

Ischemic Heart Disease

Coronary supply–demand imbalance, myocardial injury, and
clinicopathologic consequences

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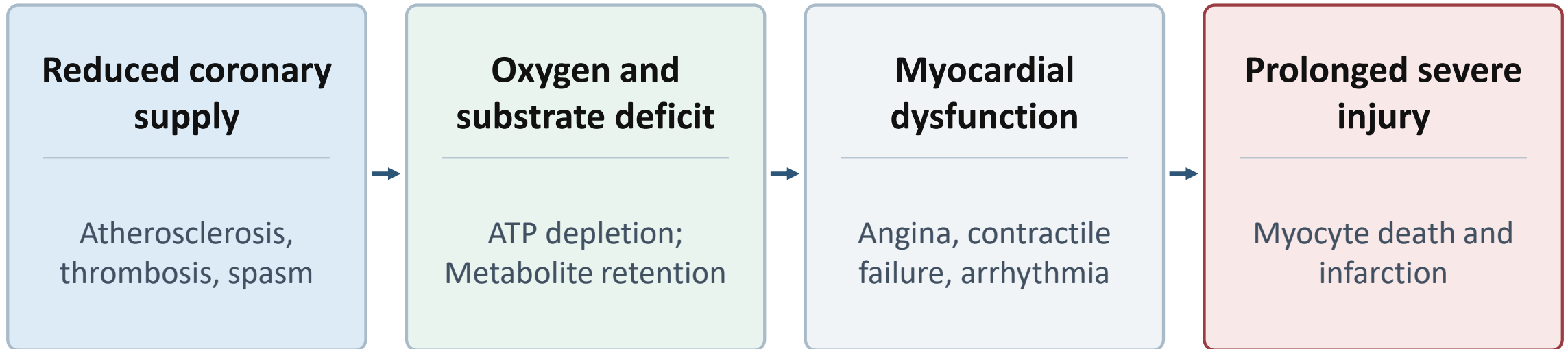
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What this lecture explains

- Define myocardial ischemia and relate oxygen supply to cardiac workload.
- Explain how fixed coronary obstruction and acute plaque change generate different clinical syndromes.
- Trace the myocardial response to ischemia, infarction, and reperfusion.
- Interpret infarct morphology, major complications, chronic IHD, and sudden cardiac death.

Ischemia is a supply–demand mismatch

Schematic



Why coronary perfusion matters

Oxygen and nutrients

Myocytes depend on oxidative ATP generation

Ischemia rapidly reduces energy production

Contractile dysfunction arises before necrosis

Reperfusion restores substrate delivery

Metabolic clearance

Perfusion also removes metabolic by-products

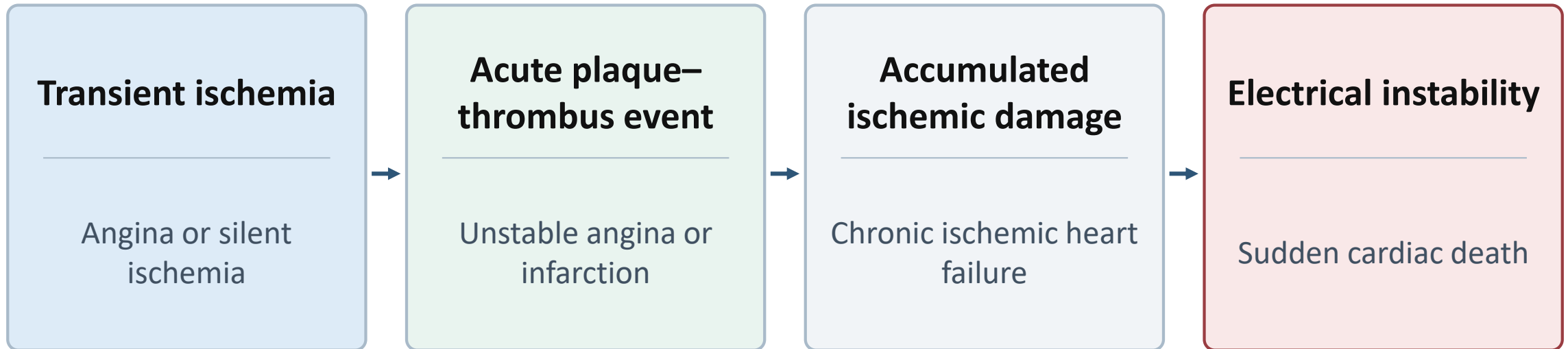
Accumulated metabolites participate in injury and pain

Decreasing flow compromises waste removal

Reperfusion also helps clear metabolites

The major clinical expressions of IHD

Schematic



Coronary atherosclerosis dominates IHD

- Atherosclerosis involving epicardial coronary arteries is the principal substrate.
- Fixed stenosis restricts flow reserve, especially under stress.
- Plaque disruption, thrombosis, and superimposed spasm produce abrupt reductions in flow.
- Less common causes include coronary spasm, embolism, vasculitis, and systemic perfusion deficits.

Population burden reflects preventable vascular disease

- Robbins characterizes IHD as the leading single cause of death globally.
- Tobacco exposure, dyslipidemia, hypertension, and diabetes contribute to coronary disease burden.
- Earlier diagnosis and treatment have reduced IHD mortality in many high-resource settings.
- Population-level prevention and emergency access influence disease outcomes.

Risk modification acts before plaque rupture

Risk-factor intervention	Clinical purpose
Smoking cessation	Limit vascular injury and thrombosis risk
Cholesterol reduction	Slow atherosclerotic progression; Favor plaque stability
Blood-pressure control	Reduce vascular stress and cardiac oxygen demand
Exercise, weight, glycemic control	Reduce metabolic and cardiovascular risk

Coronary territories connect lesion to infarct

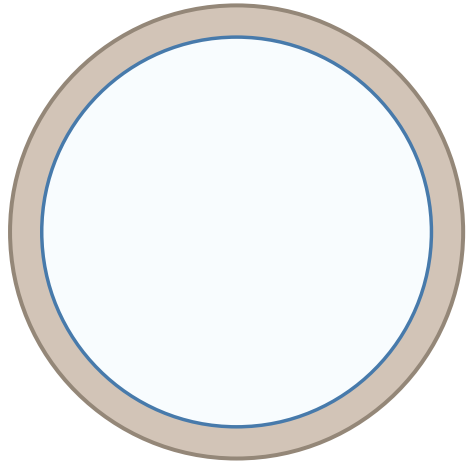
Artery	Typical major myocardial territory
Left anterior descending (LAD)	Anterior LV, apex, anterior two-thirds of septum
Right coronary artery (RCA)	Inferior/posterior LV and posterior septum in right dominance; RV involvement possible
Left circumflex (LCX)	Lateral LV free wall (typical right-dominant circulation)

Coronary dominance refers to septal supply

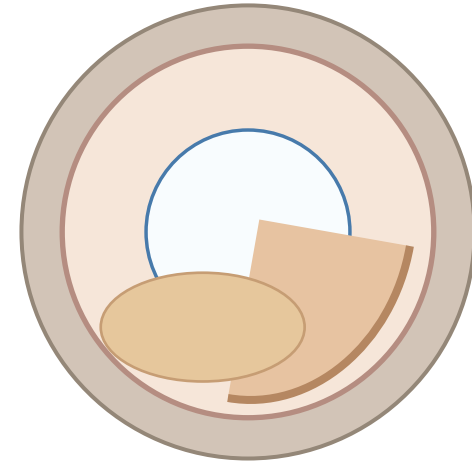
- Dominance is assigned by the artery supplying the posterior third of the interventricular septum.
- In right-dominant hearts, the RCA perfuses this posterior septal territory.
- An RCA occlusion may therefore cause LV as well as right-sided injury.
- Anatomic variation means the injured territory must be interpreted using actual coronary distribution.

Fixed stenosis consumes coronary flow reserve

Schematic



Unobstructed epicardial lumen



Atherosclerotic lumen with reduced reserve

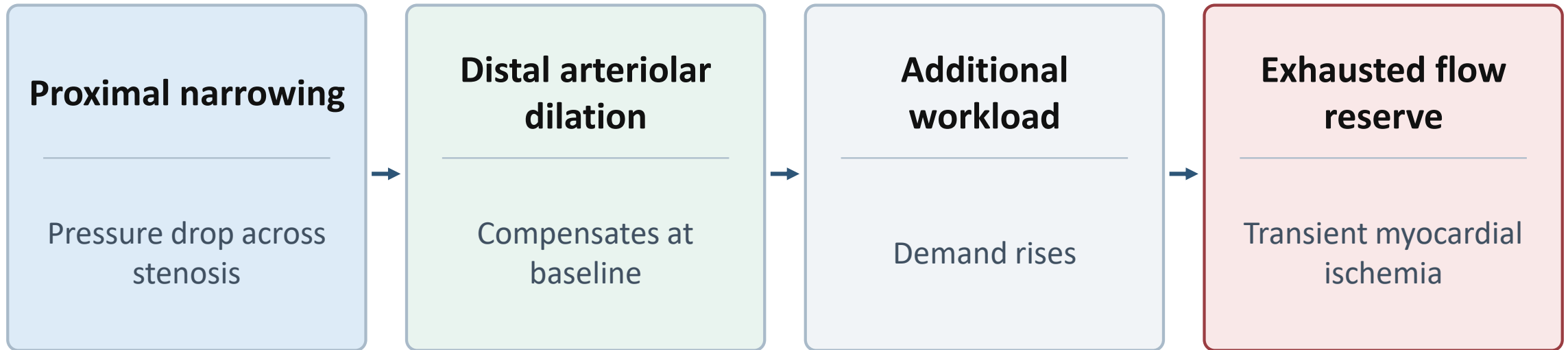
Exercise raises demand; Maximal vasodilation cannot fully compensate for fixed obstruction.

