Heart Failure

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Objectives:

By the end of the lecture the student should be able to:

1. Know different classifications of heart failure.
2. Know the causes and precipitation factors for heart failure decompensation.
3. Describe the Pathophysiology, therapies that improve survival, and prognosis.

DEFINITION: Complex clinical syndrome secondary to a functional or structural abnormality of the heart which impairs the capacity of the ventricle to eject blood (and perfuse tissues) or to be adequately filled

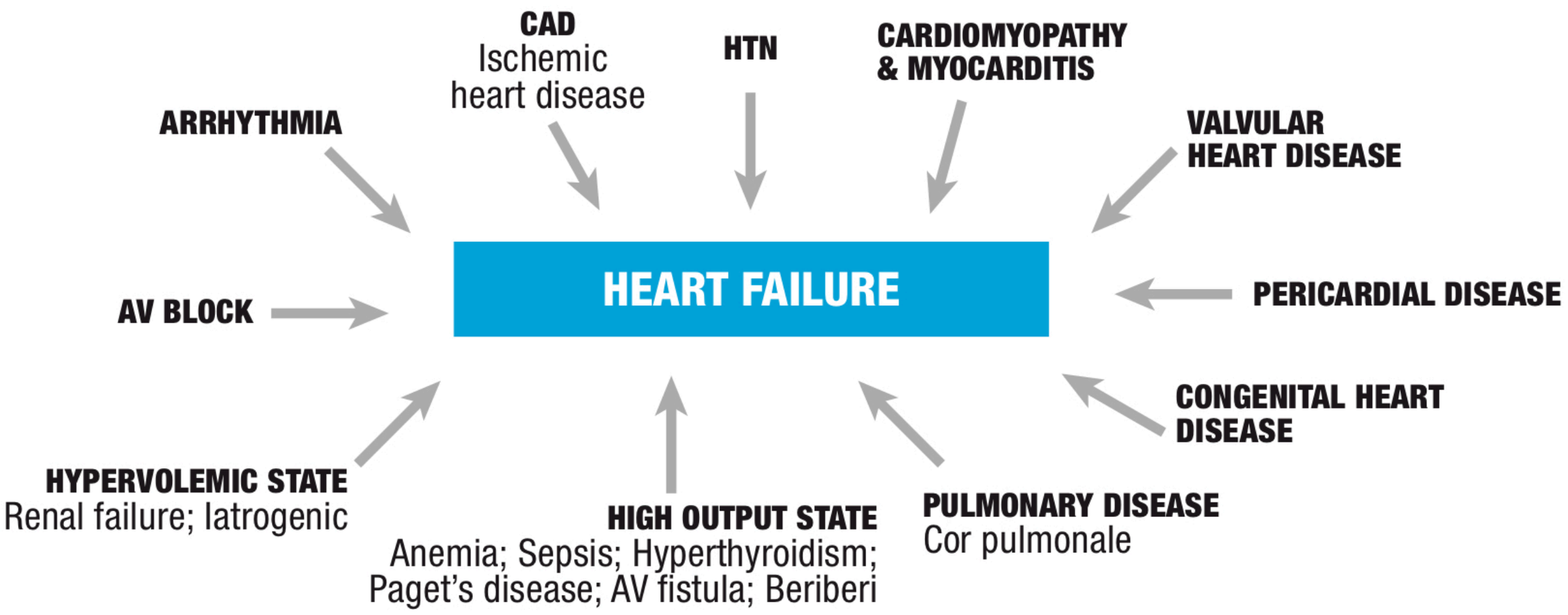
SYSTOLIC HEART FAILURE	HEART FAILURE WITH PRESERVED LVEF
1. Typical symptoms **2. Typical signs** **3. ↘ LVEF**	1. Typical symptoms 2. Typical signs 3. Normal or slightly decreased LVEF; non-dilated LV 4. Structural heart disease (LVH; LAH) and/or diastolic dysfunction

LVEF = stroke volume (end-diastolic volume – end-systolic volume) / end-diastolic volume

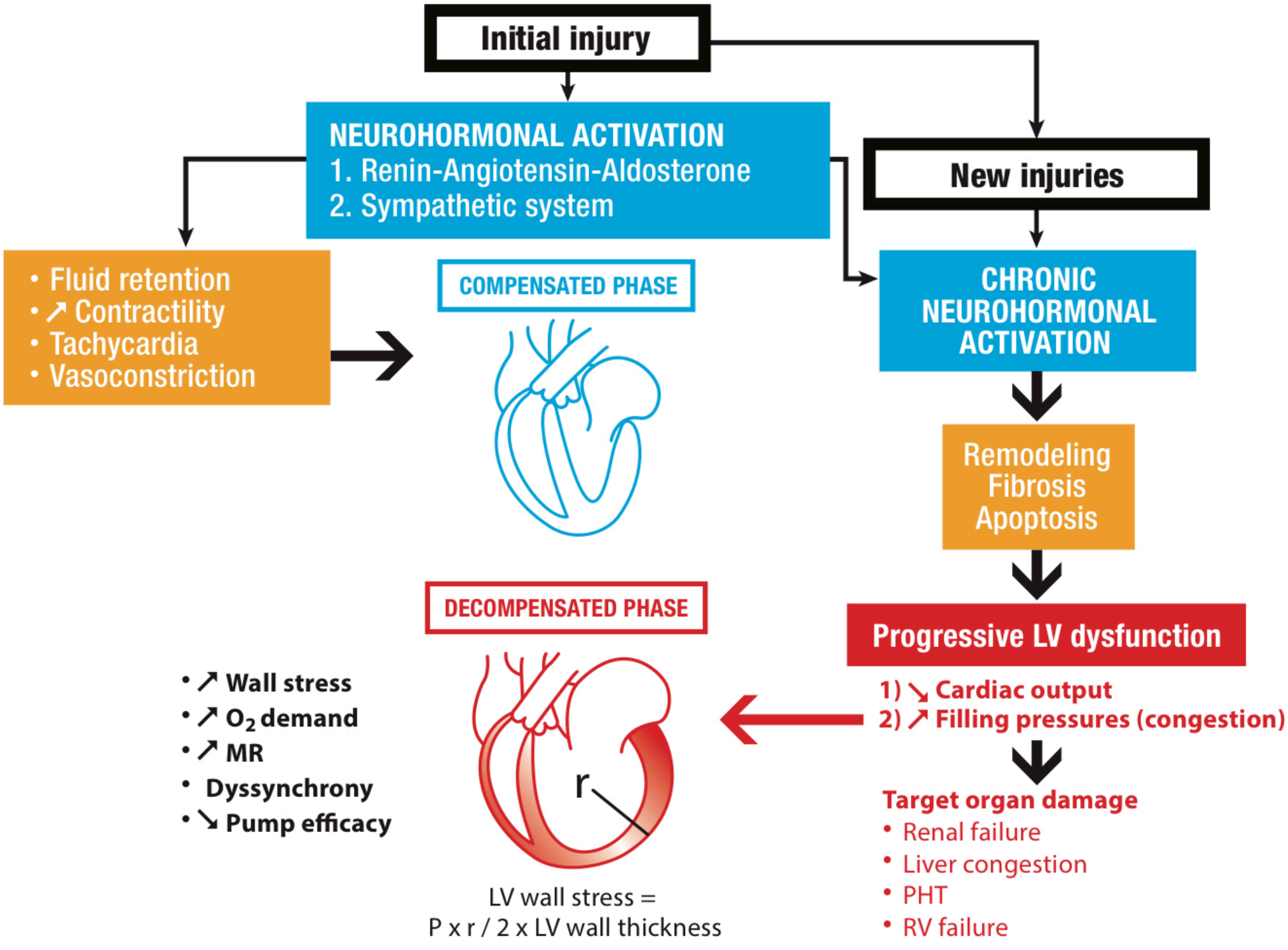
- **When LVEF is decreased: stroke volume is maintained by increasing end-diastolic volume** (eccentric LVH)

