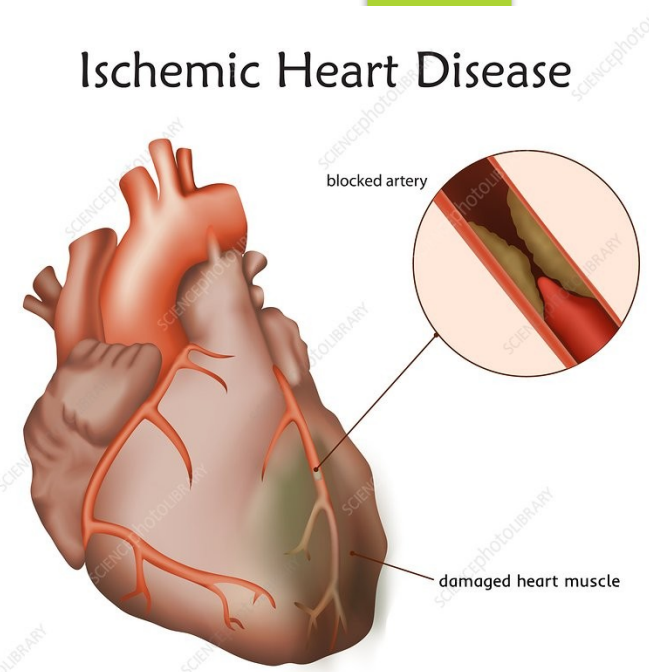
CVS module -7
ISCHEMIC HEART DISEASE



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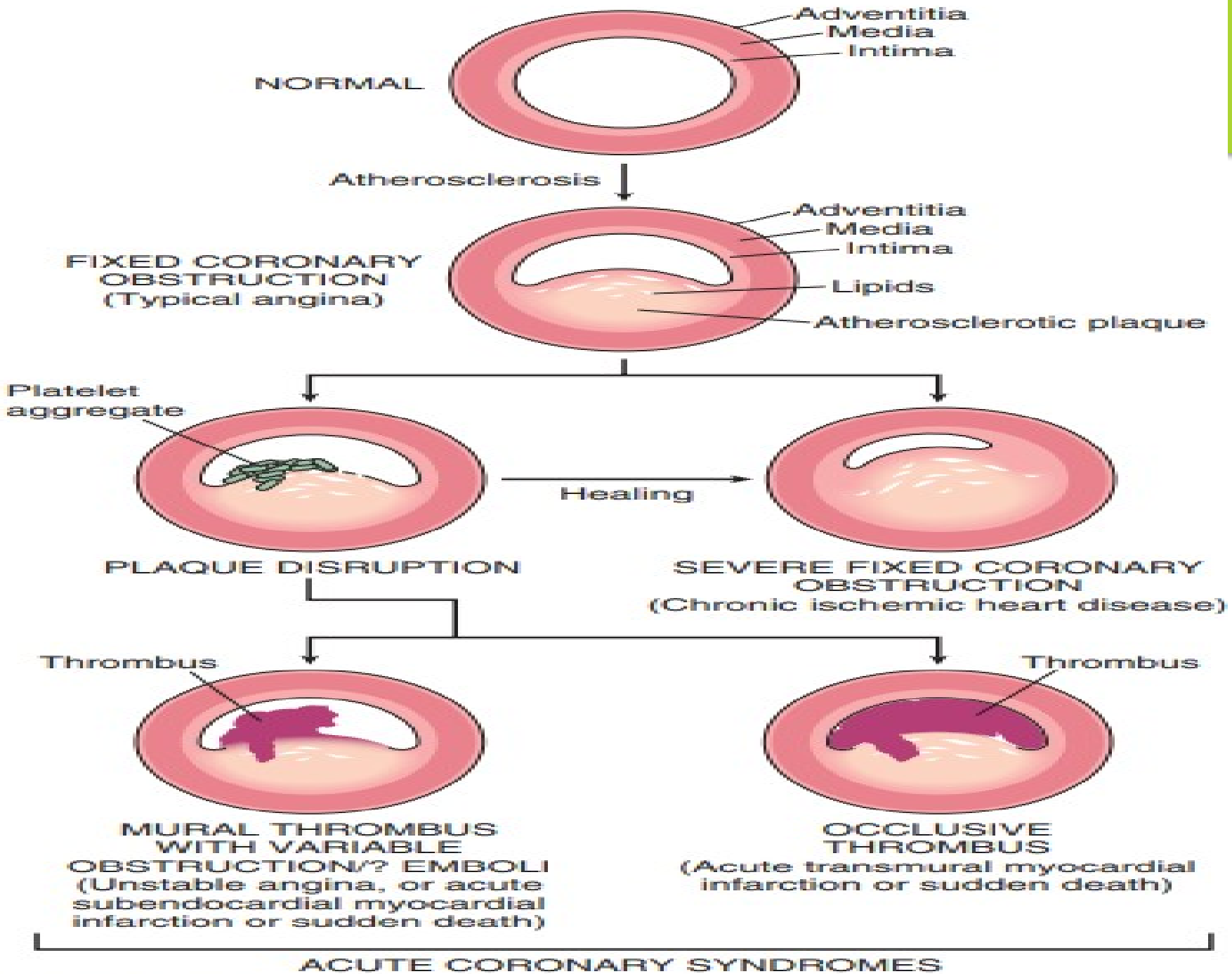
ISCHEMIC HEART DISEASE (IHD)

- A broad term including several closely related syndromes caused by myocardial ischemia (an imbalance between cardiac blood supply (perfusion) and myocardial oxygen and nutritional requirements).

