

Myocardial Infarction

Mechanisms · Morphologic evolution · Clinical consequences

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Learning outcomes

- Trace atherothrombosis to ischemic myocyte necrosis.
- Distinguish transmural, subendocardial, and microinfarct patterns.
- Interpret the chronology of myocardial injury and repair.
- Relate troponin, reperfusion, and complications to pathology.

Myocardial infarction: Definition

- Death of cardiac muscle due to prolonged ischemia.
- Most commonly arises in the setting of coronary atherosclerosis.
- The extent of injury reflects the severity and duration of impaired perfusion.

Myocardial ischemia is not synonymous with irreversible myocardial infarction.

Atherosclerotic context and susceptibility

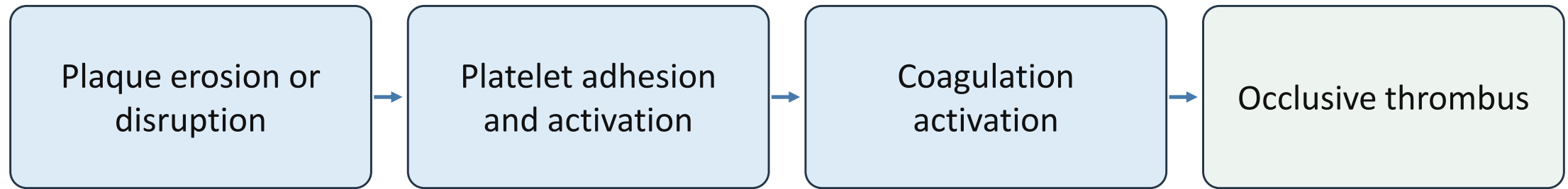
- Myocardial infarction becomes more frequent with increasing age.
- Risk increases with the burden of atherosclerotic risk factors.
- Male sex carries higher relative risk through middle age.
- Coronary disease becomes increasingly important after menopause.

Postmenopausal risk: A source-specific caution

- The postmenopausal transition is associated with worsened coronary risk.
- Hormone replacement therapy has not demonstrated protection against MI.
- The source notes possible harm in some contexts, including prothrombotic effects.

Risk modification is not equivalent to hormonal replacement as coronary prevention.

Typical pathogenesis: Coronary atherothrombosis

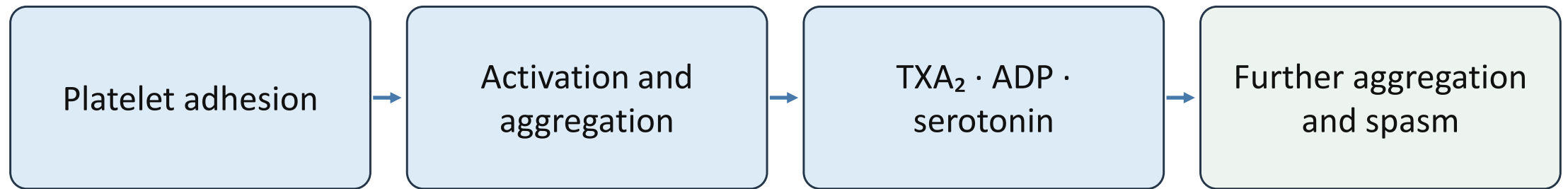


A rapidly evolving thrombus may completely obstruct the coronary lumen within minutes.

Plaque injury exposes thrombogenic material

- Endothelial injury, intraplaque hemorrhage, or mechanical forces destabilize the lesion.
- Subendothelial collagen and necrotic plaque contents contact circulating blood.
- The exposed material initiates platelet and coagulation responses.

Platelet amplification and vasospasm



Platelet mediators reinforce both thrombus growth and vasoconstriction.

Coagulation consolidates coronary occlusion

- Tissue factor and additional mechanisms activate the coagulation cascade.
- Fibrin-rich coagulation is superimposed on platelet aggregates.
- A coronary lumen can become fully occluded within minutes.

A plaque need not have produced a critical fixed stenosis before acute rupture.

Thrombus detection changes with time

Angiography after MI	Observed coronary thrombosis	Interpretation
Within 4 hours	Almost 90% of cases	High detection early after onset
12–24 hours	About 60% of patients	Spontaneous lysis or spasm resolution may occur

Why early reperfusion can salvage myocardium

- Some early coronary occlusions are thrombotic and potentially reversible.
- Spontaneous clearing may occur, but prolonged ischemia progressively kills myocytes.
- Thrombolysis or angioplasty can limit infarct size when performed early.