Critical stenosis is a functional threshold

- >70% reduction in luminal cross-sectional area as a conventional threshold for exertional ischemia.
- Very severe obstruction (~90% of area) can impair flow even at rest.
- Extent of stenosis alone does not fully predict symptoms or events.
- These refer to cross-sectional area—not interchangeable diameter measurements.

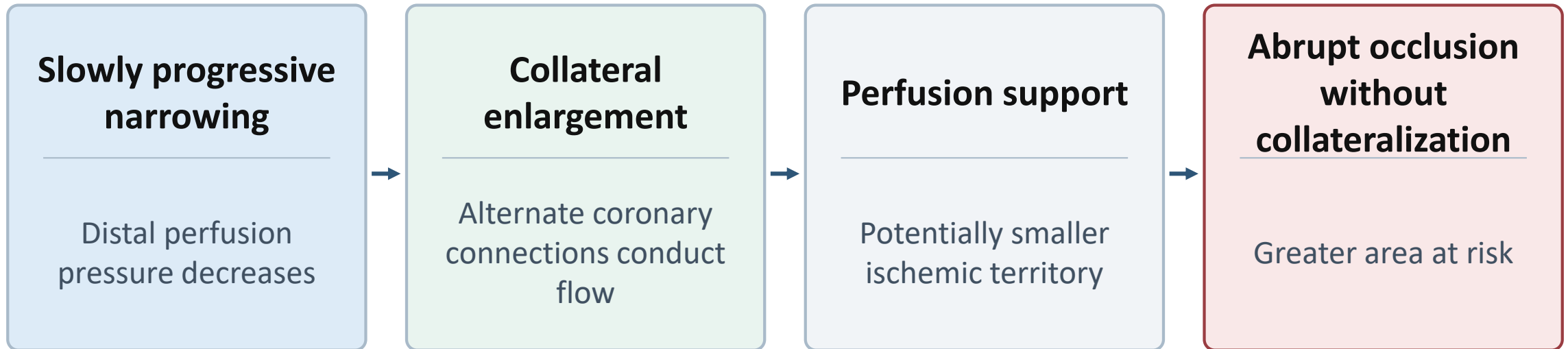
Coronary flow reserve is more than anatomy

Schematic



Collateral channels modify ischemic injury

Schematic

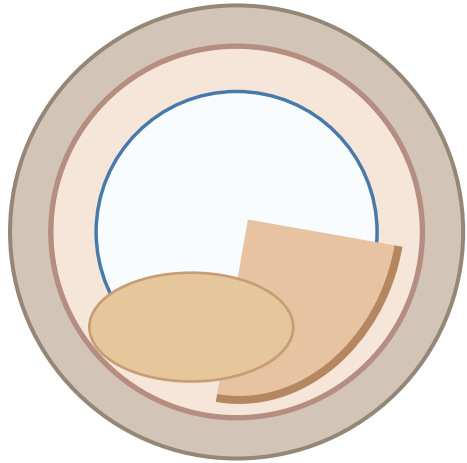


Single- and multivessel disease coexist

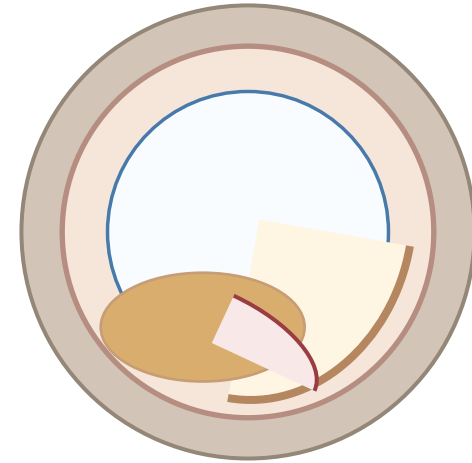
- LAD, LCX, and RCA may be affected singly or in combination.
- Major stenoses tend to occur in proximal portions of epicardial arteries.
- Intramyocardial penetrating arteries are less commonly the primary site of atherosclerotic plaque.
- Lesion distribution, collateralization, and physiological reserve jointly determine risk.

Stable plaque and vulnerable plaque differ

Schematic



Fibrous-cap-rich lesion

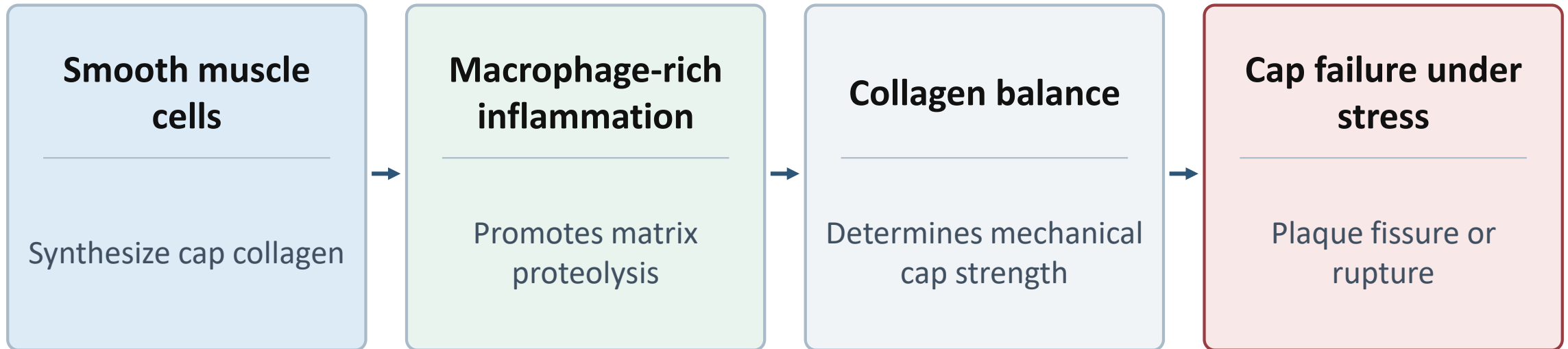


Thin-cap, lipid-rich lesion

Rupture propensity depends on cap strength, inflammation, plaque structure, and mechanical stress.

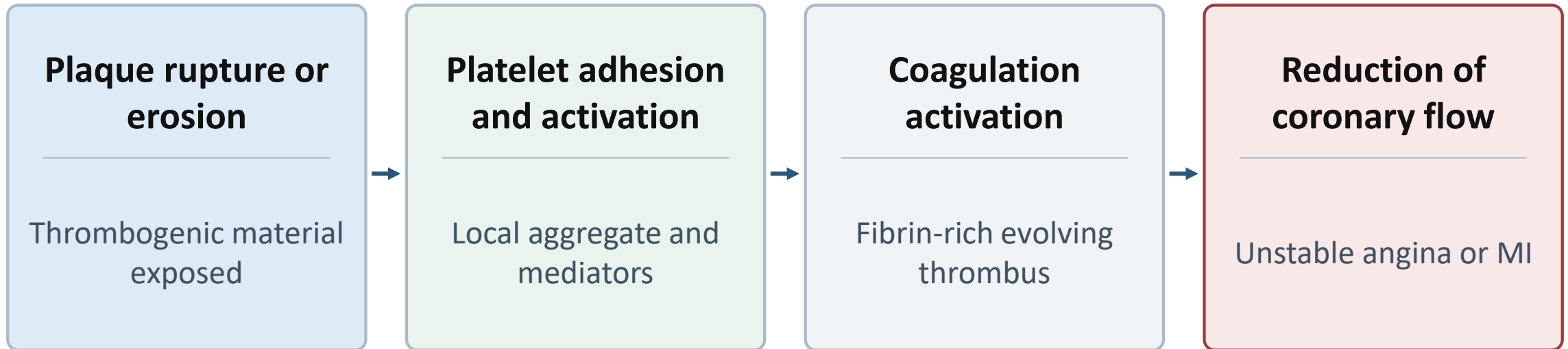
Plaque stability depends on matrix turnover

Schematic



Acute coronary syndrome starts at the plaque

Schematic

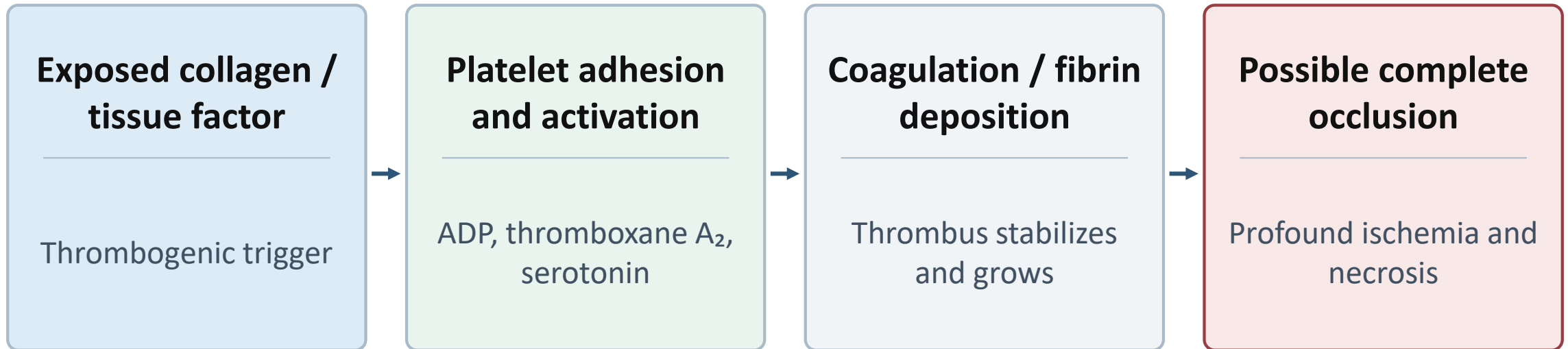


Erosion and rupture expose different surfaces

Plaque rupture	Plaque erosion
Structural failure of fibrous cap	Loss/dysfunction of surface endothelial cells
Exposes thrombogenic atheromatous contents	Exposes prothrombotic subendothelial matrix
Often associated with large lipid core, thin cap, inflammation	Can occur without overt cap rupture
Both may provoke an acute coronary thrombosis	Both may provoke an acute coronary thrombosis