SYMPTOMS	SIGNS
• Dyspnea • **Orthopnea** • **PND** (1-2 h after going to bed; resolution in 15-30 min) • **↘ Exercise tolerance** • Tiredness • Lower limb edema • **Peripheral edema** • **Nocturnal cough** • Wheezing • Weight gain • Loss of appetite • RUQ pain • Nocturia	• Cachexia • Hypotension; OH; Narrow pulse pressure • Pulsus alternans; ↘ Pulse amplitude • **Tachycardia** • Tachypnea • Cheyne-Stokes breathing • **JVD** ; HJ reflux • Lateralized and widened apex • Left parasternal heave / Signs of PHT • Decreased S1 • **S3** - S4 (± palpable) • AV valve regurgitation • **Crackles** • Wheezing • **Signs of pleural effusion** • **Hepatomegaly (± pulsatile)** • **Peripheral edema** (leg edema; scrotum; presacral; ascites) • Cold extremities • Confusion / Decreased level of consciousness

ETIOLOGIES


CAD
Ischemic heart disease
HTN
CARDIOMYOPATHY & MYOCARDITIS
ARRHYTHMIA
VALVULAR HEART DISEASE
HEART FAILURE
AV BLOCK
PERICARDIAL DISEASE
CONGENITAL HEART DISEASE
HYPERVOLEMIC STATE
Renal failure; Iatrogenic
HIGH OUTPUT STATE
Anemia; Sepsis; Hyperthyroidism; Paget's disease; AV fistula; Beriberi
PULMONARY DISEASE
Cor pulmonale

NYHA class	Symptoms
I	No limitation in normal physical activity
II	Mild symptoms only in normal activity
III	Marked symptoms during daily activities, asymptomatic only at rest
IV	Severe limitations, symptoms even at rest


Initial injury
NEUROHORMONAL ACTIVATION
1. Renin-Angiotensin-Aldosterone
2. Sympathetic system
• Fluid retention
• ↗ Contractility
• Tachycardia
• Vasoconstriction
COMPENSATED PHASE
New injuries
CHRONIC NEUROHORMONAL ACTIVATION
Remodeling
Fibrosis
Apoptosis
Progressive LV dysfunction
1) ↘ Cardiac output
2) ↗ Filling pressures (congestion)
Target organ damage
• Renal failure
• Liver congestion
• PHT
• RV failure
DECOMPENSATED PHASE
• ↗ Wall stress
• ↗ O_2 demand
• ↗ MR
• Dyssynchrony
• ↘ Pump efficacy
r
LV wall stress =
P x r / 2 x LV wall thickness

ASSESSMENT

WORK-UP: CBC; Electrolytes (including Ca^{2+}/Mg^{2+}); Creatinine - BUN; LFTs; Blood glucose; HbA1c; TSH; Urinalysis; Lipids

- **If necessary**: CK; Iron assessment; HIV; ANA; RF; Urine metanephrines; SPEP - UPEP; Uric acid; CRP; Troponin; Polysomnography

ECG: Sinus tachycardia; arrhythmia (AF; PVCs; NSVT); Conduction disorder / LBBB; LVH; LAH; Q waves; ischemia; low voltage QRS

- **AV block**: Drug-induced; myocardial infarction; myocarditis; sarcoidosis; familial cardiomyopathy (LMNA; SCN5A); Lyme disease

CXR: prominent hila; Kerley B lines (fine horizontal linear opacities extending to the pleura); peribronchial edema; interstitial / alveolar edema; redistribution to apices; pleural effusion; fluid in the fissure; cardiomegaly; other cause of dyspnea

TTE (± CONTRAST): chamber dimensions; LVH; systolic and diastolic function; LVEF (Simpson); valves; PAP; thrombus; cardiac output (LVOT VTI)

RADIONUCLIDE VENTRICULOGRAPHY: LVEF; RVEF

CARDIAC MRI: cardiac structure and function; LVEF; tissue characterization; evaluation of cardiomyopathy / myocarditis

CORONARY ANGIOGRAPHY (± FFR): rule out significant CAD

- **Noninvasive evaluation** (MIBI-P; stress echocardiography; coronary CT angiography) possible if few risk factors / low pre-test probability / low impact of the result on management

STRESS TEST / 6MWT / VO_2MAX: **A)** Objective evaluation of functional class; **B)** Rule out ischemia; **C)** Pre-transplant (VO_2max); **D)** Prescription of exercise; **E)** Prognosis; **F)** Distinguish cardiac from pulmonary cause

- **VO_2max < 12 mL O_2/kg/min** associated with poorer survival than in patients with a heart transplant
- **6MWT**: normal > 600 m; < 350 m roughly equivalent to NYHA III

BIOPSY

BNP: released by the failing heart or in response to hemodynamic stress; reflects wall stress and filling pressures

- Increases with age; decreases with obesity
- **DDx ↗**: CRF; arrhythmia; ACS; pulmonary embolism; severe COPD / PHT; sepsis; cirrhosis
- **Indications**: **A)** Identify the cause of dyspnea (cardiac versus non-cardiac); **B)** Prognosis
  - BNP-guided management of heart failure remains controversial; studies report divergent results

ACUTE HEART FAILURE UNLIKELY	NT-proBNP < 300 pg/mL (NPV 98 %)	BNP < 100 pg/mL
PROBABLE ACUTE HEART FAILURE	NT-proBNP > 450 pg/mL (< 50 years) > 900 pg/mL (50-75 years) > 1800 pg/mL (> 75 years)	BNP > 500 pg/mL

› **Variation**: a change of > 30% in BNP level should call for more intesive follow-up / treatment

