

# Pathophysiology of heart failure

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symptoms/signs due to structural/functional cardiac abnormality causing **low output, high filling pressures, or both**

## HEART FAILURE

" CLINICAL SYNDROME RESULTING FROM INABILITY OF THE HEART TO MEET THE PERFUSION DEMANDS OF THE BODY. "

INEFFECTIVE PUMPING

↳ SYSTOLIC FAILURE

↳ HF<sub>r</sub>EF

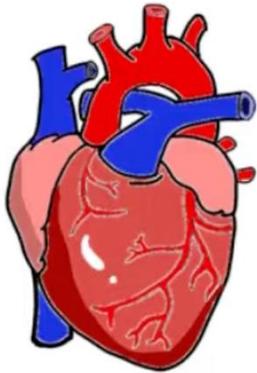
INEFFECTIVE FILLING

↳ DIASTOLIC FAILURE

↳ HF<sub>p</sub>EF

# ACUTE HEART FAILURE

HEART FAILURE — HEART IS UNABLE TO MEET PERFUSION DEMANDS OF THE BODY



## ACUTE HEART FAILURE

↳ SUDDEN DETERIORATION IN CARDIAC FUNCTION

PREVIOUSLY HEALTHY  
DE NUOVO  
ACUTE HEART FAILURE

CHRONIC (BUT STABLE)  
HEART DISEASE  
ACUTE DECOMPENSATED  
HEART FAILURE

# ACUTE HEART FAILURE

CARDIAC OUTPUT:  
HEART RATE x STROKE VOLUME

$$70 \text{ BPM} \times 70 \text{ mL} \\ = 4900 \text{ mL/min}$$



STROKE VOLUME  
(~70mL)

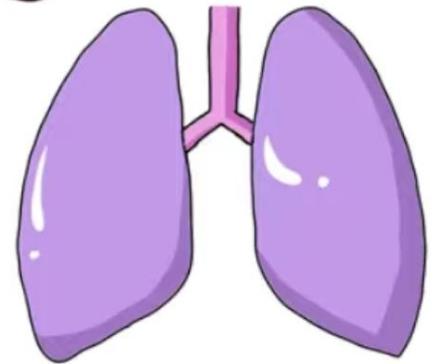
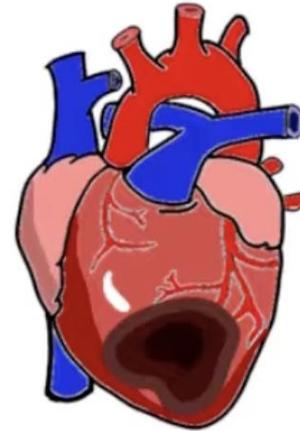
$$\text{EJECTION FRACTION} = \frac{\text{STROKE VOLUME (70)}}{\text{END DIASTOLIC VOLUME (110)}} \\ = \underline{64\%}$$

NORMAL RANGE: 55 - 70%.

# ACUTE HEART FAILURE

## CAUSES

- ① MYOCARDIAL INFARCTION
- ② ACUTE VALVULOPATHY
  - ↳ MITRAL REGURGITATION
- ③ ARRHYTHMIAS
  - ↳ VENTRICULAR FIBRILLATION
- ④ PULMONARY EMBOLISM
- ⑤ MYOCARDITIS
- ⑥ DRUGS
  - ↳ BETA BLOCKERS +  $Ca^{2+}$  CHANNEL BLOCKERS



# ACUTE HEART FAILURE

## SIGNS AND SYMPTOMS

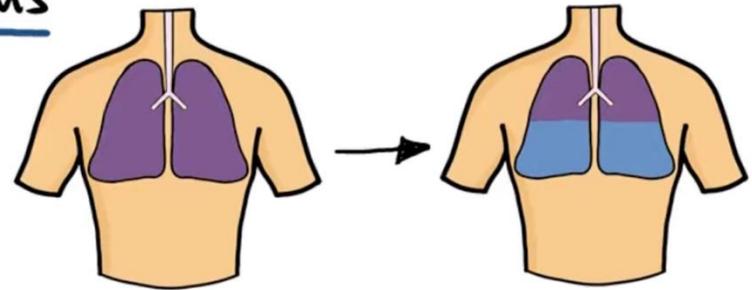
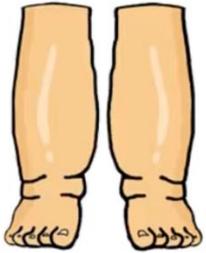
① SHORTNESS OF BREATH / DYSPNEA  
↳ PULMONARY EDEMA

