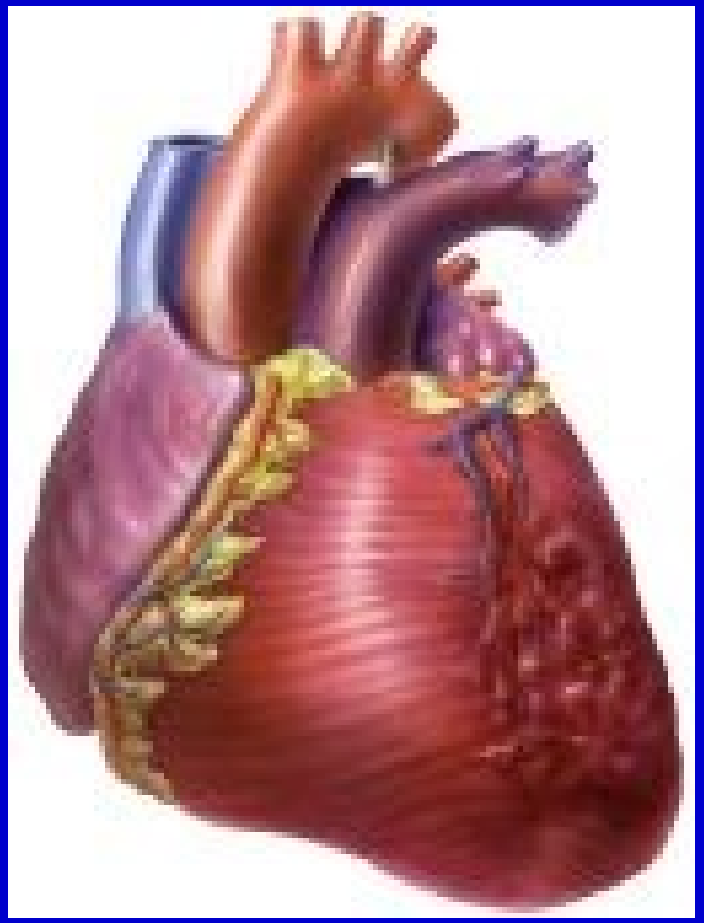


Coronary heart disease (CHD)

CASE REPORT

A) Patient, 59 years

Symptoms:
Sudden and strong chest pain with no relief
irradiation, the beginning at rest, anxiety, sweating

B) Patient, 68 years

Symptoms:
chest pain occurs regularly during the effort,
e.g. walking upstaris, run…
Relief at rest

CASE REPORT

Pain occurs due to *ischemia of myocardium*

Inbalance between blood supply and the need of the tissue

A) Absolute occlusion
B) Partial occlusion + effort
C) Microvascular dysfunction

ISCHEMIC (CORONARY) HEART DISEASE

Ischemia vs. hypoxia

- insufficient *oxygen delivery* (ischemic hypoxia) and *nutrients* to the tissue

- insufficient *metabolite wash-out*

As a consequence of *perfusion limits*

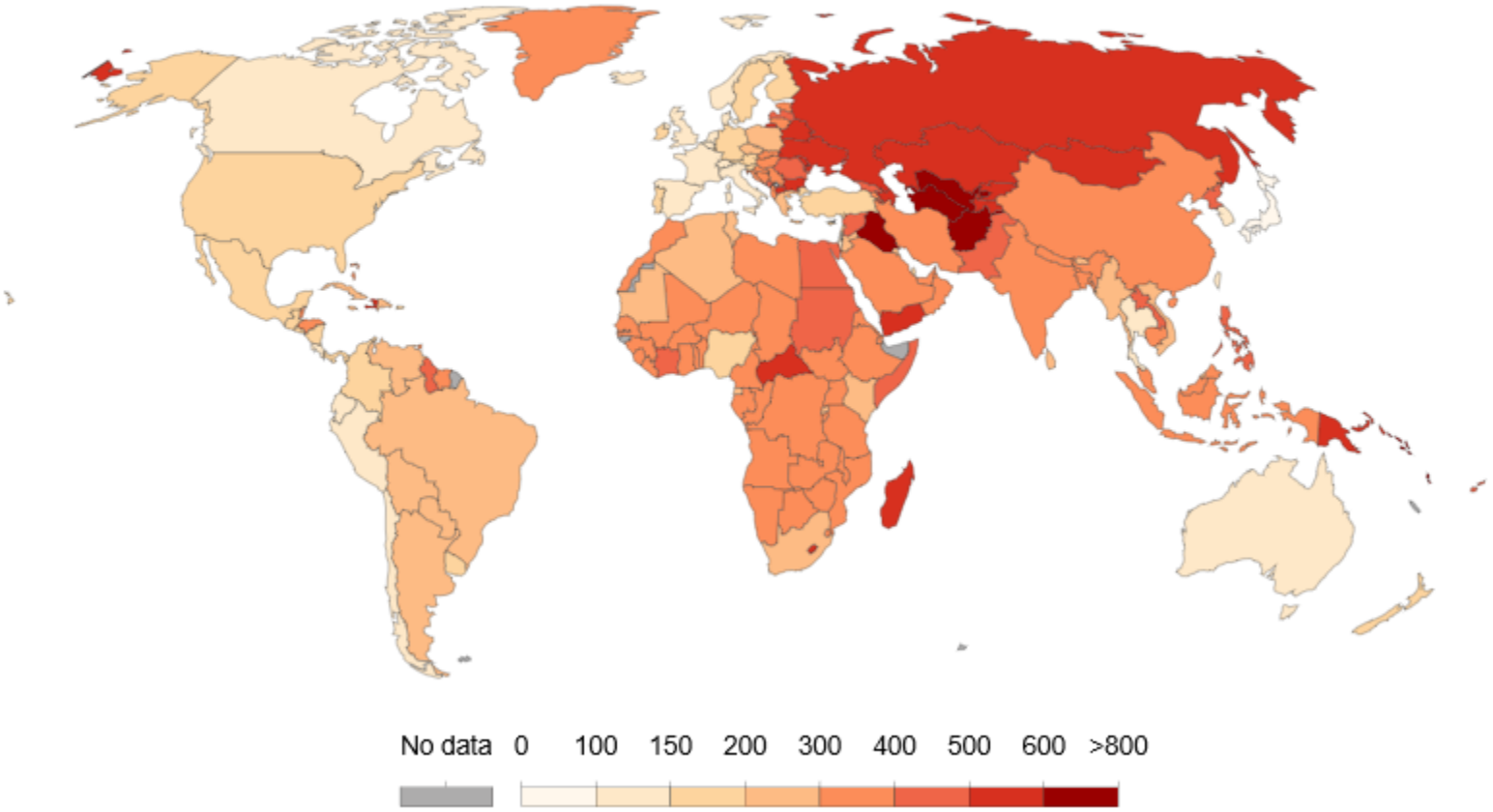
- ***narrowing*** **of the artery**
- ***occlusion*** **of the artery – embolism, thrombus**

Increased *requirements*

Cardiovascular disease death rates (per 100,000), 2016

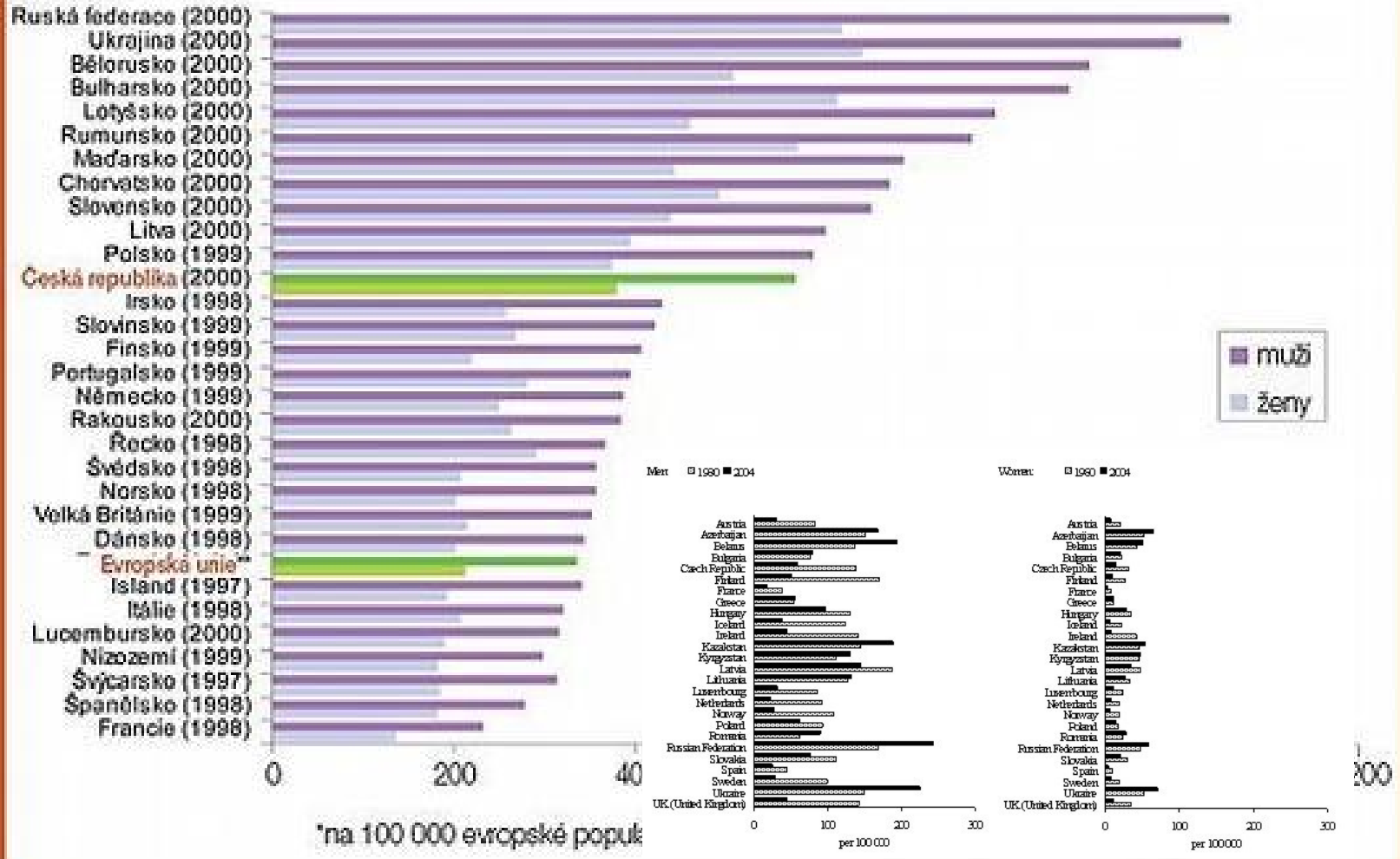
Our World in Data

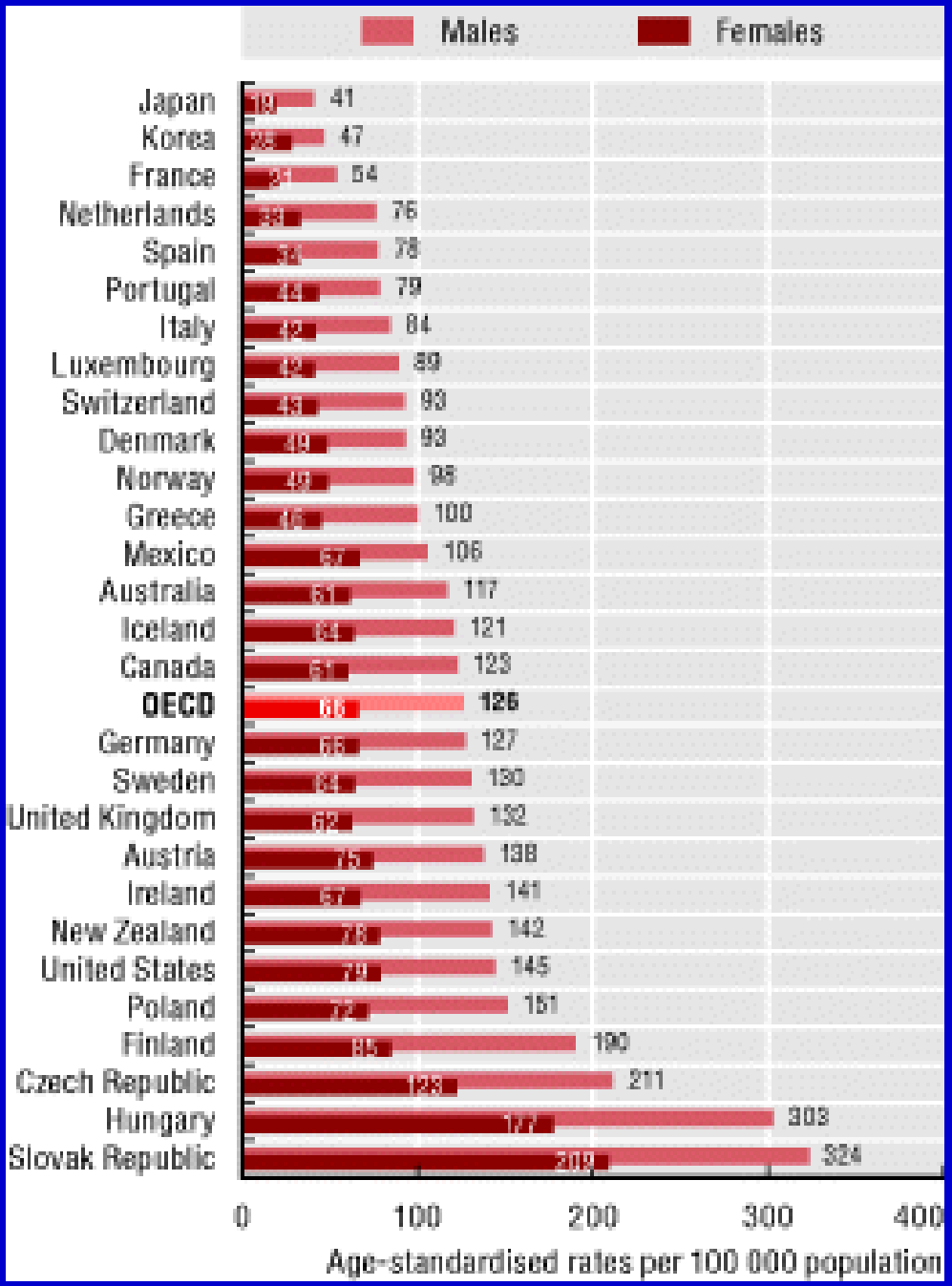
Age-standardized death rates from cardiovascular disease, measured as the number of deaths per 100,000 individuals across both sexes. Age-standardization assumes a constant population age & structure to allow for comparisons between countries and with time without the effects of a changing age distribution within a population (e.g. aging).



Source: IHME, Global Burden of Disease (GBD)

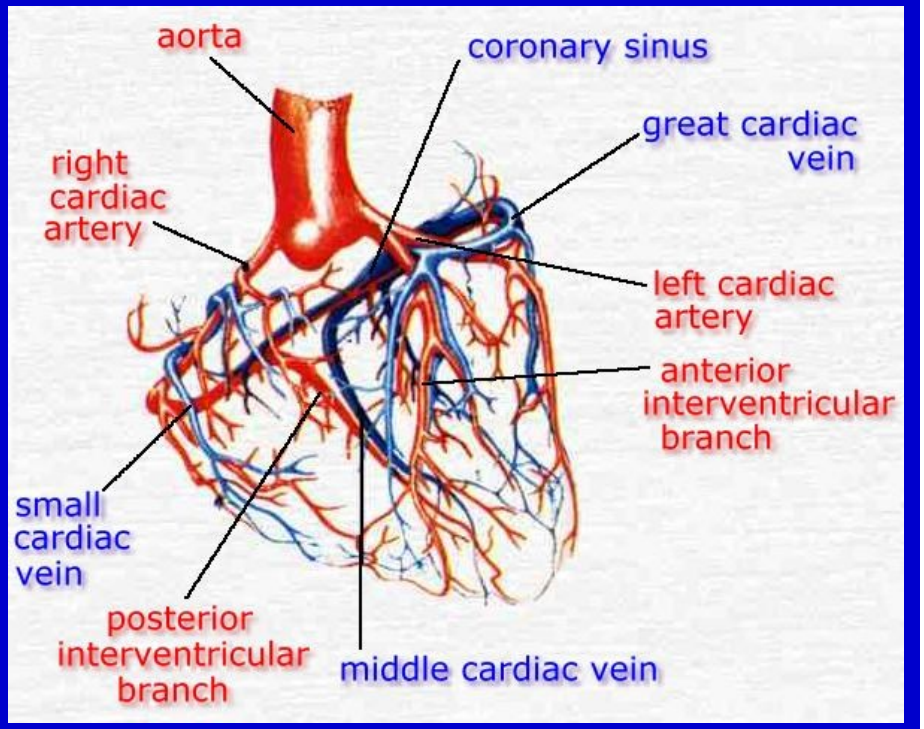
Obr. 2 – Úmrtnost na kardiovaskulární onemocnění v evropských zemích*

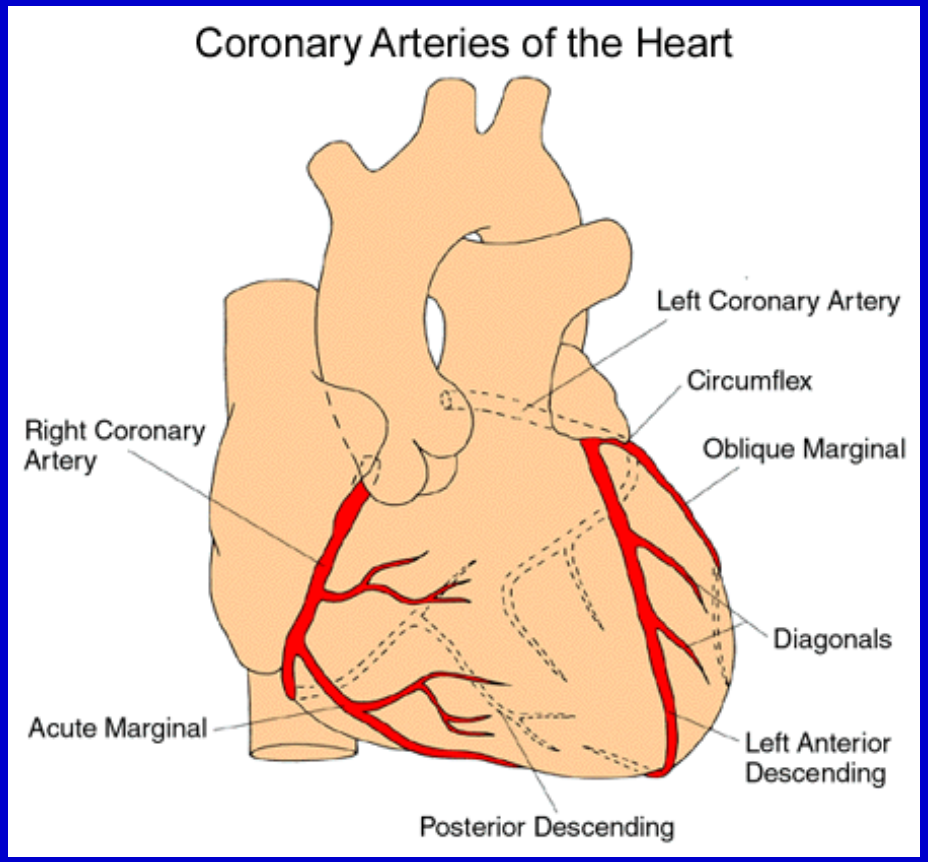




Ischemic heart disease, mortality rates, 2006 (or latest year available)

CORONARY CIRCULATION AND MYOCARDIAL METABOLISM


aorta
coronary sinus
great cardiac vein
right cardiac artery
left cardiac artery
anterior interventricular branch
small cardiac vein
posterior interventricular branch
middle cardiac vein


Coronary Arteries of the Heart
Left Coronary Artery
Circumflex
Right Coronary Artery
Oblique Marginal
Diagonals
Acute Marginal
Left Anterior Descending
Posterior Descending