- IHD usually is a consequence of reduced coronary blood flow secondary to obstructive atherosclerotic vascular disease


NORMAL
Adventitia
Media
Intima
Atherosclerosis
FIXED CORONARY OBSTRUCTION (Typical angina)
Adventitia
Media
Intima
Lipids
Atherosclerotic plaque
Platelet aggregate
Healing
PLAQUE DISRUPTION
SEVERE FIXED CORONARY OBSTRUCTION (Chronic ischemic heart disease)
Thrombus
Thrombus
MURAL THROMBUS WITH VARIABLE OBSTRUCTION/? EMBOLI (Unstable angina, or acute subendocardial myocardial infarction or sudden death)
OCCLUSIVE THROMBUS (Acute transmural myocardial infarction or sudden death)
ACUTE CORONARY SYNDROMES

clinical presentation

- Angina pectoris : Ischemia induces pain but is insufficient to cause myocyte death, can be:
- stable (occurring predictably at certain levels of exertion).
- Prinzmetal angina :caused by vessel spasm .
- unstable (occurring with progressively less exertion or even at rest).

- Myocardial infarction (MI): cardiomyocyte death.

- Chronic IHD with CHF.
- This progressive cardiac decompensation, which occurs after acute MI or secondary to accumulated small ischemic insults, eventually precipitates mechanical pump failure.

- Sudden cardiac death (SCD): result from tissue damage from MI, or from lethal arrhythmia .

- Generally, cardiac ischemia may be the result of:

- increased demand (e.g., with increased heart rate or hypertension).
- diminished blood volume (e.g., with hypotension or shock).
- diminished oxygenation (e.g., due to pneumonia or CHF).
- diminished oxygen-carrying capacity (e.g., due to anemia or carbon monoxide poisoning).

Pathogenesis

- IHD is a consequence of inadequate coronary perfusion relative to myocardial demand.
  - Due to preexisting atherosclerosis/new, superimposed thrombosis/vasospasm.

fixed obstructions that occlude less than 70%:

asymptomatic

Fixed lesions that occlude more than 70%:

Critical stenosis

Stable angina

fixed stenosis that occludes 90% :

Unstable angina

Then any **dynamic changes** in coronary plaque morphology followed by thrombosis leading to :

ACUTE CORONARY SYNDROME

Acute coronary syndrome

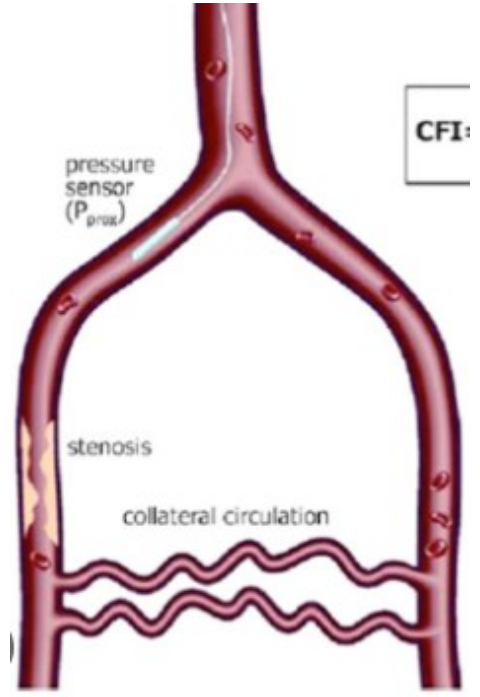
- **Acute coronary syndromes result from acute obstruction of a coronary artery, and** applied to any of the three catastrophic manifestations of IHD:

1. unstable angina
2. MI
3. SCD.

collateral perfusion

- if an atherosclerotic lesion progressively occludes a coronary artery at a sufficiently slow rate over years, other coronary vessels may undergo remodeling and provide compensatory blood flow to the area at risk; such collateral perfusion can subsequently protect against MI, even if the original vessel becomes completely occluded.

- Unfortunately, with acute coronary blockage, there is no time for collateral flow to develop and infarction results.