OBJECTIVES

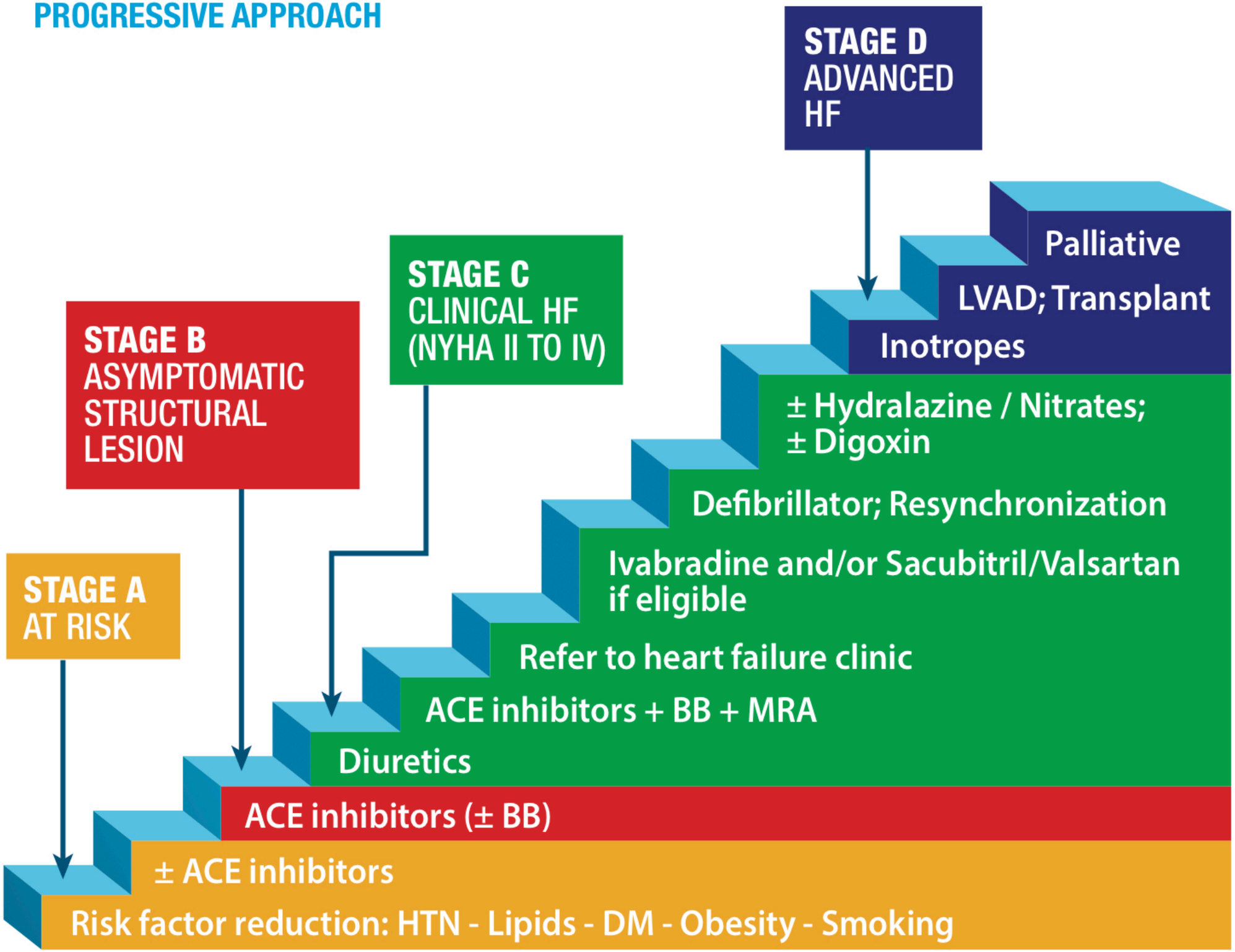
QUALITY OF LIFE

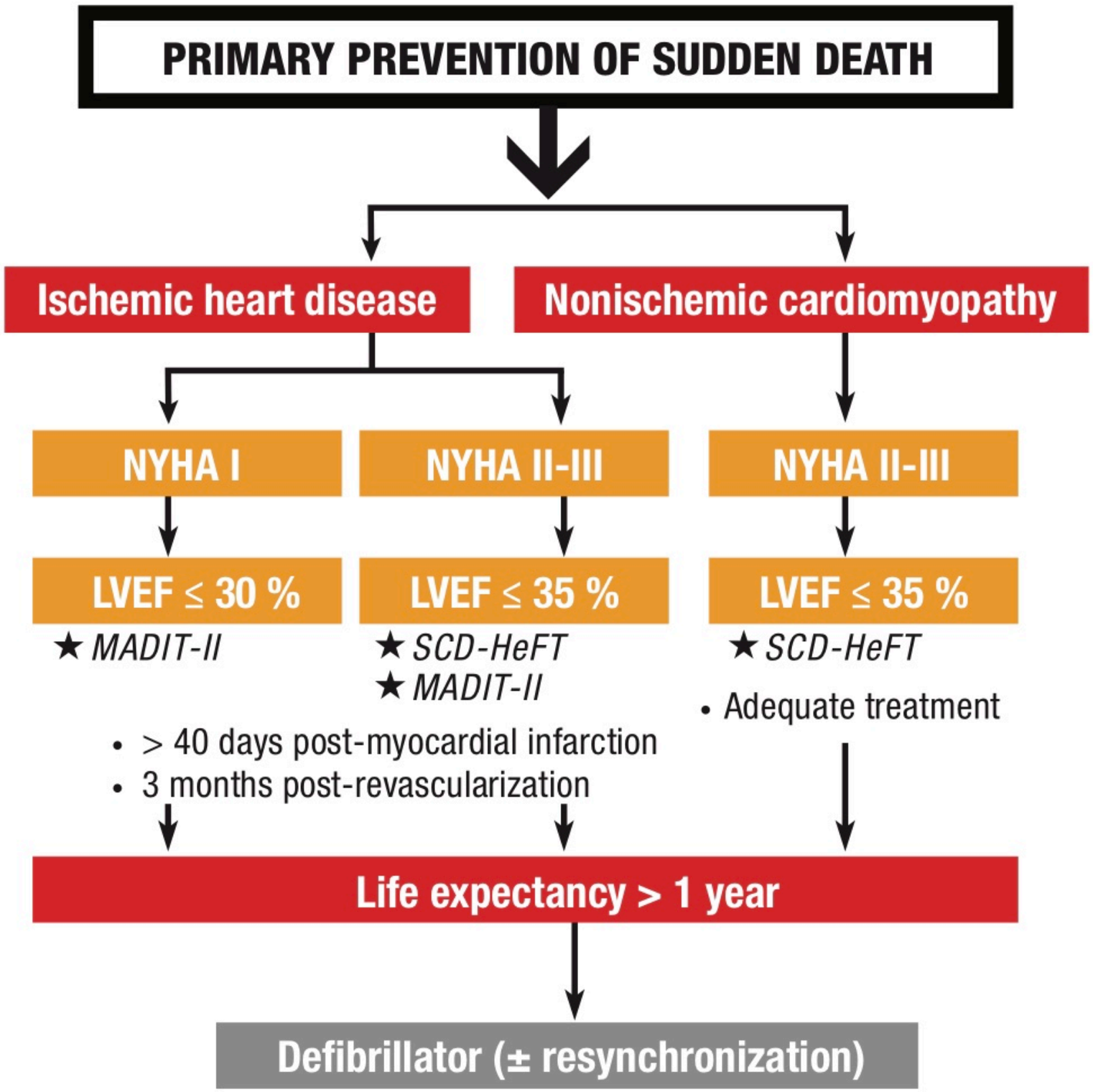
- ↓ Symptoms
- ↓ Hospitalizations
- Improve functional class
- Prevent disease progression

QUANTITY OF LIFE

- ↑ Survival

PROGRESSIVE APPROACH




PRIMARY PREVENTION OF SUDDEN DEATH
Ischemic heart disease
Nonischemic cardiomyopathy
NYHA I
NYHA II-III
NYHA II-III
LVEF ≤ 30 %
LVEF ≤ 35 %
LVEF ≤ 35 %
★ MADIT-II
★ SCD-HeFT
★ MADIT-II
★ SCD-HeFT
• Adequate treatment
• > 40 days post-myocardial infarction
• 3 months post-revascularization
Life expectancy > 1 year
Defibrillator (± resynchronization)