The platelet–coagulation amplification loop

Schematic



Occlusive and nonocclusive thrombi diverge

Nonocclusive or transient thrombus

Residual flow may be sufficient to delay transmural necrosis

Unstable angina, microembolism, or limited MI

Clinical outcome depends on duration and flow

Not reliably predicted from previous angina severity

Persistent occlusive thrombus

Severely compromises supplied myocardium

Often produces extensive acute MI

Myocyte loss expands without reperfusion

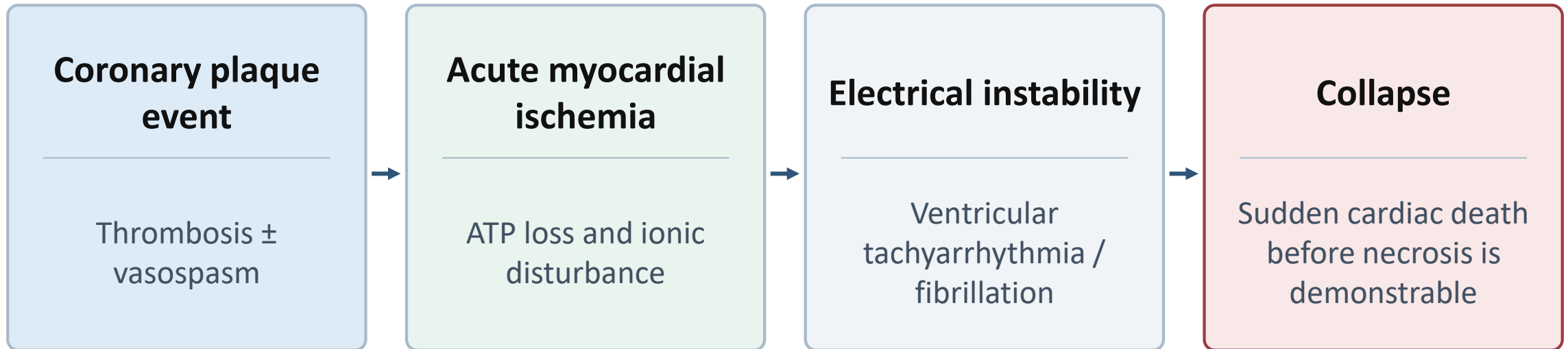
May arise from a previously noncritical plaque

The culprit lesion may not be critically stenotic

- Most infarct-related disruptions do not occur at a lesion previously causing severe fixed flow limitation.
- Vulnerability and thrombotic response matter, not only plaque bulk.
- Clinically silent plaque injury and healing can enlarge stenoses over time.
- A history without exertional angina does not exclude an abrupt coronary event.

Why plaque change can cause sudden death

Schematic

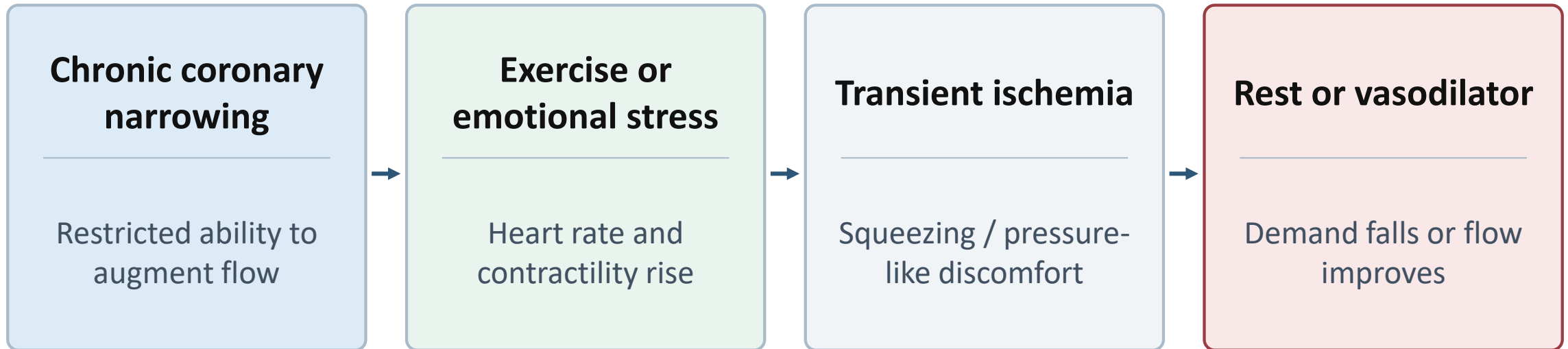


Angina is reversible ischemia without myocyte necrosis

- Transient myocardial ischemia may provoke substernal or precordial discomfort.
- Ischemic metabolites stimulate visceral afferent pathways.
- A typical attack resolves when coronary supply–demand balance improves.
- Angina and acute MI differ fundamentally by the presence of irreversible cardiomyocyte death.

Stable angina: Demand exceeds fixed supply

Schematic



Vasospastic angina: Transient dynamic obstruction

- Coronary arterial spasm can produce ischemia without increased physical demand.
- Episodes may occur at rest and may coexist with coronary atherosclerosis.
- Attacks generally respond to vasodilator treatment.
- Distinguish the dynamic vascular lesion from a fixed exertional stenosis.

Unstable angina signals acute plaque pathology

- Episodes become more frequent, longer, more severe, or occur with less exertion and at rest.
- Plaque disruption with thrombosis, distal embolization, and/or spasm underlies the syndrome.
- Necrosis is absent by definition; Evolving myocardial injury may instead establish MI.
- Unstable symptoms represent an urgent risk of complete coronary occlusion.

Silent ischemia is clinically consequential

- Not all ischemic episodes produce recognizable chest pain.
- Older adults and patients with diabetic neuropathy may report atypical or absent pain.
- Dyspnea, diaphoresis, fatigue, palpitations, and gastrointestinal symptoms can predominate.
- Absence of pain must not be equated with absence of myocardial ischemia.

Anginal phenotypes at a glance

Pattern	Dominant mechanism	Usual setting
Stable	Fixed atherosclerotic flow limitation	Predictable demand-related episodes
Vasospastic	Dynamic coronary vasoconstriction	Often at rest; Responds to vasodilators
Unstable	Plaque disruption $\pm$ thrombus / spasm	Crescendo or rest symptoms; Risk of MI
Silent	Ischemia without recognized anginal pain	Older age or autonomic neuropathy

Case: Recurrent exertional pressure

Clinical vignette

A person experiences reproducible substernal pressure during uphill walking. Symptoms disappear soon after resting. There is no evidence of myocardial necrosis.

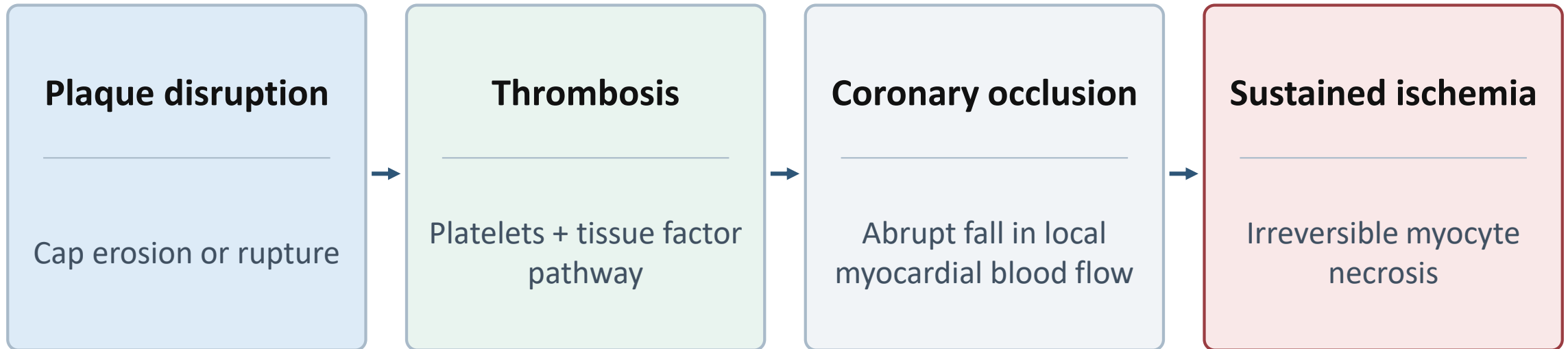
What coronary pathophysiology best explains this pattern?

Myocardial infarction is ischemic myocyte death

- MI is necrosis of cardiac myocytes caused by sufficiently severe or prolonged ischemia.
- Atherosclerotic plaque change and thrombosis are the usual proximate events.
- The extent of infarction depends on time, perfusion territory, collateral flow, and myocardial demand.
- Nonatherothrombotic mechanisms must be considered when no culprit plaque thrombus is found.

