MUNI
PHARM

# CARDIOVASCULAR SYSTEM DISEASES

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Lecture from Geriatric Pharmacotherapy 21.4. 2023

# Cardiovascular changes in old age

- **decreased compliance and elasticity** of the central arteries
- **abnormal functions of endothelium**
- **loss of coronary perfusion**
  - myocardial ischemia
- **left ventricular hypertrophy**
- **fibroblast heart remodelling**
  - from increased afterload because of atherosclerosis
- **left ventricular ejection fraction decreases**
- **heart valves sclerosis**
- **progresive fibrosis of the heart conduction system**

# Valvular heart disease

## Aortic valve stenosis

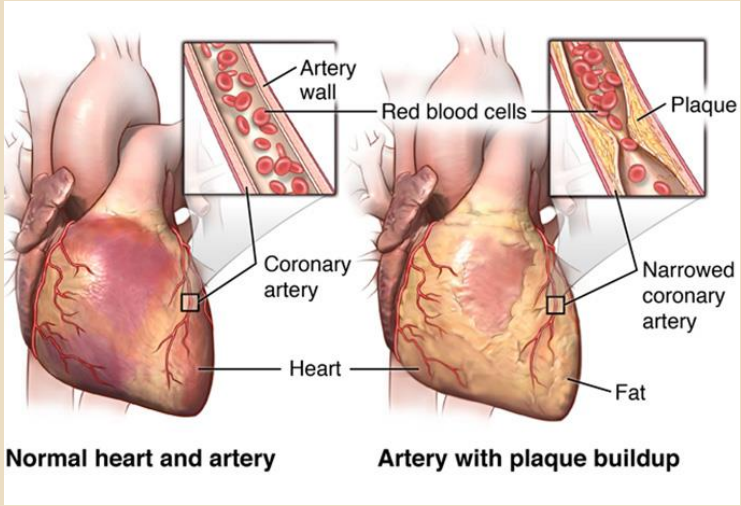
- aortic valve narrowing due to calcific degeneration
- dyspnoea, fainting (syncope), heart murmur
- **therapy:** surgical valve replacement

## Mitral insufficiency

- mitral valve does not close properly when the heart pumps out blood
  - regurgitation of blood back into the left atrium
- cause of congestive heart failure
- **therapy:** surgical valve replacement

# Coronary artery disease (CAD)

- reduction of blood flow to the myocardium due to atherosclerotic plaques in the heart coronary arteries
  - leading cause of death of elderly patients
- **risk factors:** diabetes, hypertension, tobacco smoking, alcohol abuse, dyslipidemia, obesity, family history, physical inactivity
- **typical symptoms:** chest pain or discomfort which may spread into the shoulder, arm, back, neck or jaw
  - usually occur during exertion
- **atypical chest pain** complaints
- **nonchest presentations:**
  - fatigue, dyspnea, abdominal pain, nausea, vomiting, syncope



# Coronary artery disease

**Stable angina pectoris**

- classic type of angina related to myocardial ischemia
- chest discomfort and associated symptoms precipitated by some activity

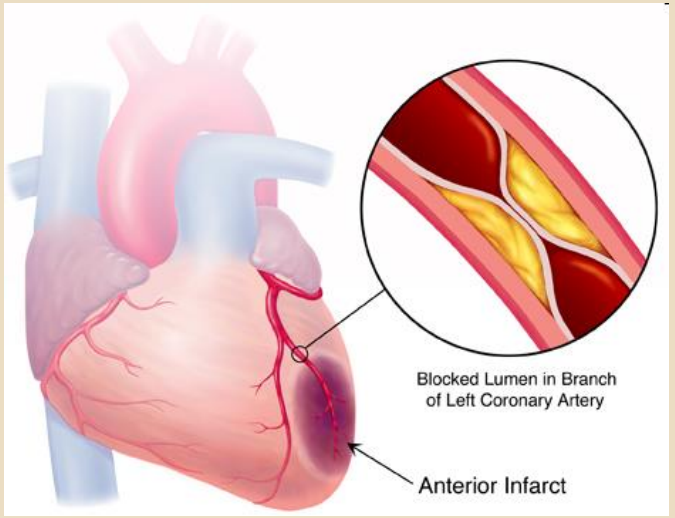
**Unstable angina pectoris**

- occurs at rest or with minimal exertion
- more severe, prolonged, or frequent than before
- the reduction of coronary flow due to transient platelet aggregation on apparently normal endothelium
- **coronary artery spasms**
- **coronary thrombosis**

# Coronary artery disease

## Myocardial infarction

- occlusion of a coronary artery leading to ischemia
- typical **central diffuse chest pain radiating** most often to the left arm or to the lower jaw, neck, right arm, back and upper abdomen
- atypical dyspnoea without pain, confusion, syncope, vertigo, epigastric pain
- may be **silent** in elderly patients