HEART FAILURE WITH LVEF < 40%

Triple therapy

ACEi

★ *SOLVD*
★ *CONSENSUS*
ARB if intolerant

BB

★ *CIBIS* ★ *MERIT-HF*
★ *COPERNICUS*

MRA

★ *RALES*
★ *EMPHASIS-HF*
LVEF ≤ 35 %; NYHA II to IV

Titrate to target doses / Maximum tolerated dose

↓

NYHA II to IV

★ *SHIFT* **Ivabradine**
LVEF ≤ 35%; HR ≥ 70 bpm (SR)

Sacubitril/Valsartan ★ *PARADIGM-HF*
↗BNP; Replace ACEi or ARB

↓

Resynchronization - CRT (± ICD)

LVEF ≤ 35%; NYHA III-IV; QRS ≥ 120 ms; LBBB
★ *COMPANION*
★ *CARE-HF*

LVEF ≤ 30%; NYHA II; QRS ≥ 130 ms; LBBB
★ *RAFT*
★ *MADIT-CRT*

↓

NYHA II to IV

★ *DIG* **Digoxin**

Hydralazine / Nitrates
★ *V-HeFT*
★ *A-HeFT*

↓

NYHA III to IV

Inotropes | **Transplant** | **LVAD** | **Palliative**

	INITIAL DOSE (mg)	**TARGET DOSE (mg)** (to be reached whenever possible)
ACE INHIBITORS - ANGIOTENSIN-CONVERTING ENZYME INHIBITORS		
Captopril	6.25 tid	50 tid
Enalapril	1.25 bid	10-20 bid
Lisinopril	2.5 qd	20-40 qd
Ramipril	1.25 bid	5 bid
Perindopril	2.5 qd (2 qd in Canada)	10 qd (8 qd in Canada)
Trandolapril	0.5 qd	4 qd
BB - BETA-BLOCKERS		
Bisoprolol	1.25 qd	10 qd
Carvedilol	3.125 bid	25-50 bid
Metoprolol succinate XL	12.5-25 qd	200 qd
ARB - ANGIOTENSIN RECEPTOR BLOCKERS		
Candesartan	4 qd	32 qd
Valsartan	20-40 bid	160 bid
NEPRILYSIN INHIBITOR		
Sacubitril / Valsartan	50 (24/26) - 100 (49/51) mg bid	200 (97/103) mg bid
I_F CHANNEL INHIBITOR		
Ivabradine	5 bid	7.5 bid
LOOP DIURETICS		
Furosemide	20-40 qd or bid (adjusted to renal function)	max 600 /24h
Bumetanide	0.5-1 qd or bid	max 10 /24h

MRA - MINERALOCORTICOID RECEPTOR ANTAGONISTS		
Spironolactone or Eplerenone	**Eplerenone** CrCl > **50 mL/min**: 25 mg qd; CrCl **30-49 mL/min**: 25 mg every 2 days **Spironolactone** CrCl > **50 mL/min**: 12.5 to 25 mg qd; CrCl **30-49 mL/min**: 12.5 mg qd or every 2 days	**Eplerenone** CrCl > **50 mL/min**: 50 mg qd; CrCl **30-49 mL/min**: 25 mg qd **Spironolactone** CrCl > 50 mL/min: 25 mg qd or bid; CrCl 30-49 mL/min: 12.5 to 25 mg qd
THIAZIDE DIURETICS		
Hydrochlorothiazide	25 qd ou bid	max 200 /24h
Metolazone	2.5-5 qd	max 20 /24h
Indapamide	2.5 qd	max 5 /24h
DIGOXIN		
Digoxin	0.125 **Adjusted to renal function** Total loading dose of 1 mg PO per 24 h in 4 doses divided on the 1st day when rapid effect is required; adjusted to renal function	Plasma target: **0.5 to 0.9 ng/mL** (1 week after titration)
HYDRALAZINE / NITRATES		
Hydralazine / Nitrates	Hydralazine: 10-25 tid Isosorbide dinitrate: 10 tid	Hydralazine: 75 tid Isosorbide dinitrate: 40 tid

ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS

↘ Mortality; ↘ Hospitalization; Stabilizes remodeling; ↘ Symptoms

STUDIES: ★ CONSENSUS - ★ SOLVD; ★ SOLVD-Prevention (asymptomatic ↘ LVEF - NYHA I); ★ SAVE - ★ AIRE - ★ TRACE (myocardial infarction with heart failure and/or ↘ LVEF); ★ ATLAS (low-dose vs high-dose Lisinopril)

ADVERSE EFFECTS: ARF; hyperkalemia; hypotension; cough (secondary to ↗ bradykinins); angioedema

CONTRAINDICATIONS: angioedema; bilateral renal artery stenosis; pregnancy

› **Caution**: creatinine > 221 µmol/L (> 2.5 mg/dL) or GFR < 30 mL/min/1.73m^2; hyperkalemia > 5.5 mmol/L; SBP < 90 mmHg
  - **< 30% rise in creatinine** or elevation of **K+ up to 5.5 mmol/L** is acceptable +

› **Follow-up**: assessment 1 week after titration (creatinine; BUN; electrolytes)

BETA-BLOCKERS (BB)

↘ Mortality; ↘ Hospitalization; ↘ Remodeling; ↘ Symptoms

STUDIES: ★ CIBIS (Bisoprolol) - ★ COPERNICUS (Carvedilol) - ★ MERIT-HF (Metoprolol succinate XL); ★ SENIORS (Nebivolol; > 70 years); ★ COMET (Carvedilol vs Metoprolol tartrate); ★ B-CONVINCED (BB continued in the presence of decompensation); ★ CAPRICORN - ★ BEAT (post-myocardial infarction)

ADVERSE EFFECTS: decompensated heart failure; bronchospasm; bradycardia / block; hypotension; tiredness; depression; nightmares; erectile dysfunction; glucose intolerance

CONTRAINDICATIONS: **active decompensated heart failure** (continue BB if already used predecompensation); shock - hypoperfusion; asthma; 2nd or 3rd degree AV block; severe PAD (ischemia at rest)

- **Treat congestion before initiating a BB; target euvolemia**
- **Titrate the dose every 2 weeks**
- **Caution**: HR < 60 bpm; recent decompensation; NYHA IV; SBP < 90 mmHg
- **COPD**: favor beta-1 selective BB (Bisoprolol; Metoprolol)

MINERALOCORTICOID RECEPTOR ANTAGONISTS (MRA)

↘ Mortality; ↘ Hospitalization; ↘ Symptoms

STUDIES: ★ RALES (NYHA III-IV; LVEF < 35 %); ★ EMPHASIS-HF (NYHA II; LVEF < 30 % or < 35 % with QRS > 130 ms; Recent hospitalization or ↗ BNP); ★ EPHESUS (myocardial infarction; LVEF < 40%; heart failure or DM)

ADVERSE EFFECTS: hyperkalemia; ARF; gynecomastia - impotence - ↘ libido - menstrual irregularities (Spironolactone)

CONTRAINDICATIONS: CRF **(creatinine > 221 µmol/L in males or > 177 µmol/L in females or GFR < 30 mL/min); hyperkalemia > 5 mmol/L**