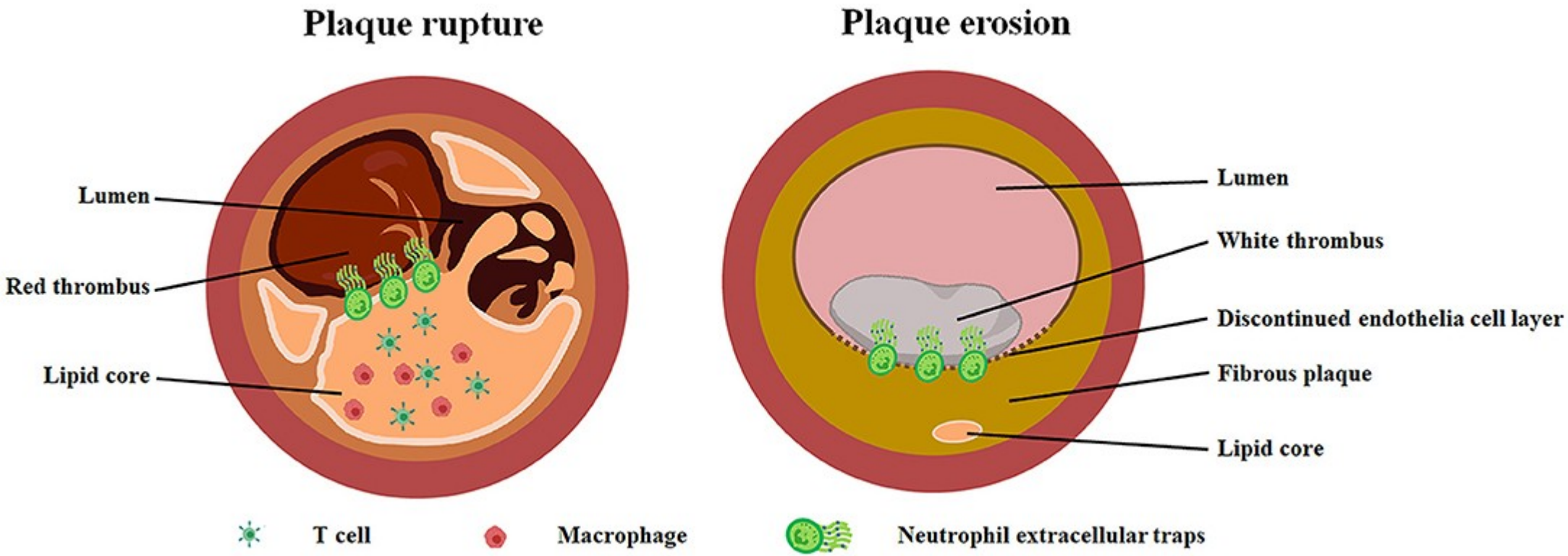
Acute Plaque Change

- The initiating event is typically a sudden disruption (ranging from erosion to rupture) of a partially occlusive plaque.

- More than one mechanism of injury may be involved:
- rupture,
- Fissuring.
- ulceration of plaques.
- hemorrhage into the core of plaques .

Expose highly thrombogenic constituents or underlying subendothelial basement membrane, leading to rapid thrombosis.

Picture for rupture, fissuring



Participating factors

- Inflammation: plays an essential role from inception to plaque rupture.

- Thrombosis : eroded or ruptured plaque triggers the acute coronary syndromes.

- Vasoconstriction, mediated by:
- Circulating adrenergic agonists.
- Locally released platelet contents.
- Imbalance between endothelial cell–relaxing factors (e.g., nitric oxide) and –contracting factors (e.g., endothelin) due to endothelial dysfunction.
- Mediators released from perivascular inflammatory cells.

1. Angina Pectoris

- Angina pectoris is an intermittent chest pain caused by transient, reversible myocardial ischemia.
- The pain is a consequence of the ischemia-induced release of adenosine, bradykinin, and other molecules that stimulate autonomic nerves.

- Subtypes:
- 1. Stable angina:
- episodic chest pain associated with particular levels of exertion or some other increased demand .
- The pain is described as a crushing or squeezing substernal sensation that radiates down the left arm or to the left jaw (referred pain).
- The pain usually is relieved by rest (reducing demand) or by drugs such as nitroglycerin, a vasodilator that increases coronary perfusion.

- 2• Prinzmetal angina:
- occurs at rest and is caused by coronary artery spasm.
- such spasms typically occur on or near existing atherosclerotic plaques or completely normal vessel .
- Prinzmetal angina typically responds promptly to vasodilators such as nitroglycerin and calcium channel blockers.

- 3• Unstable angina (also called crescendo angina):
- Characterized by increasingly frequent pain, precipitated by progressively less exertion or even occurring at rest.
- Associated with plaque disruption and superimposed thrombosis, distal embolization of the thrombus, and/or vasospasm; it can be a harbinger of MI, portending complete vascular occlusion.

2. Myocardial Infarction (heart attack).

- necrosis of the heart muscle resulting from ischemia.
- The major underlying cause is atherosclerosis.
- In general, women tend to be protected against MI during their reproductive years.
- Menopause with declining estrogen production, is associated with exacerbation of coronary artery disease, and IHD is the most common cause of death in older adult women.

Pathogenesis

- The vast majority of MIs are caused by acute thrombosis within coronary arteries, in form of:

- disruption or erosion of preexisting atherosclerotic plaque.
- vascular occlusion, and subsequent infarction of the perfused myocardium.