Reopening a vessel has maximal benefit while downstream muscle remains viable.

Infarction without typical atherothrombosis

- The source attributes approximately 10% of MIs to other mechanisms.
- Reduced flow may reflect coronary vasospasm or embolism.
- Small-vessel disease, dissection, systemic hypotension, and major hypertrophy are other causes.

Coronary vasospasm as a mechanism

- Transient severe constriction may occur with or without atherosclerosis.
- Cocaine or ephedrine exposure is cited as a potential trigger.
- Catecholamines also increase heart rate and contractility, increasing oxygen requirements.

Spasm can impair supply while adrenergic stimulation increases demand.

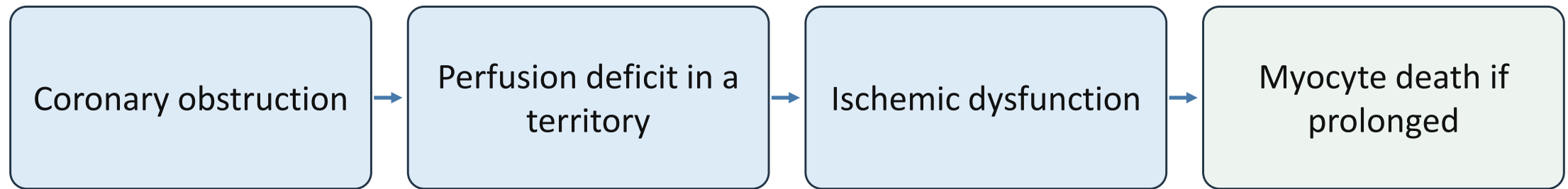
Coronary emboli: Potential origins

- Left atrial mural thrombi associated with atrial fibrillation.
- Infective endocarditis vegetations or intracardiac prosthetic material.
- Right-sided or venous emboli crossing a patent foramen ovale.

Other routes to ischemic necrosis

- Small intramural vascular disease, such as vasculitis or amyloid deposition.
- Sickle cell disease and coronary vascular dissection.
- Severe ventricular hypertrophy or profound systemic hypotension.
- Inadequate myocardial protection during cardiac surgery.

Area at risk: From arterial flow loss to necrosis



The perfusion territory downstream of the culprit artery is the “area at risk.”

Ischemia rapidly disrupts energetics

- Aerobic metabolism ceases within seconds of severe ischemia.
- Creatine phosphate and ATP production become inadequate.
- Lactate and potentially injurious metabolites accumulate.
- Mechanical contractility fails before necrosis becomes established.

Contractile failure precedes cell death

- Severely ischemic myocardium may cease contracting within about one minute.
- Early systolic dysfunction can arise while myocytes remain viable.
- This disconnect is central to the opportunity for myocardial salvage.

Loss of function is an early physiologic event, not proof of irreversible injury.

Reversible early ultrastructural injury

- Myofibrillar relaxation accompanies loss of mechanical function.
- Glycogen stores are depleted during ischemia.
- Cellular and mitochondrial swelling develop within minutes.
- These earliest changes may still reverse after blood flow is restored.

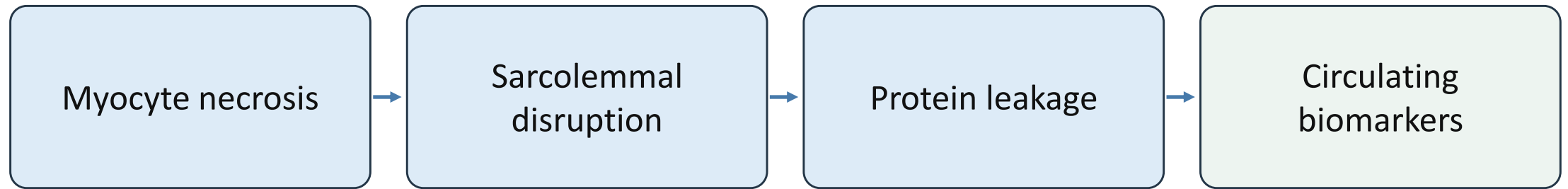
Approximate onset of ischemic events

Event	Approximate time after severe ischemia
ATP depletion begins	Seconds
Contractile function lost	Less than 2 minutes
ATP falls to 50%	10 minutes
ATP falls to 10%	40 minutes
Irreversible cell injury	20–40 minutes
Microvascular injury	More than 1 hour

Duration determines irreversibility

- Severe flow reduction to 10% or less of normal can cause necrosis after 20–30 minutes or longer.
- Loss of viability progresses across the jeopardized muscle after that threshold.
- Infarct extent is usually complete by 6–12 hours without effective salvage.