An acute infarct usually follows four linked events

Schematic

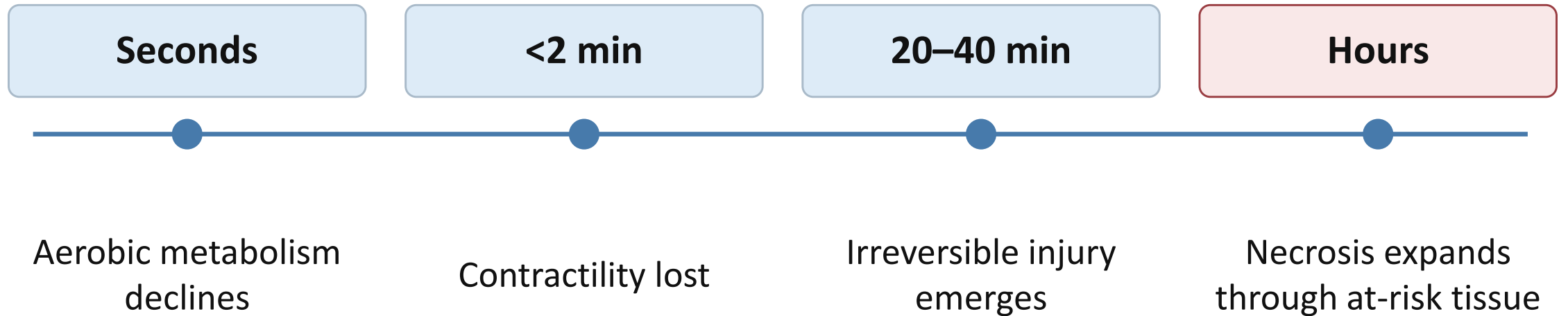


Not every infarct is caused by plaque thrombosis

Alternative mechanism	Illustrative setting
Coronary vasospasm	Spasm with/without atherosclerosis; Stimulant exposure
Coronary embolus	Atrial mural thrombus; Endocarditis vegetation
Small-vessel disease	Vasculitis or vascular amyloid
Reduced systemic oxygen delivery	Shock, hypotension, or hematologic abnormalities
Other vascular injury	Coronary dissection; Selected postoperative settings

ATP falls before tissue necrosis appears

Schematic



Contractile failure precedes cell death

- Oxidative phosphorylation falls within seconds of major perfusion loss.
- ATP depletion and metabolite accumulation impair excitation–contraction coupling.
- Severe ischemia can abolish mechanical contraction within approximately 1–2 minutes.
- Early contractile dysfunction may be reversible even when function is severely reduced.

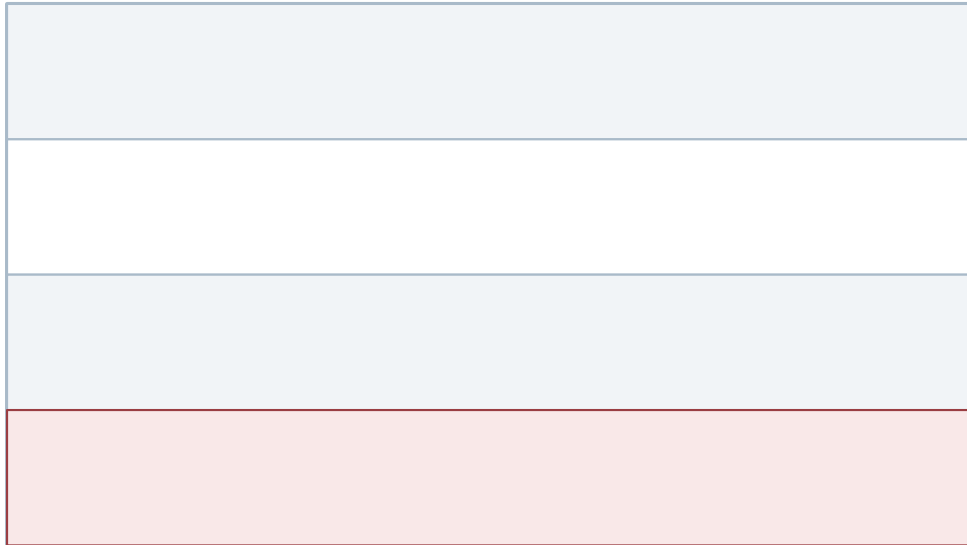
The myocardial injury threshold is time-dependent

- Very severe ischemia sustained for roughly 20–40 minutes produces irreversible injury.
- Cell death spreads through the area at risk as perfusion deprivation continues.
- An infarct may become near-complete within approximately 6–12 hours without intervention.
- Restoring flow rapidly provides the greatest potential to salvage viable myocardium.

Subendocardium is the earliest vulnerable zone

Schematic

Epicardial side



Endocardial side

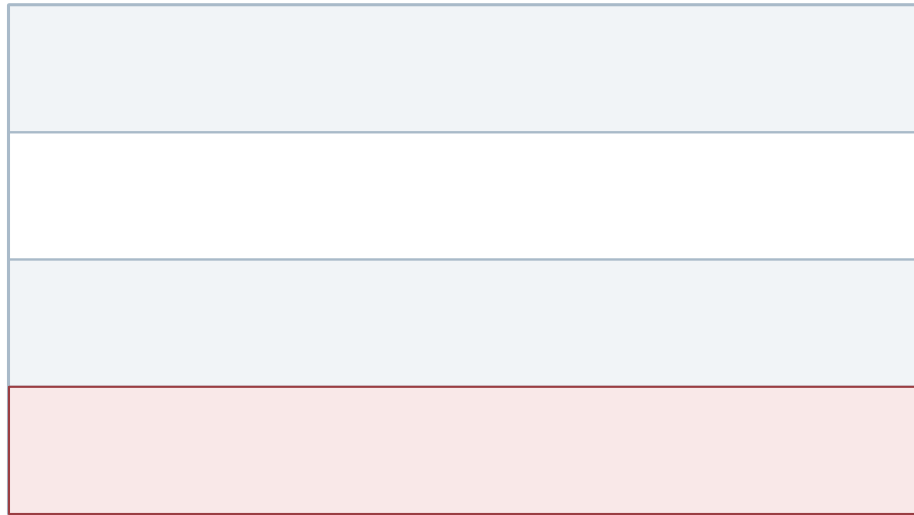
Endocardial surface lies at bottom

The subendocardium receives blood last and experiences greater intramural compressive pressure.

Necrosis advances as a wavefront

Schematic

Epicardial side



Later near-transmural zone

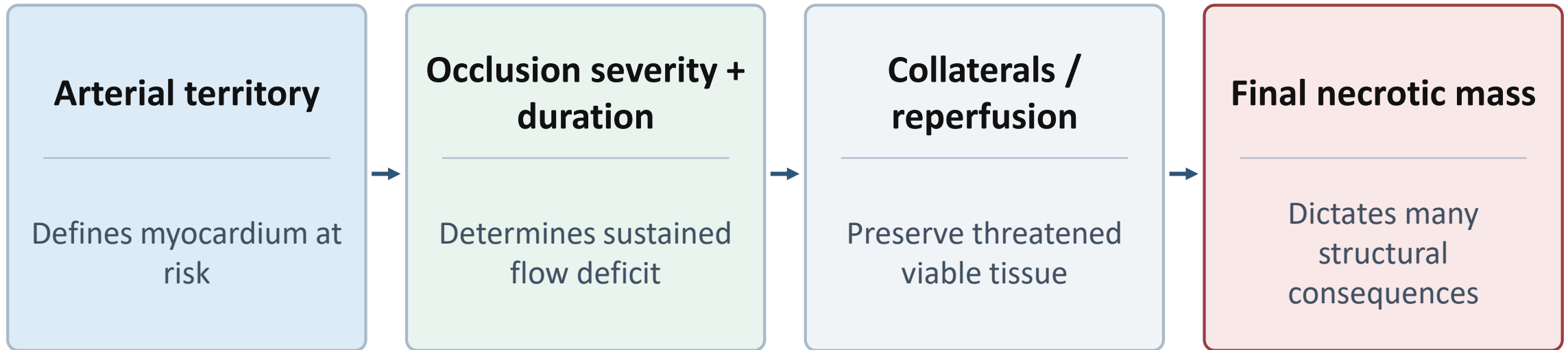
Endocardial side Early subendocardial zone

Early: Inner-wall injury

Prolonged severe ischemia: Necrosis extends toward epicardium within the supplied territory.

Area at risk is not identical to final infarct size

Schematic



Location, time, and flow determine infarct size

- Coronary anatomy establishes the perfusion zone and size of myocardium at risk.
- Obstruction site and severity modify residual tissue flow.
- Collateral channels and reperfusion can reduce completed necrosis.
- Heart rate, oxygenation, spasm, and metabolic demand further modify injury.

Transmural and subendocardial infarcts differ

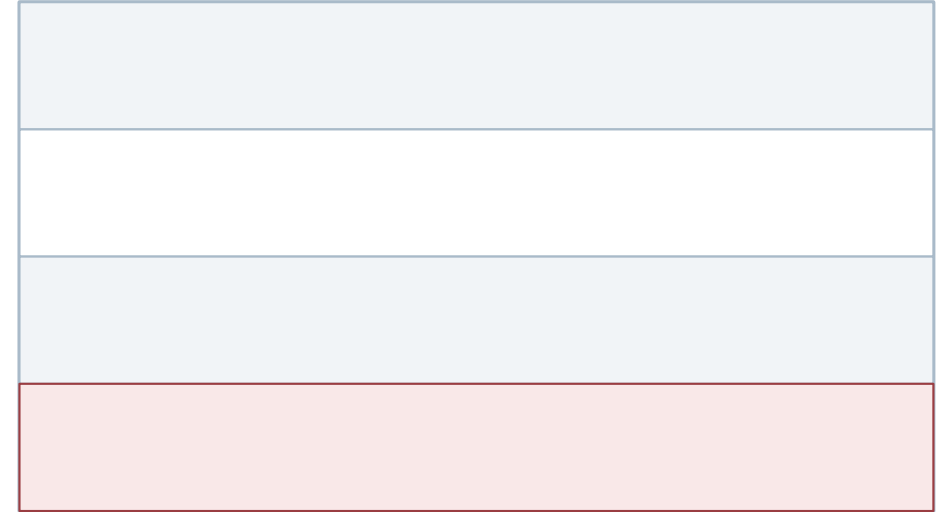
Schematic

Epicardial side



Endocardial side Transmural necrosis

Persistent epicardial occlusion may cause nearly full-thickness infarction.