② CHEST PAIN

③ SWELLING IN PERIPHERIES  
↳ JUGULAR VEIN DISTENSION  
↳ ACUTE HEPATOMEGALY → PAIN

④ WEAKNESS

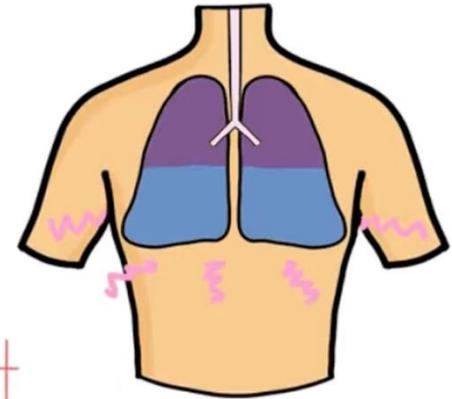
⑤ CYANOSIS



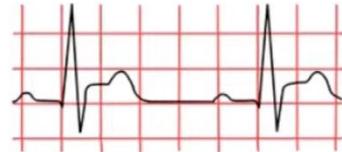
# ACUTE HEART FAILURE

## DIAGNOSIS

- PHYSICAL EXAM:
- CRACKLES AT LUNG BASES
  - ADDITIONAL HEART SOUNDS
  - JUGULAR VEIN DISTENTION
  - PERIPHERIES
  - DRUG HISTORY



- ECG:
- ISCHEMIA / INFARCTION
  - ARRHYTHMIA



- LABS:
- TROPONIN
  - B-TYPE NATRIURETIC PEPTIDE (BNP)
  - ELECTROLYTES →  $\text{Na}^+$  /  $\text{K}^+$  /  $\text{Ca}^{2+}$

- IMAGING:
- CHEST X-RAY
  - CARDIAC ULTRASOUND
    - ↳ VOLUMES, EJECTION FRACTION, ANATOMICAL CHANGES

# ACUTE HEART FAILURE

## TREATMENT

- STABILIZE: SURGERY (VALVE REPAIR)  
REPERFUSION (MYOCARDIAL INFARCTION)  
OXYGEN  
MEDICATION - DIURETICS  
IONOTROPES  
NITRATES  
PAIN RELIEF  
MECHANICAL ASSIST DEVICE - AORTIC BALLOON PUMP
- LONG TERM: LIFESTYLE MODIFICATION  
MEDICATION - ACE INHIBITORS / ARBs  
BETA BLOCKERS  
STATINS  
DIURETICS

# Classification

- Classifications:
  - **Acute vs chronic** HF (tempo matters for compensation).
  - **Left vs right** HF (dominant congestion compartment).
  - **HFrEF vs HFpEF** (dominant remodeling and loading problem).
- ❖ Two dominant pathophysiologic “outputs”:
  - 1.Congestion** (elevated filling pressures → pulmonary/systemic venous congestion).
  - 2.Hypoperfusion** (inadequate forward flow) — often later/advanced HF.

# HFrEF

- **(Heart Failure with reduced Ejection Fraction) = heart failure with reduced left ventricular ejection fraction (LVEF)  $\leq$  40%.**
- Symptoms: Shortness of breath, limited physical fitness, edema.
- Pathophysiology: Impaired systolic function, progressive left ventricular dilation.
- Diagnostics: Echocardiography to measure EF, increased natriuretic peptide levels.
- HFrEF is the main form of chronic heart failure that requires targeted pharmacotherapy.

# HFmrEF

- **(Heart Failure with Mildly Reduced Ejection Fraction, or Heart Failure with Mid-Range Ejection Fraction) = a category of heart failure where the LV pumps blood less efficiently, but not as poorly as in HFrEF, with an EF in the range of 40-49% (sometimes specified as 41-49%).**
- It is an intermediate form between HFrEF (heart failure with reduced EF) and HFpEF (heart failure with preserved EF).
- Prevalence: up to 10-20% of heart failure cases
- Treatment includes drugs similar to HFrEF (beta blockers, ACE inhibitors, SGLT2 inhibitors) and diuretics, but more detailed research is still needed on optimal therapy

# HFpEF

- **(heart failure with preserved ejection fraction) = the heart muscle contracts normally (EF >50%), but the LV is stiff (diastolic dysfunction), which prevents sufficient filling with blood, leading to increased filling pressure and accumulation of blood in the lungs.**
- Often affects older patients, especially women with AHT, obesity or DM, the risk of death is high, comparable to HFrEF.
- Diagnosis: Problematic, requires ECHOKG to assess function and filling pressures, often accompanied by increased BNP/NT-proBNP values.
- Symptoms: dyspnea on exertion and at rest, fatigue and right ventricular edema.
- Treatment: management of comorbidities (AHT, DM, FiP) and symptomatic treatment, especially diuretics to reduce fluid overload.
- Prognosis: HFpEF is a serious disease with a high rate of rehospitalization. and mortality, up to 65% of patients may die within 5 years of diagnosis.