Cell membrane failure creates blood biomarkers



Biomarker release requires loss of membrane integrity in injured myocytes.

Microvascular injury develops later

- Myocytes are affected before substantial microvascular injury.
- Prolonged ischemia and reperfusion can injure the microcirculation.
- Microvascular damage can prevent effective tissue-level reperfusion even if the main artery reopens.

Why the subendocardium dies first

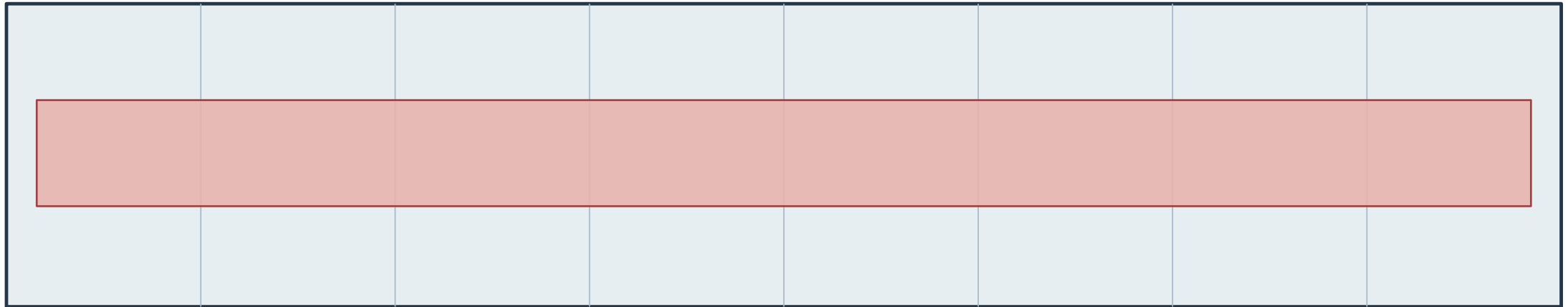
- Subendocardial tissue lies farthest along the flow path from epicardial coronary arteries.
- Higher intramural pressures impede perfusion of the inner myocardium.
- Ischemic cell death therefore starts near the endocardial surface.

Subendocardial vulnerability reflects both perfusion geometry and tissue pressure.

Wavefront necrosis can become transmural

Subendocardium

Epicardium



Schematic: Left-to-right indicates wall depth; Vertically separated areas represent distinct myocardial regions.

The conceptual wall is shown after prolonged complete ischemia; Near-complete thickness involvement.

Infarct extent has multiple determinants

- Severity, location, and speed of developing coronary obstruction.
- Duration of occlusion and size of the supplied vascular bed.
- Metabolic demand, oxygenation, heart rate, and rhythm.
- Coronary collaterals and coexisting vasospasm.

Collateral vessels may limit tissue loss

- Intercoronary anastomoses are present in many hearts.
- Slow progressive stenosis creates pressure gradients that increase collateral flow.
- Collateral enlargement can preserve tissue otherwise deprived of adequate perfusion.

Coronary collateralization modifies the same arterial occlusion's tissue impact.

Major coronary perfusion territories

Artery	Typical myocardium supplied
LAD	Apex, anterior LV wall, anterior two-thirds of septum
RCA (right dominant heart)	RV free wall, posterobasal LV wall, posterior third of septum
LCX	Lateral LV wall, usually sparing apex

Coronary dominance describes septal supply

- Dominance is assigned by which artery supplies the posterior third of the septum.
- Right coronary dominance is present in approximately 80% of individuals in this source.
- RCA occlusion in a right-dominant heart may also damage the left ventricle.

“Dominant” does not mean the artery supplies most LV myocardium.