- 10% of MI occurs in the absence of occlusive atherosclerotic vascular disease; such infarcts are mostly result from :
- coronary artery vasospasm .
- embolization from mural thrombi (e.g., in the setting of atrial fibrillation) or from valve vegetations.

In a typical MI, the following sequence of events takes place:

endothelial injury, intraplaque hemorrhage, or mechanical forces lead to atheromatous plaque erosion and disruption.

→

exposing subendothelial collagen and necrotic plaque contents to the blood.

→

Platelets adhere, aggregate, and are activated, releasing thromboxane A2, adenosine diphosphate (ADP), and serotonin, causing further platelet aggregation and vasospasm.

↓

Activation of coagulation by exposure of tissue factor adds to the growing thrombus

→

the thrombus can evolve to completely occlude the coronary artery lumen.

Cardiac response??

Myocardial Response to Ischemia

- Since cardiac myocytes generate energy almost exclusively through mitochondrial oxidative phosphorylation, cardiac function is strictly dependent upon the continuous flow of oxygenated blood through the coronary arteries.

- Within seconds of vascular obstruction, aerobic metabolism ceases, leading to a drop in adenosine triphosphate (ATP) and accumulation of lactic acid, leading to:

- Early (reversible) effect: rapid loss of contractility.
- prolonged ischemia lasting at least 20 to 40 minutes (irreversible):
- coagulative necrosis of myocytes.
- arrhythmias e.g. ventricular fibrilliation.

Patterns of Infarction

- The location, size, and morphologic features of an acute myocardial infarct depend on multiple factors:

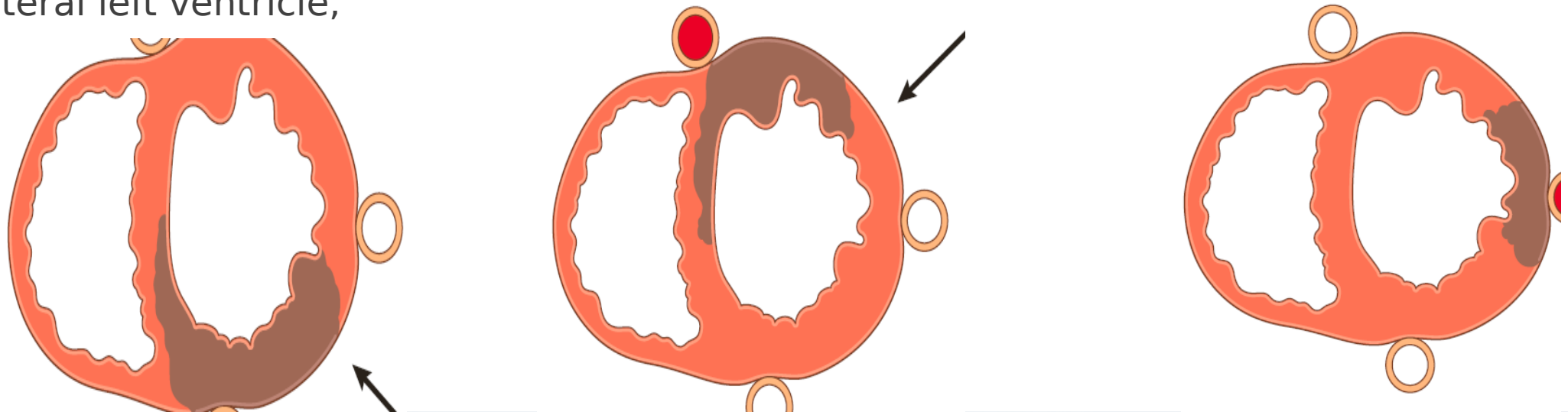
- 1• Size and distribution of the involved vessel.
- 2• Rate of development and duration of the occlusion.
- 3• Metabolic demands of the myocardium (affected, for example, by blood pressure and heart rate).
- 4• Extent of collateral supply.

According to the distribution

*Acute occlusion of the proximal left anterior descending (LAD) artery causes 40%-50% of all MIs & typically results in infarction of anterior wall of left ventricle, anterior two thirds of ventricular septum, & most of the heart apex.