# HFpEF

**HFpEF is not just “diastolic HF.” It is a multi-organ syndrome, especially in:**

- hypertension
- obesity
- type 2 diabetes (T2DM)
- older patients

## **Mechanisms:**

- systemic inflammation (visceral fat)
- endothelial dysfunction
- impaired LV relaxation
- elevated filling pressures even with mild exertion
- pulmonary hypertension

***The result is poor exercise tolerance despite a normal ejection fraction.***

# Classification of HF

## A. By ejection fraction

- **HFrEF:** EF < 40% (</=40%)
- **HFmrEF:** EF 40–49% (41-49%)
- **HFpEF:** EF ≥ 50%

## ➤ Pathophysiologic differences

- **HFrEF** = systolic dysfunction → weak contraction
- **HFpEF** = diastolic dysfunction → stiff ventricle, high filling pressures
- **HFmrEF** = transitional phenotype

## B. By speed of onset

- **Acute HF** (cardiogenic shock, acute decompensation)
- **Chronic HF** (most common)

# C. According to subjective functional load – NYHA I–IV

- **NYHA I–IV (functional classification of heart failure)**
- ❖ **NYHA I**
  - No limitation of physical activity.
  - Ordinary activity does not cause dyspnea, fatigue, palpitations, or angina.
- ❖ **NYHA II**
  - Mild limitation of physical activity.
  - Comfortable at rest, but ordinary activity causes dyspnea, fatigue, palpitations, or angina.
- ❖ **NYHA III**
  - Marked limitation of physical activity.
  - Comfortable at rest, but less-than-ordinary activity provokes symptoms.
- ❖ **NYHA IV**
  - Unable to carry out any physical activity without symptoms.
  - Symptoms (dyspnea/fatigue) are present even at rest; they worsen with exertion.

## NYHA — Walking on level ground — Stairs

### NYHA I

- **Level ground:** No symptoms with normal walking.
- **Stairs:** 1–2 flights without dyspnea/fatigue.

### NYHA II

- **Level ground:** Symptoms with fast walking or longer distances.
- **Stairs:** Dyspnea/fatigue after 1–2 flights (especially without stopping).

### NYHA III

- **Level ground:** Symptoms even with short walks (tens to a few hundred meters depending on terrain).
- **Stairs:** Symptoms after a few steps or < 1 flight; needs to stop.

### NYHA IV

- **Level ground:** Symptoms with minimal exertion (e.g., moving around the apartment) or even at rest.
- **Stairs:** Usually unable; symptoms even at rest (e.g., while dressing).
- **Note:** These are approximate examples; the threshold is individual (age, fitness, COPD, anemia, obesity).

# Main pathophysiological mechanisms

## A. Reduced cardiac output

HFrEF → ↓ contractility → ↓ CO → activation of compensatory mechanisms.

HFpEF → CO may be normal at rest, but inadequate during exertion because of:

- LV hypertrophy
  - myocardial stiffening
  - impaired relaxation
  - increased LVEDP
- 

## B. Elevated filling pressures

Key for the development of dyspnea and congestion.

High LVEDP → transmitted to the LA → to the pulmonary veins → causes pulmonary congestion and dyspnea.

## C. Neurohormonal activation – the core of pathophysiology

### 1. RAAS activation

Renal hypoperfusion → ↑ renin → ↑ angiotensin II → ↑ aldosterone

- vasoconstriction
- Na<sup>+</sup> and water retention
- myocardial hypertrophy and fibrosis
- ventricular remodeling

### 2. Sympathetic nervous system (SNS)

↑ norepinephrine

- ↑ heart rate, ↑ contractility (beneficial short-term)
- long-term: cardiomyocyte apoptosis, arrhythmias, β-receptor downregulation

### 3. ADH (vasopressin)

→ water retention, hyponatremia, higher filling pressures

### 4. Inflammatory cytokines

TNF- $\alpha$ , IL-1 $\beta$ , IL-6

→ reduce contractility, promote fibrosis

### 5. Natriuretic peptides (BNP, NT-proBNP) – the only protective system

Act against RAAS and SNS:

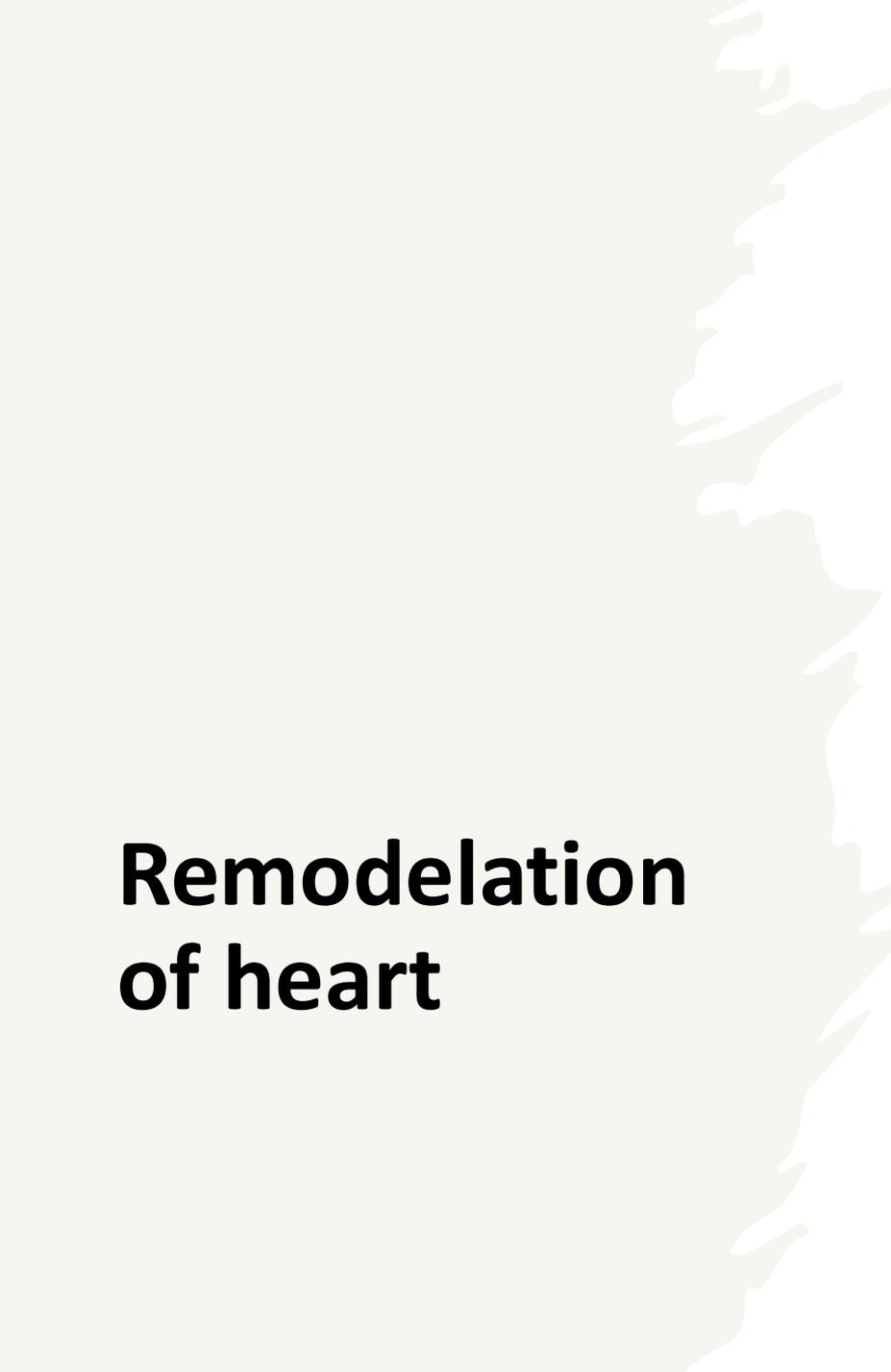
→ natriuresis

→ vasodilation

→ antifibrotic effects

In HF they are increased, but their effectiveness is reduced due to receptor resistance.

# Remodelation of heart



**Long-term overload leads to:**

**a) Eccentric hypertrophy (volume overload)**

- ventricular dilation
- wall thinning
- typical of HFrEF

**b) Concentric hypertrophy (pressure overload)**

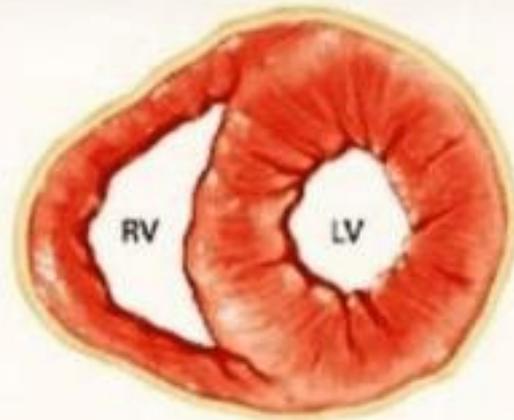
- wall thickening
- diastolic dysfunction
- typical of HFpEF (e.g., hypertension)

**Mechanisms of remodeling**

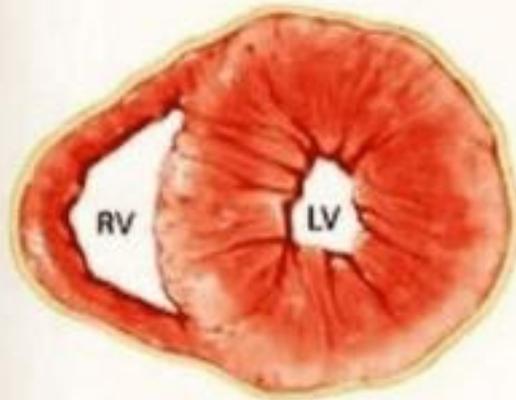
- cardiomyocyte apoptosis
- interstitial fibrosis
- changes in the extracellular matrix
- fibroblast activation