LAD infarctions: Principal territory

- The LAD is implicated in approximately 40%–50% of infarcts in the source.
- Affected areas: Anterior LV near the apex and anterior ventricular septum.
- The cardiac apex may be involved circumferentially.

RCA infarctions: Principal territory

- The RCA is implicated in approximately 30%–40% of infarcts in the source.
- Affected areas: Inferior/posterior LV wall and posterior septum.
- The adjacent right ventricular free wall can also be affected.

LCX infarctions: Principal territory

- The LCX is implicated in approximately 15%–20% of infarcts in the source.
- Its characteristic territory is the lateral left ventricular wall.
- The apex is ordinarily spared in this typical distribution.

Three principal patterns of myocardial necrosis

Transmural

Near full-thickness wall necrosis

Typical sustained epicardial occlusion

Coronary territorial pattern

Subendocardial

Inner wall involvement

Transient or partial flow loss

Can follow global hypotension

Microinfarction

Focal injury in small areas

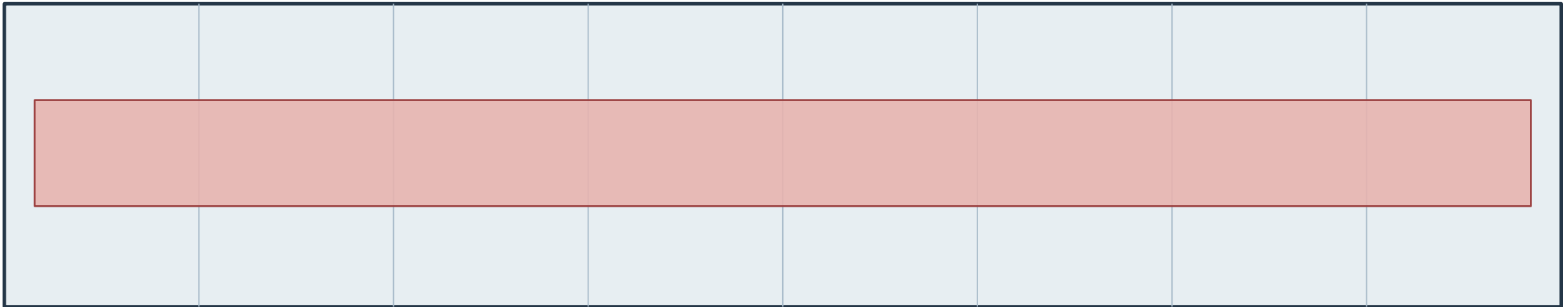
Intramural vascular pathology

Microemboli, spasm, vasculitis

Transmural necrosis: Full wall-depth pattern

Subendocardium

Epicardium



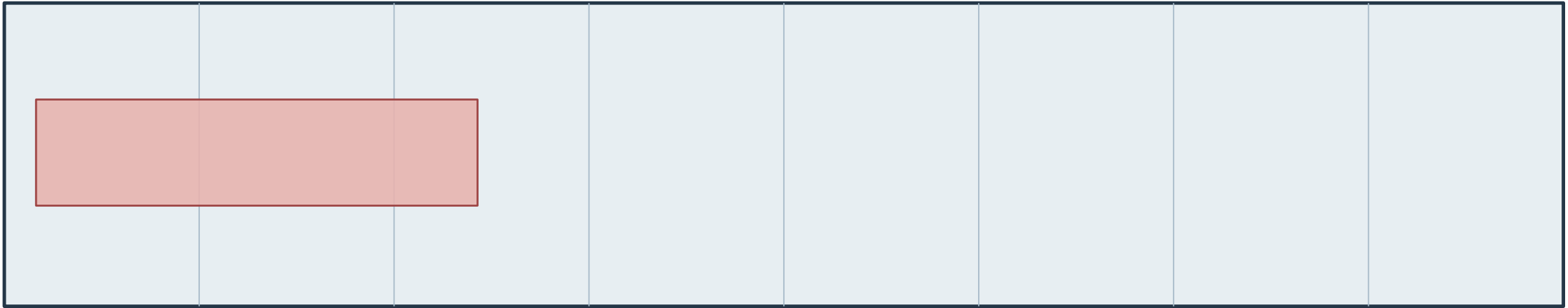
Schematic: Left-to-right indicates wall depth; Vertically separated areas represent distinct myocardial regions.

A sustained epicardial coronary occlusion may injure nearly the full ventricular wall.