Subendocardial necrosis

Partial/transient occlusion or global hypoperfusion may leave necrosis limited to the inner wall.

Subendocardial infarction can be circumferential

- Transient thrombotic occlusion may injure the inner portion of one coronary territory.
- Global hypotension superimposed on stenosis may produce a circumferential subendocardial pattern.
- Reperfusion before completion can limit the depth of necrosis.
- Thus, transmural extent and coronary territory do not always correspond one-to-one.

Small intramural vessel injury produces microinfarcts

- Microemboli, vasculitis, and vasospasm can obstruct small intramyocardial vessels.
- Injury is patchy and may not form a single large epicardial-territory infarct.
- Adrenergic stimulation can combine coronary constriction with increased oxygen demand.
- Interpret microinfarcts in the context of vascular pathology and systemic illness.

Regional infarcts reflect arterial supply

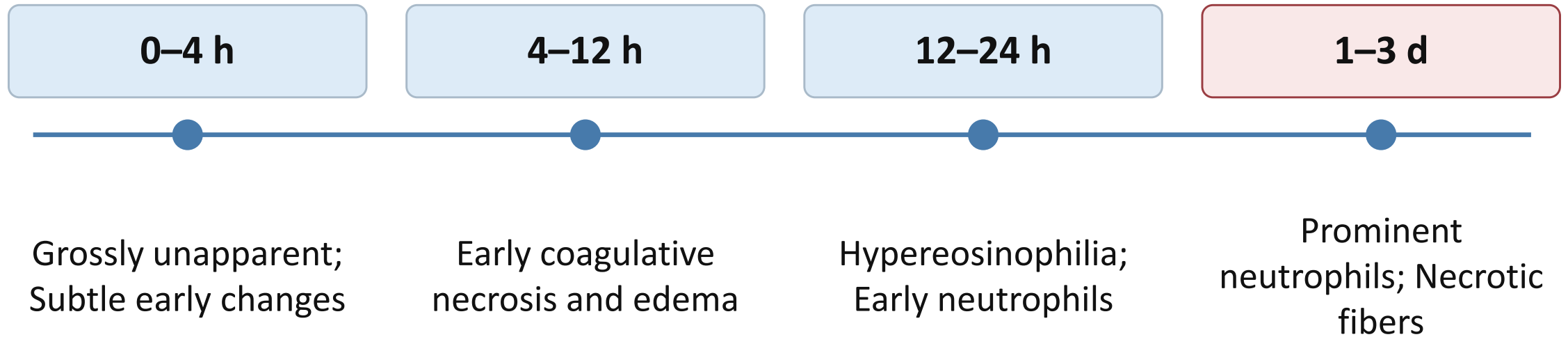
Occluded artery	Common myocardial pattern	Potential additional injury
LAD	Anterior left ventricular wall, apex, anterior septum	Extensive anteroapical injury
RCA (right dominance)	Inferior/posterior LV, posterior septum	Right ventricular involvement; Conduction disturbance
LCX	Lateral left ventricular wall	Posterolateral injury varies with dominance

The earliest infarct is grossly inconspicuous

- MI generally cannot be diagnosed from gross appearance in the first several hours.
- Triphenyl tetrazolium chloride staining can reveal loss of dehydrogenase activity after early necrosis.
- Viable myocardium stains red; Infarcted nonviable regions remain pale.
- Apparent absence of a gross infarct does not exclude fatal early ischemic injury.

Coagulative necrosis evolves over hours

Schematic



Wavy fibers mark early mechanical injury

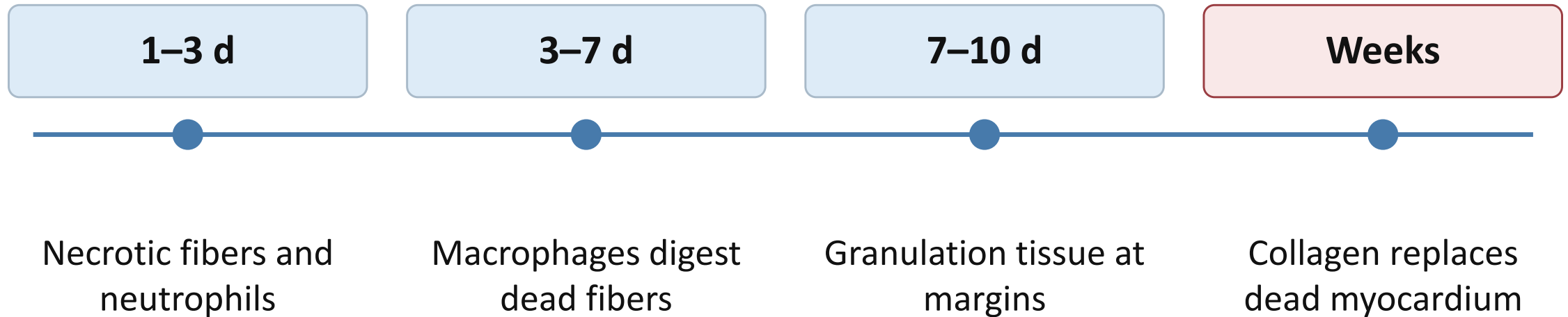
- Noncontractile necrotic fibers are stretched by adjacent viable contracting myocardium.
- At the infarct margin, fibers may appear narrowed and wavy.
- Edema separates injured myocardial fibers.
- The finding must be interpreted against postmortem interval and adjacent morphology.

Neutrophils dominate the early infarct

- Coagulative myocyte necrosis triggers an acute inflammatory response.
- Neutrophilic infiltration becomes prominent during the first several days.
- Inflammation clears injured tissue but contributes to transient tissue fragility.
- The cellular composition changes predictably as healing advances.

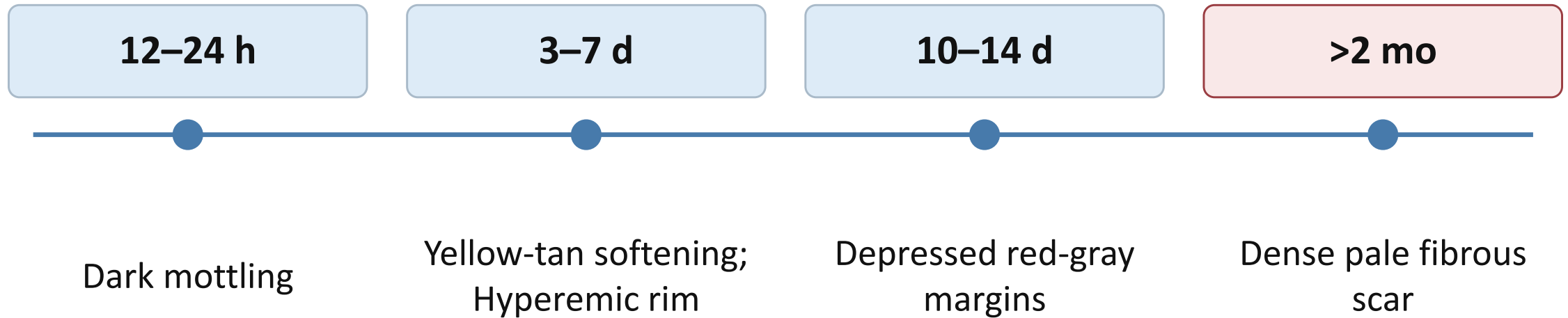
Macrophage clearance creates a vulnerable wall

Schematic



Gross healing changes from mottling to scar

Schematic



Granulation tissue replaces cleared necrosis

- Capillary ingrowth and fibroblast activity begin at the margins of necrotic tissue.
- Vascular granulation tissue forms a matrix for subsequent collagen deposition.
- Large infarcts heal from border toward center and may take longer to scar.
- Adult cardiomyocytes do not replace the lost contractile cell population by meaningful regeneration.

Old infarcts become mechanically distinct scar

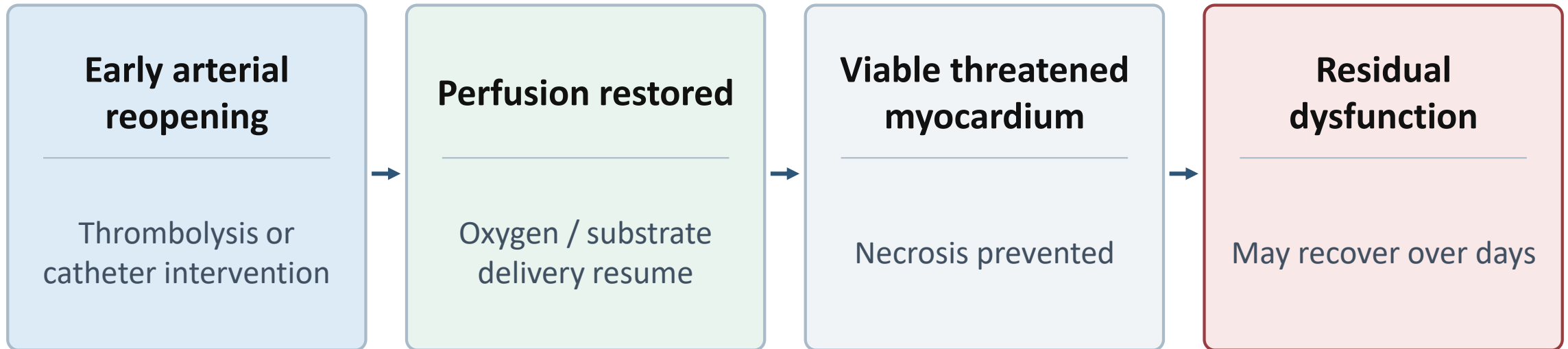
- Mature infarcts contain dense collagen replacing dead myocytes.
- Scar lacks normal force-generating properties and disrupts local conduction.
- Adjacent viable cardiomyocytes can become hypertrophic.
- The microscopic age of a fully healed scar cannot be determined reliably from appearance alone.