# Eccentric and concentric cardiac hypertrophy

@Echo\_tips



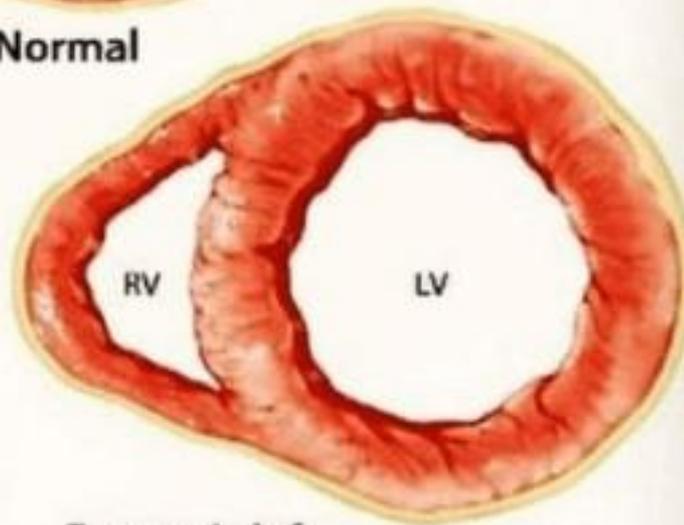
Normal



**Concentric left ventricular hypertrophy**

Pressure overload

- Chronic hypertension
- Aortic stenosis



**Eccentric left ventricular hypertrophy**

Volume overload

- Aortic or mitral regurgitation
- Myocardial infarction
- Dilated cardiomyopathy

# Hemodynamic consequences

## 1. Forward failure – insufficient output

- fatigue
- muscle weakness
- renal hypoperfusion → RAAS activation

## 2. Backward failure – congestion

- dyspnea, orthopnea
- lower limb edema
- hepatomegaly
- ascites

# Pathophysiology of symptoms

- **Dyspnea**
- pulmonary congestion → transudation of fluid
- reduced lung compliance
- activation of J receptors → sensation of “air hunger”
- **Fatigue**
- low cardiac output (CO)
- reduced perfusion of skeletal muscle
- muscle atrophy and mitochondrial dysfunction (cardiac cachexia)
- **Edema**
- increased venous pressure
- activated RAAS and ADH
- reduced lymphatic drainage
- **Arrhythmias**
- fibrosis
- atrial dilation → atrial fibrillation
- $\beta$ -receptor downregulation

# Cardiogenic shock

- extremely ↓ CO
- systemic vasoconstriction
- elevated lactate
- severe hypoperfusion of kidneys, liver, CNS
- mortality 40–50%

# Clinical phenotypes of heart failure (ESC) according to perfusion and congestion

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## 1) ESC “clinical profiles”

The ESC uses bedside stratification of acute heart failure along two axes:

### **Congestion (“wet” vs “dry”)**

“**wet**” = symptoms/signs of fluid overload are present (pulmonary congestion or systemic venous congestion)

“**dry**” = no significant congestion

### **Perfusion (“warm” vs “cold”)**

“**warm**” = adequate peripheral perfusion

“**cold**” = hypoperfusion (low output) – clinical signs of “low output”

This yields 4 profiles: **warm–dry, warm–wet, cold–dry, cold–wet.**

## **2) How to clinically determine congestion and perfusion**

### **2.1 Signs of congestion ("wet")**

- dyspnea, orthopnea, PND
- crackles (rales), pleural effusion
- elevated JVP, hepatojugular reflux
- peripheral edema, ascites, hepatomegaly
- weight gain, oliguria (also with renal venous congestion)

### **2.2 Signs of hypoperfusion ("cold")**

- cold extremities, mottling, prolonged capillary refill
- hypotension (not required, but common), narrow pulse pressure
- altered mental status, dizziness
- oliguria (from low flow), elevated lactate, metabolic acidosis

# Clinical profile of acute HF (ESC)

Clinical profile (ESC)	Congestion	Perfusion	Typical bedside findings	Typical hemodynamics (approx.)	“What I do first” (principle)
<b>Warm–Dry</b> (“warm–dry”)	<b>No</b>	<b>Yes</b>	No orthopnea/crackles, no edema/JVP↑; stable BP; warm extremities; normal capillary refill	<b>PCWP normal</b> ( $\approx \leq 18$ mmHg), <b>CI preserved</b> ( $\approx \geq 2.2$ L/min/m <sup>2</sup> )	Continue/optimize chronic therapy; monitor; <b>no urgent decongestion</b>
<b>Warm–Wet</b> (“warm–wet congestion”)	<b>Yes</b>	<b>Yes</b>	Dyspnea, orthopnea, crackles/CXR congestion; JVP↑, edema; warm extremities; BP often normal to high	<b>PCWP ↑</b> ( $\approx > 18$ ), <b>CI preserved</b> ( $\approx \geq 2.2$ )	<b>IV diuretic</b> (decongestion); if BP is higher consider <b>vasodilation</b> ; O <sub>2</sub> /ventilation as needed
<b>Cold–Dry</b> (“cold–dry”)	<b>No (or minimal)</b>	<b>No</b>	Cold extremities, prolonged capillary refill, weakness, dizziness, oliguria; minimal congestion; BP may be low or normal	Two subtypes: <b>(A)</b> PCWP low/normal + <b>CI ↓</b> ; <b>(B)</b> PCWP normal to mildly ↑ + <b>CI ↓</b>	Clarify preload: if hypovolemia suspected → <b>cautious fluid challenge</b> ; otherwise with low output consider <b>inotrope</b> and search for the cause
<b>Cold–Wet</b> (“cold–wet”)	<b>Yes</b>	<b>No</b>	Combination: dyspnea/crackles, JVP↑, edema <b>plus</b> cold extremities, hypotension/narrow pulse pressure, oliguria, altered mental status, lactate ↑	<b>PCWP ↑</b> ( $\approx > 18$ ), <b>CI ↓</b> ( $\approx < 2.2$ )	<b>Urgent stabilization:</b> O <sub>2</sub> /ventilation; <b>inotrope</b> for low output; in hypotensive shock add a <b>vasopressor</b> ; decongest cautiously; treat trigger (ACS, arrhythmia, mechanical cause); consider <b>mechanical support</b>