Regional subendocardial necrosis

Subendocardium

Epicardium



Schematic: Left-to-right indicates wall depth; Vertically separated areas represent distinct myocardial regions.

Early thrombus lysis or restoration of flow can spare outer myocardium.

Circumferential subendocardial necrosis

Subendocardium

Epicardium



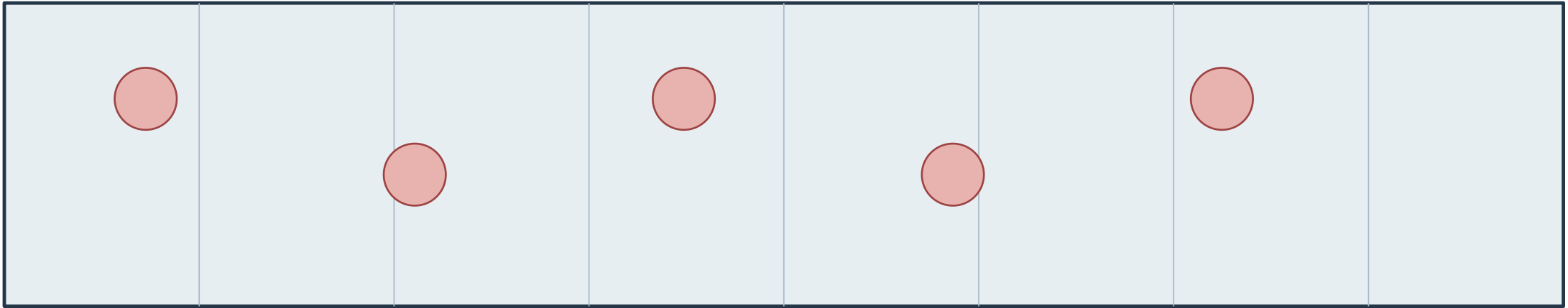
Schematic: Left-to-right indicates wall depth; Vertically separated areas represent distinct myocardial regions.

Systemic hypotension with underlying stenoses can affect the inner myocardium widely.

Multifocal microinfarction

Subendocardium

Epicardium



Schematic: Left-to-right indicates wall depth; Vertically separated areas represent distinct myocardial regions.

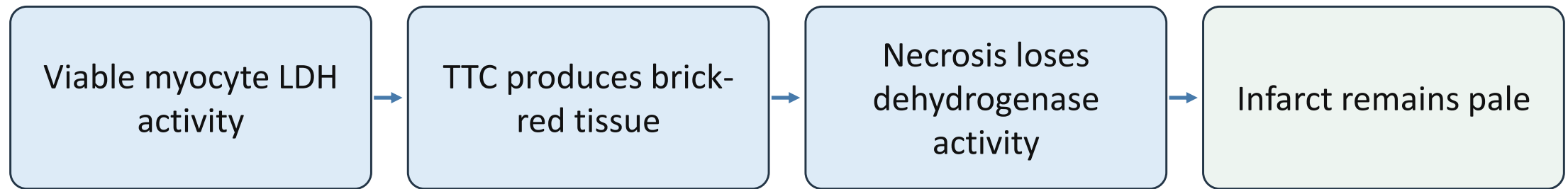
Scattered microinfarcts reflect small intramural vessel injury or obstruction.

Pathologic aging requires elapsed time

- Gross and histologic appearances evolve after the acute event.
- Very early infarcts can escape gross recognition.
- The appearance reflects ischemic necrosis, inflammation, clearance, and scar formation.

A normal-looking early gross specimen does not exclude acute myocardial infarction.

Triphenyl tetrazolium chloride highlights necrosis



This is the source-described histochemical principle—not a reproduced pathology specimen.

Early gross change is subtle

- Infarcts younger than 12 hours are often not visible grossly.
- A 2–3-hour-old area of necrosis may be detected using TTC staining.
- At 12–24 hours, reddish-blue mottling may become apparent.

Gross appearance evolves during repair

- At 3–7 days: Hyperemic margin around a softening yellow-tan center.
- At 7–10 days: Maximal softness and a depressed red-tan border.
- During subsequent weeks: Progressive gray-white scar formation.

Coagulative necrosis is the dominant injury

- Irreversible ischemic injury predominantly causes coagulative necrosis.
- Loss of nuclei and striations accompanies progressive myocyte death.
- Some apoptosis may also occur.