- Titration every 4-8 weeks
- **Follow-up**: assessment 1 week and 4 weeks after titration; at 8 weeks - 12 weeks; at 6 - 9 - 12 months; then every 4 months

ANGIOTENSIN RECEPTOR BLOCKERS (ARB)

INDICATIONS: A) Intolerance to ACE inhibitors (cough; angioedema); **B)** In combination with ACE inhibitors if intolerant to mineralocorticoid receptor antagonists and persistent symptoms

STUDIES

- **Intolerance to ACE inhibitors**: ★ CHARM-Alternative (Candesartan); ↘ Cardiovascular mortality; ↘ Hospitalization
- **ARB combined with ACE inhibitors**: ★ Val-HeFT (Valsartan) - ★ CHARM-ADDED (Candesartan); ↘ Cardiovascular mortality (Candesartan); ↘ Hospitalization; ↘ Symptoms
- **Post-myocardial infarction** (with heart failure and/or ↘ LVEF): ★ VALIANT (Valsartan vs Captopril vs Combinaison) → Valsartan non-inferior to Captopril

NEPRILYSIN INHIBITOR

↗ Active natriuretic peptides

★ **PARADIGM-HF**: LVEF ≤ 35-40 %; NYHA II-IV; NTproBNP ≥ 600 pg/ml (or ≥ 400 pg/ml if hospitalized < 12 months); Sacubitril + Valsartan vs Enalapril → ↘ Mortality; ↘ Hospitalization; ↘ Symptoms; ↗ Hypotension; ↗ Angioedema

DOSING (SACUBITRIL/VALSARTAN): stop ACEi 36 h before; start with 50 (24/26) or 100 (49/51) mg bid; double the dose after 2-4 weeks; target dose of 200 (97/103) mg bid if tolerated

DIGOXIN

Inhibits the Na-K-ATPase pump: ↗ intramyocyte Ca^{2+} (positive inotropic agent); ↗ vagal tone

INDICATIONS: **A)** Persistent symptoms despite standard treatment; **B)** AF (rate control)

STUDIES: ★ DIG (NYHA II-IV; LVEF < 45 %) → ↘ Hospitalization; ↘ Symptoms

Adjustment according to renal function and serum digoxin levels

› **Target serum Digoxin level 0.5 to 0.9 ng/mL**

ADVERSE EFFECTS: atrial / junctional / ventricular arrhythmias (especially in the presence of hypokalemia) combined with blocks; visual disorders; confusion; GI symptoms

CONTRAINDICATIONS: CRF; bradycardia - blocks

MULTIPLE DRUG INTERACTIONS

› ↗ **Serum Digoxin levels**: Amiodarone; Verapamil; Nifedipine; Diltiazem; Quinidine; Propafenone; Captopril; Carvedilol; Spironolactone; Cyclosporine; Macrolides

HYDRALAZINE - ISOSORBIDE DINITRATE

↘ **Mortality in Afro-Americans;** ↘ Hospitalization; ↘ Symptoms

INDICATIONS: A) Intolerance to ACE inhibitors and ARB; **B)** Persistent symptoms despite BB - ACE inhibitors - MRA **(particularly in Afro-Americans)**

STUDIES: ★ V-HeFT-1 and 2; ★ A-HeFT (Afro-Americans)

ADVERSE EFFECTS: headache; hypotension; nausea; arthralgia; asymptomatic ↗ ANA; drug-induced lupus

NON-PHARMACOLOGICAL TREATMENT

SELF-SURVEILLANCE OF WEIGHT

› Daily weight; on waking; before getting dressed; post-voiding → increase the dose of diuretics or notify if weight ↗ > 1.5-2 kg or 3-4 lbs (x 2-3 days)

SODIUM: < 2-3 g per day

FLUIDS: < 2 liters per day (especially if hyponatremia or refractory congestion)

VACCINATION: influenza (annually); pneumococcus (every 5 years)

TREATMENTS TO BE AVOIDED: **A)** Thiazolidinediones; **B)** Non-dihydropyridine CCBs; **C)** NSAIDs; **D)** Certain AAD: Dronedarone (★ ANDROMEDA); Class I AAD (★ CAST); **E)** Alpha-blockers

EXERCISE

★ **HF-ACTION** → improves symptoms and functional capacity

Regular isotonic exercise (walking; stationary bike) after stress test (rule out ischemia - arrhythmia)

› **Prescription**: 3-5 times a week; 30-45 min; **60-70% of peak heart rate** (or peak VO_2) **or 4-5-6/10 on Borg's scale**

ATRIAL FIBRILLATION

RATE CONTROL: **non-inferior to rhythm control (★ AF-CHF)**

› **A)** BB; **B)** Digoxin; **C)** Amiodarone to control HR as necessary (patient should be anticoagulated for 1 month because of the risk of CCV); **D)** AV node ablation + PPM; consider resynchronization

RHYTHM CONTROL: patients with severe symptoms or reversible cause / precipitating factor

› **A)** ECV; **B)** Amiodarone or Dofetilide; **C)** ± PV isolation (benefit in ★ PABA-CHF and ★ AATAC-AF)

WARFARIN - ANTICOAGULATION

INDICATIONS: **A)** AF; **B)** Thrombus; **C)** History of thromboembolic disease

No benefit in ★ WARCEF study (LVEF < 35% in SR; for thromboembolic primary prevention)

SLEEP-DISORDERED BREATHING

CENTRAL SLEEP APNEA - CHEYNE-STOKES (40%): hyperventilation followed by apnea (≥ 10 s with no ventilatory effort); **associated with pulmonary congestion**; independent risk factor of mortality

- **Diagnosis**: Polysomnography
- **Treatment**: Optimize management of heart failure; CPAP (no benefit in ★ CANPAP study); Adaptive servo-ventilation associated with ↗ mortality in ★ SERVE-HF

OBSTRUCTIVE SLEEP APNEA (10%): Leads to hypoxemia / hypercapnia / intermittent sympathetic stimulation

- Look for obesity / ↗ neck circumference; snoring; daytime sleepiness; apneas
- **Complications**: refractory HTN; nocturnal HTN; PHT; arrhythmias
- **Diagnosis**: Polysomnography (screening with nocturnal saturometry)
- **Treatment**: Weight loss; CPAP

ISCHEMIC LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

REVASCULARIZATION: possible benefit in the presence of significant viability; highly controversial topic (mixed results of ★ STICH study; ★ ISCHEMIA study ongoing)

FUNCTIONAL MITRAL REGURGITATION

Carpentier I and IIIb mechanisms; maintains systolic dysfunction (which maintains MR)

MVR OR MITRAL ANNULOPLASTY: possible improvement in functional class; associated with reverse remodeling; no convincing data on survival; MVR possibly superior (★ CTSN)

› Consider in severe secondary MR with: CABG or concomitant AVR (class IIa recommendation) or refractory NYHA III - IV (class IIb recommendation)

MITRACLIP: consider in the presence of significant MR with refractory symptoms in a patient who is not a candidate for surgery

DIASTOLIC HEART FAILURE (preserved LVEF)