# RAAS in heart failure

- ↓ Renal perfusion → ↑ renin → angiotensin I → angiotensin II
- Vasoconstriction → ↑ afterload
- ↑ Aldosterone → Na<sup>+</sup>/water retention → ↑ preload
- ↑ ADH → hyponatremia
- Result: ↑ filling pressures, fibrosis, remodeling

# Myocardial remodeling

- ↑ pressure/volume load + RAAS + SNS →
  - Cardiomyocyte hypertrophy
  - Apoptosis
  - Fibroblast activation → fibrosis
- Eccentric hypertrophy → dilation, ↓ EF
- Concentric hypertrophy → stiffening, diastolic dysfunction

# RAAS in heart failure

↓ renal perfusion

↓

↑ renin (juxtaglomerular apparatus)

↓

angiotensinogen (liver)

↓

→ angiotensin I → (*ACE in the lungs*)

↓

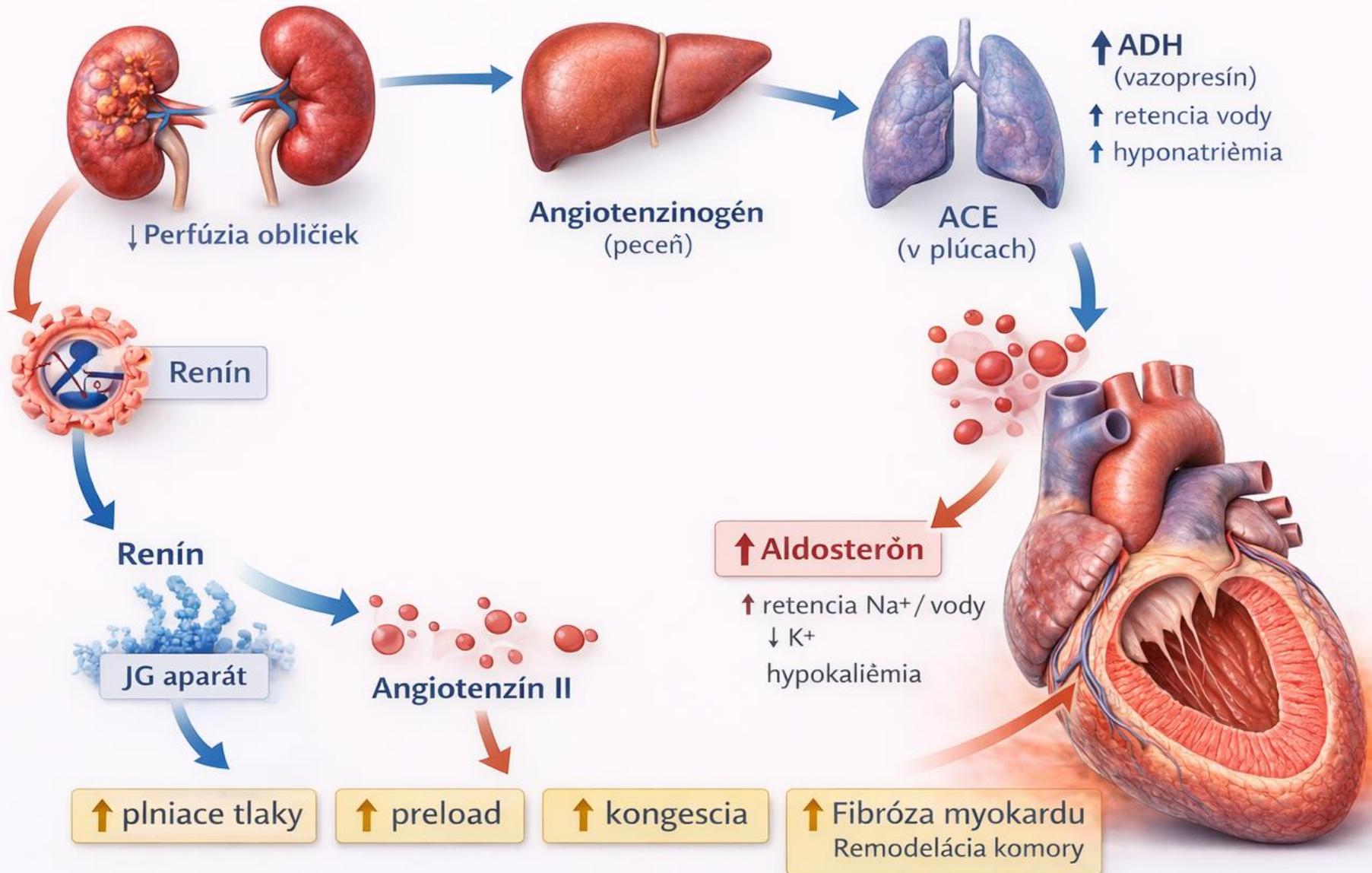
→ angiotensin II →