Morphologic dating is approximate

Time after infarction	Dominant expected finding
0.5–4 hours	Often minimal LM change; Possible wavy fibers
4–24 hours	Evolving coagulative necrosis and early neutrophils
1–3 days	Neutrophilic infiltrate
3–7 days	Macrophage removal; Tissue softening
7–14 days	Granulation tissue and beginning collagen
Weeks to months	Progressive fibrous scarring

Reperfusion salvages viable at-risk myocardium

Schematic

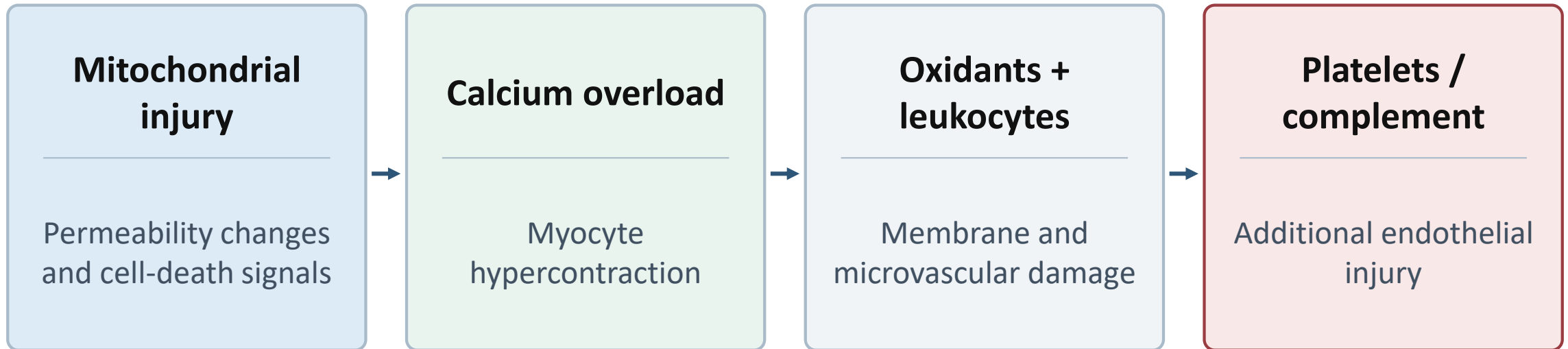


Successful reperfusion can alter morphology

- Reperfused infarcts are often hemorrhagic because previously injured microvessels leak.
- Myocytes already irreversibly injured may develop contraction band necrosis.
- Additional injury may involve reactive oxygen species, Ca^{2+} overload, and microvascular dysfunction.
- Clinical significance of reperfusion injury is an area of continuing investigation.

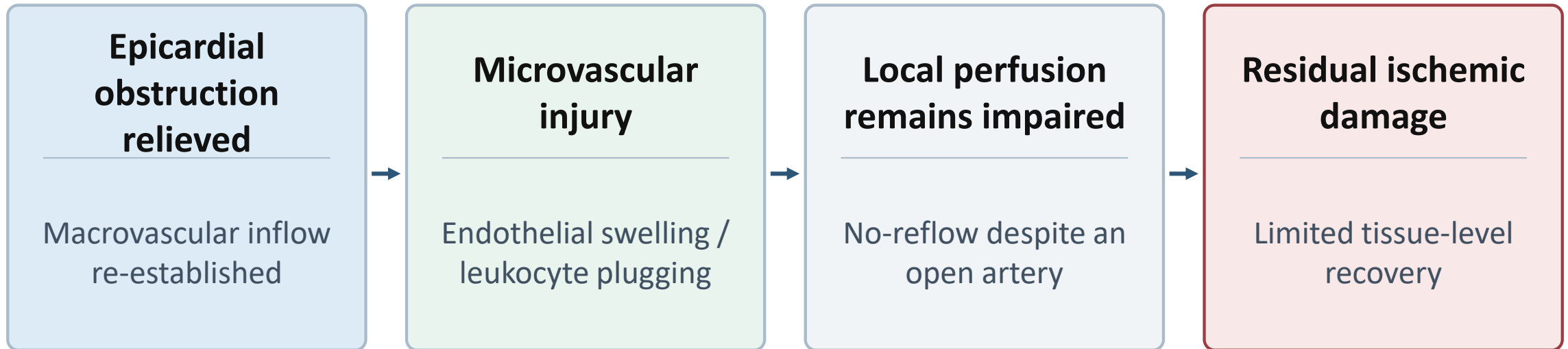
Reperfusion injury has several interacting causes

Schematic



No-reflow is a microvascular problem

Schematic



Stunning and hibernation are viable dysfunction

Stunned myocardium

Prolonged transient dysfunction after short ischemia/reperfusion

Viable cells with delayed contractile recovery

Typically improves after a recovery period

Not equivalent to infarct scar

Hibernating myocardium

Chronic downregulation under persistent sublethal ischemia

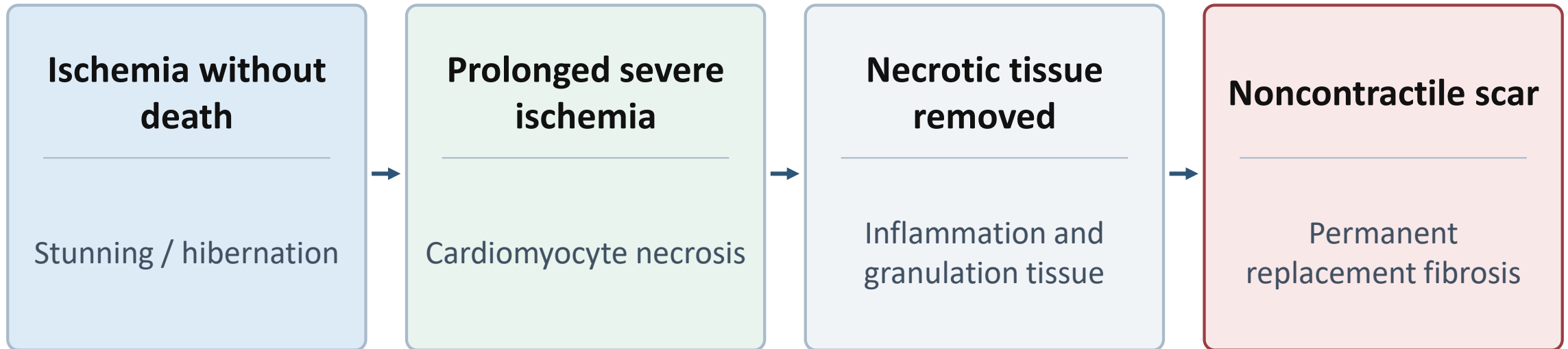
Viable but persistently low-function cells

Often improves after revascularization

Not equivalent to infarct scar

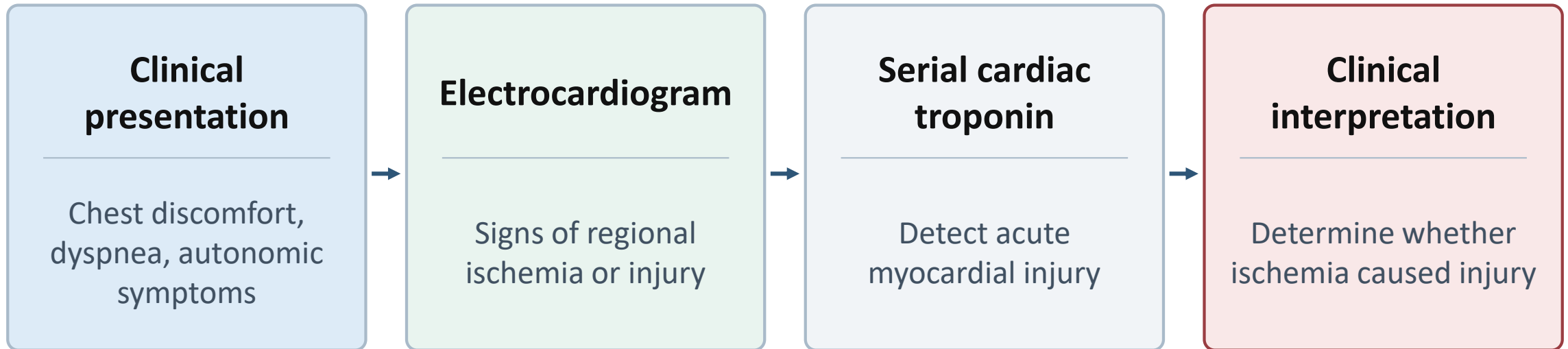
Reversible dysfunction must be separated from scar