## Sudden cardiac death

# Myocardial infarction Types

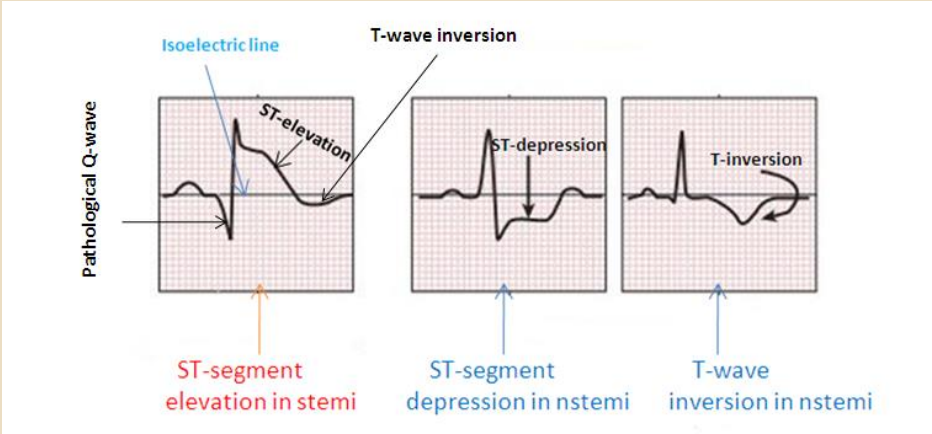
**ST-elevation (STEMI)**

- 25 – 40% of myocardial infarctions
- significant ST elevations on ECG

**Non ST-elevation (NSTEMI)**

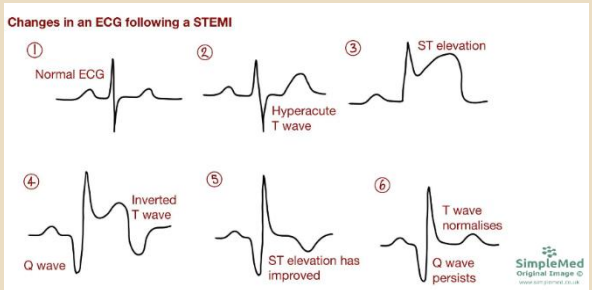
- ST depressions or T wave changes

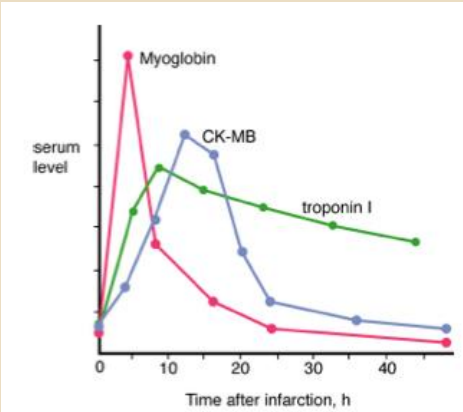
- **! ECG changes may not be typical in elderly patients !**



# Myocardial infarction Diagnosis

- symptoms related to ischemia
- pathological changes on **electrocardiograph (ECG)**
  - ST segment changes, Q waves
- **cardiac enzymes (biomarkers) elevation**
  - troponins, creatine kinase myocardial band (CK-MB), myoglobin
- **cardiac catheterization**
  - thrombus on angiogram