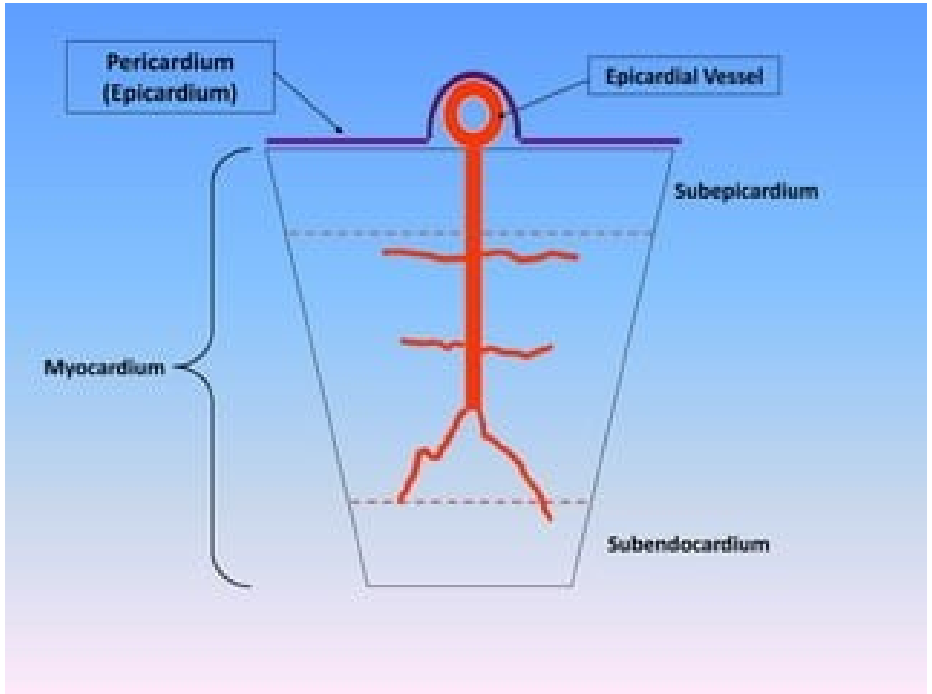
*Proximal right coronary artery (RCA) occlusion (30% to 40% of MIs) affects much of the right ventricle.

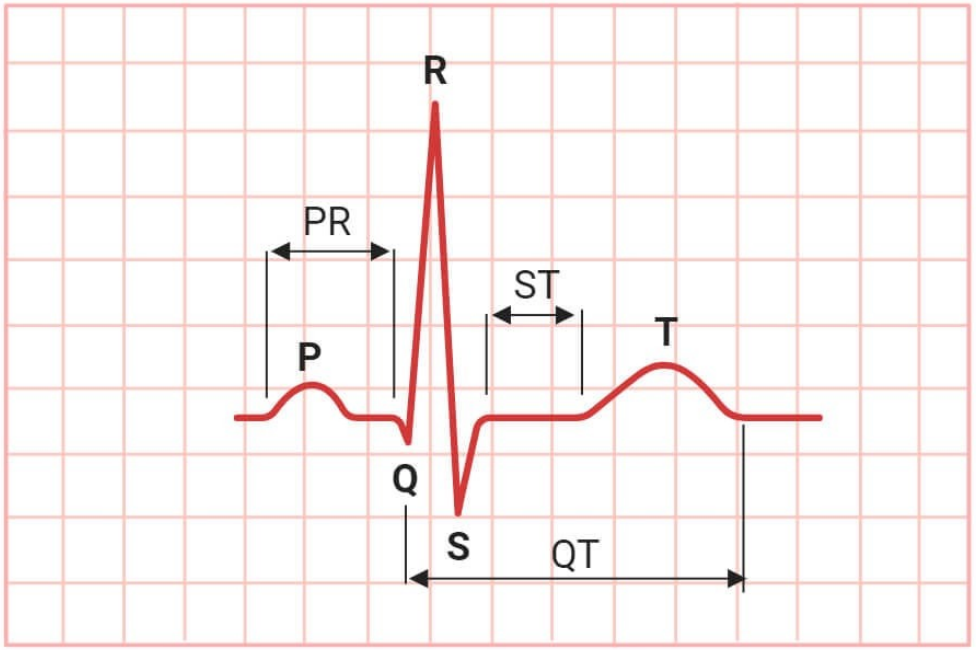
*Acute occlusion of the proximal left circumflex (LCX) artery (15%-20% of MIs) causes necrosis of the lateral left ventricle,



- Transmural infarctions (ST-segment elevated MIs (STEMIs).
- involve the full thickness of the ventricle & are caused by epicardial vessel occlusion
- Give rise to: ST segment elevations on (ECG) and can have negative Q waves.

- Subendocardial infarctions (non–ST-segment elevated MIs" /"NSTEMIs).
- are limited to the inner third of myocardium.
- No ST segment elevations on ECG





Electrocardiogram
(ECG)

Gross morphology

postmortem autopsy revealed areas of Coagulative necrosis.