## Effects of angiotensin II:

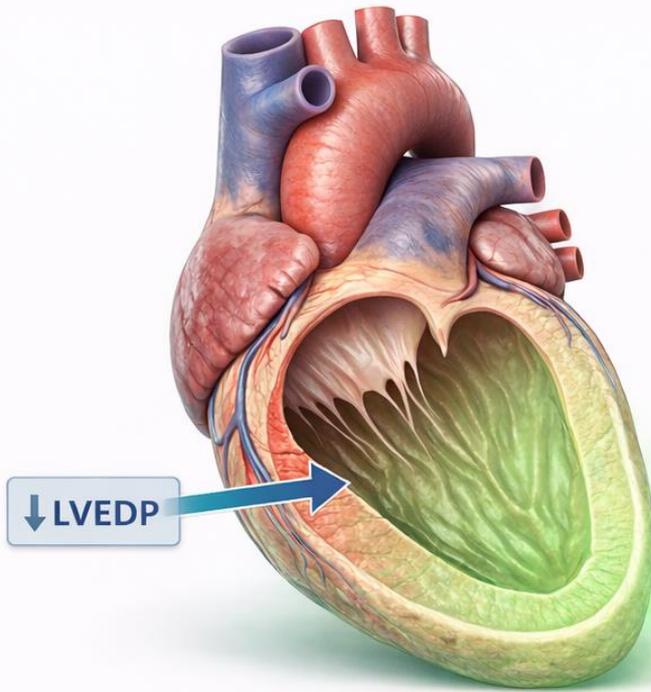
- **Vasoconstriction**
  - ↑ afterload
  - ↑ blood pressure
- **↑ Aldosterone**
  - Na<sup>+</sup>/water retention
  - hypokalemia
- **↑ ADH (vasopressin)**
  - water retention
  - hyponatremia

**Overall effect:** ↑ filling pressures, ↑ preload, ↑ cor ↓ tion, ↑ myocardial fibrosis, ventricular remodeling

# RAAS in heart failure



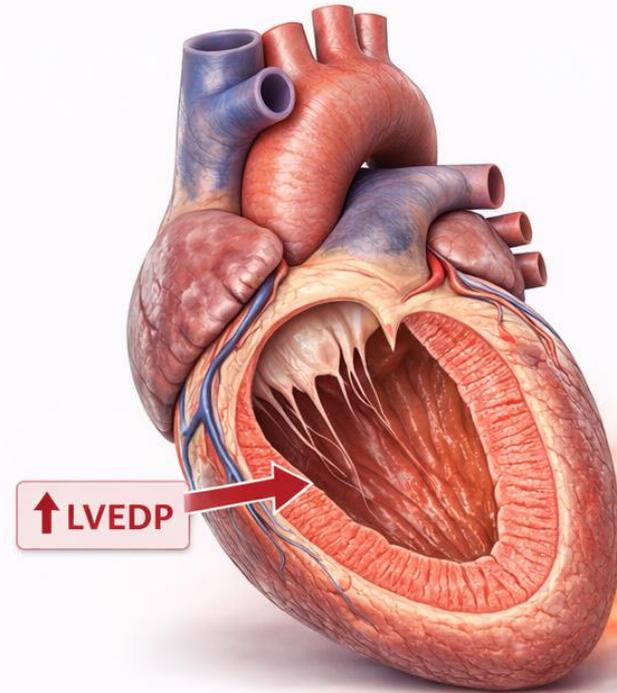
# Diastolic dysfunction



Normálna relaxácia ľavej komory (ĽK)

**Poddajnosť:** ↑ dobrá

Normálna diastolická náplň  
(nízky pľiaci tlak)



Stuhnutosť ľavej komory pri diastolickej  
dysfunkcii

**Poddajnosť:** ↓ znížená

- Dilatácia ľavej predsene
- Plúcna kongescia (↑ pľiaci tlak)