Blood supply and myocardium metabolism

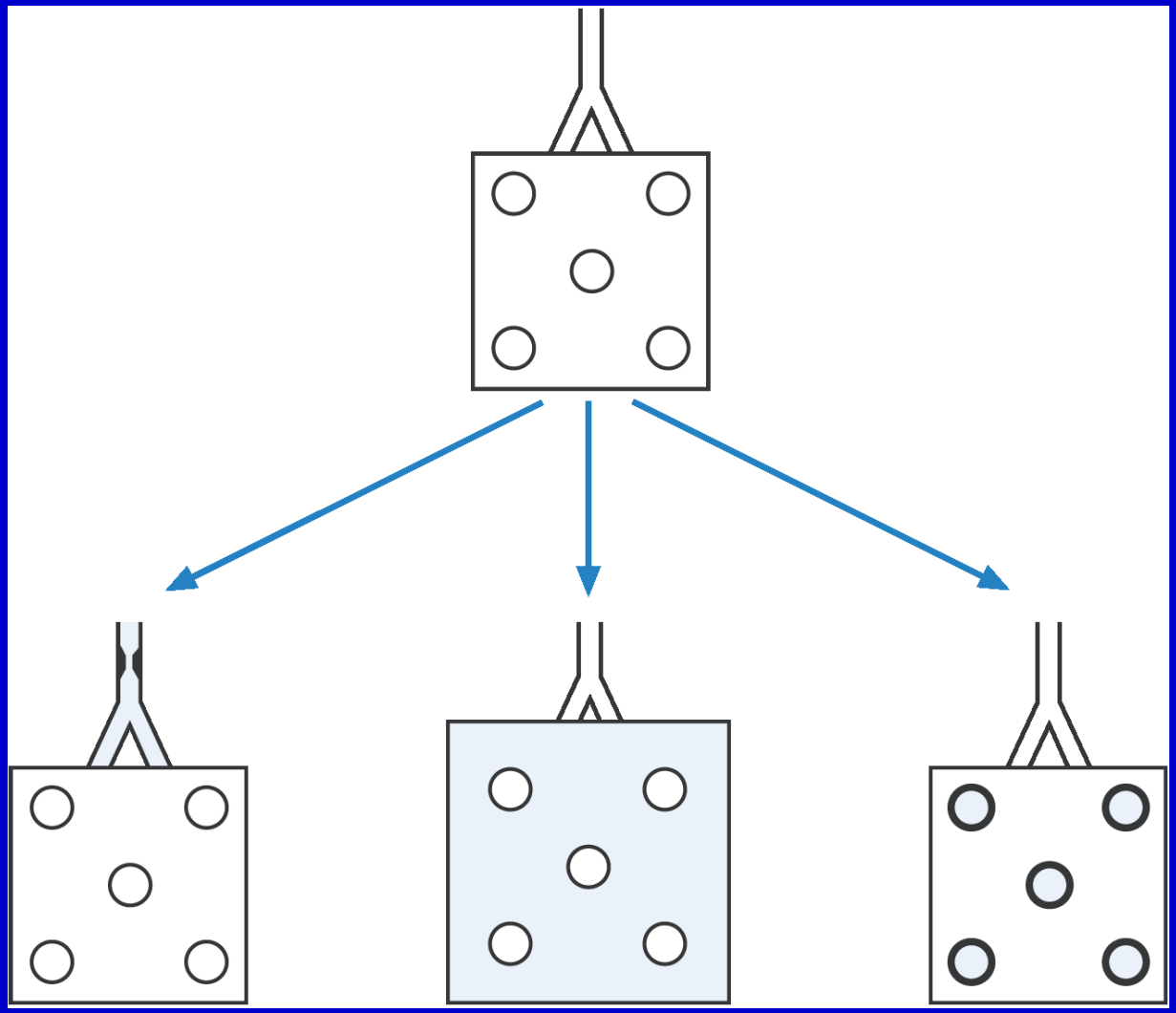
1. Blood flow
2. Oxygen

Blood flow:
resting: 250 ml/min

Main components:

- coronary arteries in epicardial part
- small coronary vessels
- myocardium

Perfusion pressure x resistance



Zátěžová echokardiografie, Maxdorf

Blood flow

Rest: **250 ml/min**
Maximal: **1000 ml/min**

Coronary reserve (CRF): **4**

Perfusion

extravascular pressure (+)

high in systole
higher in subendocardium
myocardium diseases

perfusion pressure

diastolic BP

vascular resistance

dilatation of larger epicard. arteries

VNS
$\beta_2 \times \alpha$

arteriolar dilatation

main mechanism
of increasing the blood flow

- metabolic influence
- autoregulation

endothelium

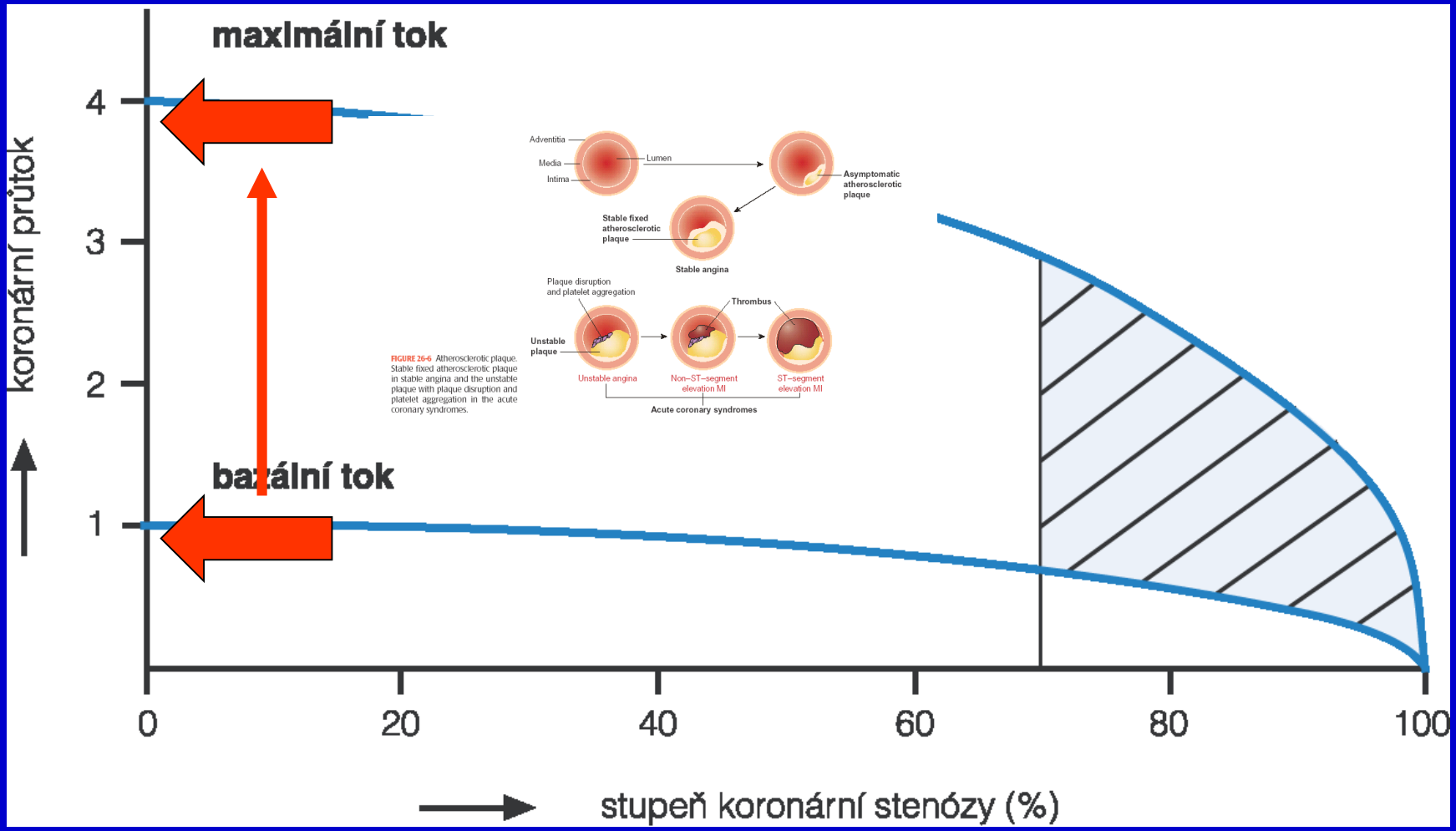
Key importance of the diastole for myocardium perfusion

Shortening of the diastole due to the tachycardia impairs the blood supply to the myocardium (but increases the demands)

Perfusion pressure:
pressure difference between the beginning of coronary arteries and estuary of coronary sinus

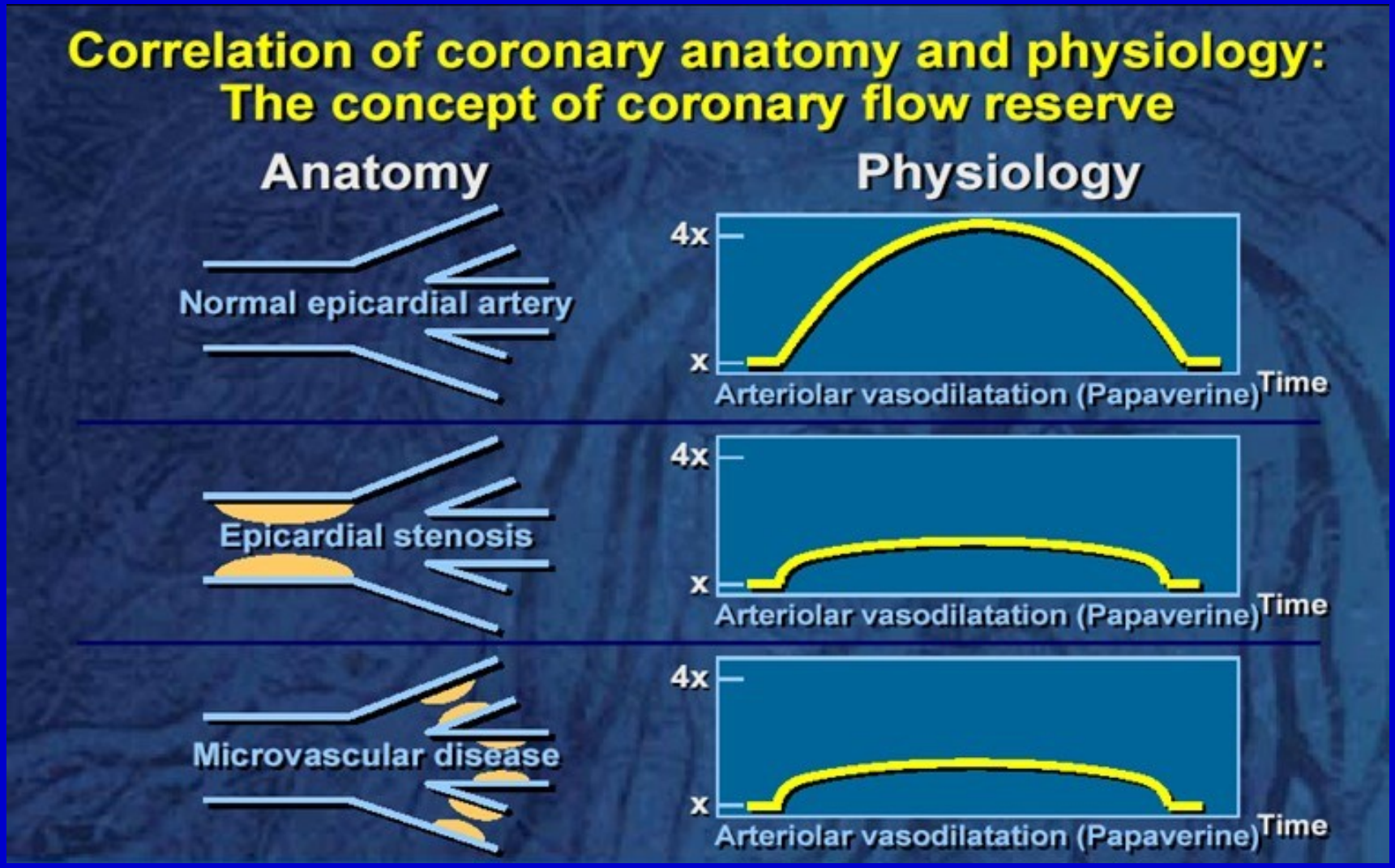
Coronary reserve:
maximal increase of blood flow through myocardium – cca 4×
vasodiatation of small vessels

Differences in perfusion:
impaired perfusion of subendocardial parts



Zátěžová echokardiografie, Maxdorf

Correlation of coronary anatomy and physiology: The concept of coronary flow reserve



Blood flow through the subendocardial vessels
is less during systole
than in the outer coronary vessels.

To compensate, *the subendocardial vessels are far more extensive* than the outermost arteries, allowing a disproportionate increase in subendocardial flow during diastole.

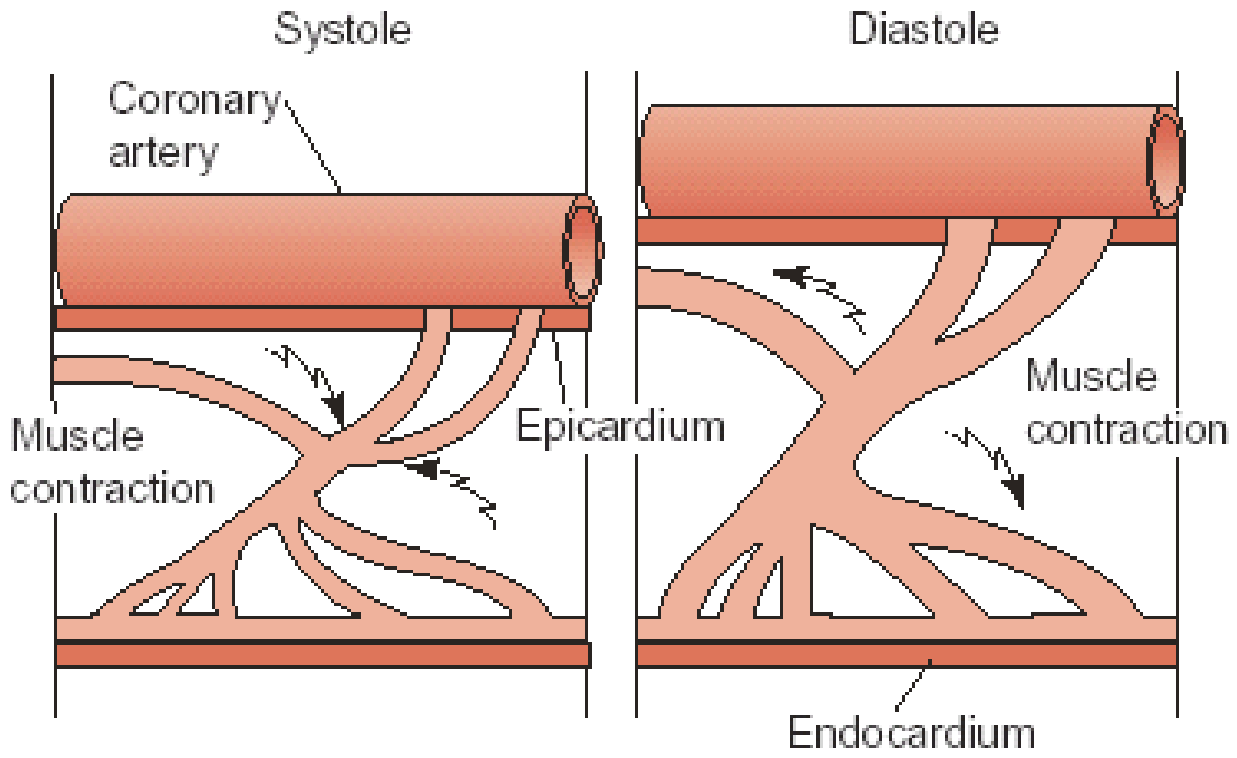
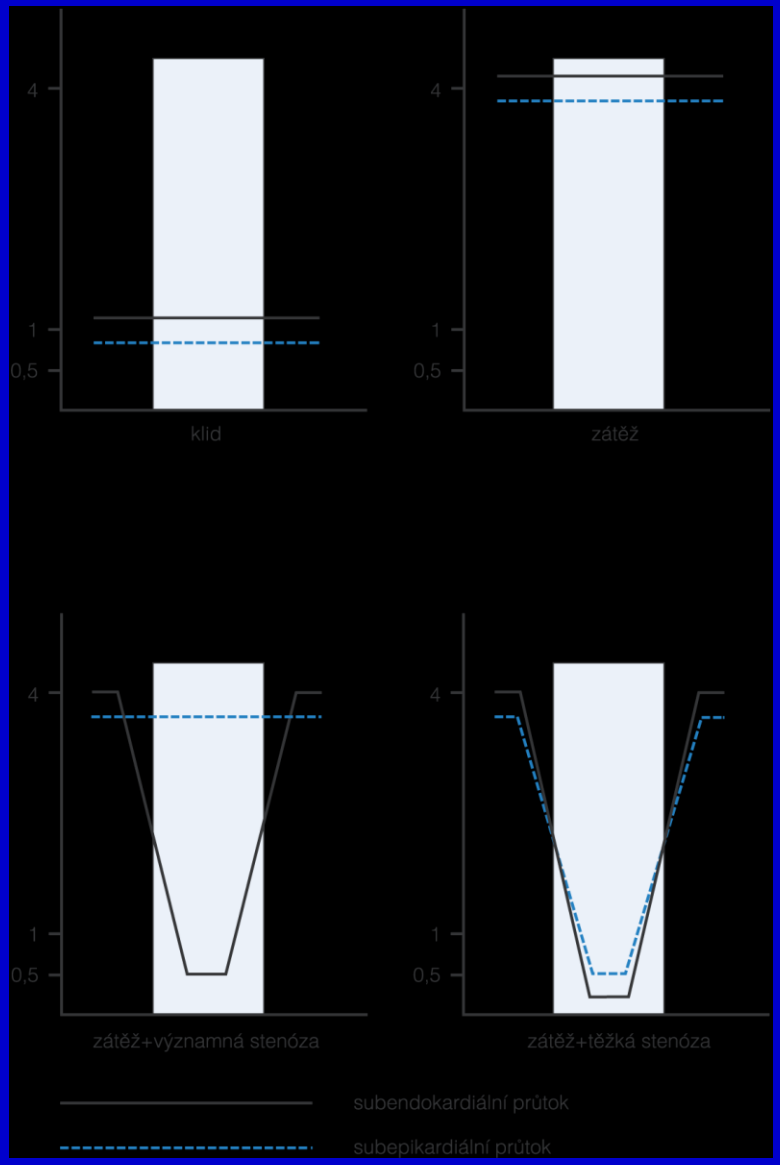


FIGURE 26-5 The compressing effect of the contracting myocardium on intramyocardial blood vessels and subendocardial blood flow during systole and diastole.



Zátěžová echokardiografie, Maxdorf

Because blood flow mainly occurs during diastole, there is a risk for subendocardial ischemia

- diastolic pressure is low
- elevation in diastolic intraventricular pressure sufficient to compress the vessels in the subendocardial plexus
- rapid heart rates, the time spent in diastole is greatly reduced

Oxygen extraction: almost maximal (as in intensively working skeletal muscles)

AV difference: 140–160 ml O_2/L blood

Oxygen consumption (AV difference × flow):
rest – 140 × 0,25 = 35 ml
exercise – 160 × 1,00 = 160 ml
Mainly achieved by increase of flow – vessel parameters are crucial for oxygen delivery to the myocardium during exercise

Energy consumption:

- 90 % mechanical activity (contraction, relaxation)
- 9,5 % proteosynthesis
- 0,5 % electrical activity

- tension in the wall of LV ~ blood pressure
- inotropy
- heart rate

Energy sources in the myocardium:
rest – FFA, glucose, lactate
exercise – increase of lactate up to 2/3

Factors infuencing oxygen consumption:

- heart work
- contractility
- heart rate
- myocardium properties: wall tension (dilatation, afterload – hypertension), hypertrophy
- adrenergic stimulation

Factors infuencing oxygen delivery to the myocardium:

- parcial tension of oxygen in the environment
- respiratory functions
- hemoglobin
- blood flow through myocardium

CASE REPORT

To evaluate:

-Heart rate
-BP
-Heart hypertrophy or dilatation
-Hemoglobin concentration,
-respiration

ISCHEMIA

Ischemia

insufficient delivery of oxygen and nutrients and insufficient outflow of metabolites from the tissues due to the impaired perfusion

Imbalance between metabolic requirements and perfusion:

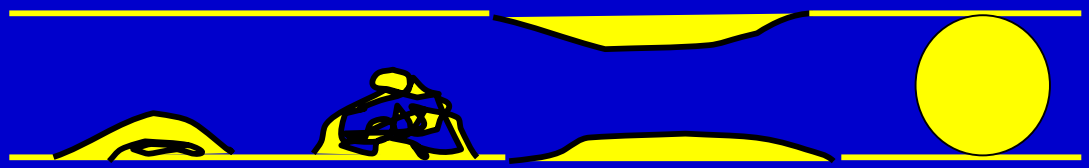
1. **increased requirements – *simulation by exercise tests***
2. **impaired perfusion**
3. **combination**