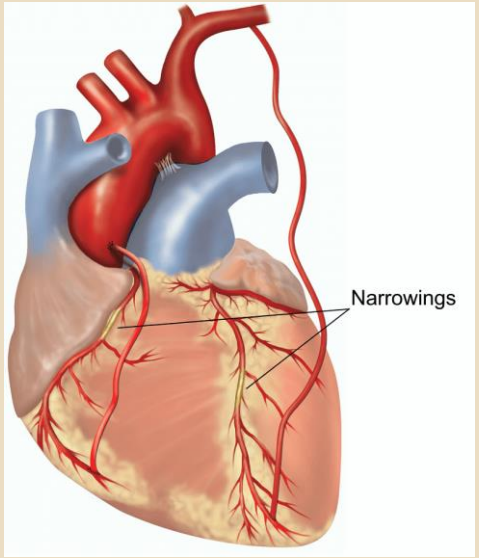



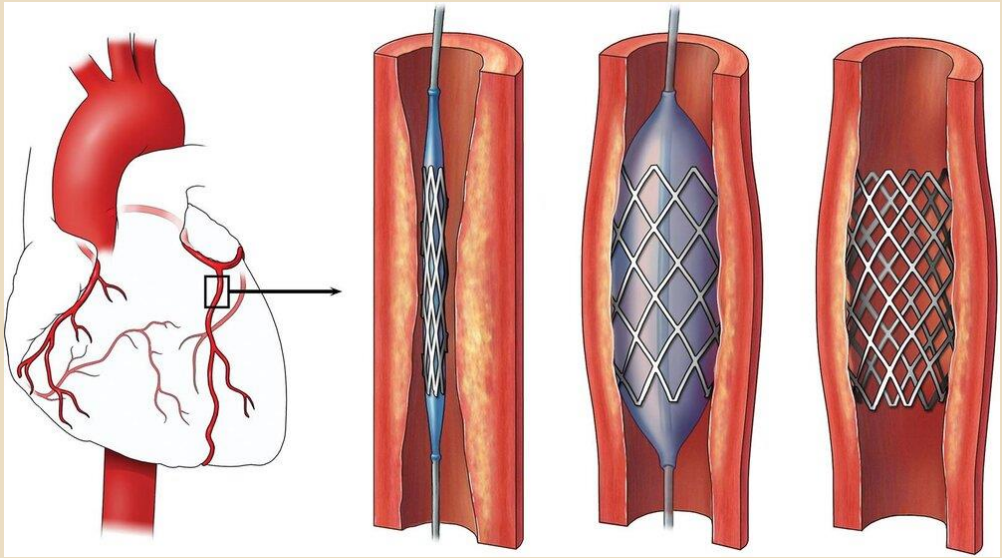
# Coronary artery disease Treatment

- **lifestyle changes**
- **antiplatelet therapy**
  - **p.o.** aspirin, prasugrel, clopidogrel
  - **i.v.** GP IIb/IIIa inh. – abciximab, tirofiban, eptifibatide
- **cholesterol-modifying medications**
- **angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs)**
- **nitrates** (nitroglycerin)
- **beta-blockers**

# Coronary artery disease Treatment

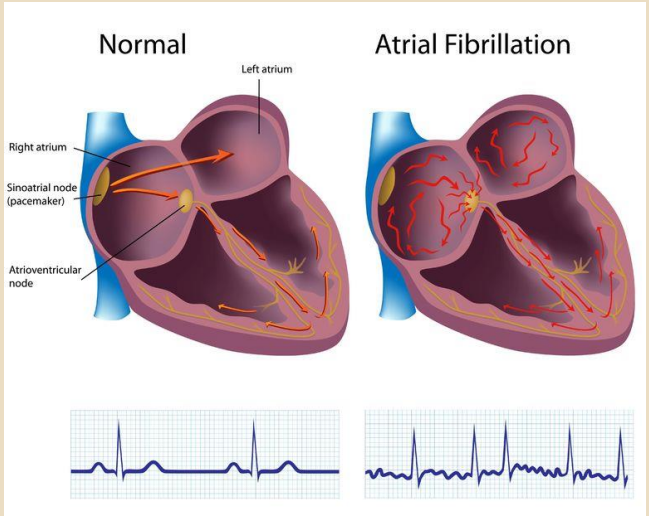
- **thrombolytic therapy**
  - tPA (alteplase), anistreplase, tenecteplase
- **percutaneous transluminal coronary angioplasty (PTCA) and stent placement** (coronary revascularization)
- **coronary artery bypass surgery**



# Arrhytmias Atrial fibrillation

- the most common clinically significant arrhytmia in the elderly
- irregular and often rapid heart rate that can increase the **risk of strokes or heart failure**
  - the major concern is a potential to develop blood clots within the upper heart chambers (cerebral stroke)



# Atrial fibrillation

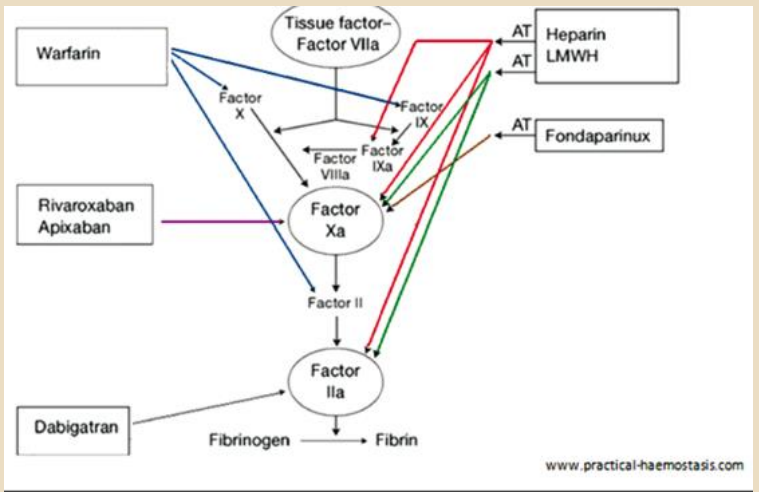
- **symptoms:** palpitations, weakness, fatigue, dizziness, shortness of breath
- could be **occasional** or **persistent**
- **risk factors:** age, hypertension, heart diseases, family history, obesity
- **$CHA_2DS_2$–VASc score** for atrial fibrillation stroke risk
- diagnosis by **ECG**

| Letter | Risk factor | Score |
|---|---|---|
| C | Congestive heart failure/LV dysfunction | 1 |
| H | Hypertension | 1 |
| $A_2$ | Age ≥75 | 2 |
| D | Diabetes mellitus | 1 |
| $S_2$ | Stroke/TIA/thrombo-embolism | 2 |
| V | Vascular disease* | 1 |
| A | Age 65–74 | 1 |
| S | Sex category (i.e., female sex) | 1 |
| | Maximum score | 9 |