# HFpEF pathophysiology

- Metabolic stress (obesity, type 2 diabetes, hypertension) →
- Systemic inflammation → endothelial dysfunction →
- ↓ NO (nitric oxide) → microvascular ischemia → LV (left ventricular) stiffening
- → ↑ LVEDP (left ventricular end-diastolic pressure), ↑ LA (left atrial) pressure, pulmonary hypertension → exertional dyspnea

# HFpEF pathophysiological model

## METABOLIC STRESS

(obesity, type 2 diabetes, hypertension, inflammation)

↓

Systemic inflammation and ↑ cytokines

↓

Endothelial dysfunction (NO↓)

↓

↓ Vasodilatory reserve

↓

Microvascular myocardial ischemia

↓

Stiffness + impaired relaxation

↙ ↓ ↘

↑ LVEDP ↑ LA pressure Pulmonary hypertension

Diastolic dysfunction LA dilation ↓ exercise tolerance  
and exertional dyspnea

**HFpEF = normal EF, but ↑ filling pressures, ↓ compliance**

Multisystem disease → treatment goal is ↓ congestion and improved relaxation

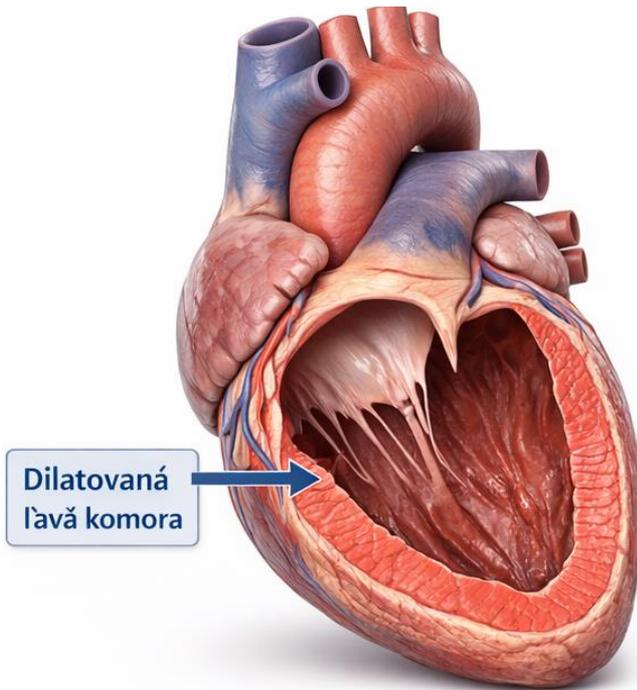
- **↑ Load (pressure / volume) + ↑ RAAS + ↑ SNS**  
↓  
**Activation of cardiomyocytes**
- **Hypertrophy (compensatory)**
- **Cardiomyocyte apoptosis (harmful)**
- **Fibroblast activation → Interstitial fibrosis**

### **CHANGES IN LV GEOMETRY (LV geometric change)**

- **Eccentric hypertrophy (volume overload)**  
→ LV dilatation  
→ ↓ EF
- **Concentric hypertrophy (pressure overload)**  
→ LV stiffening  
→ diastolic dysfunction

**Consequence:** progression of **HF**, reduced **CO**, arrhythmias, higher mortality

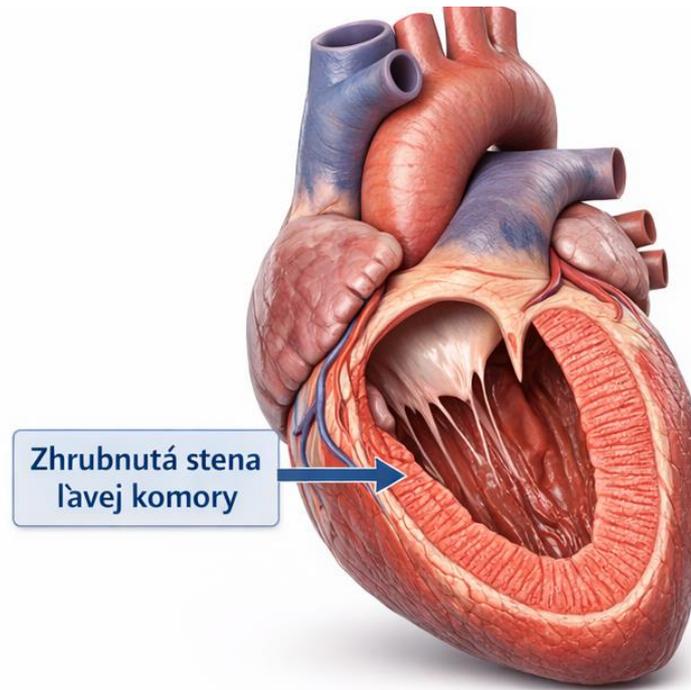
# Myocardial remodeling



## Eccentric hypertrofia

(dilatovaná komora)

- Zväčšený objem
- Nízka ejekčná frakcia



## Koncentrická hypertrofia

(zhrubnutá stena)

- Zhrubnutá stena
- Diastolická dysfunkcia