Vessel narrowing

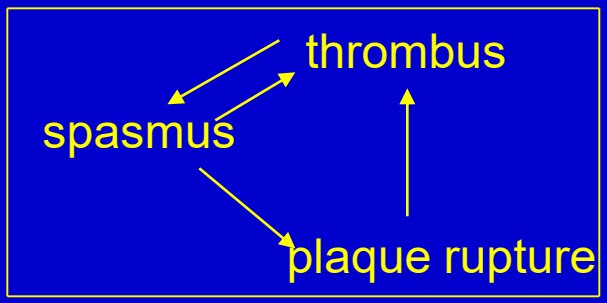
- organic
- functional
- combined

- fixed
- dynamic

plaque + thrombus + spasmus



atherom. plaque **thrombus** **spasmus** **embolus**



<u>localisation</u>
- concentric
- excentric

<u>stability</u>
- fibrotisation
- lipids
- inflammation

platelets:
vasoconstr. factors
growth factors

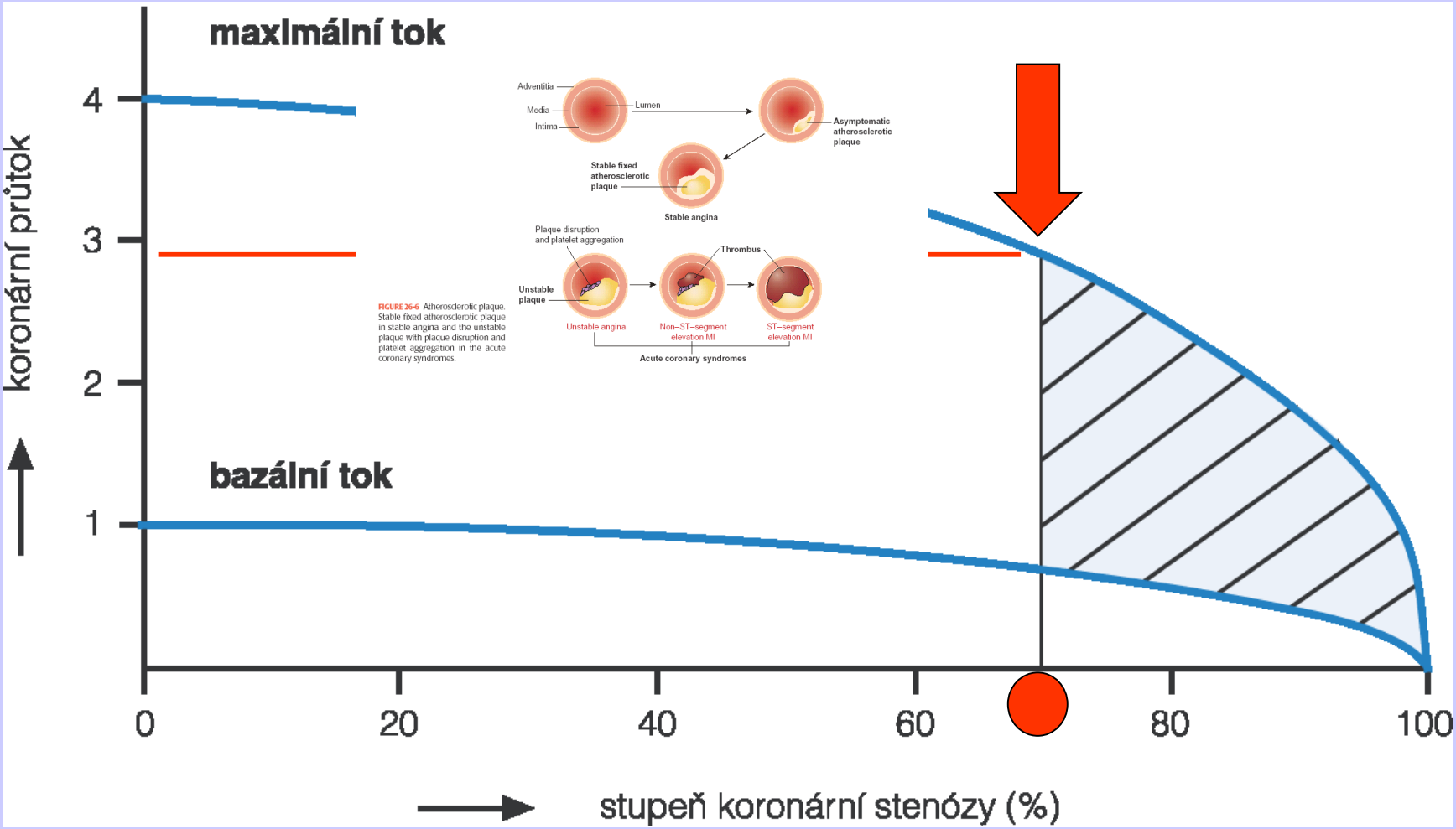
diurnal rhytm (morning!)
cold
smoking
psychic influences

Impact of the size of stenosis on hemodynamics of coronary blood flow:

- do 40 % – without influence
- 40–70 % – ischemia not apparent in physiological exercise
- 70–90 % – ischemia not in resting, distinct in exercise
- over 90 % – ischemia even in rest

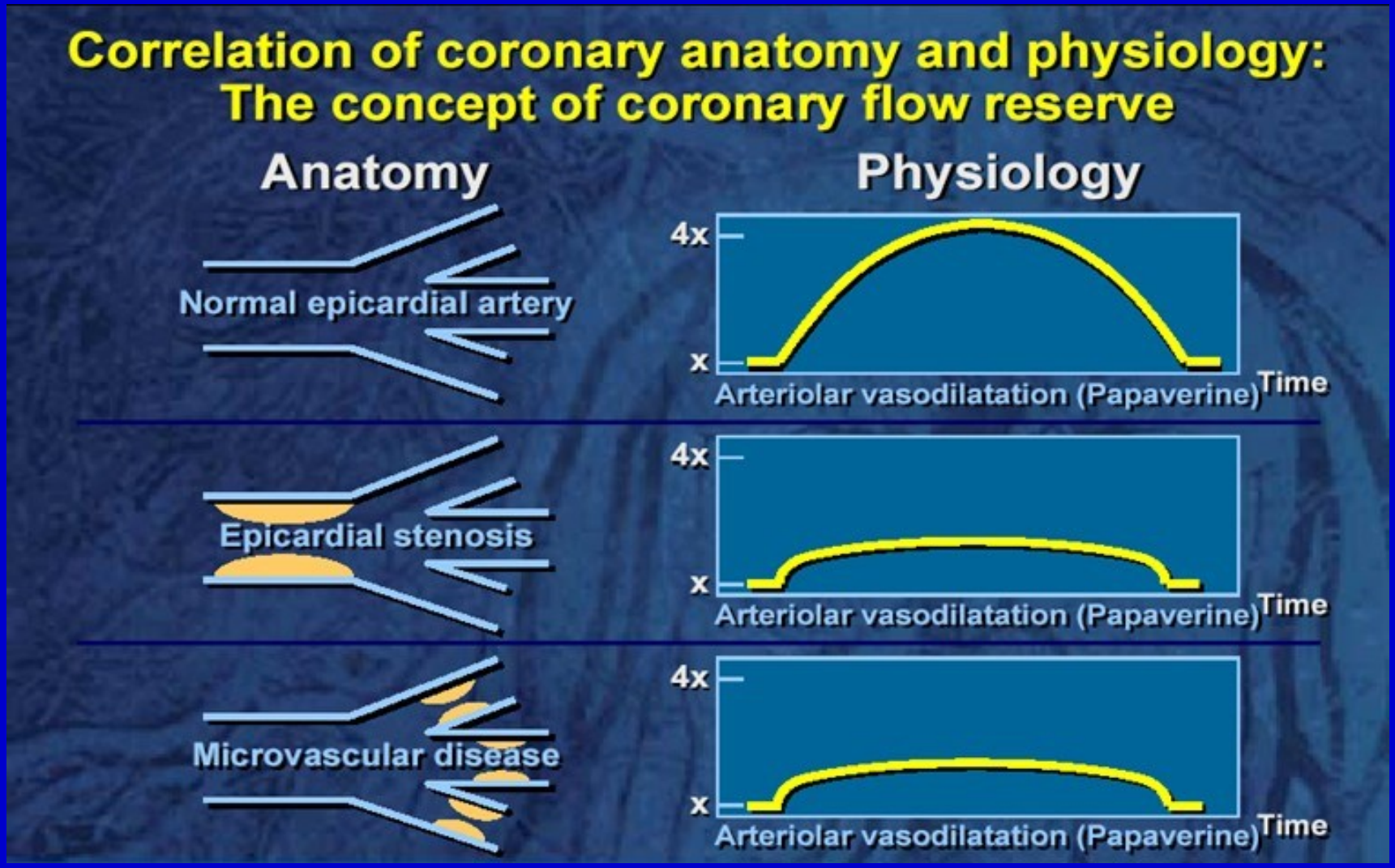
Hemodynamically unimportant atherosclerotic plaque can be the cause of life-threatening myocardial infarction:

rupture ⇒thrombus + spasmus ⇒necrosis ⇒
arrhytmia (ventricular fibrillation) ⇒death



Zátěžová echokardiografie, Maxdorf

Correlation of coronary anatomy and physiology: The concept of coronary flow reserve



Consequences of ischemia:

- metabolic changes: ATP depletion, lokal acidosis, increased inflow of *calcium* to the cells

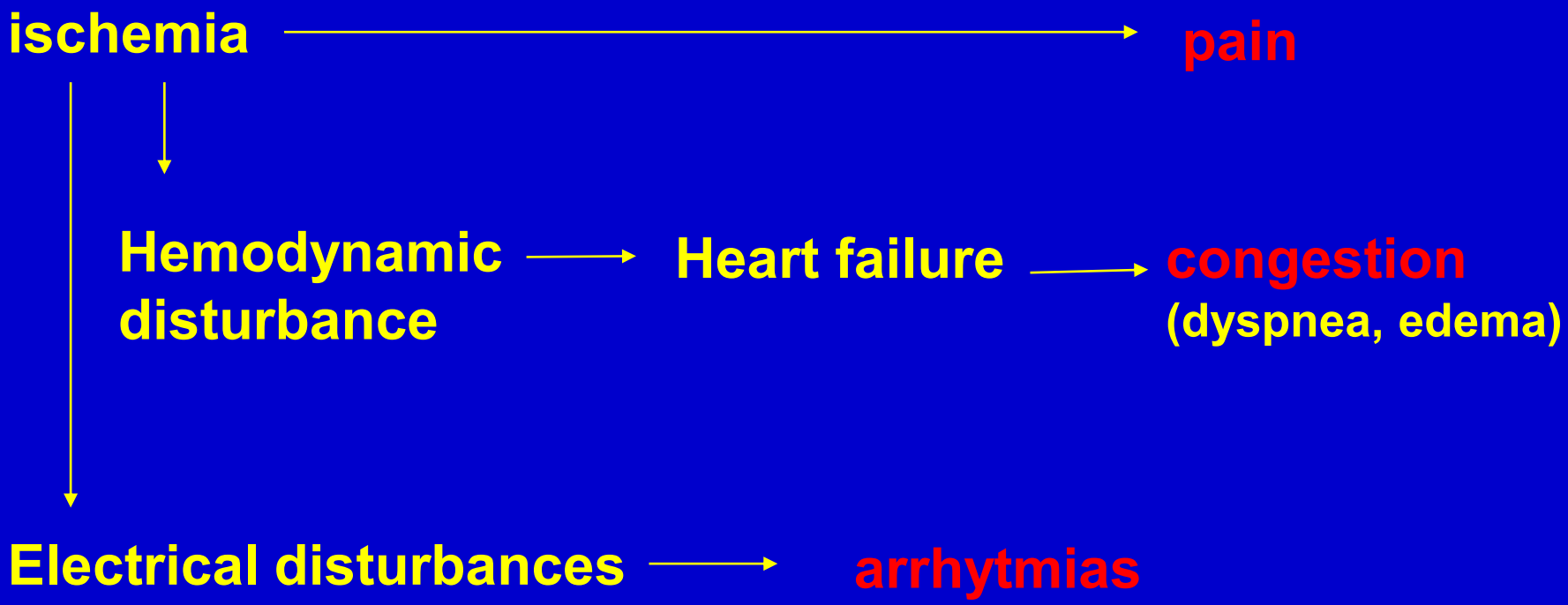
- impaired contractility (*decrease of stroke volume*):

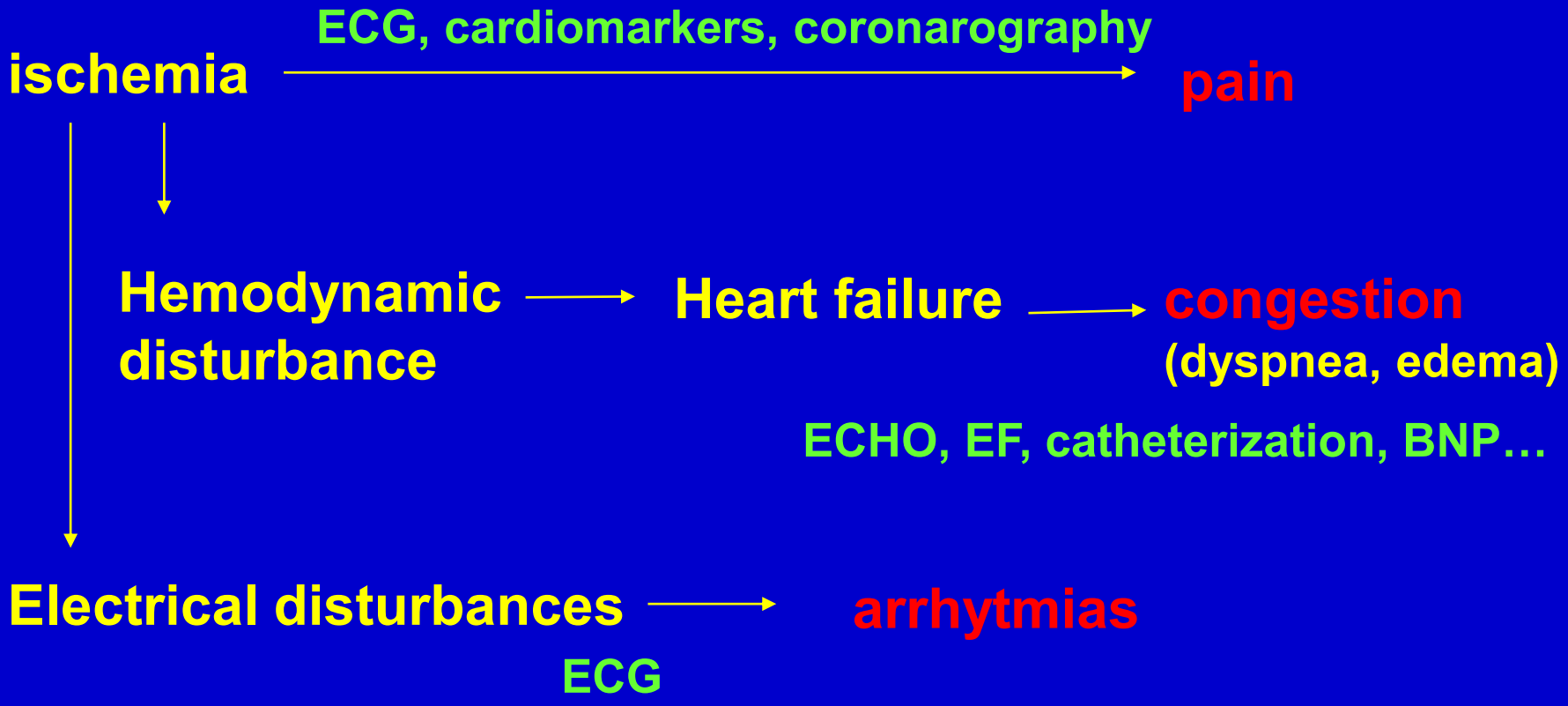
- impaired relaxation (*diastolic dysfunction*)

- impaired electrical events (*arrhytmias, ECG*)

- morphological changes (*myocytes, necrosis, fibrotisation, steatosis etc.*)

- clinical symptoms (*pain, arrhytmia, heart failure*)


ischemia
pain
Hemodynamic disturbance
Heart failure
congestion
(dyspnea, edema)
Electrical disturbances
arrhytmias

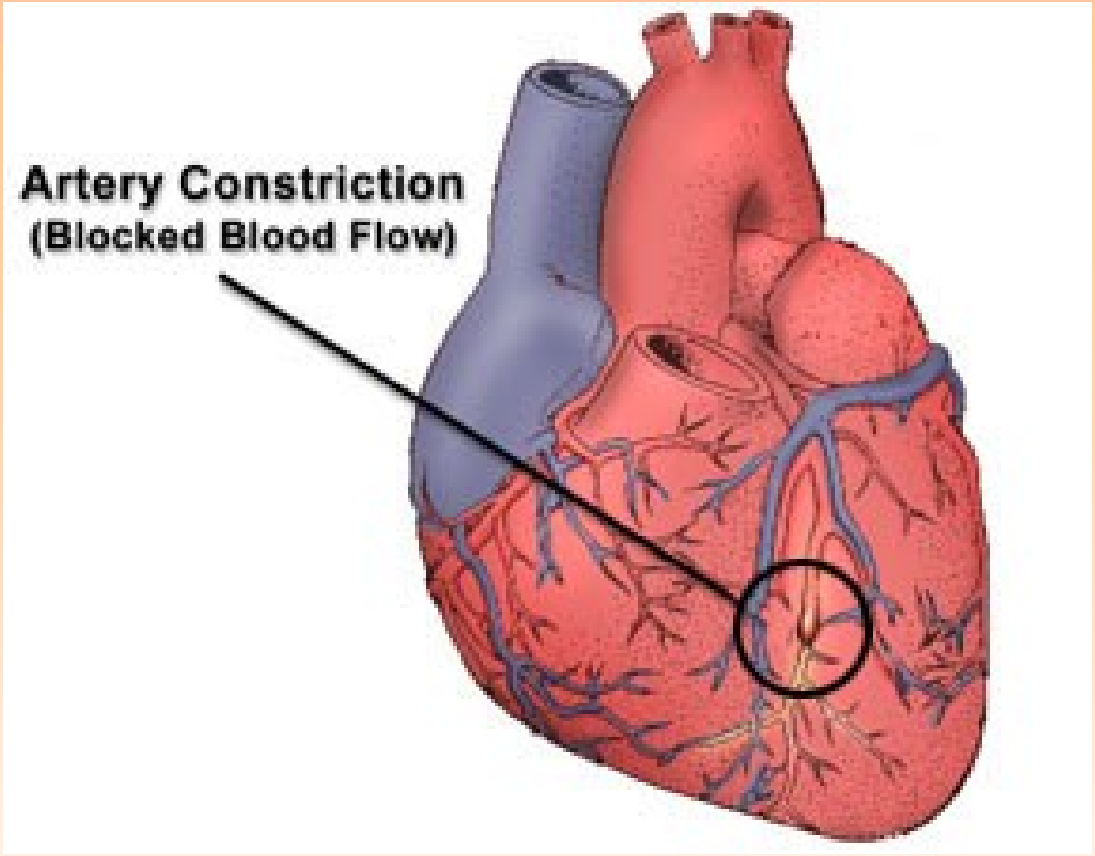

ECG, cardiomarkers, coronarography
ischemia
pain
Hemodynamic disturbance
Heart failure
congestion
(dyspnea, edema)
ECHO, EF, catheterization, BNP…
Electrical disturbances
arrhytmias
ECG

The result of ischemia

Size + duration + reperfusion

- Prolongated occlusion: necrosis
- Temporary occlusion with complete reperfusion – without necrosis

steal fenomén
rheology

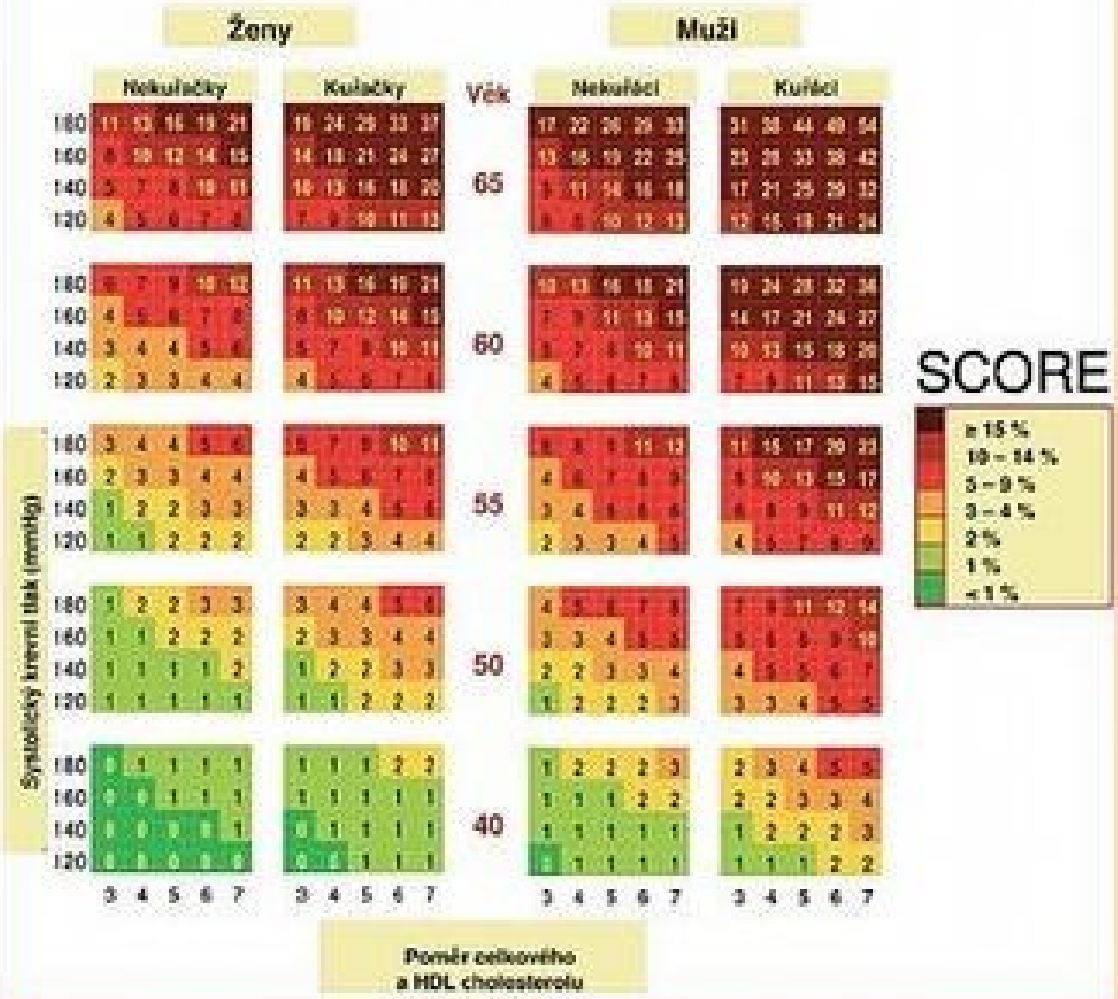


CLINICAL FORMS OF CHD

The principle cause of CHD is

ATHEROSCLEROSIS and its complications

Obr. 9 – Desetileté riziko fatálního kardiovaskulárního onemocnění v ČR podle pohlaví, věku, systolického TK, poměru celkového a HDL-cholesterolu a kuřáckých návyků



CASE REPORT – atherosclerosis

History:

-Atherosclerosis and CHD in the family
-smoking
-Life style, excersise, nutrition and other risk factors

Examine (apart from the heart):

-BP
-glycemia
-BMI, waist circumference
-Arteries, murmurs (a. carotis…)
-CRP
-lipid metabolisms
-homocystein…

