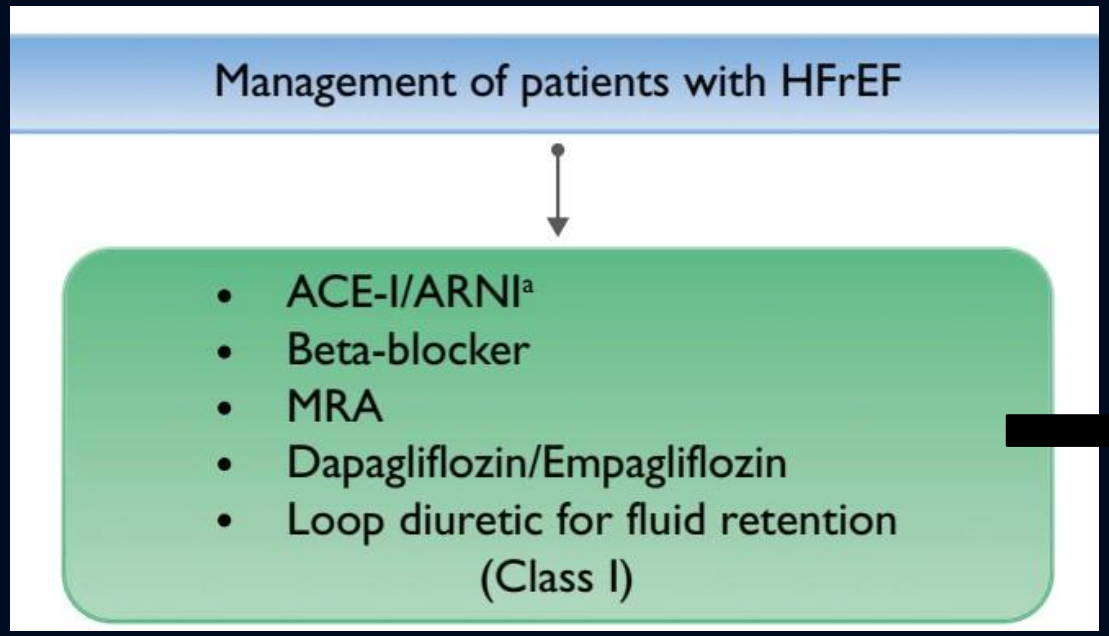
Multi-professional disease management



Schematic course of Stage C and D heart failure. Sudden death may occur at any point along the course of illness. (1) Initial symptoms of heart failure (HF) develop and HF treatment is initiated. (2) Plateaus of variable length may be reached with initial medical management or after mechanical support or heart transplant. (3) Functional status declines with variable slope, with intermittent exacerbations of HF that respond to rescue efforts. (4) Stage D HF, with refractory symptoms and limited function. (5) End of life.

Comprehensive Heart Failure Care (adapted with permission from Goodlin et al. [17])

How to treat heart failure with preserved ejection fraction (HFpEF = LVEF≥50%) ?



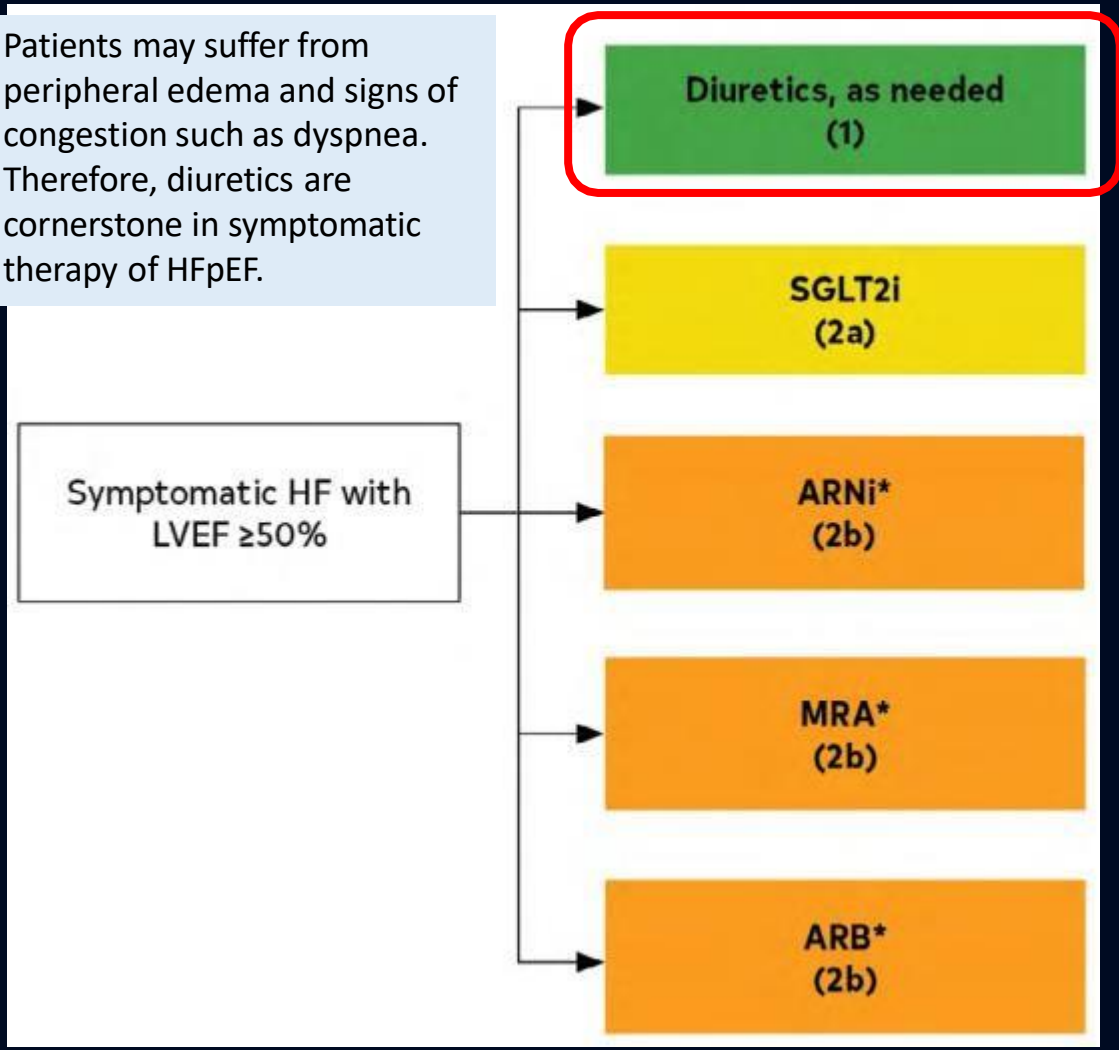
These therapies do not decrease morbidity and mortality in HFpEF