Congestive heart failure/LV dysfunction means LV ejection fraction ≤40%. Hypertension includes the patients with current antihypertensive medication. *Prior myocardial infarction, peripheral artery disease, aortic plaque. LV: left ventricular, TIA: transient ischemic attack

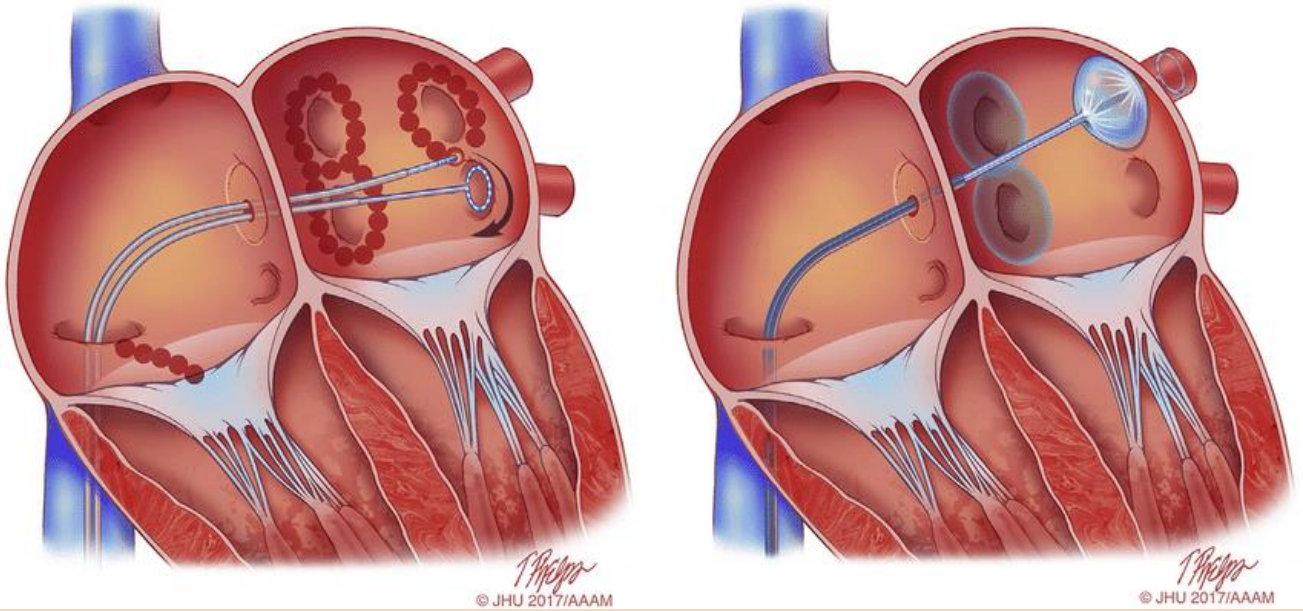
# Atrial fibrillation Treatment

- **resetting the rhythm**
  - **electrical cardioversion**
  - **cardioversion with antiarrhytmic** drugs (propafenone, amiodarone, sotalol)
- **control of the heart rate**
  - digoxin, beta-blockers, calcium channel-blockers
- **anticoagulation** as a prevention of blood clots
  - **warfarin**
  - **NOAC** (novel oral anticoagulants)
    - dabigatran, rivaroxaban



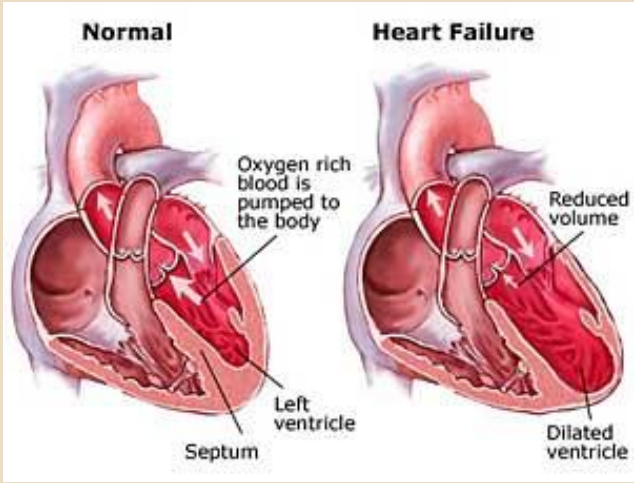
# Atrial fibrillation Treatment

- **catheter and surgical procedures**
  - **selective catheter ablation** (radiofrequency, cryotherapy, heat)
  - **atrioventricular (AV) node ablation** with cardiostimulator implant