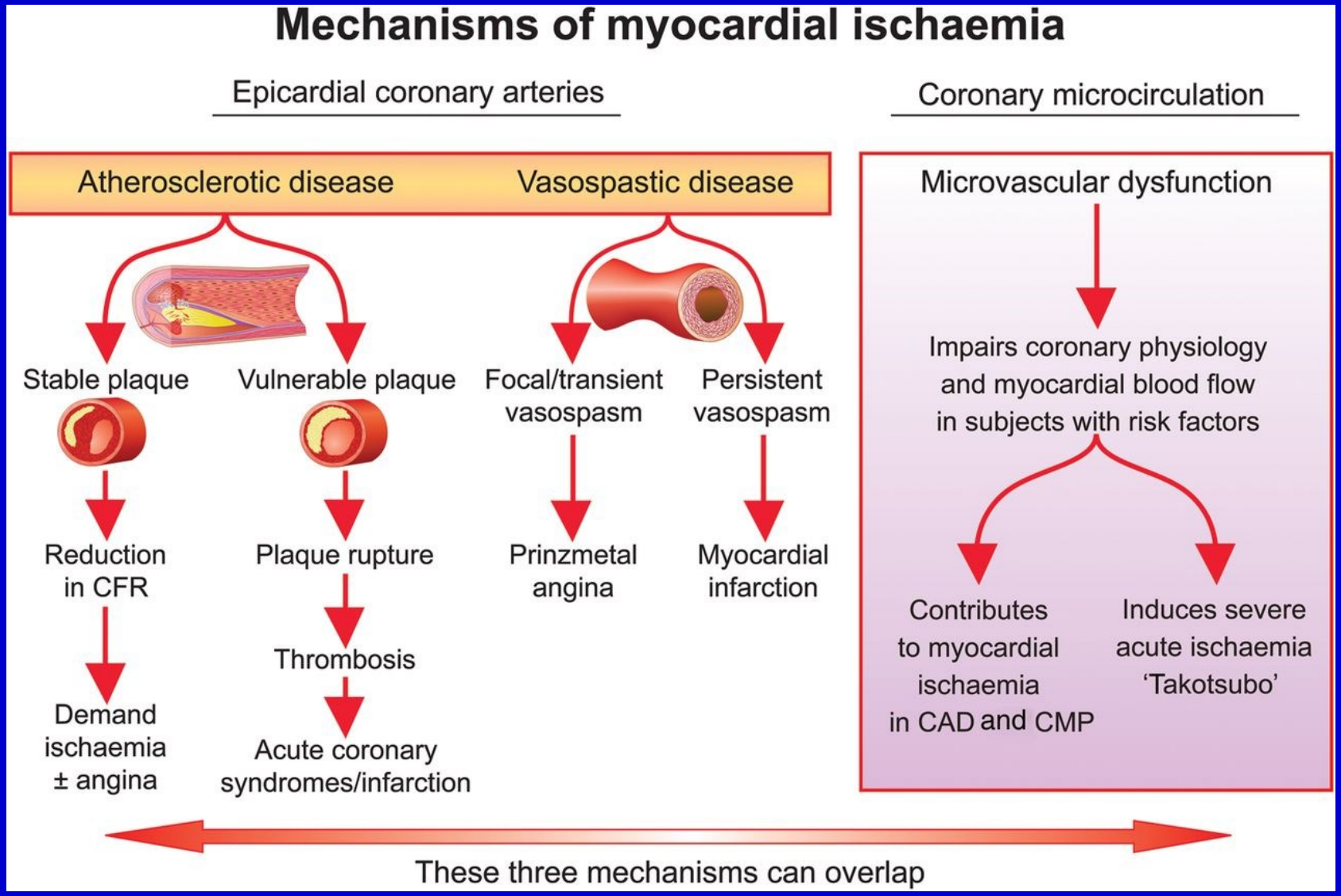
Plaque vulnerability

(1) Size of the lipid core and the stability and thickness of the fibrous cap

(2) Inflammation with the degradation processes

(3) lack of SMC with impaired healing and the plaque instability

Mechanisms of myocardial ischaemia



Coronary microvascular dysfunction: an update
Filippo Crea, Paolo G. Camici, Cathleen Noel Bairey Merz DOI: http://dx.doi.org/10.1093/eurheartj/eht513 1101-1111 First published online: 23 December 2013

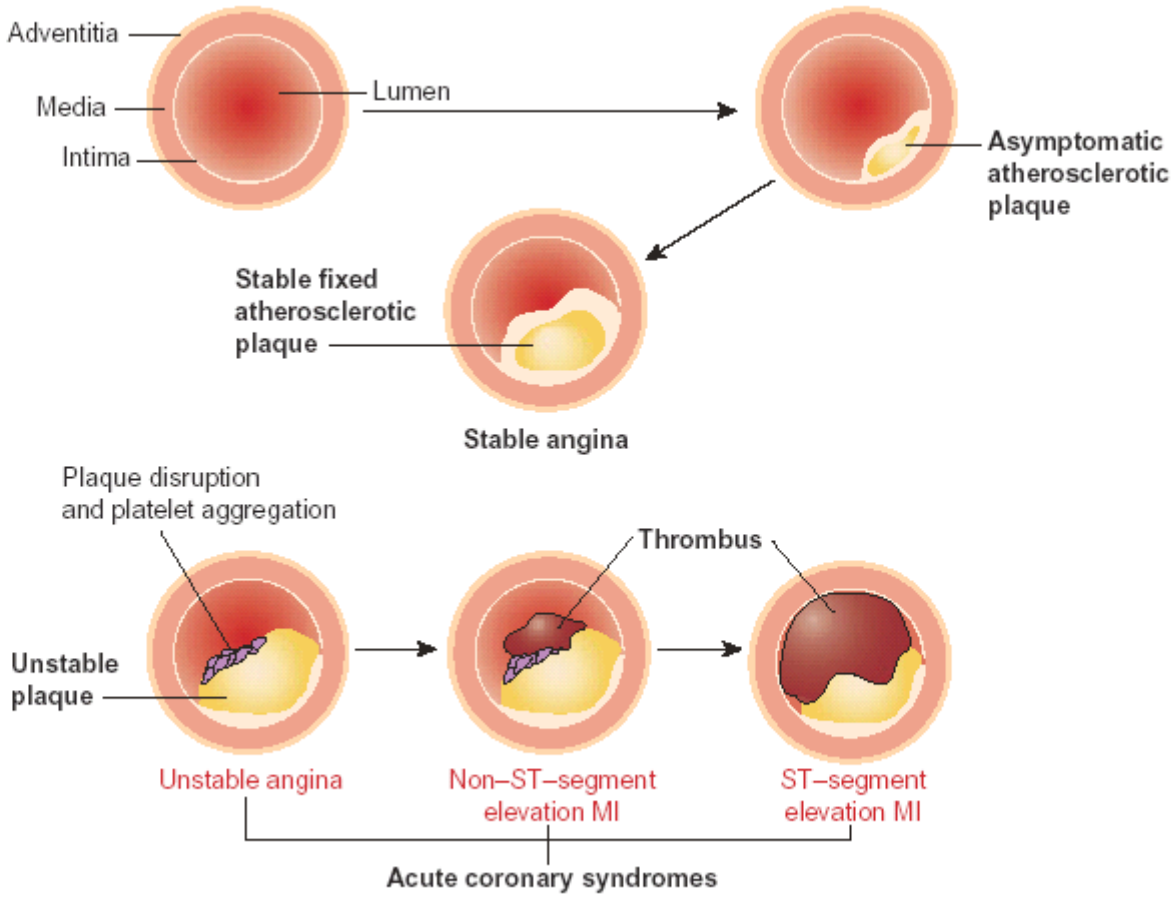
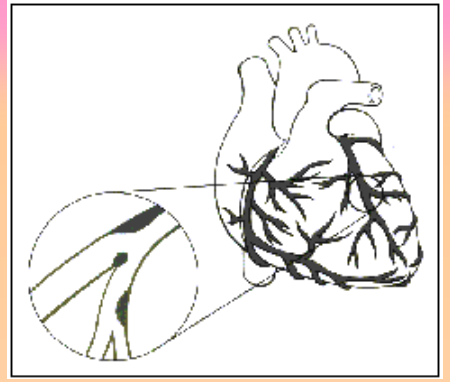


FIGURE 26-6 Atherosclerotic plaque. Stable fixed atherosclerotic plaque in stable angina and the unstable plaque with plaque disruption and platelet aggregation in the acute coronary syndromes.

Angina pectoris (AP)



- ***stable***: fixed stenosis

atherosclerotic plaque decreases coronary reserve, increased oxygen requirements of myocardium (tachycardia) ... subendocardial ischemia

Other contributing factors: anemia, increased blood viscosity, diastolic hypotension, hypertrophy of myocardium

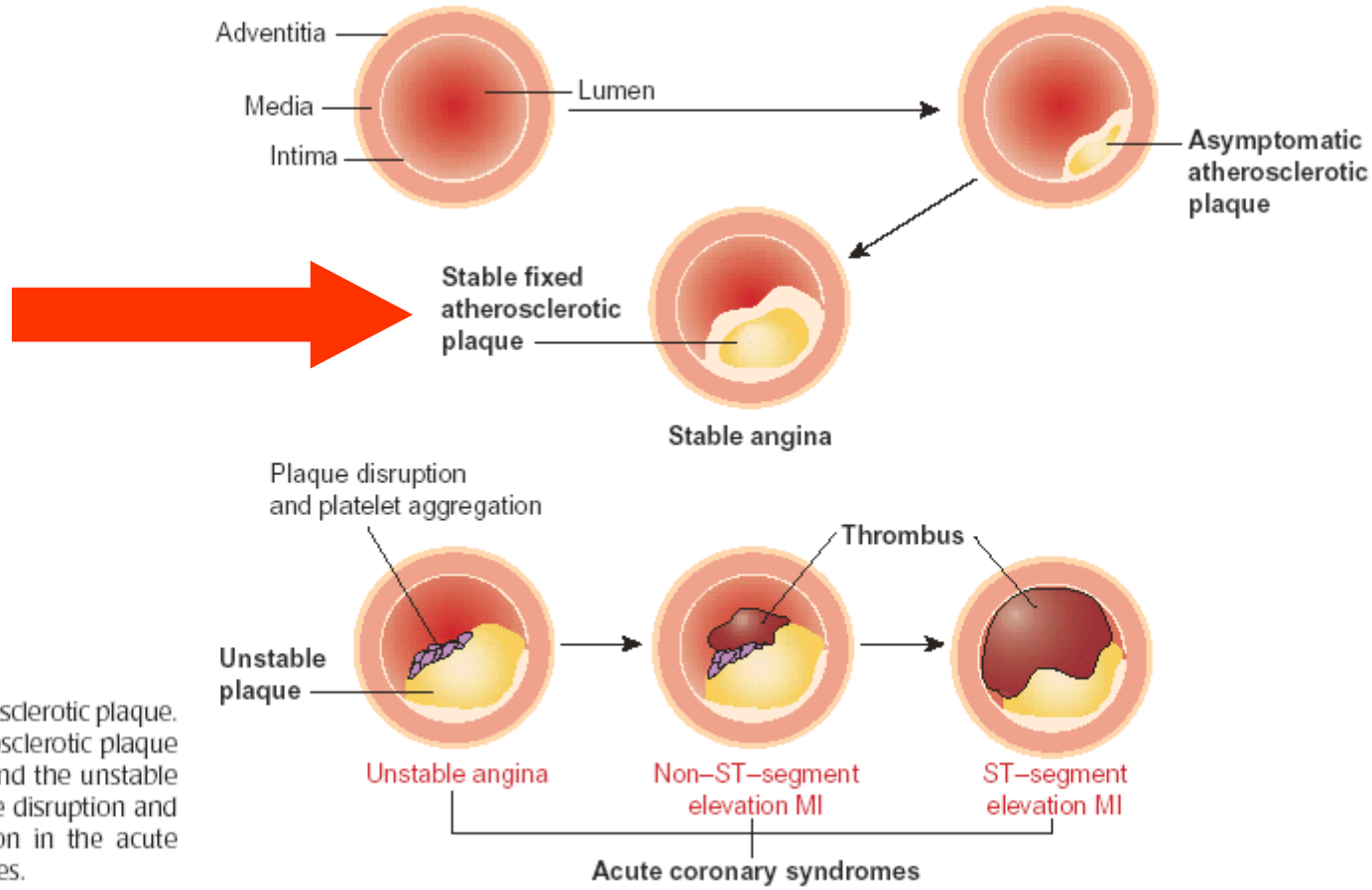
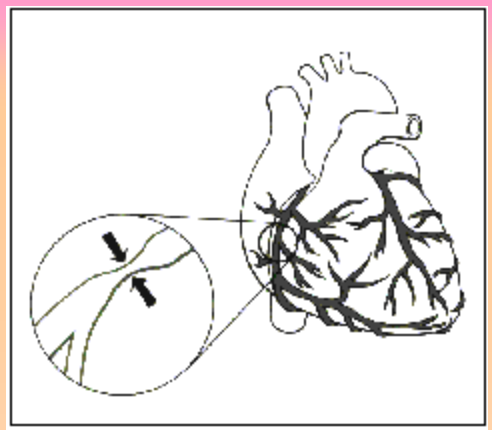


FIGURE 26-6 Atherosclerotic plaque. Stable fixed atherosclerotic plaque in stable angina and the unstable plaque with plaque disruption and platelet aggregation in the acute coronary syndromes.



- ***vasospastic*** (Prinzmetalova):

spasmus of epicardial artery,
transmural ischemic changes;
in rest (frequently nocturnally),
reperfusion may be accompanied by arrythmia

Mechanisms (?):

- hyperactive sympathetic nervous system

- defect in the handling of calcium in vascular smooth muscle

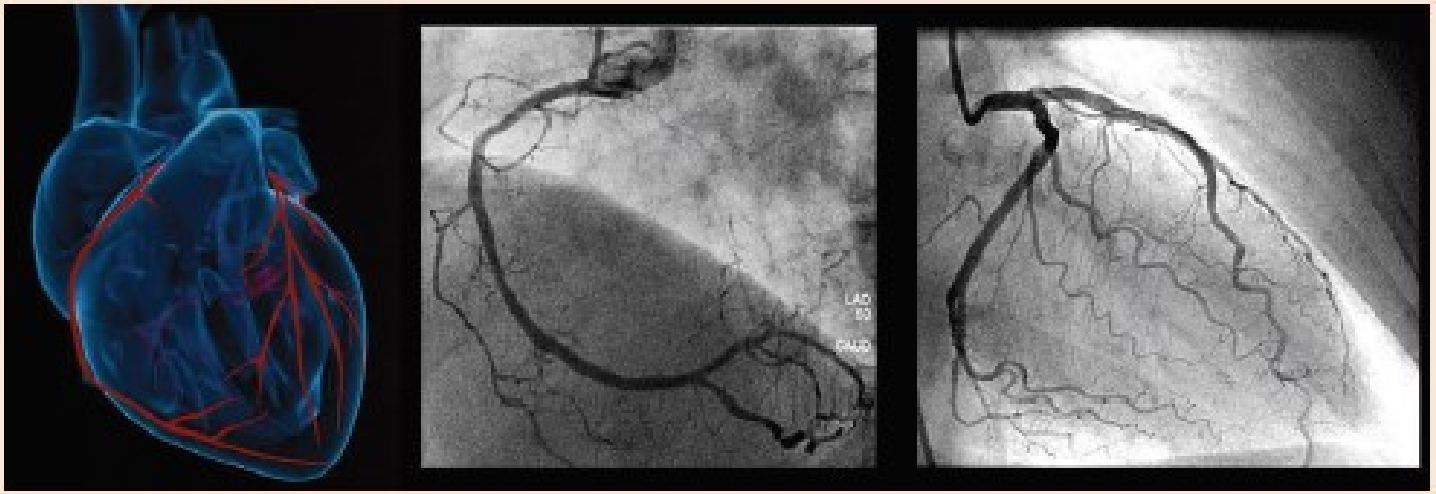
- imbalance between endothelium-derived relaxing and contracting factors, incl. NO

Microvascular angina (MVA, syndrome X)

- Retrosternal pain w/o narrowing on coronarography
- Small vessels
- More frequent in women
- Spasms, microvascular dysfunction, endothelium dysfunction …

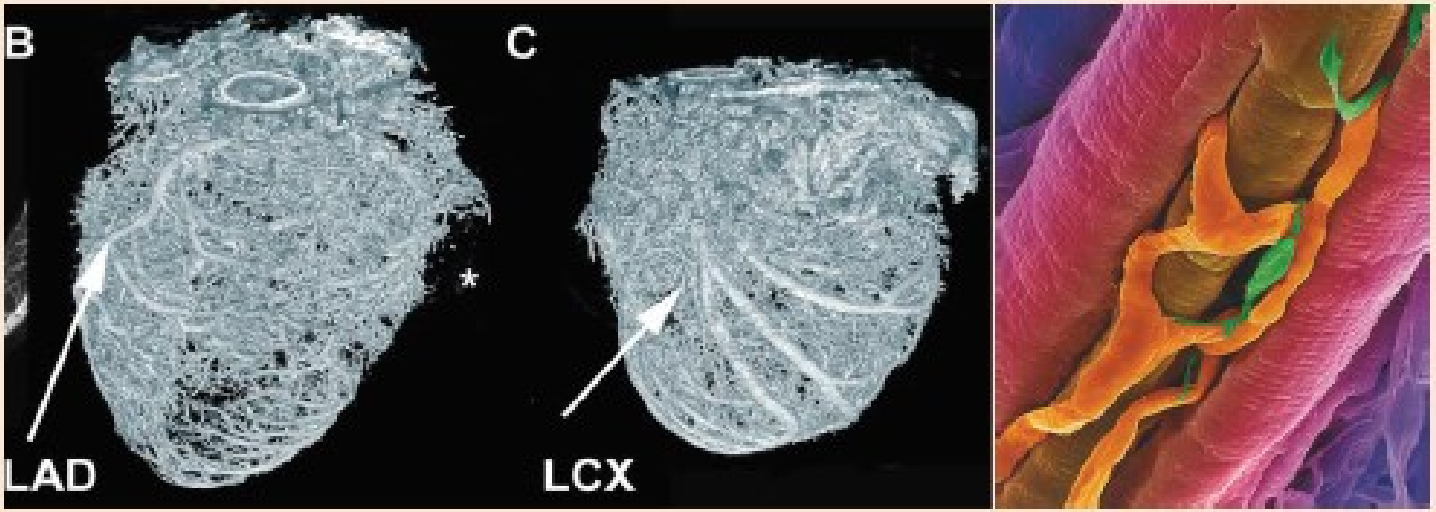
OBRÁZEK 1

Patogeneze chronické anginy: koronární arterie však nejsou jen tyto



OBRÁZEK 2

Patogeneze anginy: koronární arterie jsou také tyto



https://www.tribune.cz/clanek/42401-angina-pectoris-ma-stale-sva-tajemstvi

CASE REPORT

A) Patient, 59 years

Symptoms:
Sudden and strong chest pain with no relief
irradiation, the beginning at rest,
anxiety, sweating

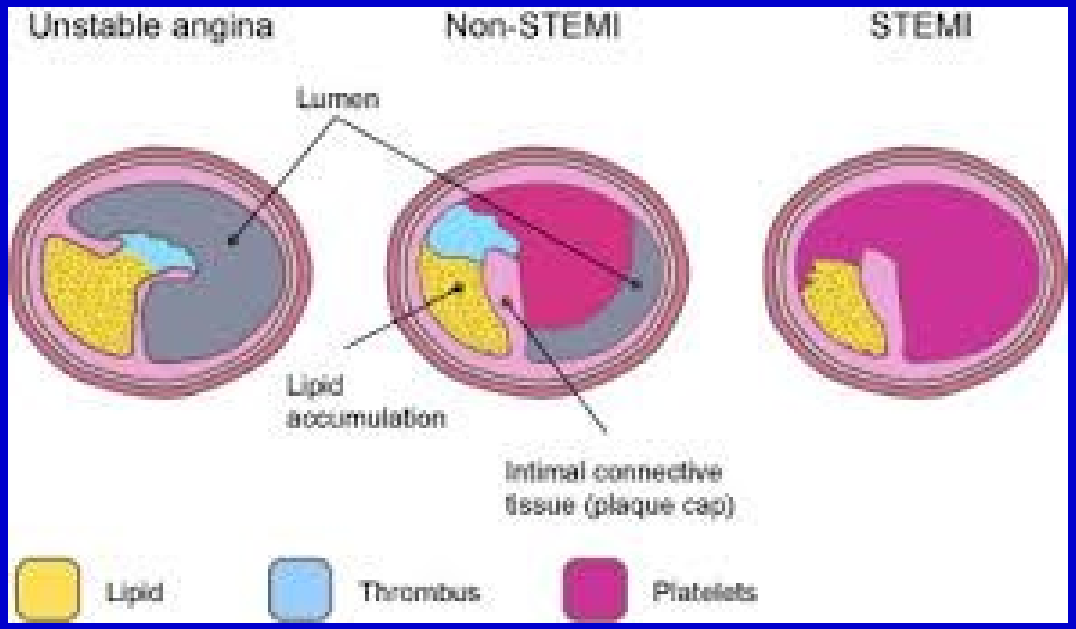
Dg: stable angina pectoris

***Other negative factors*:**
anemia,
increased blood viscosity,
diastolic hypotension,
myocardium hypertrophy

Acute coronary syndrome

- **Unstable angina pectoris** – w/o necrosis (w/o cardiomarkers elevation)
- **Myocardial infarction** – necrosis, cardiomarkers, ECG
  - NSTEMI
  - STEMI
  - Q infarction

Coronary arteries and blood flow



http://www.nottingham.ac.uk/nursing/practice/resources/cardiology/acs/non_stelevation.php

Acute coronary syndromes

unstable AP + acute MI: NSTEMI, STEMI

ECG + cardiac markers

Unstable AP: unstable stenosis
rupture, thrombosis, spasmus,
uncomplete obturation + shorter time of ischemia
without necrosis – no or minimal increase in cardiac markers

Unstable AP

- **NONocclusive** thrombus without necrosis but important blood flow impairment and ischemia
- Cardiomarkers negative
- Chest pain similar to AP but at rest, longer, more frequent
- ECG: various changes but sometimes can be normal, often ST depression and T wave inversions
- Further development ??