The morphologic sequence reflects necrosis followed by inflammation and replacement repair.

Early wavy fibers: A mechanical explanation

- Necrotic fibers lose active contraction and resist normal force generation.
- Adjacent viable myocardium continues to contract.
- Dead fibers may be stretched and buckled, producing a wavy appearance.

First day: Early microscopic evolution

- Within 0.5–4 hours, light microscopy is often unrevealing.
- By 4–12 hours, edema, hemorrhage, and early coagulative necrosis may be seen.
- At 12–24 hours, hypereosinophilia, nuclear pyknosis, and early neutrophils appear.

Days 1–3: Neutrophilic inflammation

- Coagulative necrosis becomes prominent, with loss of myocyte nuclei and striations.
- A brisk interstitial neutrophilic infiltrate accompanies acute tissue injury.
- This is an inflammatory response to necrotic myocardium.

Days 3–7: Macrophage clearance

- Dead fibers begin to disintegrate and neutrophils die.
- Macrophages phagocytose necrotic cells, especially from the infarct margins.
- Developing granulation tissue produces a hyperemic peripheral zone.

Days 7–14: Granulation tissue

- Macrophage phagocytosis becomes well established.
- New blood vessels and loose collagen appear at the infarct margins.
- Collagen accumulation prepares the site for fibrous replacement.

Weeks to months: Scar maturation

- Between 2 and 8 weeks, collagen increases while cellularity falls.
- After approximately two months, a dense collagenous scar is complete in the source table.
- Once healed, histology cannot reliably date a scar as weeks versus years old.

Morphology timeline: Acute injury to scar

Interval	Predominant microscopic finding	Typical gross appearance
0.5–4 h	Usually none; possible wavy border fibers	None
4–24 h	Early coagulative necrosis; edema; early neutrophils	Mottling may appear
1–3 d	Necrosis and brisk neutrophils	Yellow-tan center begins
3–7 d	Macrophages; early granulation tissue	Soft center, hyperemic rim
7–14 d	Phagocytosis and vascular granulation tissue	Depressed margins
2–8 wk and later	Progressive collagen to dense scar	Gray-white scar

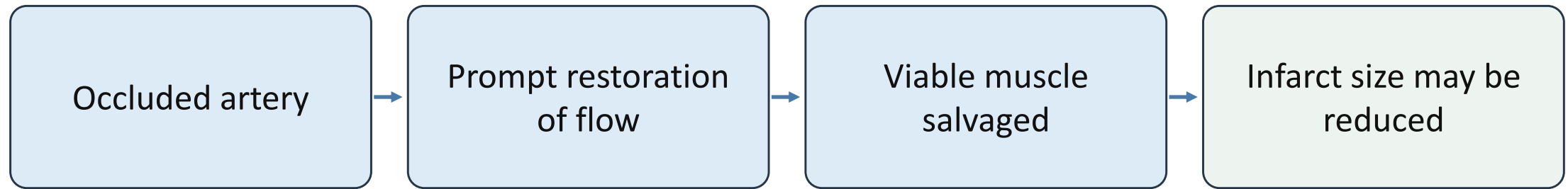
Why healing proceeds from the border

- Inflammatory cells and ingrowing vessels enter from surviving tissue margins.
- Granulation tissue moves inward toward the necrotic core.
- Large infarcts may require longer repair than smaller lesions.
- Malnutrition, poor vascularity, and anti-inflammatory steroids can impair healing.

Infarct repair does not regenerate cardiac muscle

- Adult cardiomyocytes are terminally differentiated in the source's account.
- The injured zone is replaced by granulation tissue and collagenous scar.
- Residual myocardium may hypertrophy, but the necrotic area does not regain myocyte mass.

Reperfusion: Tissue salvage and its limits



Earlier perfusion restoration generally preserves more myocardium at risk.

Pathways to restoring coronary flow

- Thrombolysis dissolves an obstructing clot.
- Angioplasty restores coronary arterial lumen patency.
- Coronary artery bypass grafting can provide an alternative path for perfusion.

These are methods named by the Robbins source, not a treatment-selection guideline.