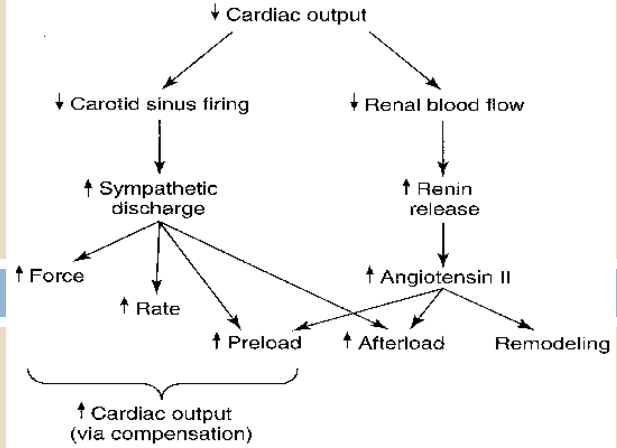


# Heart failure

- can involve the **left or right side** of the heart or both
  - the left side is rather affected first
- usually a chronic disease
- the heart tries to compensate for the loss in pumping function by:
  - developing more muscle mass (**ventricular hypertrophy**)
  - enlarging (**dilation**)
  - pumping faster (**tachycardia**)



# Heart failure Types




## LEFT HEART FAILURE

- involves the left ventricle of the heart
- **Systolic failure**
  - loss of heart´s ability to contract or pump blood into the circulation
- **Diastolic failure**
  - loss of heart´s ability to relax because it becomes stiff and can´t be filled properly

## RIGHT HEART FAILURE

- usually result of left heart failure
- occasionally **isolated right heart failure** can occur due to lung disease or pulmonary embolism

# Heart failure Types

- measurement of **ejection fraction (EF)**
  - how much blood the left ventricle pumps out with each contraction
  - EF of 60 % means that 60 % of the total amount of blood in the left ventricle is pushed out with each heartbeat

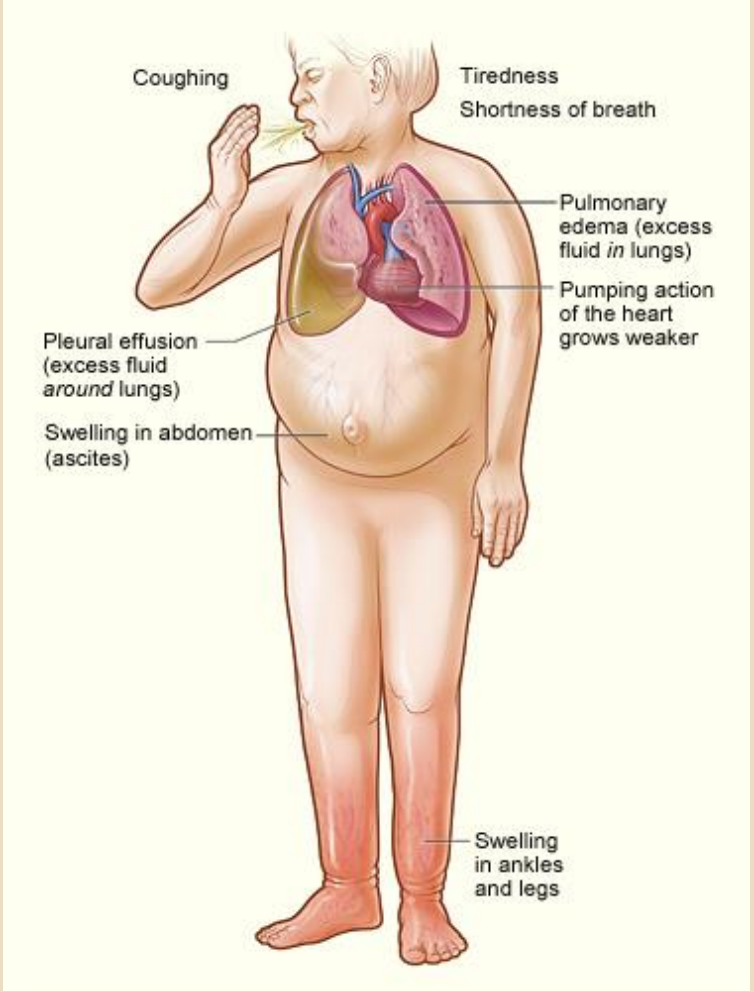
- **HFrEF** (heart failure with reduced ejection fraction)
  $EF_{LK} \leq 40\ \%$
- **HFpEF** (heart failure with preserved ejection fraction)
  $EF_{LK} \geq 50\ \%$
- **HFmrEF** (heart failure with mid-range ejection fraction)
  $EF_{LK} = 40–49\ \%$