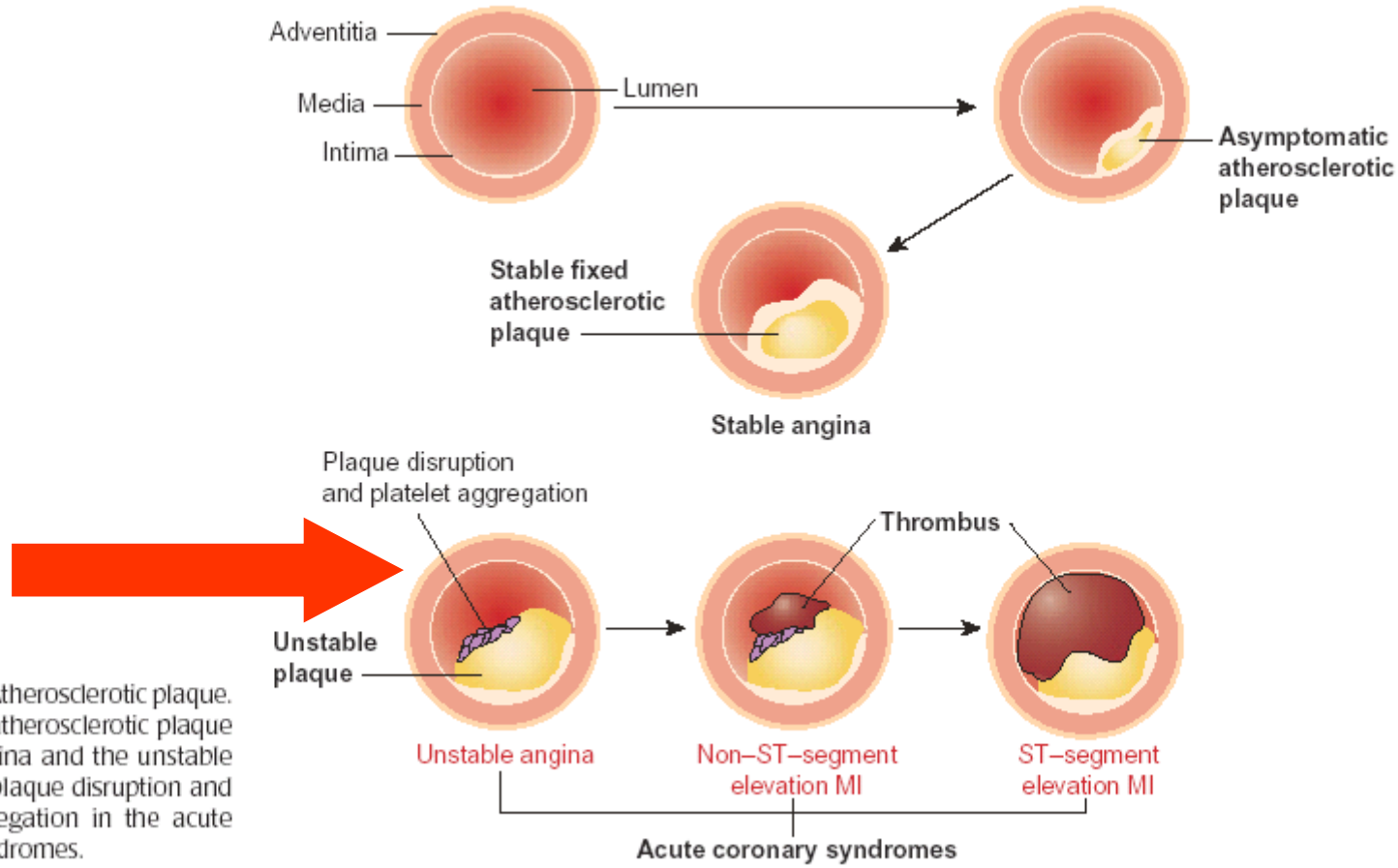


FIGURE 26-6 Atherosclerotic plaque. Stable fixed atherosclerotic plaque in stable angina and the unstable plaque with plaque disruption and platelet aggregation in the acute coronary syndromes.

Plaque rupture

- spontaneously
- triggered by hemodynamic factors
  - blood flow characteristics
  - vessel tension.

Sudden surge of sympathetic activity: an increase in blood pressure, heart rate, force of cardiac contraction, and coronary blood flow

Plaque rupture also has a diurnal variation, occurring most frequently during the first hour of arising.

It has been suggested that the sympathetic nervous system is activated on arising, resulting in changes in platelet aggregation and fibrinolytic activity that tend to favor thrombosis. This diurnal variation in plaque rupture can be minimized by β-adrenergic blockers and aspirin

Acute myocardial infarction (AMI)

thrombosis leading to the ***necrosis*** of myocardium

NSTEMI – non ST segment elevation MI
Usually ST depression, T wave inversion
increase in cardiac markers,not all wall is necrotic (non Q)

STEMI
Complete occlusion, ST elevation, Q wave usually develops (Q – transmural – infarction)

NSTEMI, STEMI

- **NSTEMI** – necrosis of myocytes but w/o ST elevation and pathological Q – subendocardial necrosis
- **STEMI – occlusive** atherothrombosis with complete blocking of blood flow, necrosis and ST elevation

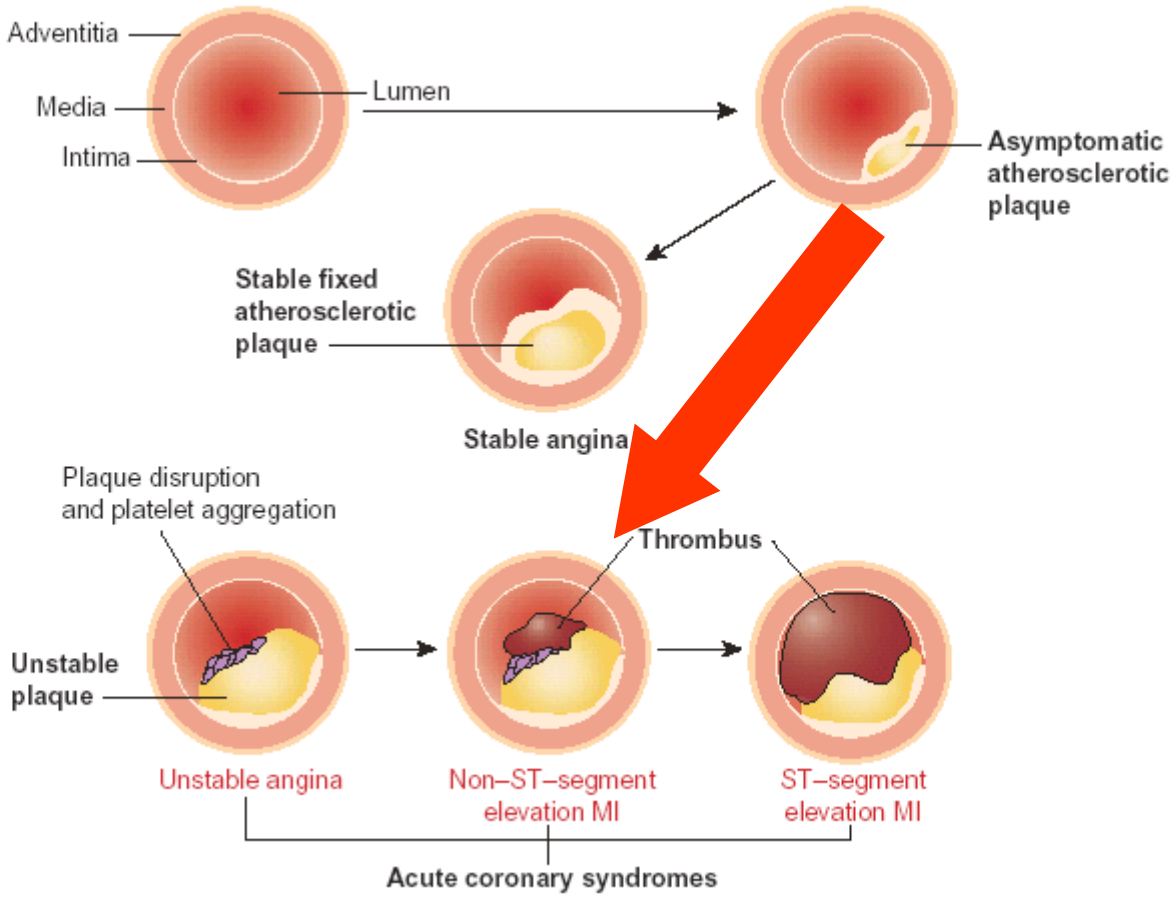
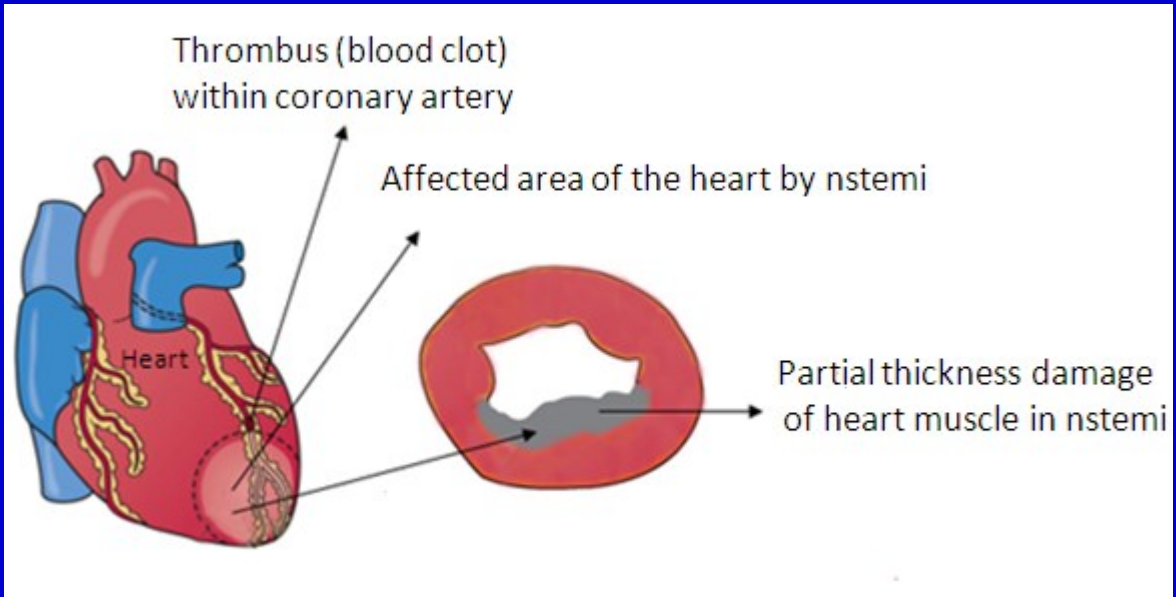
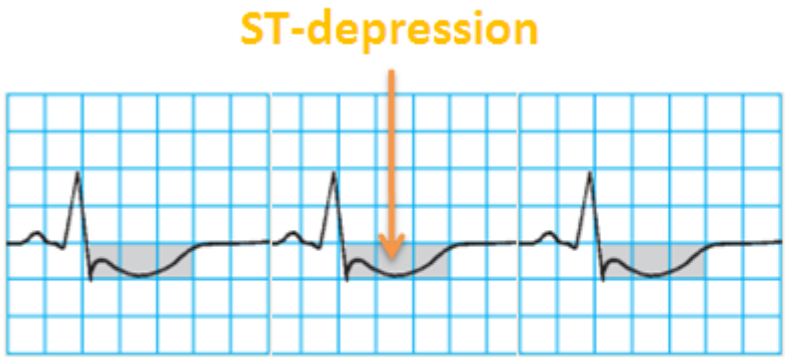


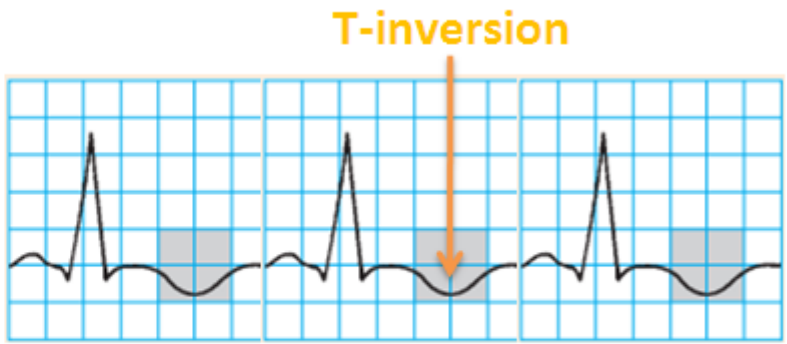
FIGURE 26-6 Atherosclerotic plaque. Stable fixed atherosclerotic plaque in stable angina and the unstable plaque with plaque disruption and platelet aggregation in the acute coronary syndromes.

NSTEMI

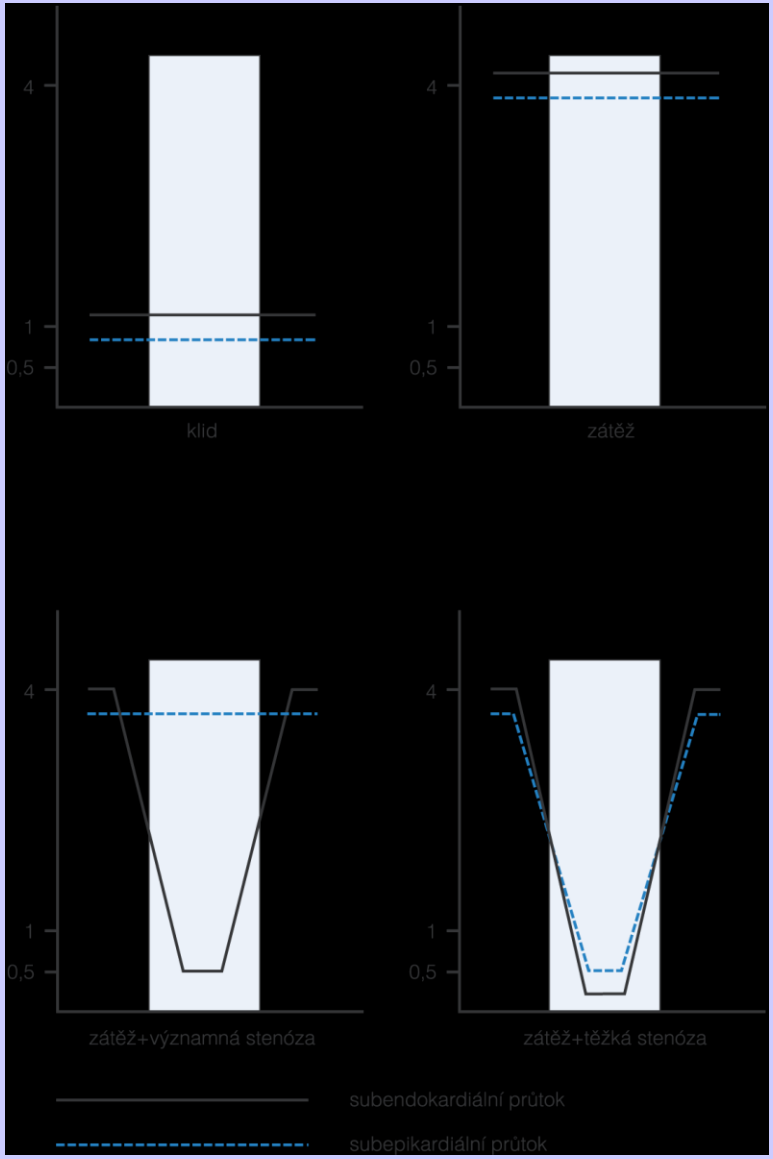




ST-segment depression in nstemi

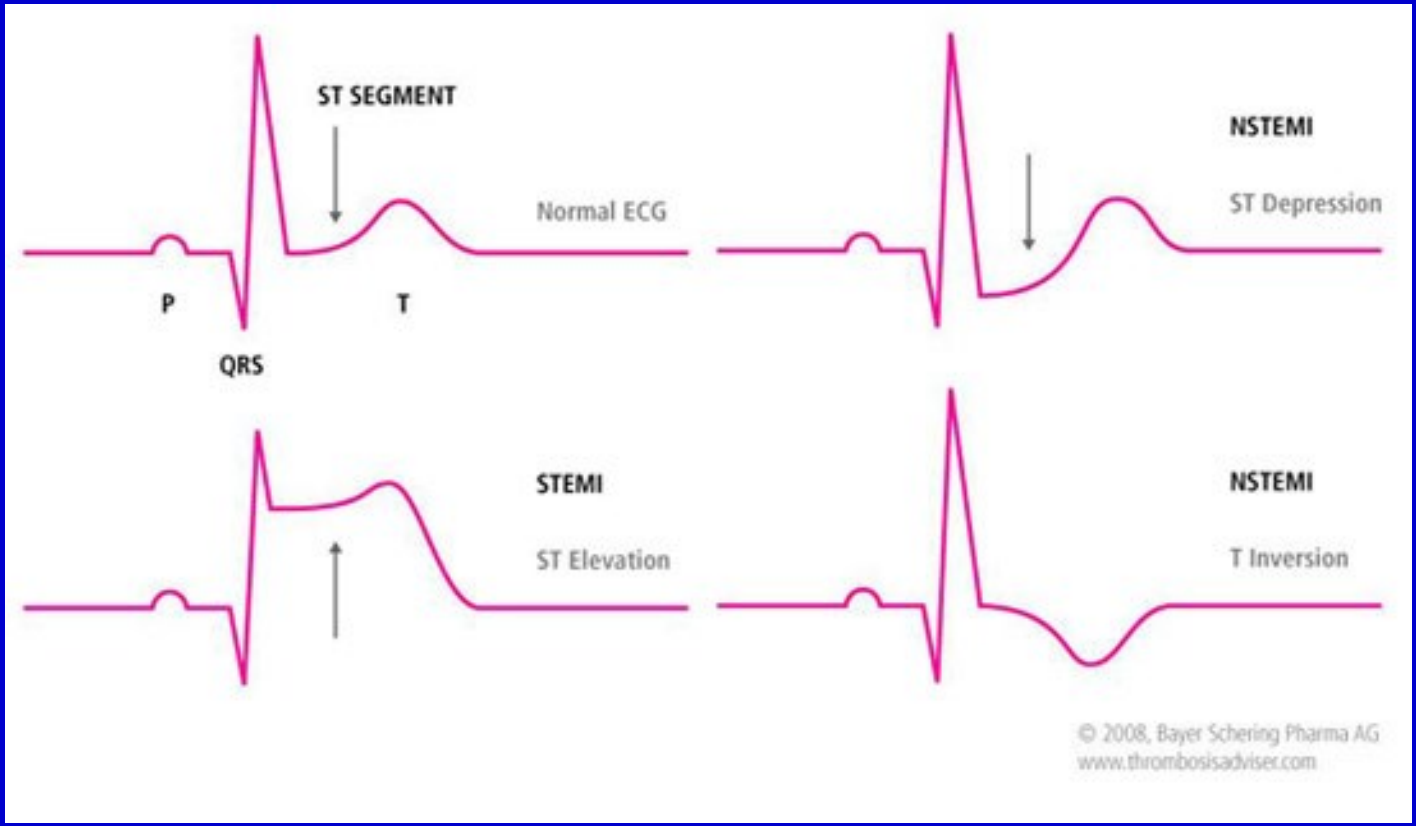


T-wave inversion in nstemi



Zátěžová echokardiografie, Maxdorf

STEMI


ST SEGMENT
Normal ECG
P
QRS
T
NSTEMI
ST Depression
STEMI
ST Elevation
NSTEMI
T Inversion
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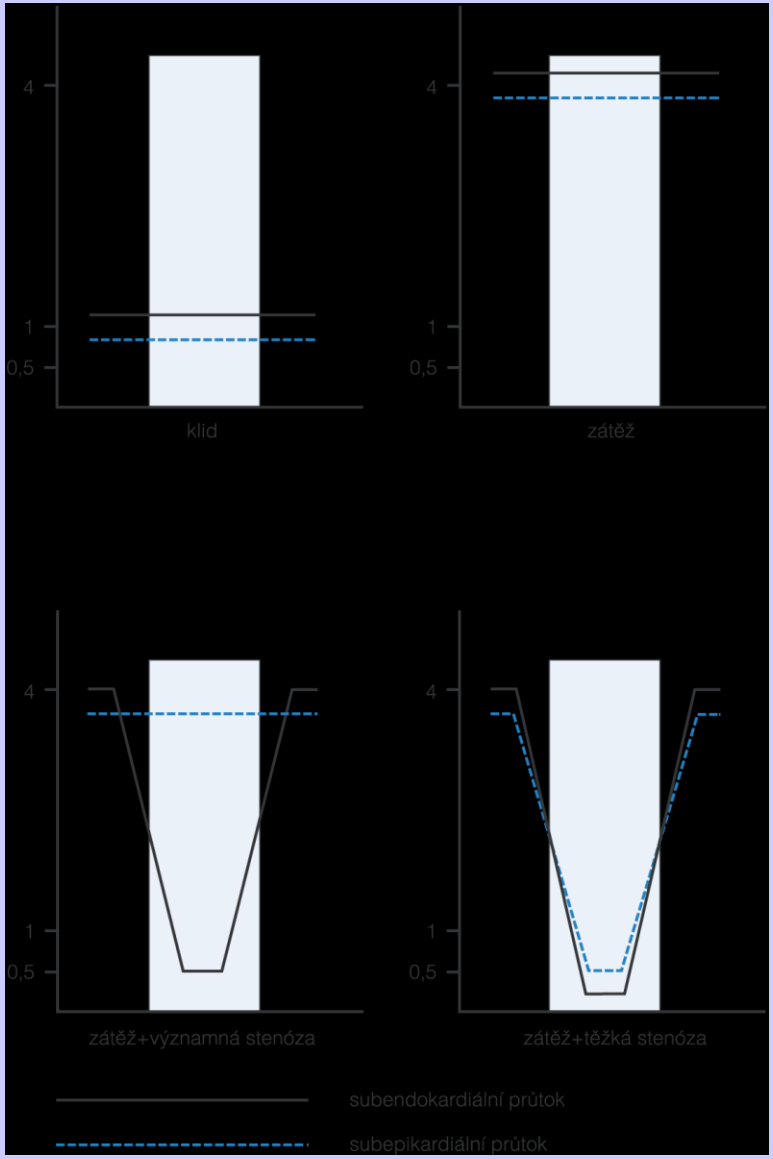
www.thrombosisadviser.com