Schematic



Acute MI diagnosis integrates different evidence

Schematic



Myocardial injury may occur without classic pain

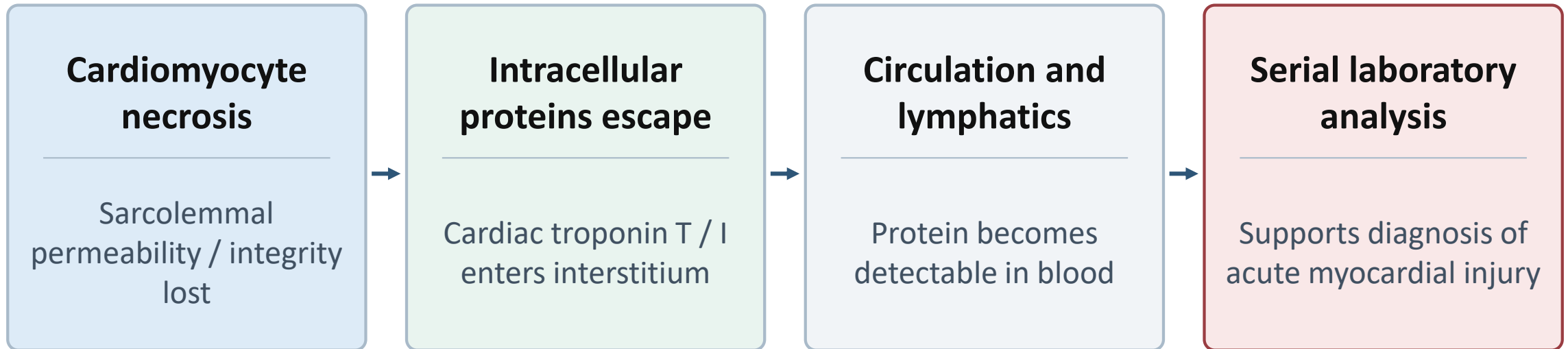
- Crushing or pressure-like prolonged chest discomfort is typical but not universal.
- Diaphoresis, nausea, vomiting, dyspnea, and weakness may accompany acute MI.
- Some patients have clinically silent or atypical presentations.
- Symptoms alone cannot establish the presence, extent, or mechanism of myocyte necrosis.

STEMI and NSTEMI are clinical ECG categories

- ST-elevation and non–ST-elevation MI describe electrocardiographic presentation.
- The ECG pattern reflects ischemic injury distribution and electrical manifestations.
- Many transmural infarcts with STEMI and many subendocardial infarcts with NSTEMI.
- Anatomical transmurality and ECG labels are not perfectly interchangeable in individual patients.

Troponin release requires membrane injury

Schematic



Troponin is a marker of injury, not etiology

- Cardiac troponins T and I are sensitive indicators of myocardial injury.
- An acute rising/falling pattern is interpreted with symptoms, ECG, and clinical context.
- Myocarditis and myocardial trauma can cause substantial troponin release.
- Heart failure, pulmonary embolism, sepsis, and renal disease may also show elevated troponin.

Case: Elevated troponin with systemic illness

Clinical vignette

A critically ill patient with sepsis has elevated cardiac troponin but no clear acute coronary symptoms or regional ECG changes.

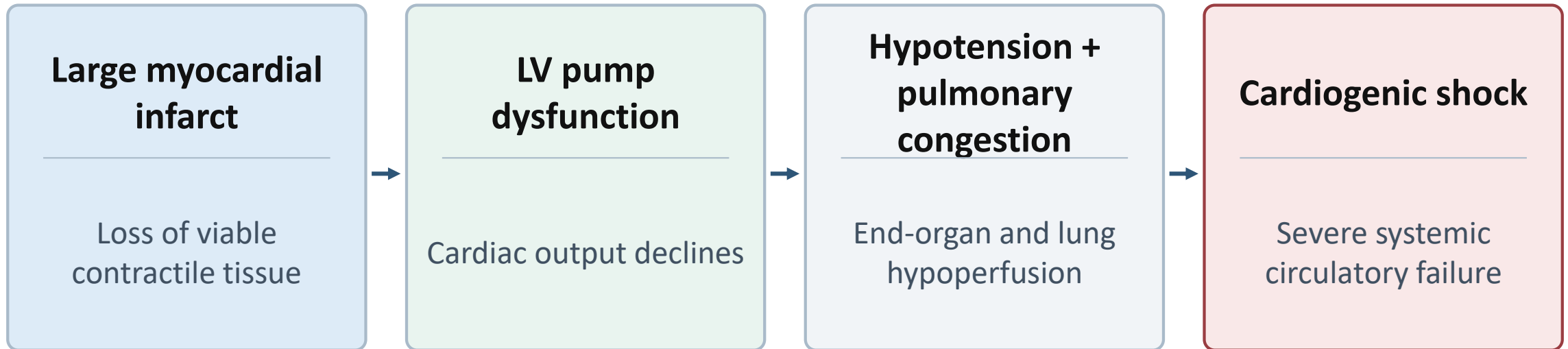
What should be concluded from the troponin result alone?

Postinfarction outcomes track injury extent

- Infarct size, location, and wall thickness predict complication patterns.
- Large transmural infarcts carry substantial risk of pump failure, arrhythmia, and structural complications.
- Residual LV function is an important determinant of prognosis.
- Stenoses supplying remaining viable myocardium influence long-term outcome.

Loss of contractile mass can cause shock

Schematic

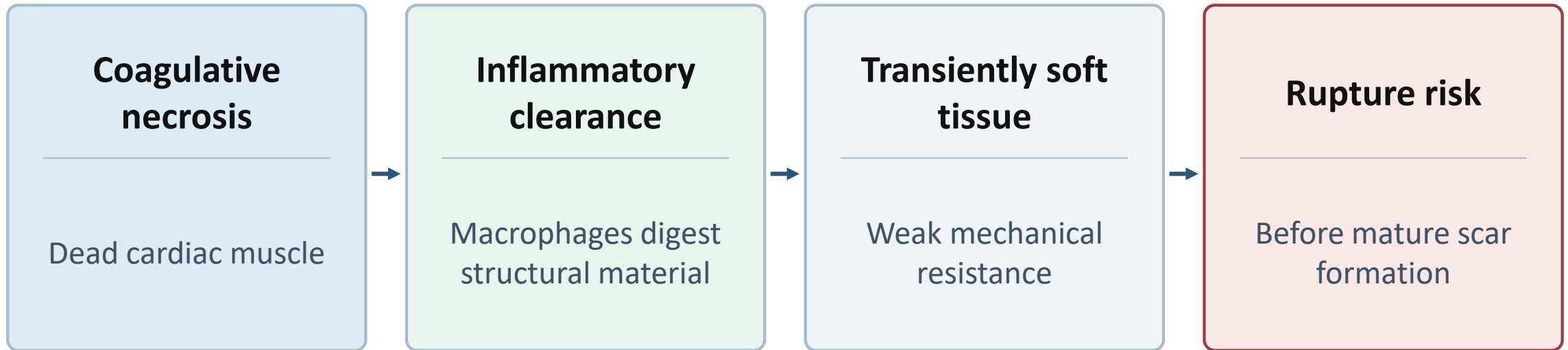


Rupture targets three distinct structures

Site of rupture	Immediate result	Clinical consequence
LV free wall	Blood enters pericardial space	Hemopericardium and tamponade
Ventricular septum	New interventricular communication	Acute left-to-right shunt
Papillary muscle	Acute loss of valve support	Severe mitral regurgitation

Days 3–7 are a major rupture-risk interval

Schematic



Ischemic papillary muscle dysfunction causes MR

- Ischemia or infarction can impair papillary muscle contraction without anatomic rupture.
- Complete rupture causes abrupt severe regurgitation.
- Later ventricular dilation or papillary scarring also alters mitral geometry.
- Clinical severity depends on the mechanism and timing of valve incompetence.

Arrhythmia may be the earliest fatal event

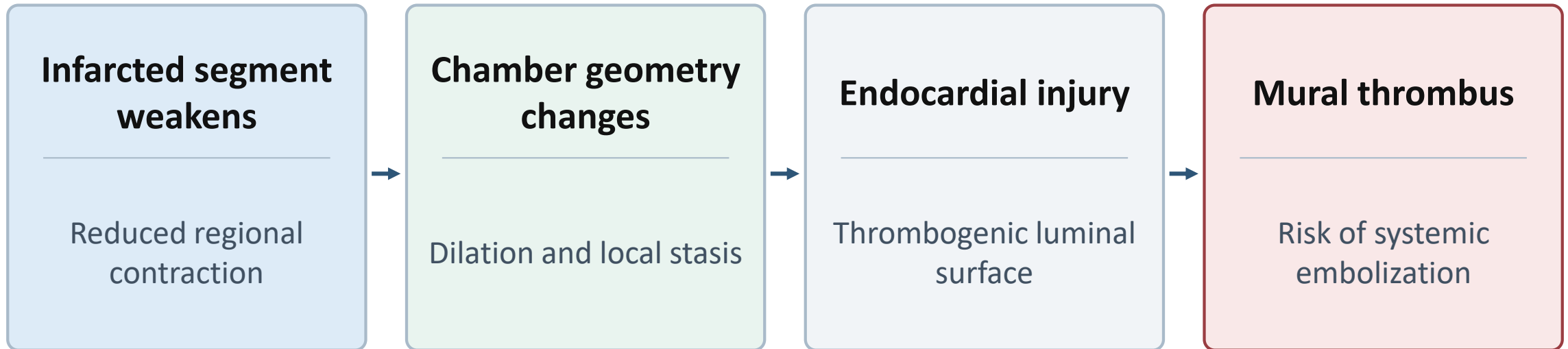
- Acute ischemia and infarction create heterogeneous electrical conduction and irritability.
- Potential disturbances include conduction block, ectopy, ventricular tachycardia, and fibrillation.
- Risk of malignant rhythm disturbance is particularly high soon after symptom onset.
- Electrical death can precede grossly or biochemically apparent infarction.