Secondary to abnormal active relaxation and/or ↗ passive rigidity

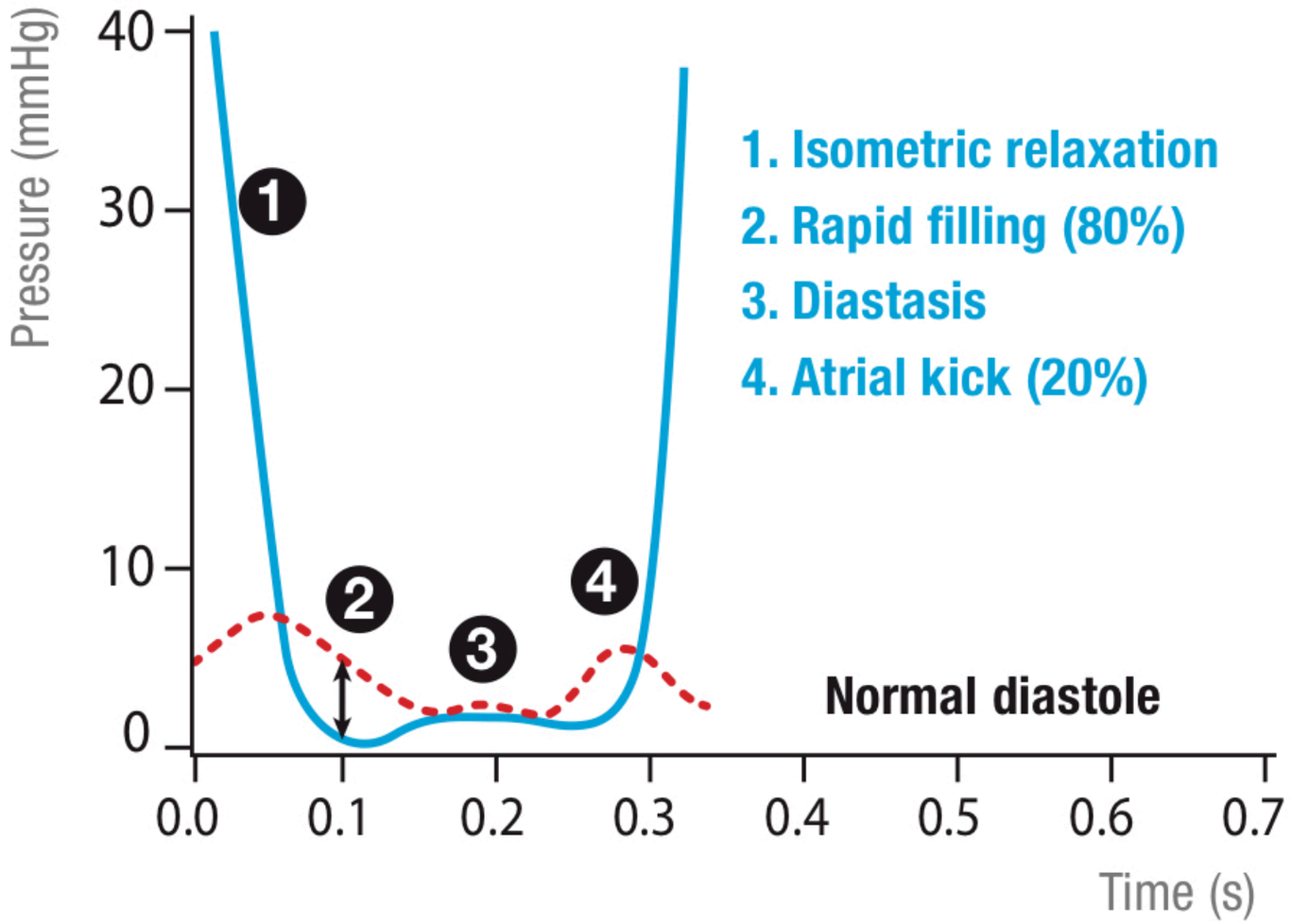
50% of patients with heart failure

ALL-CAUSE MORTALITY similar to that of heart failure with ↘ LVEF

› Mortality is mostly due to non-cardiovascular causes

RISK FACTORS: Age; Female; HTN; LVH; Ischemia; DM; Obesity; RCM; HCM

FACTORS ASSOCIATED WITH DECOMPENSATION: uncontrolled / labile HTN; AF; Ischemia; Volume overload; Extracardiac cause



1. Isometric relaxation
2. Rapid filling (80%)
3. Diastasis
4. Atrial kick (20%)

DIASTOLIC DYSFUNCTION

Abnormal relaxation
and/or ↑ passive rigidity

↓

↑ Filling pressures

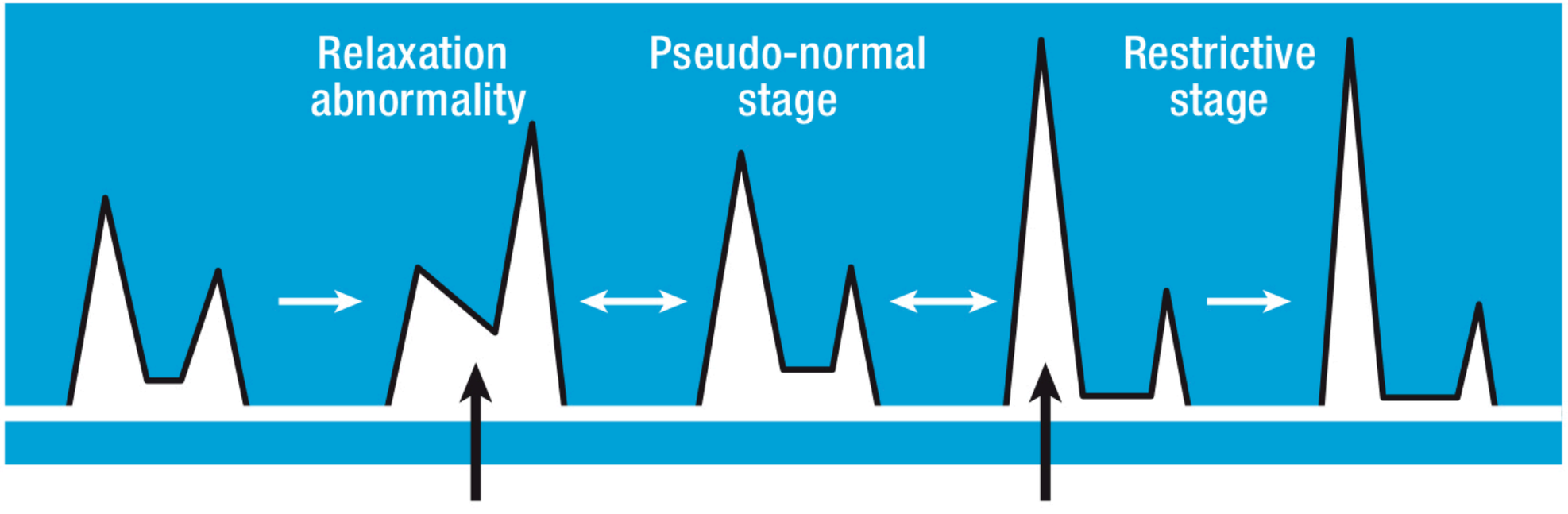
↓

↑ LA pressure

ETIOLOGIES OF ↓ RELAXATION VELOCITY

- ↑ LV afterload
- Ischemia
- Age
- Systolic dysfunction (↓ recoil)
- LVH

MANAGEMENT



No treatment proven to decrease morbidity or mortality

› **No benefit in**: ★ CHARM-Preserved - ★ PEP-CHF - ★ I-Preserve - ★ TOPCAT - ★ NEAT-HFpEF