Zátěžová echokardiografie, Maxdorf

Q infarction

- STEMI with the development of the pathological Q as a sign of transmural necrosis

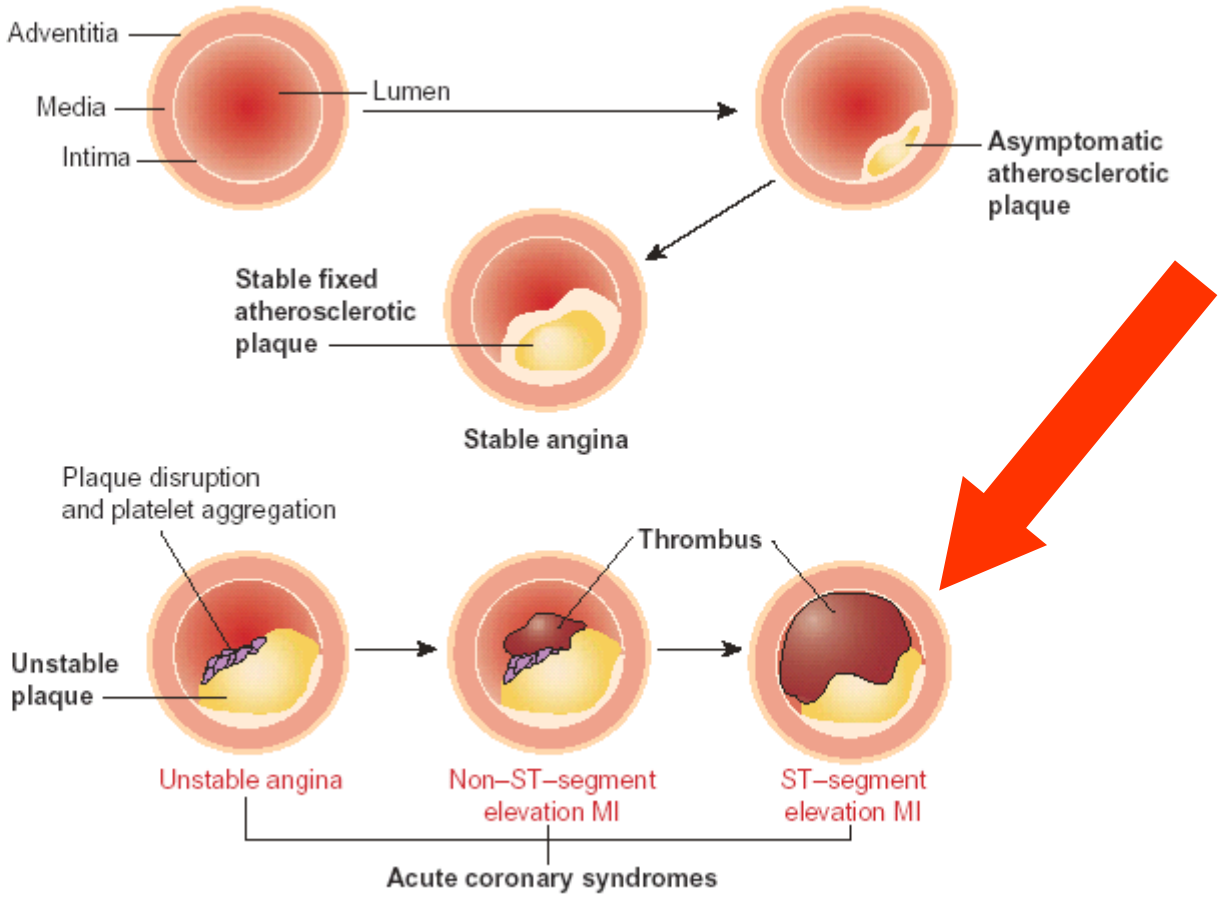
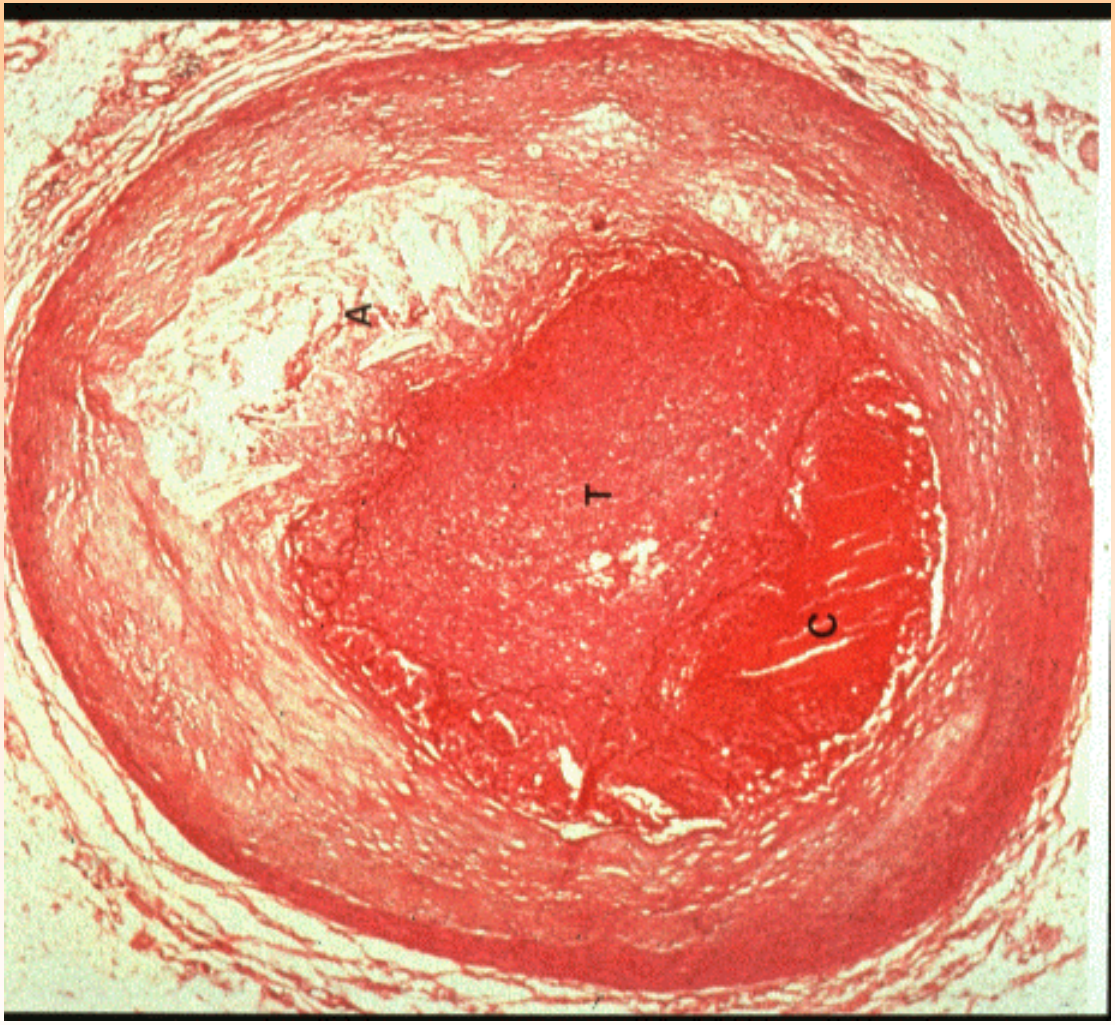
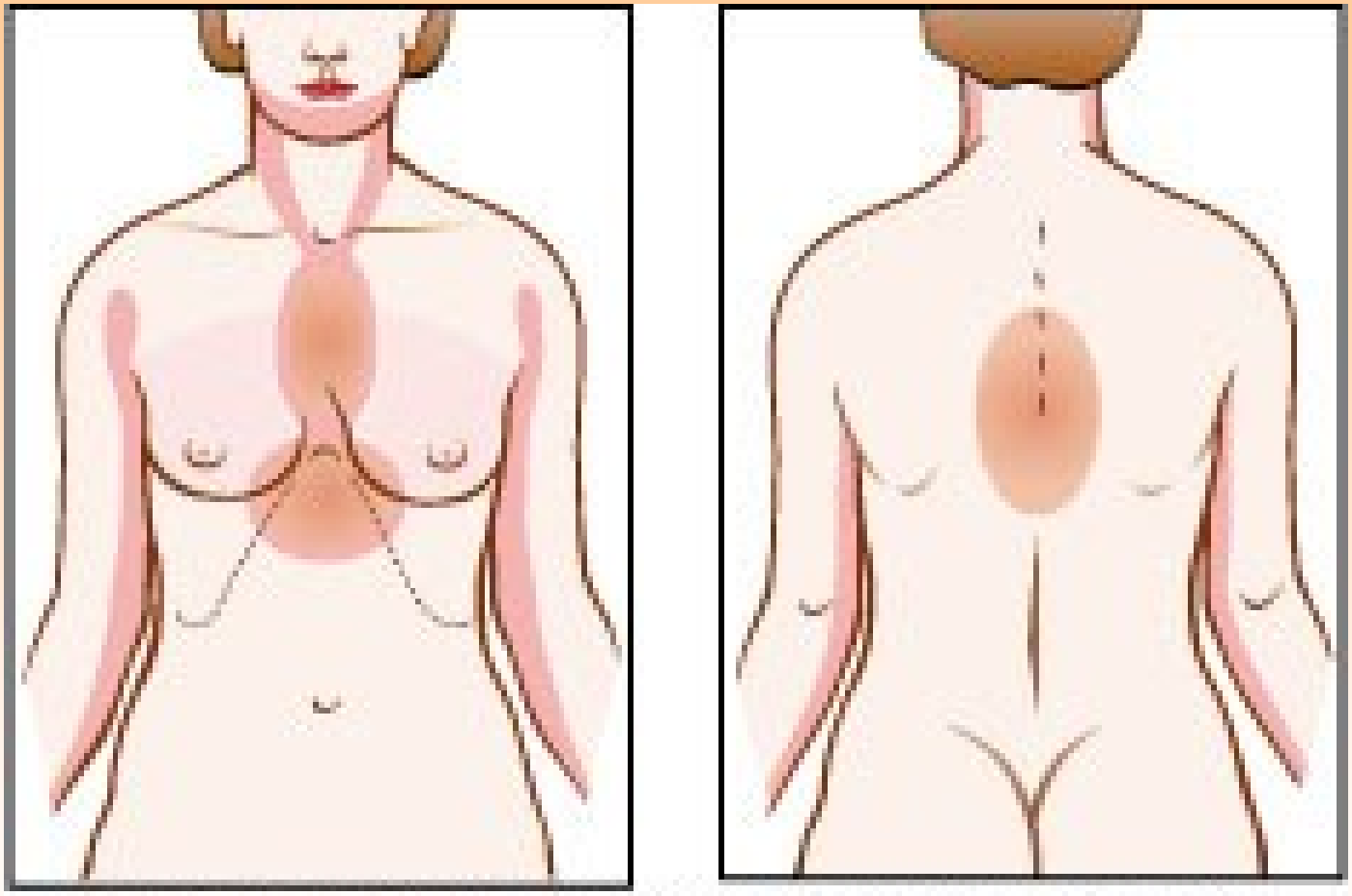


FIGURE 26-6 Atherosclerotic plaque. Stable fixed atherosclerotic plaque in stable angina and the unstable plaque with plaque disruption and platelet aggregation in the acute coronary syndromes.


A
T
C

Symptoms

- pain
- vegetative nerves activation (anxiety, sweating, tachycardia)
- atypical (without important pain, abdominal symptoms)
- arrhytmias
- heart failure



Schmerzlokalisation bei koronarer Herzkrankheit

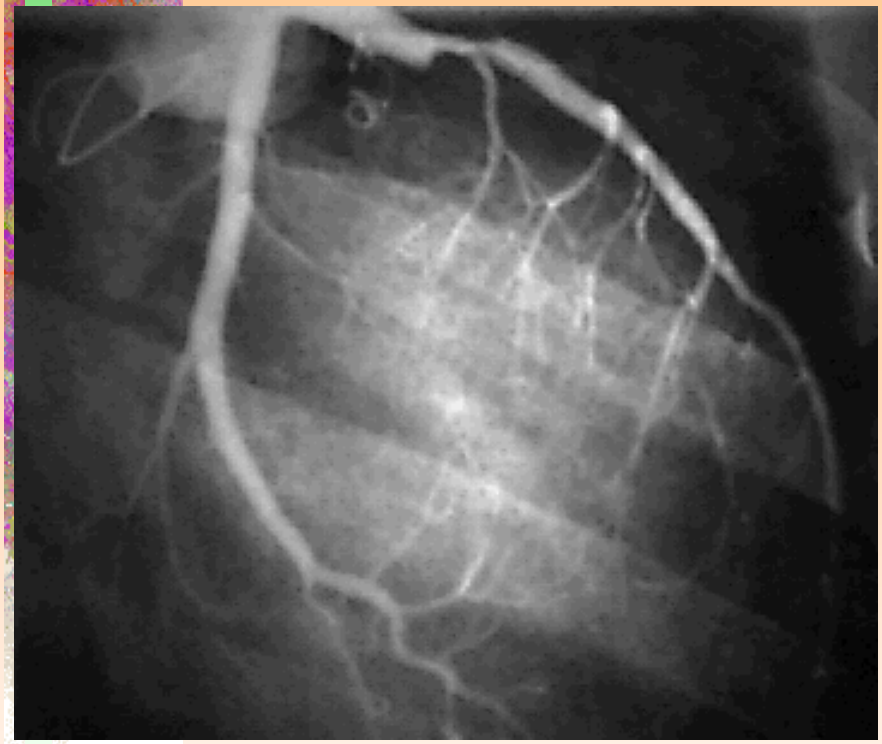
Clinical consequences

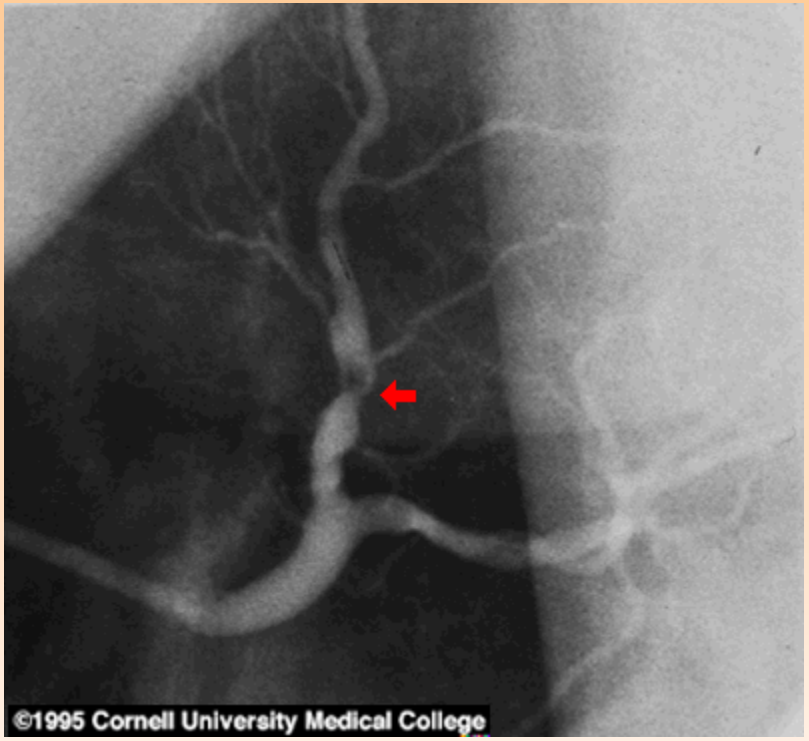
PAIN

DECREASE OF CONTRACTILITY – HEART FAILURE OR CARDIOGENIC SHOCK

ARRHYTMIAS

NECROSIS AND ITS SYMPTOMS cardiomarkers

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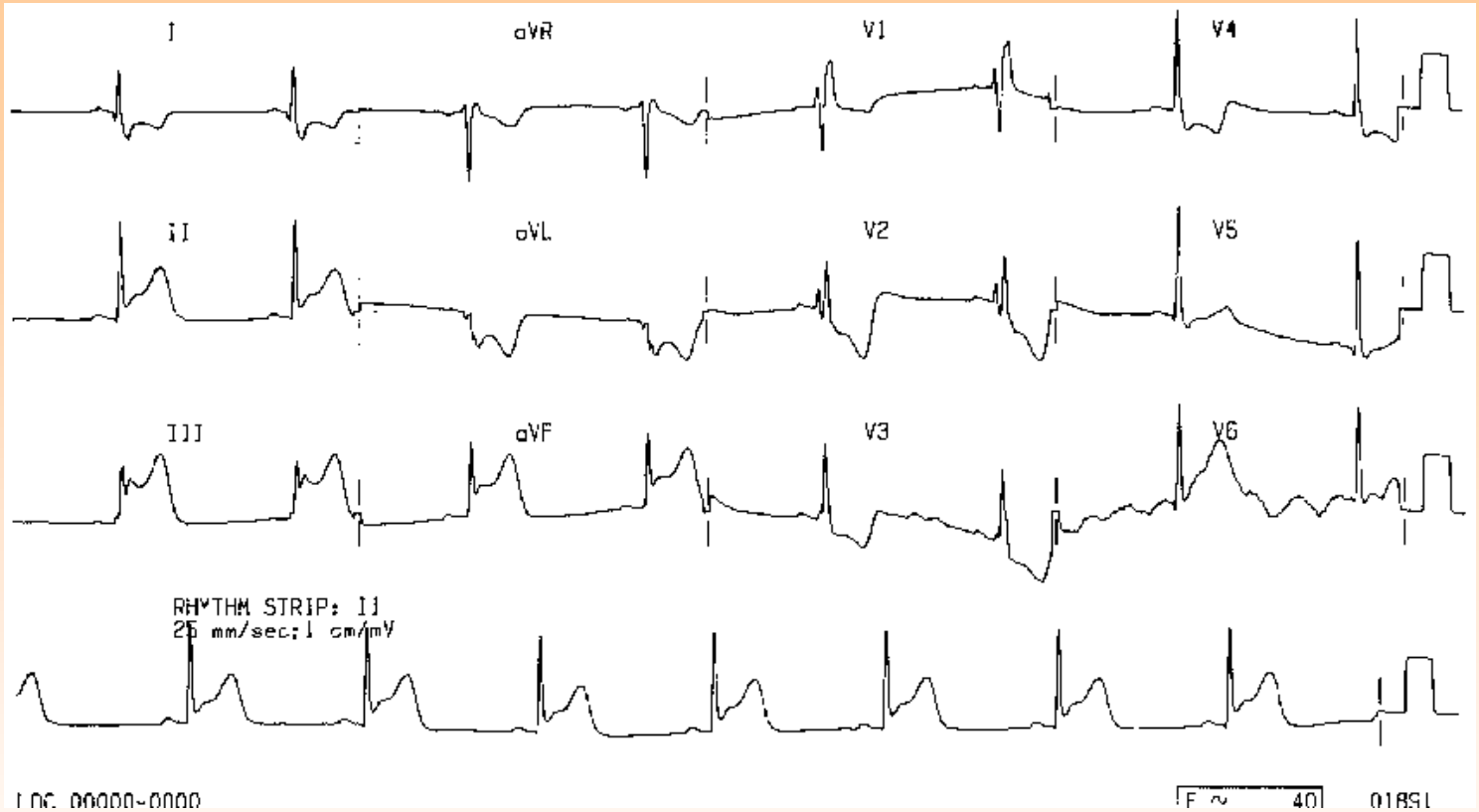
Size of the necrosis

- extent of the blood flow
- collaterals
- myocardial needs of oxygen (heart rate, wall tension - afterload / systolic BP)
- ischemic preconditioning

Localisation of the necrosis

- ***layer of the wall***: transmurale, subendocardial, intramural

- ***part of the heart***: according to the coronary artery
anterior wall (RIA)
lateral wall (RC)
diaphragmatic (RIP)


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
RHYTHM STRIP: II
25 mm/sec;1 cm/mV

Layers of myocardium and their impairments

- anatomy
- Higher tension in subendocard. layers

Subendocardial ischemia
Classical stable angina pectoris (no necrosis)
depression ST segment – NSTEMI (necrosis)

Subepicardial ischemia
variant AP (no necrosis)
Myocardial infarction (necrosis)
ST segment elevation – STEMI

Sequelae of the necrosis

• ***hemodynamic*** (disturbances of contractility, decrease of ejection fraction) – large necrosis or repeated infarction - heart failure, if about 40% of myocardium destroyed, *cardiogenic* shock can develop

• ***electrical instability*** – arrhytmias, ventricular fibrillation, sudden death

• ***remodelation*** of the ventricle – scarring, aneurysma (dyskinesis, thrombosis with embolism), dilatation – importance for prognosis

• ***rupture*** of the wall, aneurysma (pericardial tamponade), septum, papillary muscle