Persistent occlusion versus reperfusion

Persistent occlusion

Loss of contraction precedes necrosis

Progressive loss of at-risk viability

Extensive tissue death if prolonged

Early reperfusion

Some ischemic myocardium survives

Reperfusion injury can coexist

Functional recovery may be delayed

Reperfusion injury: Mechanisms

- Mitochondrial injury and membrane permeability alterations.
- Calcium-related hypercontracture of myocytes.
- Reactive oxygen and nitrogen species injury.
- Leukocyte, platelet, and complement-mediated microvascular injury.

Mitochondrial injury after flow restoration

- Ischemia can alter mitochondrial membrane permeability.
- Mitochondrial swelling and outer-membrane rupture may release pro-apoptotic contents.
- This can add cell injury in tissue exposed to reperfusion.

Calcium drives contraction-band damage

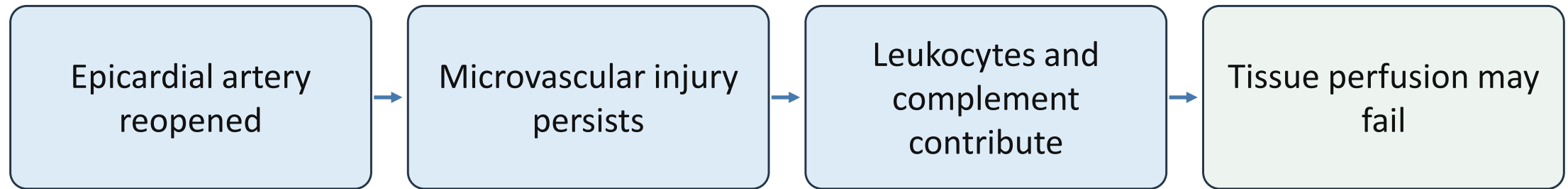
- Ischemia impairs calcium cycling and damages sarcolemmal integrity.
- Restored perfusion can intensify uncontrolled actin–myosin contraction.
- Hypercontracted sarcomeres become visible as eosinophilic contraction bands.

Contraction-band necrosis is a pathologic consequence of severe calcium dysregulation.

Reactive species exacerbate injury

- Superoxide, hydrogen peroxide, and hydroxyl radicals are cited among reactive species.
- Peroxynitrite and hypochlorous acid are also noted by the source.
- Oxidative reactions damage membrane proteins and phospholipids.

No-reflow: Vessel open, tissue still ischemic



“No reflow” refers to failure of microvascular tissue reperfusion despite removal of the main obstruction.

Reperfused infarcts may be hemorrhagic

- Microvascular damage increases vascular leakiness.
- Reperfused infarcted tissue often contains hemorrhage.
- Irreversibly injured cells may exhibit contraction-band necrosis.

Reperfusion changes the appearance of injury; It does not reverse already necrotic myocardium.

Myocardial stunning versus hibernation

Stunned myocardium

After brief ischemia and reperfusion

Contractile dysfunction persists temporarily

Usually recovers over days

Hibernating myocardium

Due to chronic sublethal ischemia

Metabolism and function downregulated

May recover after revascularization

Classical clinical presentation

- Prolonged chest pain, often described as crushing, stabbing, or squeezing.
- A rapid, weak pulse and diaphoresis may accompany the episode.
- Nausea and vomiting can be associated with posterior-inferior infarction.
- Dyspnea may reflect pulmonary congestion due to impaired contractility.

An infarction may be clinically silent

- The source reports up to one quarter of patients as initially asymptomatic.
- Diabetic neuropathy is given as one possible setting.
- The infarction may only be recognized through ECG findings or biochemical evidence.

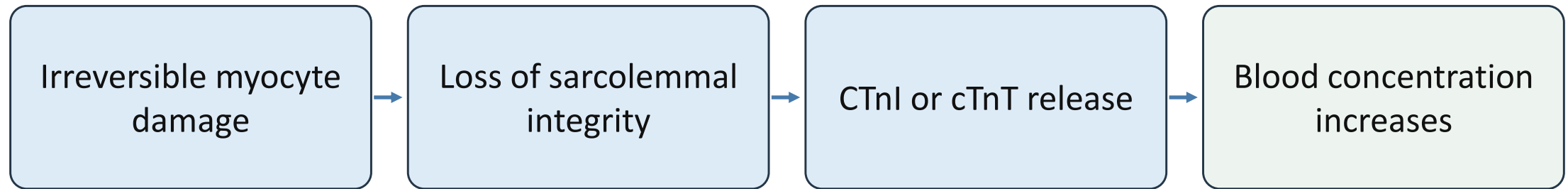
Absence of typical pain does not exclude myocardial injury.