HFpEF Treatment - HFSA 2022

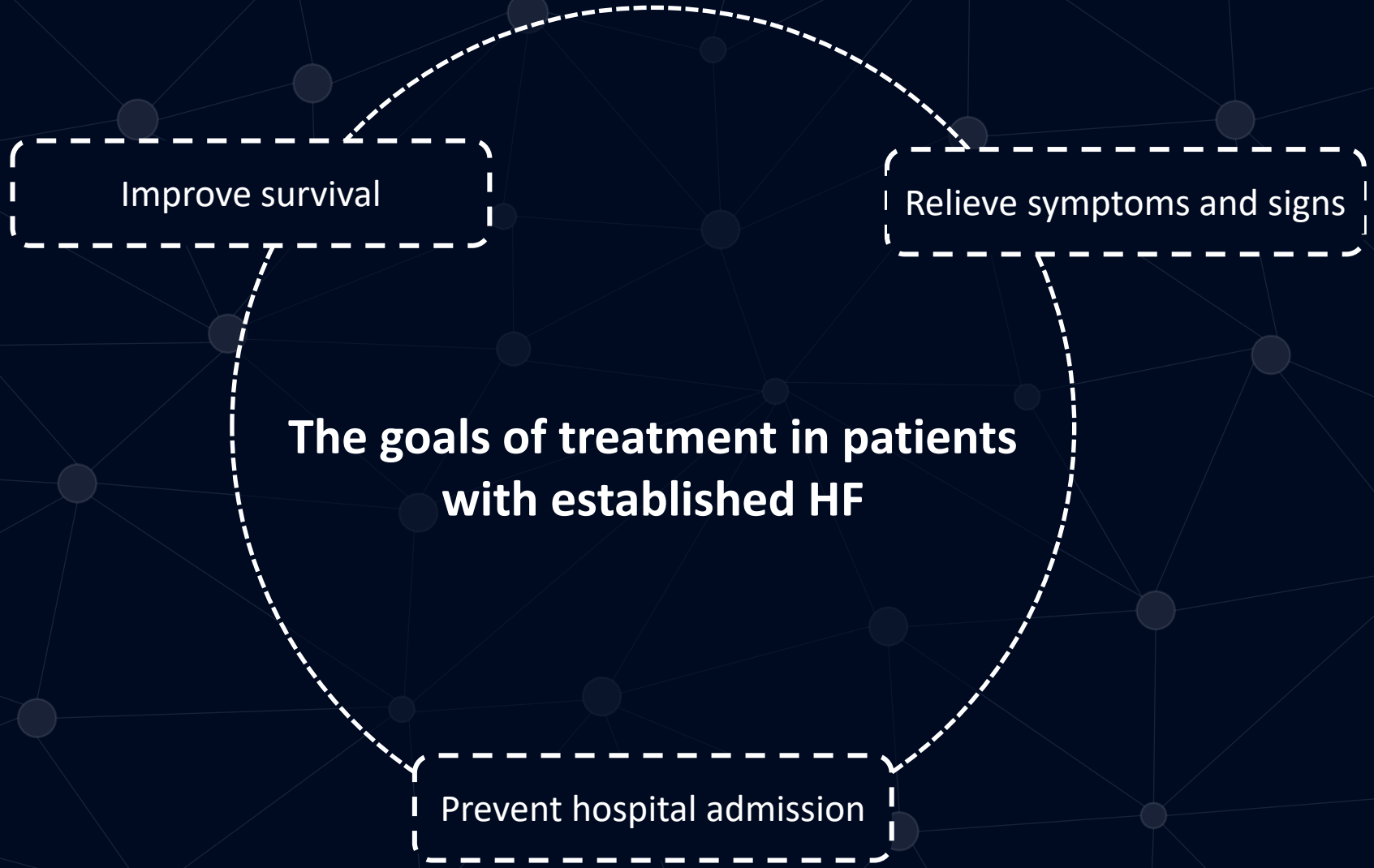
Recommendations for HF With Preserved Ejection Fraction*
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

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.[1–3]
2a	B-R	2. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.[4]
2a	C-EO	3. In patients with HFpEF, management of AF can be useful to improve symptoms.
2b	B-R	4. In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[5–7]
2b	B-R	5. 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.[8,9]
2b	B-R	6. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[10,11]
3: No-Benefit	B-R	7. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QOL is ineffective.[12,13]

Patients may suffer from peripheral edema and signs of congestion such as dyspnea. Therefore, diuretics are cornerstone in symptomatic therapy of HFpEF.



Heidenreich et al. Circulation. 2022;145:e895–e1032.



McMurray et al,2012

THANK YOU