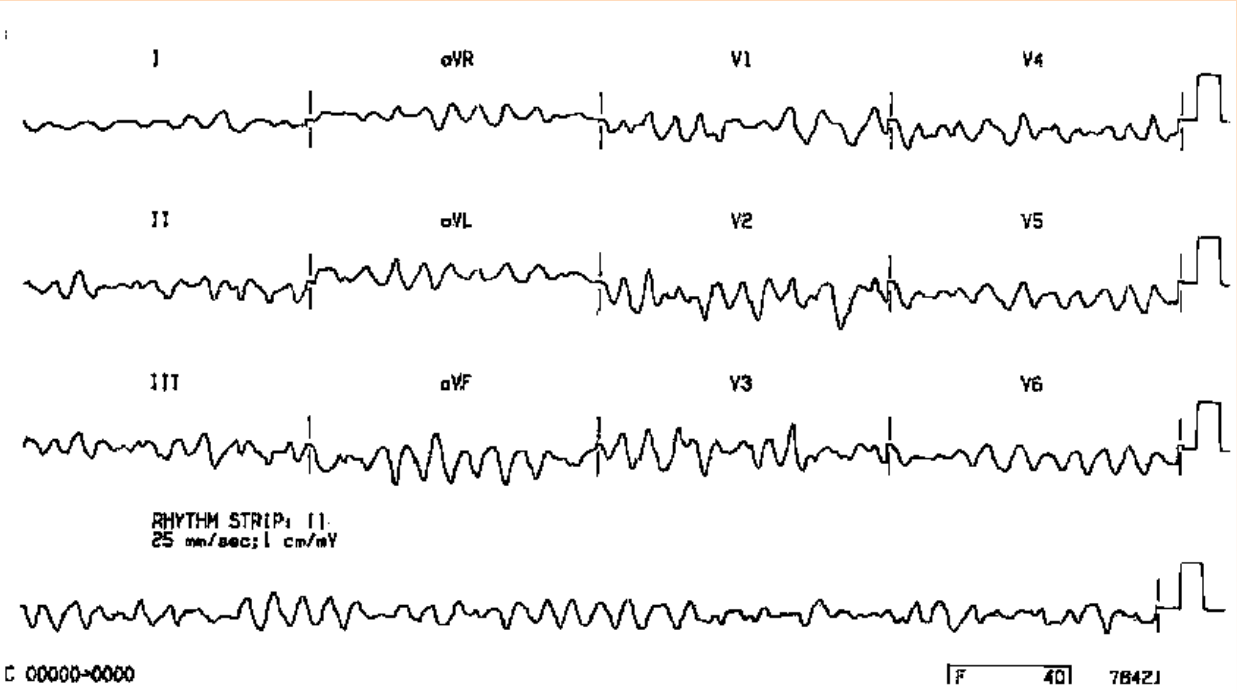
Cardiogenic shock

- Severe dysfunction of the pumping heart function with the dramatic decline of CO
- Severe hypoperfusion of the tissues with their ischemia
- EDV in the myocardium is increased, symptoms of congestion (different from hypovolemic shock with the decrease of preload as the cause of the low stroke volume)
- **„extreme heart failure“ with dominating hypoperfusion and organ failure**

Sequelae of the necrosis

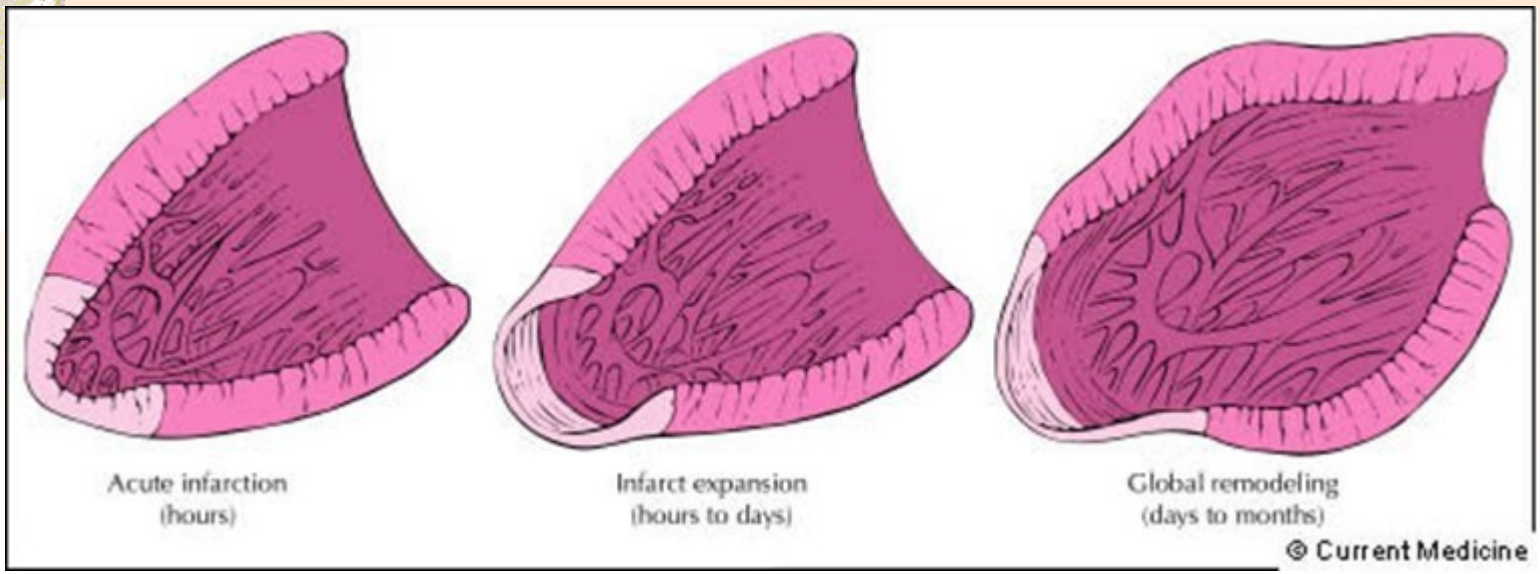
Electrical instability

arrhytmias, ventricular fibrilation, sudden death



PostIM remodelation

- changes of cardiomyocytés and intersticium
- cell, molecular and gene changes
- change in size, shape and function
- thinning IM part,
compensatory hypertrophy of others,
changes of wall tension – O2, el. events



Pain vs. dyspnea

- **Pain** – muscle ischemia, angina pectoris, AIM (and others…)
- **Dyspnea** – lung congestion („hemodynamic“ sign, heart failure, or others (mitral stenosis)
- Obviously they can combine (e.g. Heart failure in AIM)

Tests for ischemia

- ECG – **poškození/nekróza/el. nestabilita**
- Cardiac markers (troponin, myoglobin, CK-MB) – sings of **injury/necrosis**
- Echo – impaired **contractility (function)** of the ischemic/necrotic part
- Coronarography – **flow**
- CFR – coronary flow reserve
- FFR – fractional flow reserve

Basic diagnostics

Necrosis

- enzymes: CK-MB, AST, LD

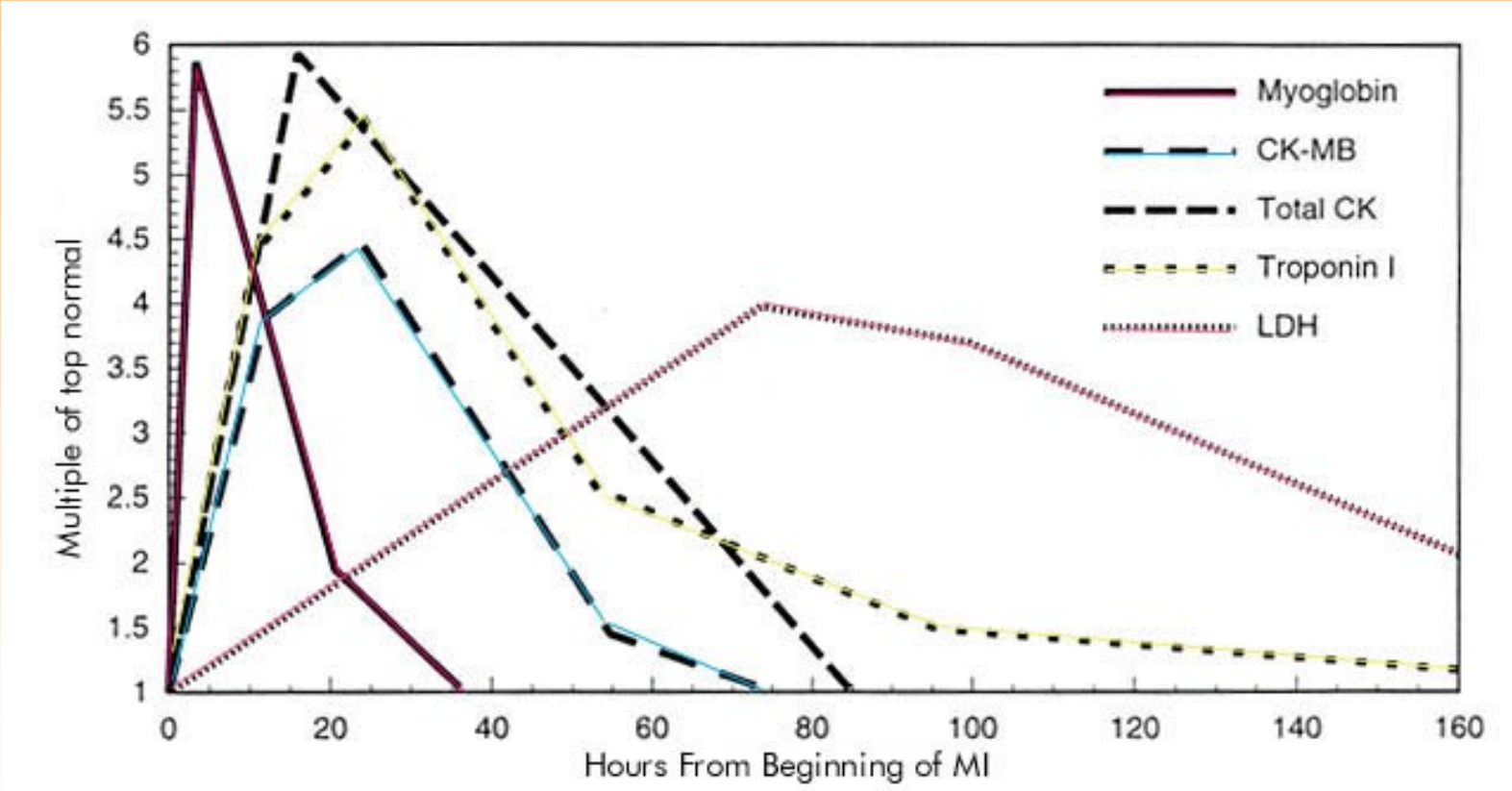
- structural proteins: myoglobin, troponin

- reaction to the necrosis: leucocytosis, RBC sedimentation rate

Electrical changes

- ECG: development of the curve
localisation + infarction extent

- arrhytmias


Myoglobin
CK-MB
Total CK
Troponin I
LDH
Multiple of top normal
Hours From Beginning of MI
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0
20
40
60
80
100
120
140
160

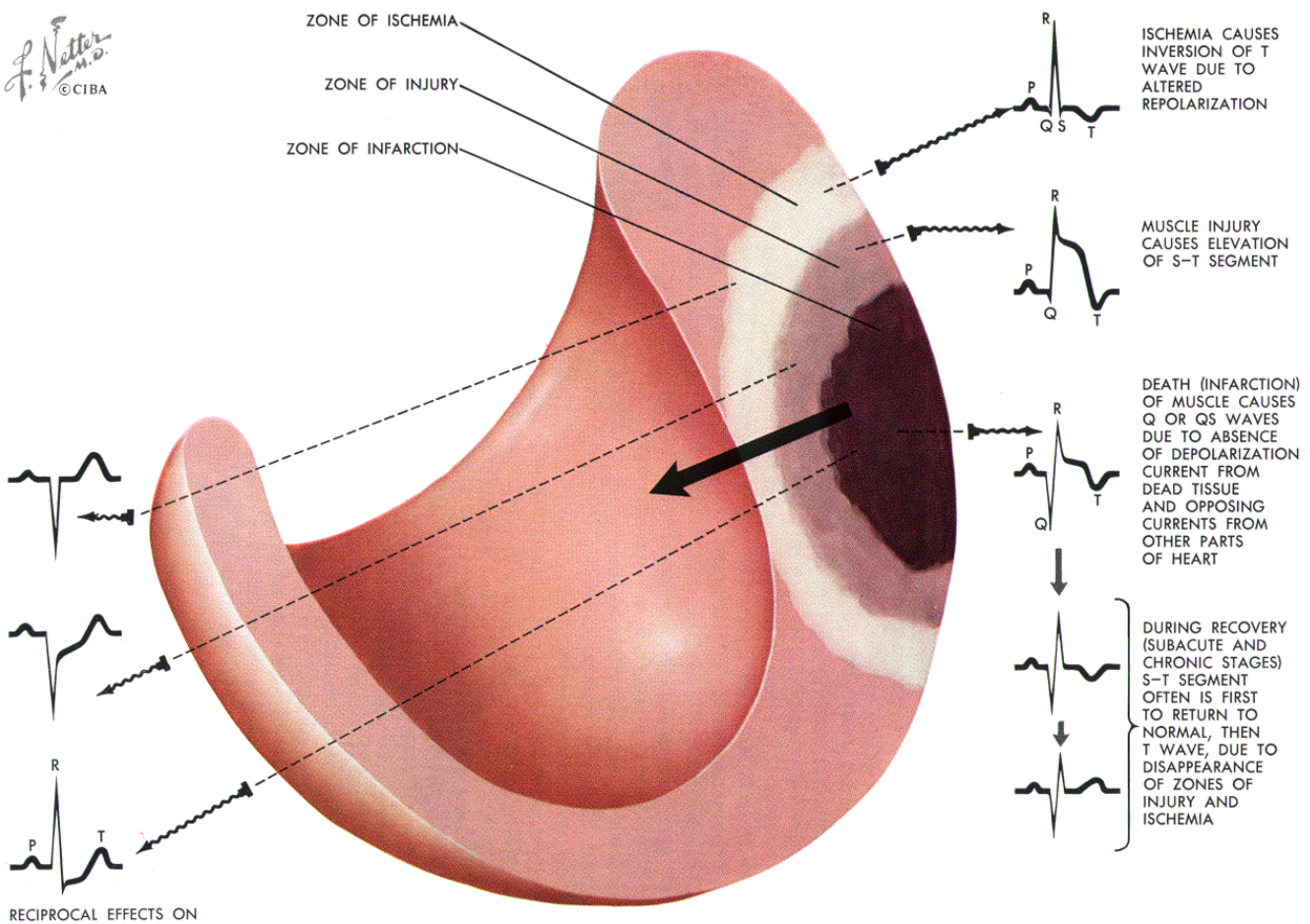


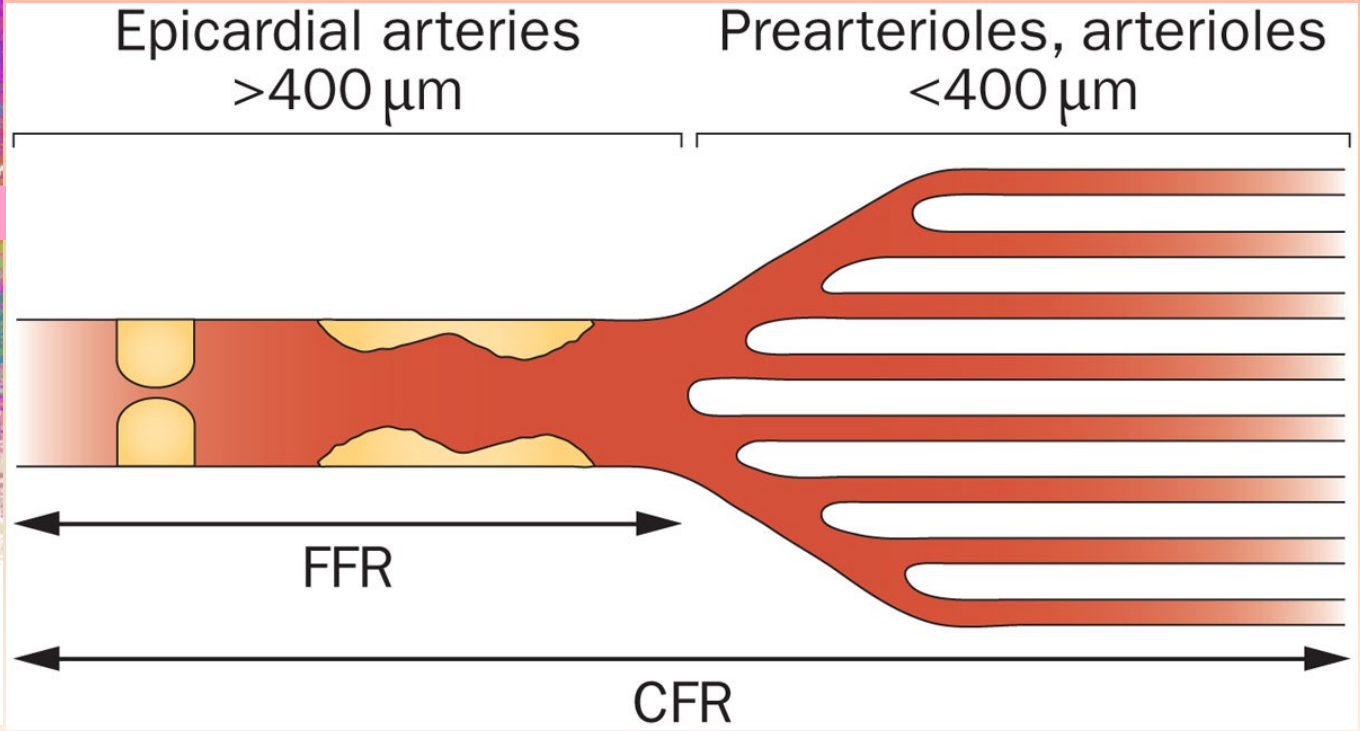
PLATE IX

EFFECT OF CARDIAC INFARCTION, INJURY, AND ISCHEMIA

FFR

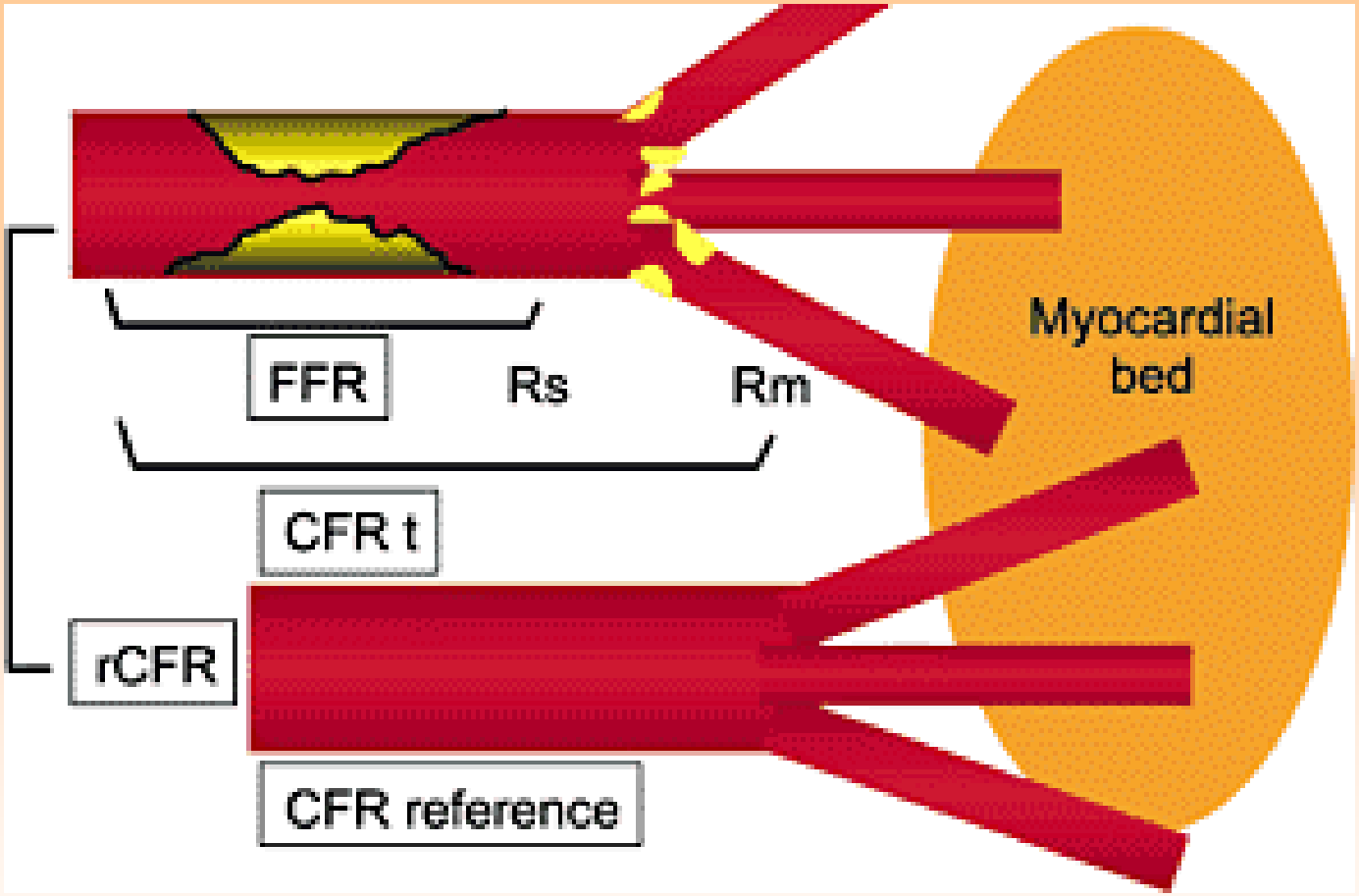
- Fractional flow reserve (FFR) measurement involves determining the ratio between the maximum achievable blood flow in a diseased coronary artery and the theoretical maximum flow in a normal coronary artery. An FFR of 1.0 is widely accepted as normal. An FFR lower than 0.75-0.80 is generally considered to be associated with myocardial ischemia (MI).