Infarction can inflame the overlying pericardium

- Transmural injury may induce fibrinous or fibrinohemorrhagic pericarditis.
- Early post-MI pericarditis may develop within a few days.
- Later immune-mediated postinfarction pericarditis is described as Dressler syndrome.
- These phenomena differ from free-wall rupture with hemopericardium and tamponade.

Mural thrombus arises from stasis and injury

Schematic



Infarct expansion and ventricular aneurysm

Early infarct expansion

Stretching and thinning of necrotic wall

May worsen wall stress and dilation

Occurs before stable collagen scar

Structural weakness raises concern for rupture

Late true ventricular aneurysm

Outpouching formed by scarred ventricular wall

Associated with mural thrombus, arrhythmia, and failure

Usually follows a large transmural infarct

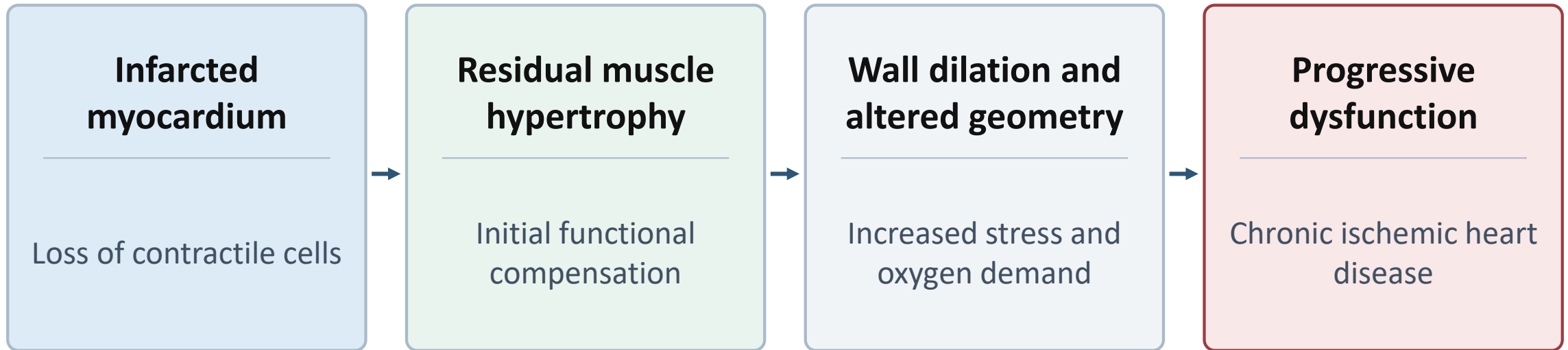
Scarred true aneurysm typically does not rupture

Mechanical complications depend on infarct depth

More often with transmural injury	Less characteristic of limited subendocardial injury
Pericardial inflammation	Epicardial surface usually spared
Free-wall or septal rupture	Wall retains more full-thickness myocardium
Scarred ventricular aneurysm	Less extensive full-wall scar substrate
Marked chamber dysfunction	May still occur if ischemic burden is large

Ventricular remodeling links MI to chronic failure

Schematic



Chronic IHD reflects accumulated injury

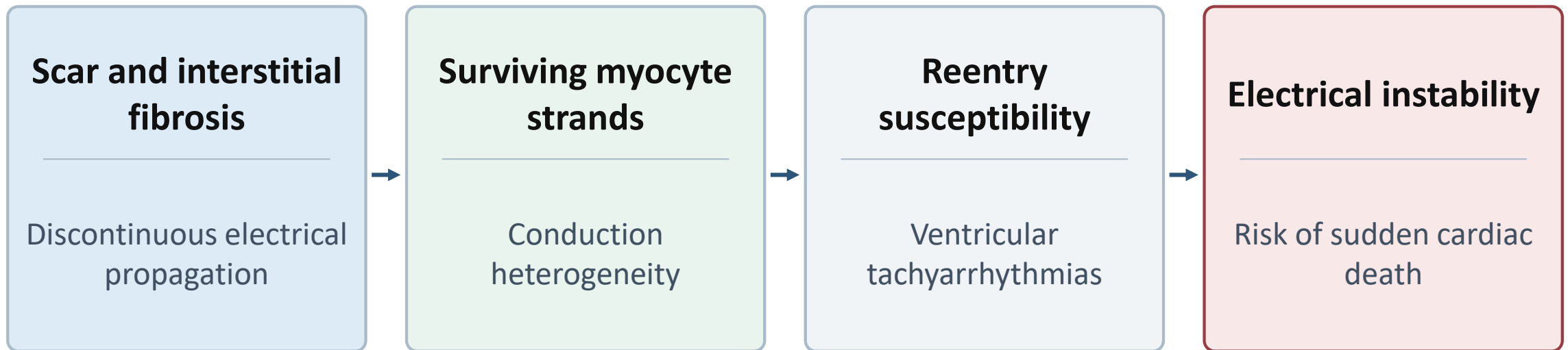
- Chronic ischemic heart disease denotes progressive cardiac failure from prior infarction and/or ongoing inadequate perfusion.
- Decompensation of hypertrophied viable myocardium compounds earlier ischemic loss.
- Some patients develop heart failure with severe CAD but without a recognized prior MI.
- Coronary obstruction and ventricular remodeling act together.

Chronic IHD has a characteristic pathology

Gross morphology	Microscopic morphology
Cardiomegaly; LV hypertrophy and dilation	Hypertrophied remaining cardiomyocytes
Stenotic epicardial atherosclerosis	Interstitial and replacement fibrosis
Discrete healed infarct scars	Subendocardial myocyte vacuolization
Endocardial fibrous thickening ± mural thrombi	Mixed chronic ischemic and remodeling changes

Chronic ischemia is also an electrical substrate

Schematic



Sudden cardiac death is usually arrhythmic

- SCD as unexpected cardiac death soon after symptom onset or after being last seen well.
- Ventricular fibrillation and other fatal rhythm disturbances are the common mechanism.
- Coronary artery disease is the leading underlying cause.
- SCD may be the first clinical manifestation of IHD.

Sudden death need not follow a completed MI

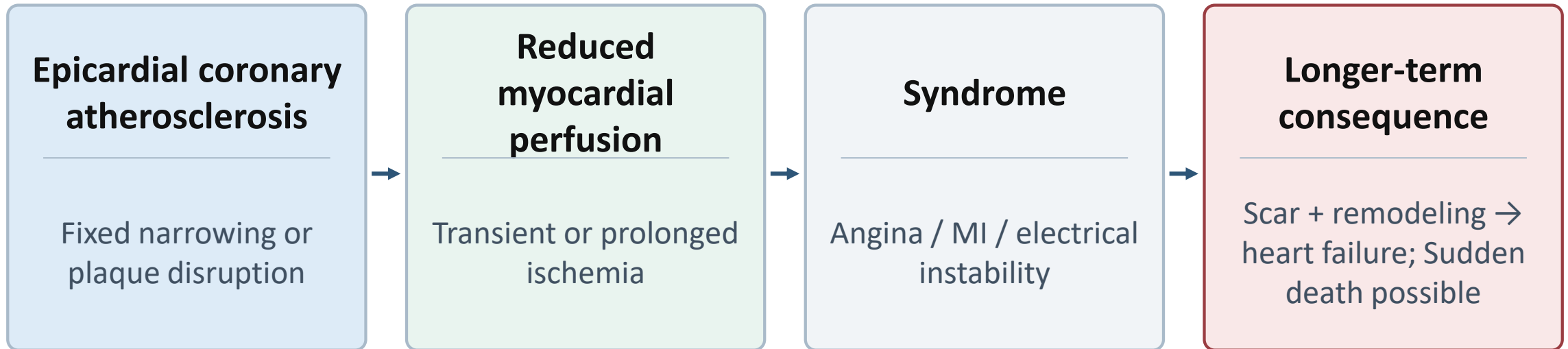
- Severe fixed CAD can trigger fatal ischemic arrhythmia without a new thrombosis.
- An acute plaque disruption is not demonstrable in every coronary-related sudden death.
- Old infarct scars can provide reentrant electrical pathways.
- At autopsy, absence of an acute infarct does not exclude ischemic arrhythmic death.

Consider other causes of sudden death in younger patients

Category	Examples listed by Robbins
Electrical disease	Inherited / acquired conduction disease and channelopathies
Structural myocardial disease	Hypertrophic or dilated cardiomyopathy; Myocarditis
Congenital abnormality	Anomalous coronary origins / courses
Other cardiac and systemic processes	Mitral valve prolapse, pulmonary hypertension, embolism, stimulant use

An integrated causal map of IHD

Schematic



Case: Collapse after brief chest discomfort

Clinical vignette

A patient with advanced coronary atherosclerosis collapses unexpectedly after brief chest discomfort. No established acute myocardial necrosis is found.

Which mechanism must remain high on the differential?

Five pathology principles to retain

- Coronary oxygen supply must be evaluated relative to myocardial demand.
- Fixed stenosis predicts exertional ischemia; Acute plaque thrombosis predicts abrupt coronary syndromes.
- Early severe ischemia causes rapid dysfunction; Irreversible necrosis requires sustained flow deprivation.
- Myocyte necrosis is followed by inflammation, granulation tissue, and permanent collagen scar.
- Infarct complications and chronic sequelae follow from lost muscle, mechanical fragility, fibrosis, and electrical instability.

Primary reference and scope

Primary course source

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 12: The Heart, pp. 492–504.
- Primary project transcript: robbins.md, chapter section “Ischemic Heart Disease” and adjacent subsections.
- This lecture includes the parent disease section and directly related manifestations through sudden cardiac death.