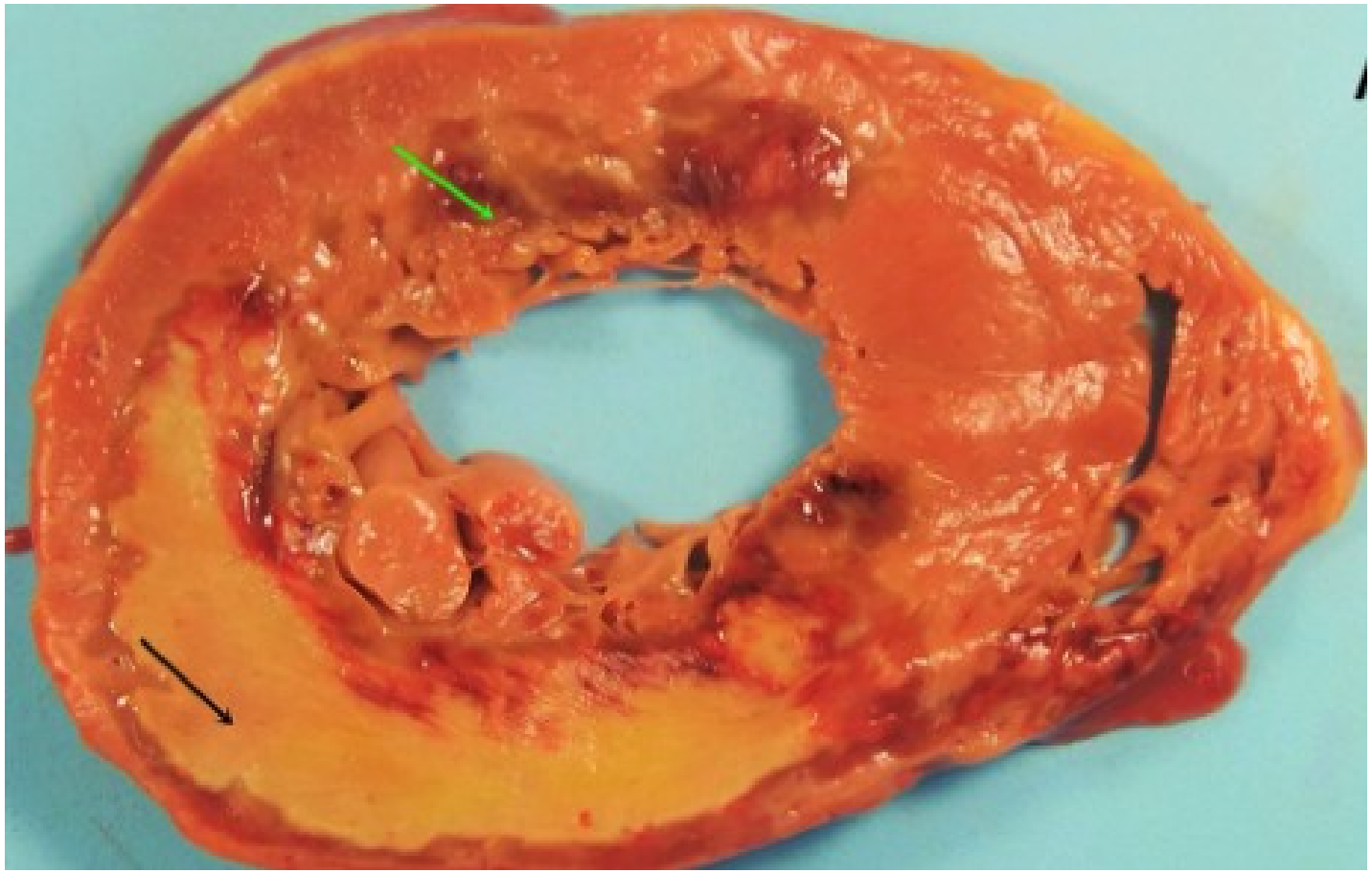
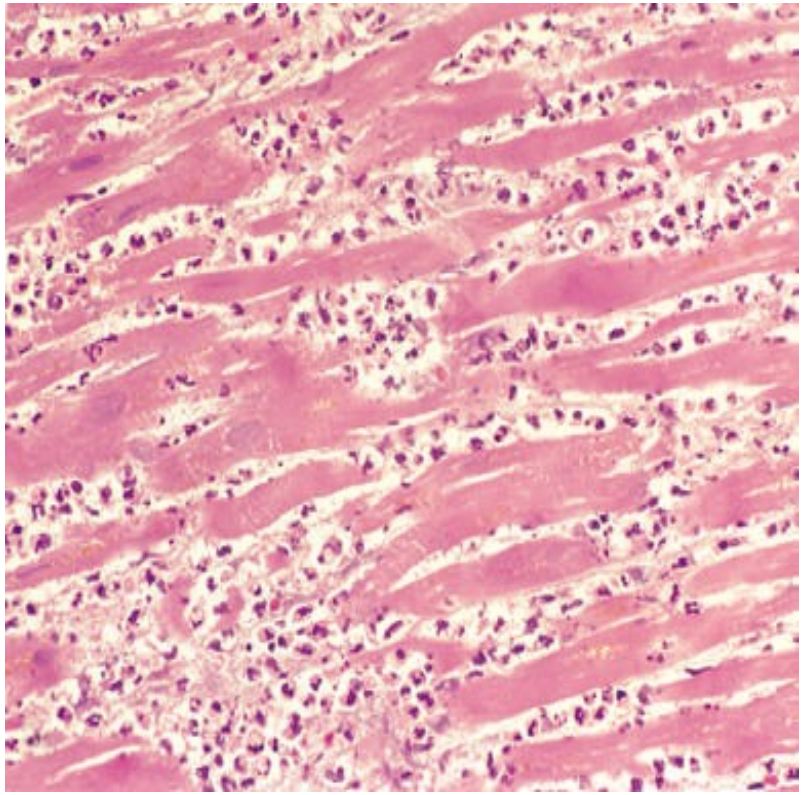