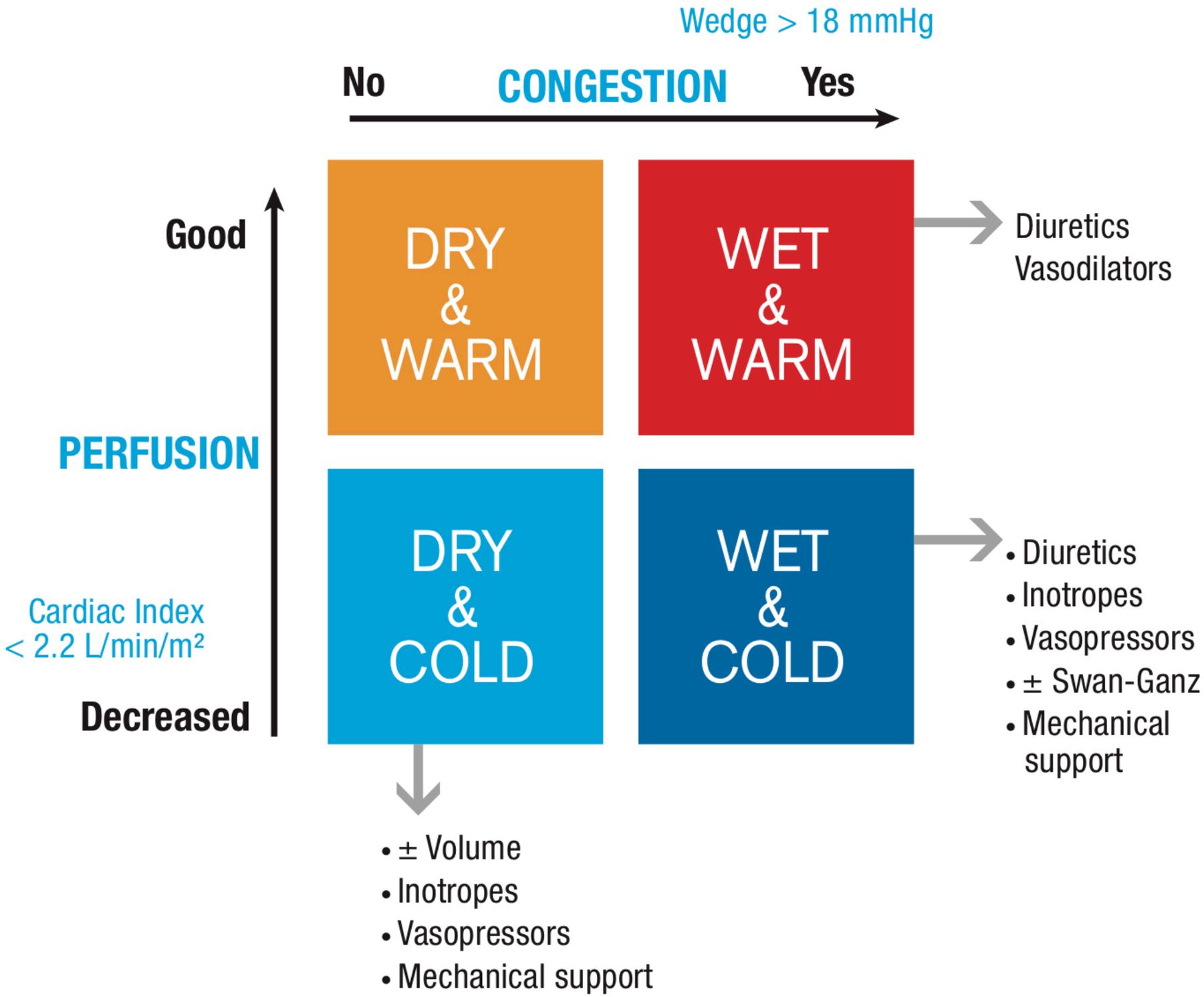
DIURETICS: symptoms / congestion control

RISK FACTOR REDUCTION: CAD; HTN (rule out renovascular syndrome in the presence of refractory HTN)

REVASCULARIZATION: if significant ischemia / symptoms

RATE CONTROL during AF (± rhythm control)

CONSIDER: ACE inhibitor or ARB; BB; MRA


Wedge > 18 mmHg
No
CONGESTION
Yes
Good
PERFUSION
Cardiac Index
< 2.2 L/min/m²
Decreased
DRY & WARM
WET & WARM
Diuretics
Vasodilators
DRY & COLD
WET & COLD
• Diuretics
• Inotropes
• Vasopressors
• ± Swan-Ganz
• Mechanical support
• ± Volume
• Inotropes
• Vasopressors
• Mechanical support

- Monitor
- Vital signs - SaO_2
- Urine output
- SVO_2

ACUTE HEART FAILURE

↗ FILLING PRESSURES / CONGESTION
(Wedge > 18 mmHg and/or CVP > 8 mmHg)

and/or

↘ CARDIAC OUTPUT
(< 2.2 L/min/m²)

- Diuretics (Lasix)
- Vasodilators (Nitrates)
- Morphine
- O_2 (target SaO_2 > 92 %)
- BiPAP or Mechanical ventilation if respiratory failure

TARGET ORGAN HYPOPERFUSION

- Cold skin
- Urine output < 20 mL/h
- SVO_2 < 70 %
- Confusion
- Ischemia

Rule out reversible cause

Hemodynamic instability and/or ↘ systemic vascular resistance

Maintain perfusion of vital organs (heart; CNS)
- Vasopressors (Norepinephrine; Dopamine)
- Non-vasodilator inotropes

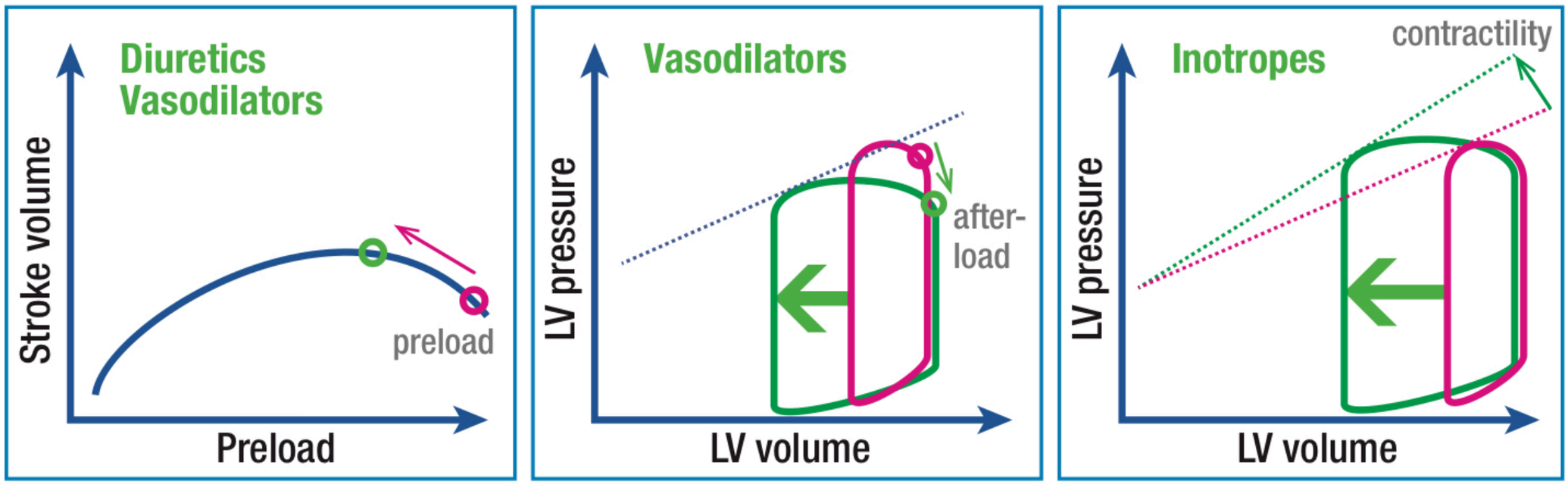
Normal systemic vascular resistance (1000 - 1200 dynes x s/cm⁵)