# Heart failure Causes

- **coronary artery disease**
  - cholesterol and fatty deposits build up in the heart's arteries
  - work of the heart is harder and occasionally damages the heart muscle
- **myocardial infarction**
- **hypertension**
  - uncontrolled high blood pressure doubles a persons risk of developing heart failure
  - heart must pump harder to keep blood circulating
  - chamber first thickens, then gets larger and weaker

# Heart failure Symptoms

- **shortness of breath (dyspnoea)**
  - **main symptom** in elderly
  - dyspnea on exertion or at rest
  - difficulty breathing when lying flat
  - waking up short of breath
- **persistent cough or wheezing**
- **edemas**
  - swelling in feet, ankles and legs
  - ascites
  - weight gain
- **confusion, impaired thinking**



# NYHA Heart failure Classification

| Class | % of patients | Symptoms |
|---|---|---|
| I | 35 % | No symptoms or limitations in ordinary physical activity |
| II | 35 % | Mild symptoms and slight limitation during ordinary activity |
| III | 25 % | Marked limitation in activity even during minimal activity. Comfortable only at rest |
| IV | 5 % | Severe limitation. Experiences symptoms even at rest |

# Heart failure Treatment

**Non-pharmacological rules**

- salt and water intake restriction
- alcohol reduction
- weight maintenance
- physical exercise

# Heart failure Treatment

**Diuretics**

- management of symptoms of congestion and volume overload
- frequent monitoring of serum electrolytes and renal functions
- **loop diuretics**
  - **furosemide**
- **thiazide diuretics**
  - ineffective when the GF rate is less than 30–40 ml/min.
  - **indapamide, hydrochlorothiazide**
- **potassium sparing diuretics (aldosterone-antagonists)**
  - **spironolactone, eplerenone, amiloride**
  - should be reduced because of risk of hyponatremia, hyperkalemia and uremia

# Heart failure Treatment

**Angiotensin-converting enzyme (ACE) inhibitors**

- hemodynamic, functional and mortality benefits for elderly patients with systolic heart failure
- renal functions should be monitored closely
  - creatinine and serum potassium
- cough is frequent adverse effect
- **ramipril, enalapril, lisinopril, cilazapril,**

# Heart failure Treatment

**Angiotension II receptor blockers**

- significant benefit in cardiovascular death and hospitalization
- recommended as treatment in patients who are intolerant of ACE-I
  - lower rates of cough
- **losartan, valsartan**

**Dual inhibitor of AT1 receptors for angiotensin II and neprilysin – neutral endopeptidase (ARNI)**

- **natriuretic peptides (BNP, NT-proBNP)**
  - vasodilatation, natriuresis, antiproliferative effects
  - inhibition of endopeptidase prevents the breakdown
- **sacubitril/valsartan**

# Heart failure Treatment

**Beta-blockers**

- slow the heart rate and decreases the blood pressure
  - reduce the risk of tachyarrhytmias
- initiation with very low doses and slow titration
- careful monitoring of heart rate is necessary because of bradycardia risk
- **bisoprolol, carvedilol, metoprolol, nebivolol**

**Sinus node inhibitors**

- **ivabradin**
- can be used as an alternative to beta-blocker or in combination

# Heart failure Treatment

## Positive inotropes

- increase the strength of the heart muscle contractions by intracellular calcium increase in myocardial cells, by inhibiting the sodium–potassium pump
- **digoxin**
  - cardiac glycosides first drugs used for heart failure
  - beneficial for atrial fibrillation with rapid ventricular response
  - administration in small doses (0.125 mg every other day)
  - risk of **digoxin toxicity** because of narrow therapeutic window
    - GIT symptoms, arrhytmias, confusion
    - high risk in patients with hypokalaemia, hypercalcaemia, hypothyroidism
    - **TDM** monitoring of plasma digoxin levels (digoxin target levels: 0.6 - 1.6 nmol/l)

# Hypertension

- high arterial pressure in the systemic circulation, abnormal elevation in diastolic pressure and/or systolic pressure
- generally an asymptomatic condition
- the most important risk factor for **cardiovascular morbidity and mortality**

- the WHO has proposed the upper limit of normal blood pressure

| Classification | Systolic (mmHg) | Diastolic (mmHg) |
|---|---|---|
| Normal | <120 | <80 |
| Prehypertension | 120-139 | 80-89 |
| Stage 1 | 140-159 | 90-99 |
| Stage 2 | 160-179 | 100-109 |
| Stage 3 | ≥180 | ≥110 |