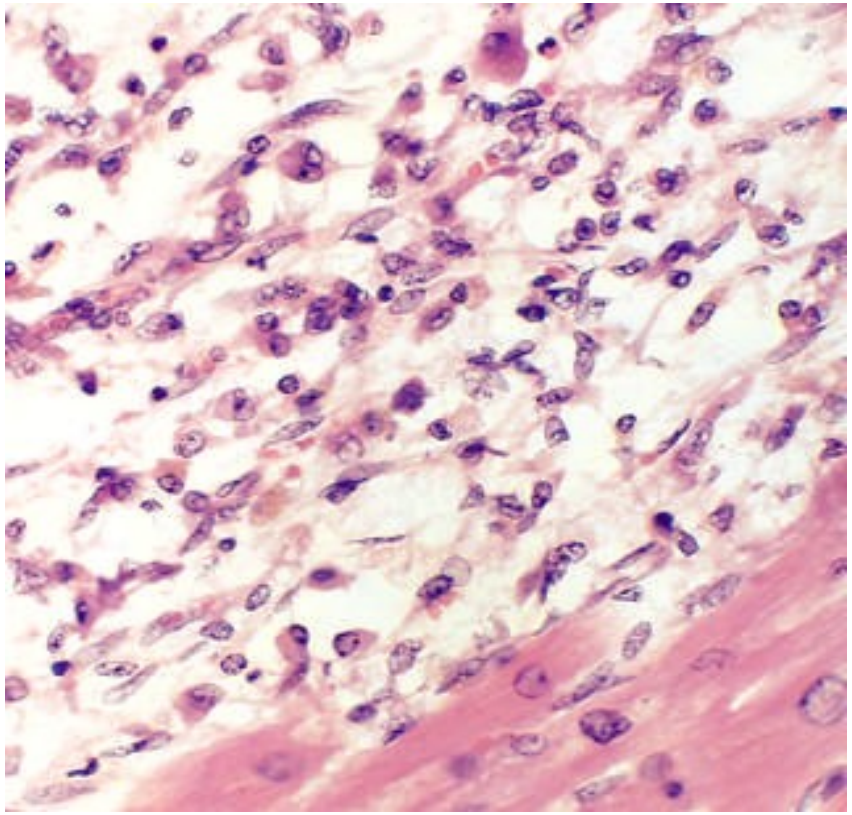
Table 11.2 Evolution of Morphologic Changes in Myocardial Infarction

Time Frame	Gross Features	Light Microscopic Findings	Electron Microscopic Findings
Reversible Injury			
0–½ hour	None	None	Relaxation of myofibrils; glycogen loss; mitochondrial swelling
Irreversible Injury			
½–4 hours	None	Usually none; variable waviness of fibers at border	Sarcolemmal disruption; mitochondrial amorphous densities
4–12 hours	Occasionally dark mottling	Beginning coagulation necrosis; edema; hemorrhage	
12–24 hours	Dark mottling	Ongoing coagulation necrosis; pyknosis of nuclei; hypereosinophilic appearance of myocytes; marginal contraction band necrosis; beginning neutrophilic infiltrate	
1–3 days	Mottling with yellow-tan infarct center	Coagulation necrosis with loss of nuclei and striations; interstitial infiltrate of neutrophils	
3–7 days	Hyperemic border; central yellow-tan softening	Beginning disintegration of dead myofibers, with dying neutrophils; early phagocytosis of dead cells by macrophages at infarct border	
7–10 days	Maximally yellow-tan and soft, with depressed red-tan margins	Well-developed phagocytosis of dead cells; early formation of fibrovascular granulation tissue at margins	
10–14 days	Red-gray depressed infarct borders	Well-established granulation tissue with new blood vessels and collagen deposition	
2–8 weeks	Gray-white scar, progressive from border toward core of infarct	Increased collagen deposition, with decreased cellularity	
>2 months	Scarring complete	Dense collagenous scar	