- Inotropes
- Vasodilators

↗↗ systemic vascular resistance

- Vasodilators
- Inotropes

- Intra-aortic balloon pump
- Short-term percutaneous ventricular support (ECMO; Impella; TandemHeart) as “bridge to decision”


Diuretics
Vasodilators
Stroke volume
preload
Preload
Vasodilators
LV pressure
after-
load
LV volume
Inotropes
contractility
LV pressure
LV volume

VASODILATORS		
Nitroglycerin	Dose: 10-20 µg/min up to 200 µg/min	• ↗ cGMP in smooth muscle cells (= vasodilatation) • Venous vasodilator (↘ filling pressures) then arterial (↘ afterload; coronary vasodilatation) • Adverse effects: Tolerance during prolonged use; Hypotension; Headache
	Standard dilution: 50 mg/250 mL D5% = 200 µg/mL	
Nitroprusside	Dose: 0.3 µg/kg/min up to 5 µg/kg/min	• Balanced vasodilator • Short half-life • Used for hypertensive emergency or acute MR • Adverse effects: Risk of cyanide toxicity; Hypotension
	Standard dilution: 50 mg/250 mL NS = 200 µg/mL	
Nesiritide	• Bolus: 2 µg/kg • Perfusion: 0.01-0.03 µg/kg/min	• Recombinant BNP • Balanced vasodilator • No benefit in ★ ROSE-AHF and ★ ASCEND-HF

INOTROPES		
Dobutamine	Dose: 2-20 µg/kg/min Standard dilution: 250 mg/ 100 mL D5% = 2500 µg/mL	• Beta-1 and beta-2 agonist • Supplementary alpha-1 effect at higher doses (neutralizing the beta-2 vasodilator effect) • **Favor to Milrinone in the presence of significant hypotension** • Arrhythmogenic
Dopamine	• Renal effect (Dopamine) < 3 µg/kg/min • Beta-1: 3-5 µg/kg/min • Alpha-1 (and Beta-1): > 5 µg/kg/min (up to 20 µg/kg/min) Standard dilution: 400 mg / 250 mL D5% = 1600 µg/mL	• Dose-dependent effect • Positive inotrope and vasopressor (vasodilator at low doses) • Norepinephrine precursor • Arrhythmogenic • ↗ Mortality in cardiogenic shock (★ SOAP II)
Milrinone	• Bolus: 25-75 µg/kg x 10-20 min (optional; avoid if hypotension) • Infusion: 0.375 - 0.75 µg/kg/min • Adjustment to GFR Standard dilution: 10 mg/100 mL D5% = 90 µg/mL	• Phosphodiesterase inhibitor (↗ intra-myocyte cAMP = ↗ intracellular Ca^{2+}) • Risk of hypotension (vasodilator) • Caution in patients with CAD (hypotension can accentuate ischemia) • Effective despite BB • Favor if BP preserved • Less arrhythmogenic than dobutamine • No benefit in ★ OPTIME-HF study

VASOPRESSORS		
Norepine-phrine	Dose: 0.2 -1 µg/kg/min Standard dilution: 4 mg / 250 mL D5% = 16 µg/mL	• Alpha-1 agonist • Beta-1 effect (but reflex bradycardia secondary to ↗ MAP)
Epinephrine	• Bolus: 1 mg IV every 3-5 min (during resuscitation) • Infusion: 0.05 - 0.5 µg/kg/min Standard dilution: 5 mg / 250 mL D5% = 20 µg/mL	• Alpha-1, beta-1 and beta-2 agonist • Arrhythmogenic
Phenylephrine	Dose: 40 - 60 µg/min Standard dilution: 10 mg / 250 mL NS = 40 µg/mL	• Pure alpha-1 agonist

MONITORING: Cardiac monitoring - Regular vital signs - SaO_2 - urine output; daily weight

LMNOP: IV Lasix; Morphine if anxiety / distress (2.5-5 mg IV); Nitrates (avoid if hypotension); O_2; Position - PEEP

- **Diuretic**: ★ DOSE study → bolus bid equivalent to IV infusion; low-dose IV (equal to usual oral doses) equivalent to high-dose IV (2.5 x usual oral doses)
- **BiPAP**: contraindicated in the presence of hypotension; Vomiting; Impaired level of consciousness; Uncooperative patient

INOTROPES (Dobutamine; Milrinone): **indicated in the presence of peripheral hypoperfusion**

› **Adverse effects**: Hypotension (vasodilator effect); Arrhythmogenic; ↗ O_2 demand; ↗ Long-term mortality

VASOPRESSORS (Norepinephrine): indicated in the presence of severe hypotension

› **Objective**: **redirect cardiac output to vital organs**

› **Adverse effects**: ↗ Afterload; ↗ O_2 demand; Arrhythmogenic

SWAN-GANZ: Indications → **A)** Cardiogenic shock despite inotropes / vasopressors;
B) Patient refractory to treatment; **C)** Uncertain hemodynamic parameters (filling pressures; SVR);
D) Hemodynamic assessment prior to transplant / mechanical support

› **Hemodynamic targets**

WEDGE	CVP	BP	SVO_2	SVR	CARDIAC INDEX
< 18 mmHg	< 8 mmHg	MAP > 60 mmHg SBP > 80 mmHg	> 70 %	1000 to 1200 dynes x s/cm^5	> 2.2 $L/min/m^2$

DISCHARGE FROM HOSPITAL: congestion resolved; **dry weight achieved**; ACE inhibitors - BB - mineralocorticoid receptor antagonist initiated; stable dose of diuretics and stable labs for > 48 h; restrictions explained; registration in specialized clinic; follow-up < 1 month (vulnerable phase)

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ORIGINAL ARTICLE FREE PREVIEW

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

John J.V. McMurray, M.D., Scott D. Solomon, M.D., Silvio E. Inzucchi, M.D., Lars Køber, M.D., D.M.Sc., Mikhail N. Kosiborod, M.D., Felipe A. Martinez, M.D., Piotr Ponikowski, M.D., Ph.D., Marc S. Sabatine, M.D., M.P.H., Inder S. Anand, M.D., Jan Bělohlávek, M.D., Ph.D., Michael Böhm, M.D., Ph.D., Chern-En Chiang, M.D., Ph.D., et al., for the DAPA-HF Trial Committees and Investigators*