# Etiology of hypertension

**Primary (essential, idiopathic)**

- 90–95 %
- strong family history

**Secondary**

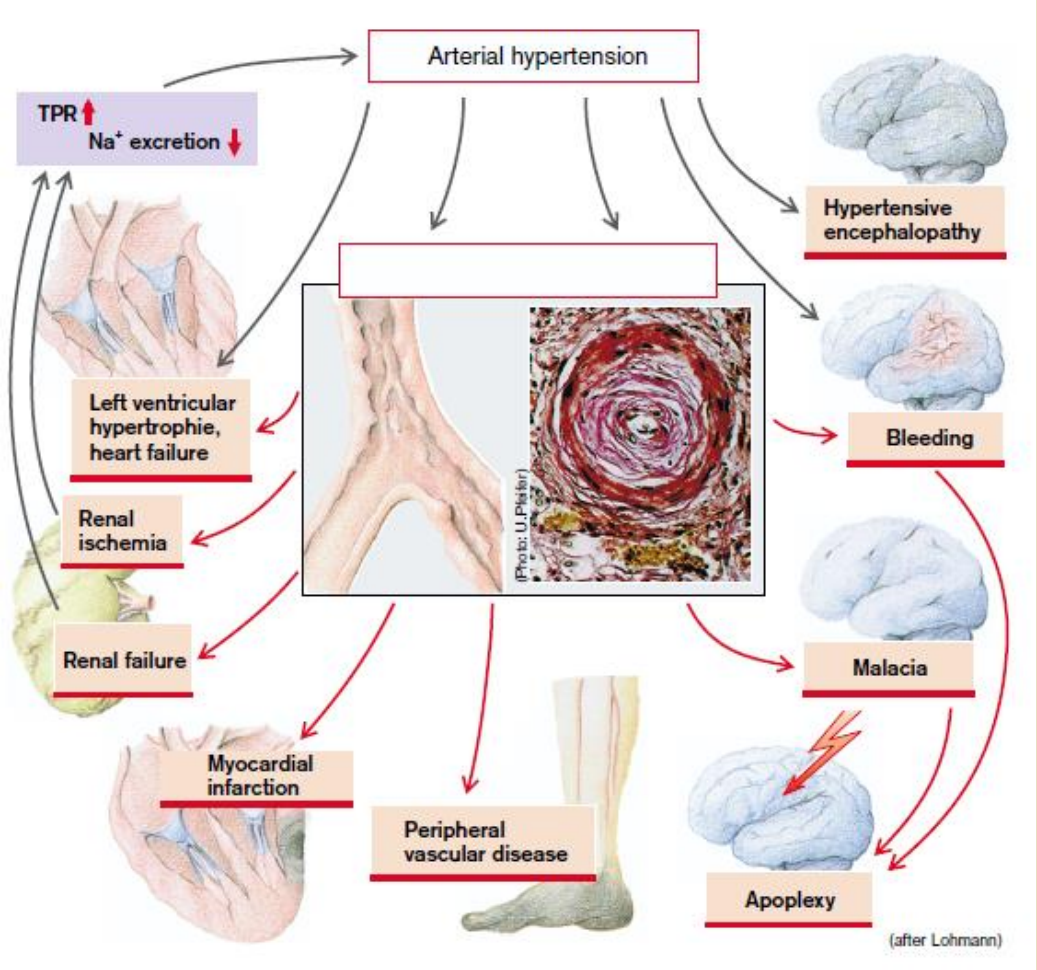
- about 5–10 %
- identifiable cause:
  - **kidney disease**
  - **renal artery stenosis**
  - **hyperaldosteronism**
  - **pheochromocytoma**

# Clinical manifestations of hypertension

- frequently asymptomatic until it becomes severe and organ diseases occur

**Target organs:**

- heart
- brain
- peripheral vessels
- kidney
- eyes



# Hypertension in elderly

- **isolated systolic hypertension (ISH)** the most common
  - systolic BP ≥140 mmHg and diastolic BP <90 mmHg
  - increasing stiffness of the arterial wall due to atherosclerosis
- important to reach a target value of BP to avoid hypertension-associated morbidities
  - **combination of 2 or 3 antihypertensive drugs** often necessary