Figure 2 Assessment of epicardial and microvascular ischaemia

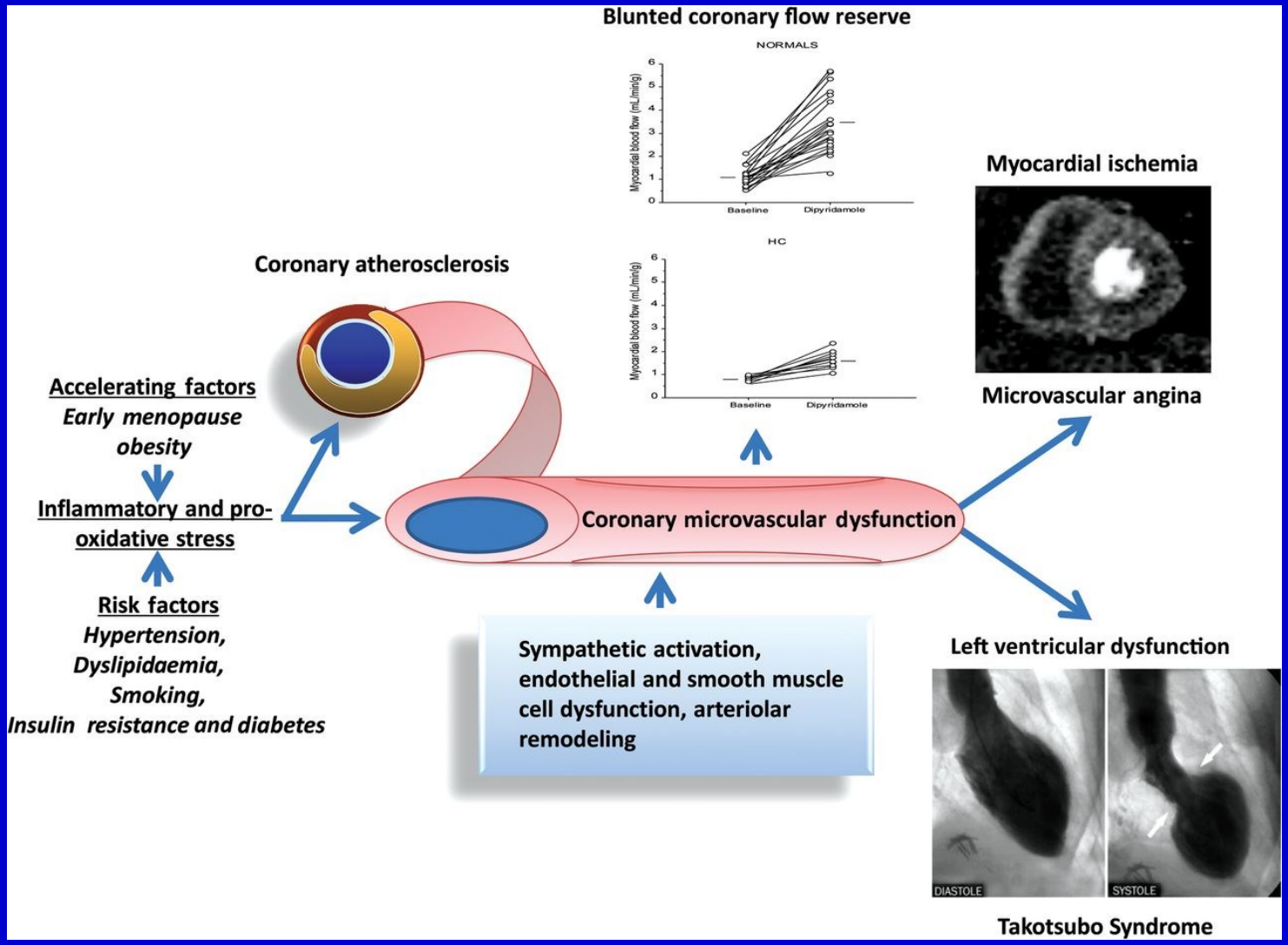


*Nat. Rev. C*Fuster, V. (2014) Top 10 cardiovascular therapies and interventions for the next decade
ardiol. doi:10.1038/nrcardio.2014.137

nature REVIEWS CARDIOLOGY



Drugs Today 2000, 36(8): 515



Coronary microvascular dysfunction: an update
Filippo Crea, Paolo G. Camici, Cathleen Noel Bairey Merz DOI: http://dx.doi.org/10.1093/eurheartj/eht513 1101-1111 First published online: 23 December 2013

„Dyspnea testing“

- Auscultation – rales
- X-ray – congestion
- High EDP
- Decrease of blood gases in the arterial blood (impaired blood oxygenation in the lungs), low Hgb saturation

CHD TREATEMENT

Reperfusion

Collaterals

Angiogenesis
VEGF (vascular endothelial growth factor)
FGF (fibroblast growth factor)
Angiopoetin
and others...

Therapeutical angiogenesis
gene therapy: direct intramyocardial aplicatioon of plasmid or use of vector (adenovirus) VEGF or FGF

Revascularization by invasive treatment
- PTCA (percutanneous transluminal coronary angioplastic)
- stents
- bypass

Primary prevention

Treatment of risk factors

Blood flow through myocardium

Vessels (calcium antagonists, vasodilatation)
Decrease of oxygen consumption (betalytics)
Coagulation (aspirin...)

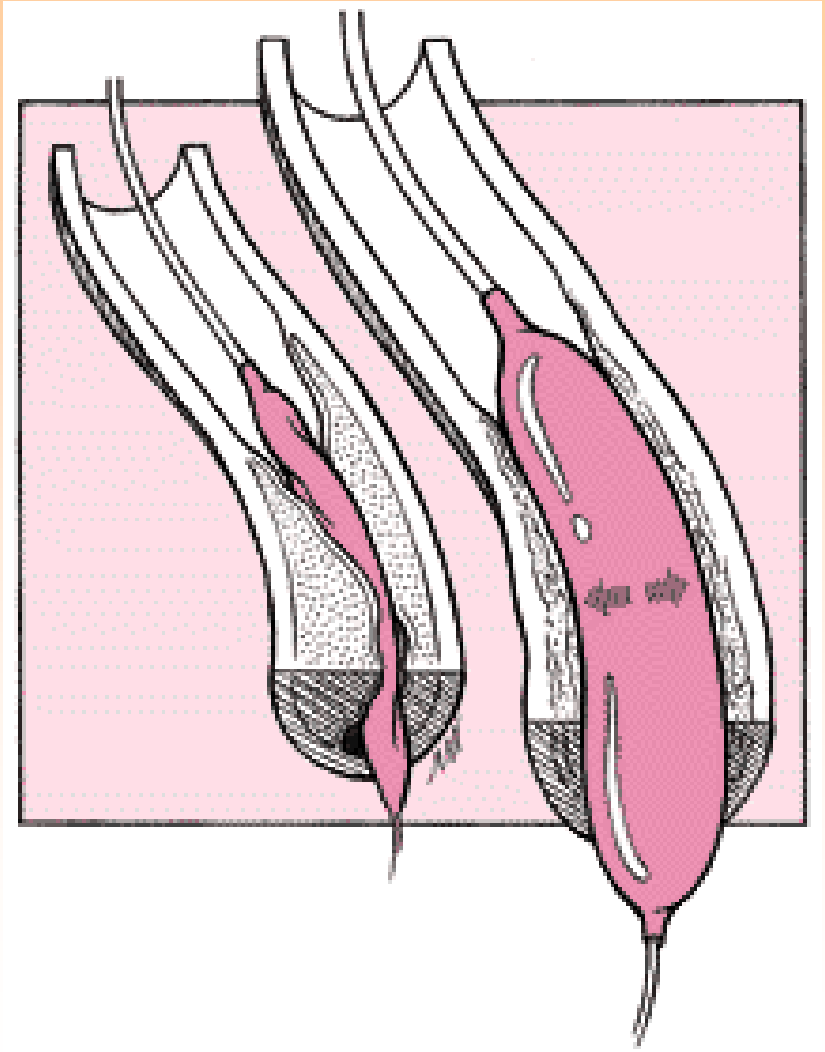
Treatment of complications

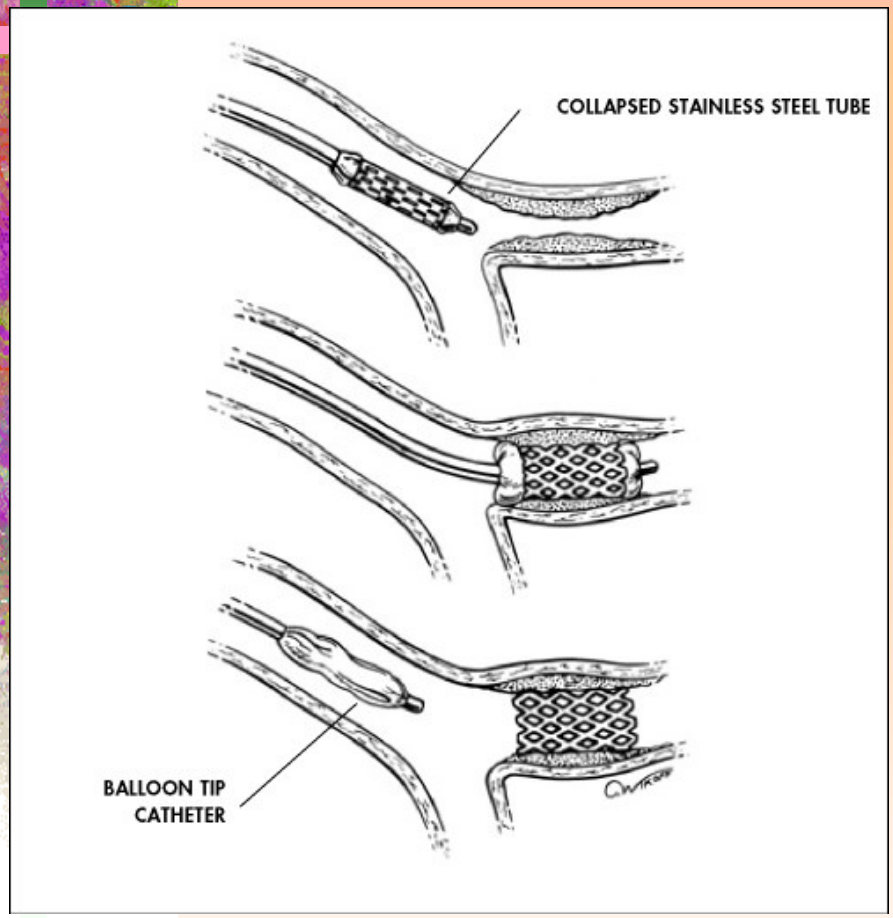
Revascularization

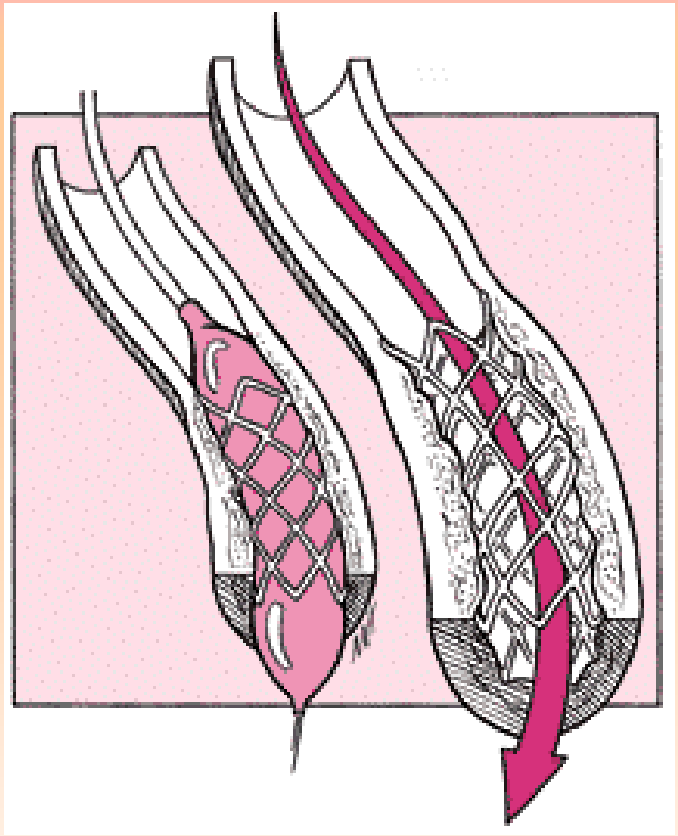
Fibrinolysis
Percutaneous coronary arteries treatment – angioplastics (PTCA), stent
Bypass
Angiogenetic therapy

Stem cells

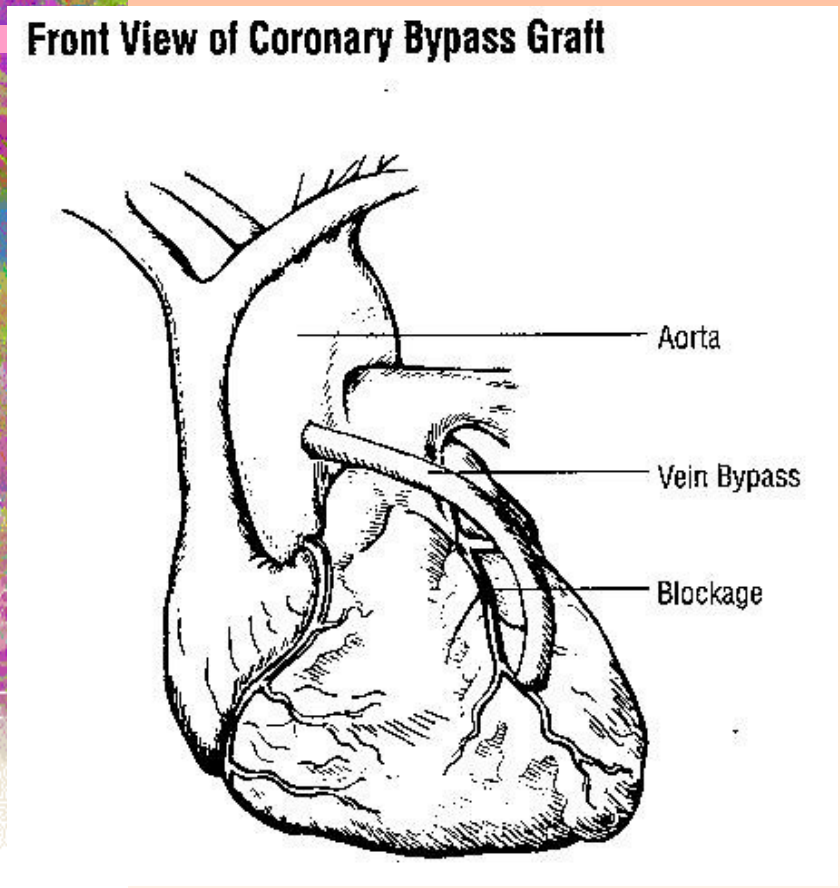
Angioplastics

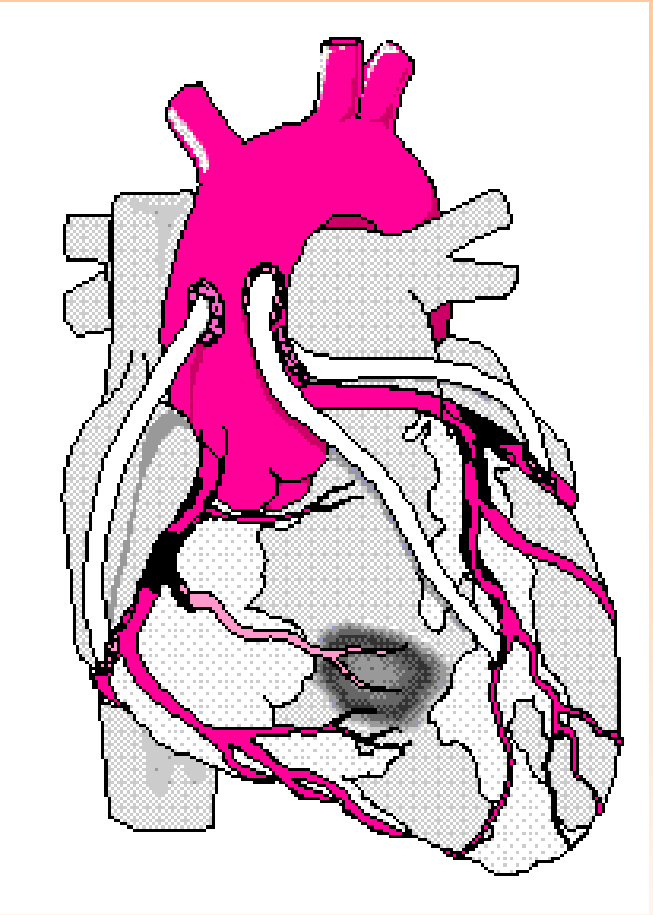






Stent


Front View of Coronary Bypass Graft
Aorta
Vein Bypass
Blockage



Reperfusion damage

* oxygen radical species: source in mitochondria, or leukocytes,
xanthinoxidase (less important in myocardium)
* increased amount of intracellular calcium
* neutrophils: radical formation, mechanical plugging of capillaries, proteolytic enzymes

clinically - ***arrhytmias***

Postischemic changes

* ischemia duration
* reperfusion

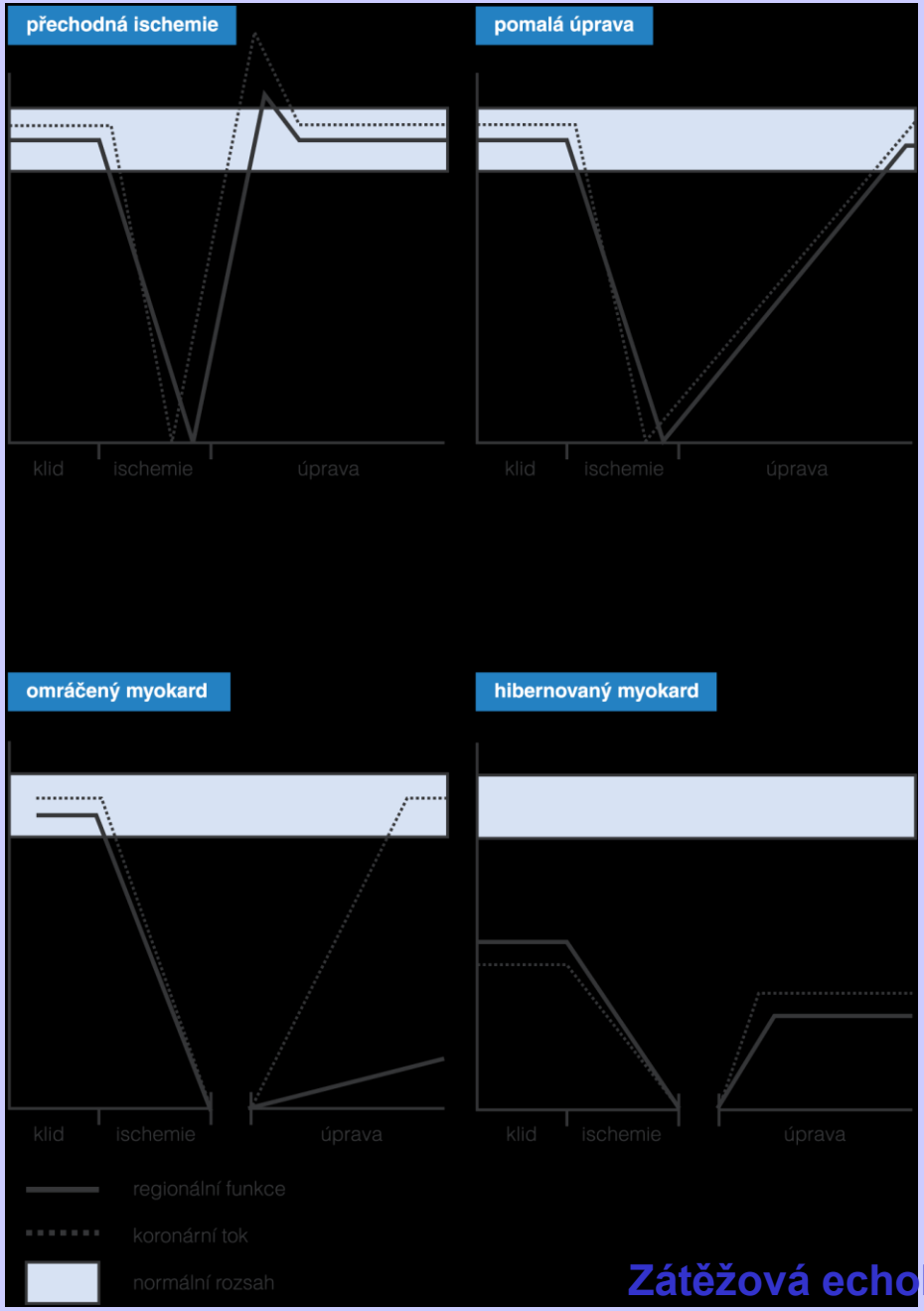
Stunned myocardium

perfused but not functioning
reversible continuous dysfunction of myocardium after reperfusion without apparent changes

Hibernating myocardium

chronically hypoperfused and functionally impaired
situation with continuously decreased blood flow
accompanied by impaired contractility

adaptation of cells to decreased energy delivery



Zátěžová echokardiografie, Maxdorf

Ischemic preconditioning

increased resistence of myocardium against damage due to ischemia

caused by preceding ischemia and reperfusion

The End

Syndrome X

stable AP + normal coronarography
small vessels