Histopathological features

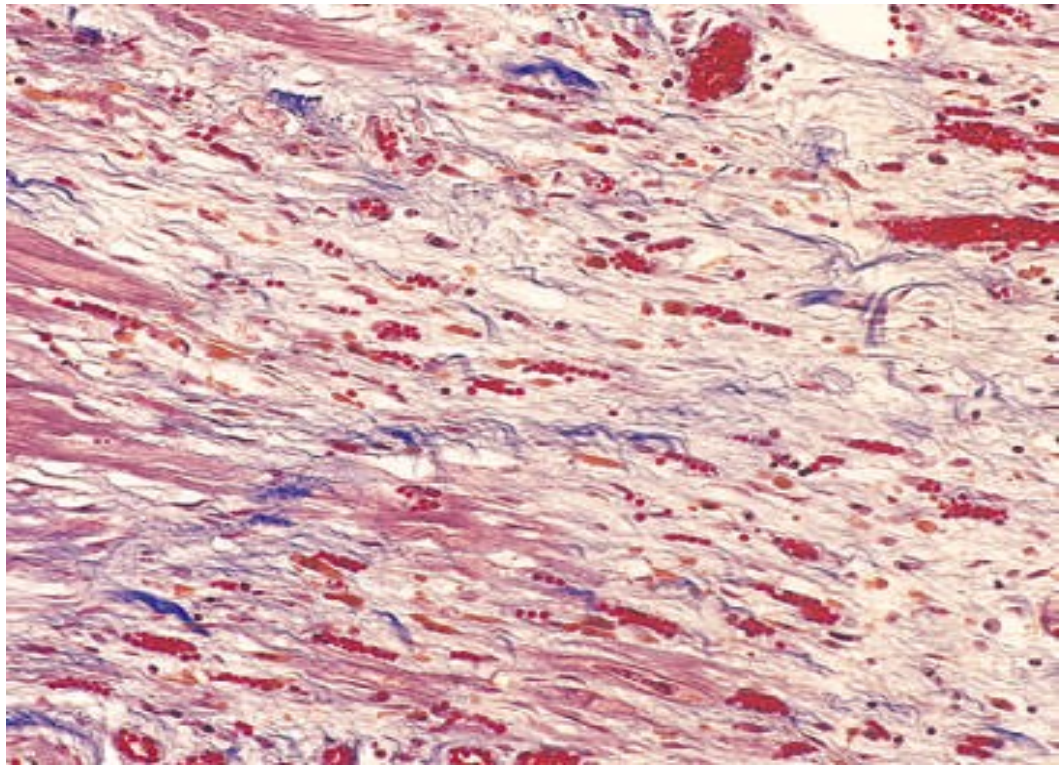


Coagulation necrosis with loss of nuclei and striations; interstitial infiltrate of neutrophils

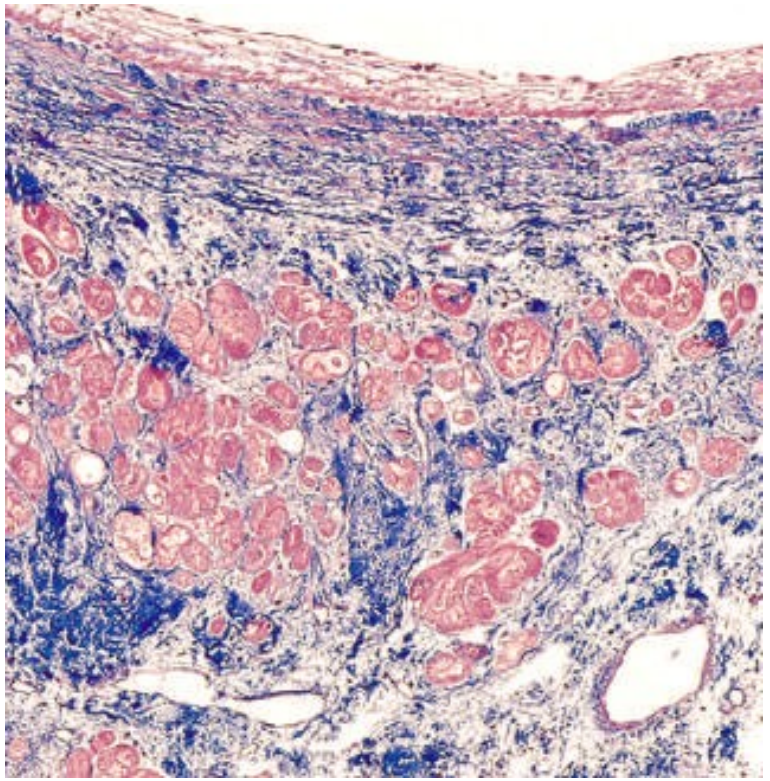


Complete removal of necrotic myocytes by phagocytic macrophages

Histopathological features cont.



well established granulation tissue with new blood vessels & collagen deposition.



Dense collagenous scar

Clinical features

- retrosternal pain radiate to the neck, jaw, epigastrium, or left arm.
- not relieved by rest or vasodilators.
- persist for several hours (>20-30 min).
- nausea, vomiting, sweating & weakness .

- LAB: elevated cardiac enzyme: leak out of injured myocardial cells through damaged cell membranes.
- E.g. troponins , creatine kinase (CK)

- Electrocardiographic abnormalities, include:
- Q waves, ST segment changes, and T wave inversions.

Complications of MI

- Contractile dysfunction in form of:
- left ventricular failure manifested as hypotension, pulmonary congestion, & pulmonary edema.
- Arrhythmias with risk of sudden cardiac death.
- Papillary muscle dysfunction or rupture.
- Myocardial rupture: during healing process, necrotic myocardium converted to soft, friable granulation tissue.
- Ventricular aneurysm.
- Mural thrombus

Chronic Ischemic Heart Disease

- Chronic IHD, also called ischemic cardiomyopathy, is a progressive heart failure secondary to ischemic myocardial damage.
- Mostly there is a known clinical history of previous MI.
- After prior infarction(s), chronic IHD appears when the compensatory mechanisms (e.g., hypertrophy) of residual myocardium begin to fail.
- severe CAD can cause diffuse myocardial dysfunction, and even micro-infarction and replacement fibrosis, without any clinically evident episode of frank infarction.