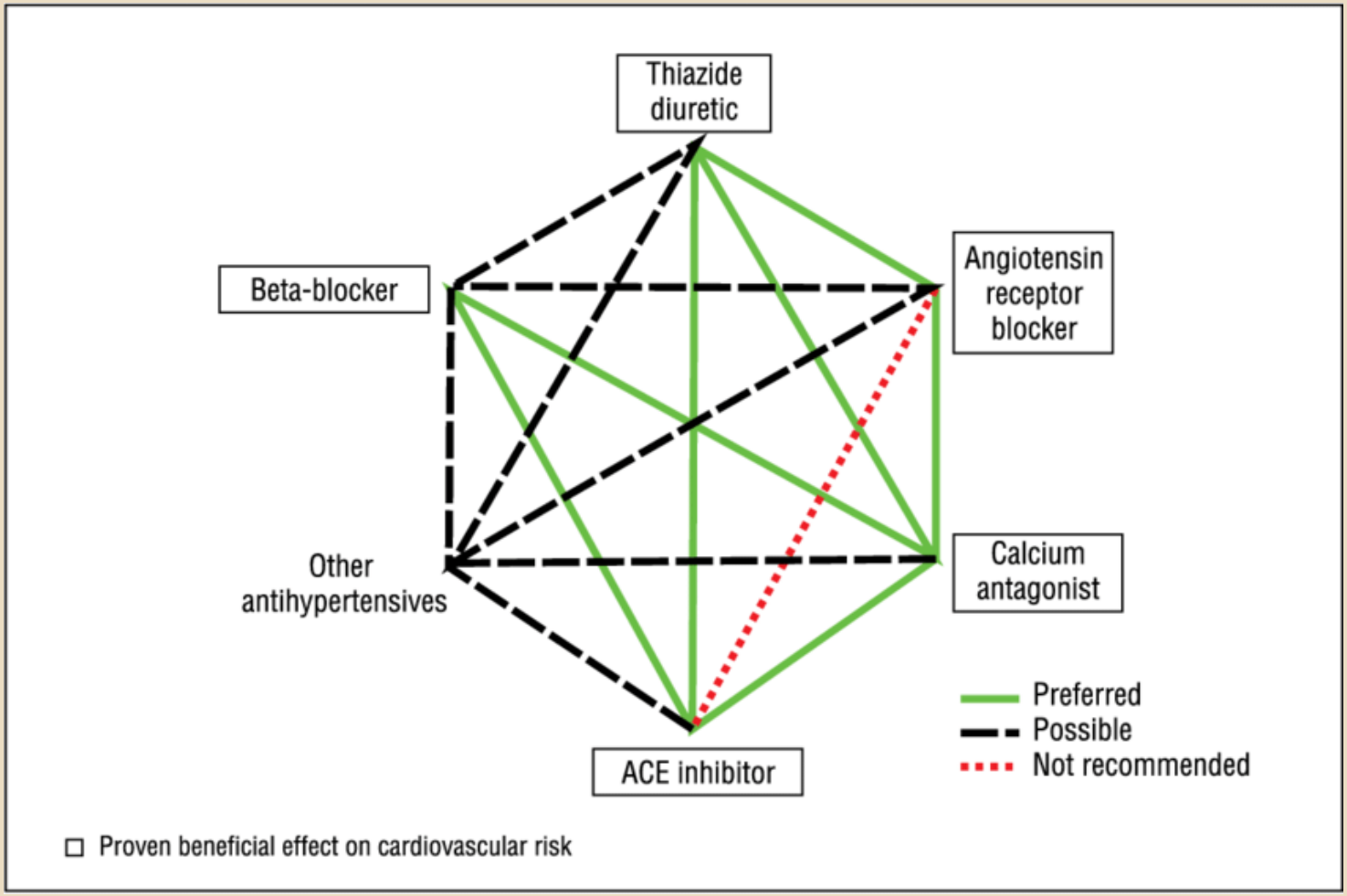
# Hypertension in elderly

- **overtreatment of hypertension** can be risky as well
  - **hypoperfusion** of target organs
  - dizziness, falls, confusion, unconsciousness
  - **orthostatic hypotension**
    - BP decreasing with at least 20 mmHg in standing form a lying position
    - regulation disturbances of the ageing autonomic NS, volume depletion
    - drug AEs (diuretics, calcium channel blockers, nitrates, antidepressants, antipsychotics, opiates, alcohol)
  - **postprandial hypotension**
    - decrease of systolic BP after meal

# Hypertension treatment

- **lifestyle changes**
- **calcium channel blockers**
- **beta blockers**
- **diuretics**
- **angiotensin-converting enzyme inhibitors (ACEis)**
- **angiotensin II receptor blockers (ARBs)**

# Antihypertensive drugs Combinations



# Antihypertensive drugs Combinations

| Dual combination | Indication |
| --- | --- |
| **ACEI/ARB + CCB** | dual combination with the widest use, in high-risk hypertension, especially associated with atherosclerosis, nephropathy, metabolic syndrome and DM |
| **ACEI/ARB + diuretic** | hypertension in the elderly, condition after CMP, hypertension with left ventricular hypertrophy, hypertension in type 2 DM |
| **ACEI/ARB + BB** | hypertension + chronic coronary heart disease, hypertension + chronic heart failure |
| **Alpha-blocker + BB** | hypertension in pheochromocytoma |

# Antihypertensive drugs Combinations

| Dual combination | Examples |
|---|---|
| ACEI + CCB | lisinopril + amlodipine<br>perindopril + amlodipine<br>ramipril + felodipine |
| ACEI+ diuretic | cilazapril + hydrochlorothiazide<br>ramipril + hydrochorothiazide<br>perindopril + indapamide |
| ARB + CCB | candesartan/telmisartan + amlodipine |
| ARB + diuretic | candesartan/losartan/valsartan + hydrochlorothiazide |

| Triple combination | Examples |
|---|---|
| ACEI + CCB + statin | perindopril + amlodipine + atorvastatin |
| ACEI+ CCB + diuretic | perindopril + amlodipine + indapamide |

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