ECG patterns do not simply equal wall anatomy

- The source links typical transmural injury with ST-elevation MI terminology.
- Subendocardial infarction is often described with non–ST-elevation terminology.
- Smaller or differently located infarcts can show nonspecific or absent ECG changes.

These are textbook associations—not a rule that ECG alone proves transmural histology.

Cardiac troponin becomes a circulating signal



Troponins detect myocardial injury; The cause requires clinical interpretation.

Troponin timing after MI

- Cardiac troponin I or T begins rising about 2–4 hours after infarction.
- Levels typically peak at 24–48 hours and stay elevated for 7–10 days.
- Reperfusion can produce an earlier, higher peak by accelerating washout.

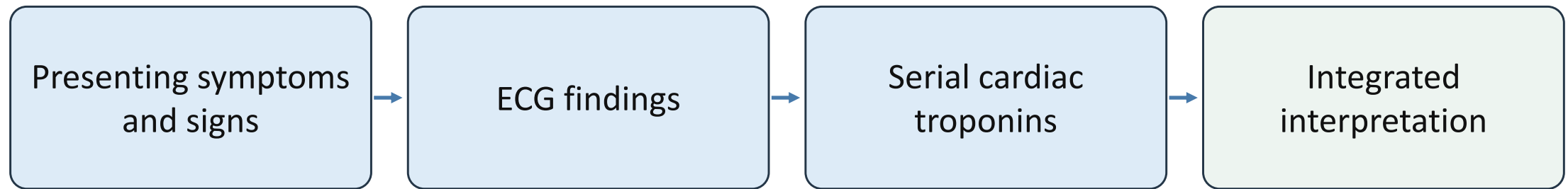
Source-reported kinetics depend on tissue injury, perfusion, drainage, and clearance.

Troponin elevation is not etiologically specific

- Myocarditis or myocardial trauma can also cause marked acute troponin elevation.
- Low-level elevation is reported with heart failure, pulmonary embolism, renal failure, and sepsis.
- Serial measurements and the entire presentation help distinguish etiologies.

Troponin above a threshold establishes myocardial injury—not its mechanism by itself.

The pathology-based diagnostic framework



The source describes diagnosis as a synthesis of clinical, electrical, and laboratory evidence.

Therapeutic logic: Interrupt thrombosis

- Antiplatelet agents reduce platelet-mediated coronary thrombus propagation.
- Anticoagulants target coagulation-dependent thrombus extension.
- Prompt reperfusion attempts to salvage viable myocardium.

Mechanistic treatment overview only; No drug doses or contemporary regimen claims.

Therapeutic logic: Rebalance oxygen supply

- Supplemental oxygen is listed for hypoxia or respiratory distress.
- Nitrates induce vasodilation and reverse vasospasm.
- Beta blockers can lower demand and arrhythmic risk when appropriate.
- Treating pain, abnormal hemodynamics, anemia, and respiratory disease can improve the balance.

Complications reflect tissue loss and instability

- Infarct volume and location influence mechanical and electrical consequences.
- Large transmural infarcts have increased risk of pump failure, arrhythmias, and rupture.
- Residual viable myocardium and ensuing repair determine long-term function.

Contractile dysfunction and cardiogenic shock

- Left ventricular dysfunction generally scales with the extent of infarcted muscle.
- Hypotension and pulmonary congestion or edema may occur.
- The source associates severe pump failure with infarcts involving about 40% or more of LV muscle.

Papillary muscle dysfunction and regurgitation

- Ischemic papillary muscles can contract poorly without rupturing.
- This dysfunction may cause postinfarct mitral regurgitation.
- Complete papillary muscle rupture can produce severe acute mitral regurgitation.
- Later fibrosis, shortening, or ventricular dilation may also impair valve competence.

Right ventricular involvement

- Isolated right ventricular infarction is uncommon.
- RCA-related posteroseptal infarcts may extend into the right ventricle.
- Resulting right-sided failure can cause systemic venous pooling and hypotension.

Three mechanical rupture pathways

LV free-wall rupture

Hemopericardium

Cardiac tamponade

Often rapidly fatal

Septal rupture

Acute ventricular septal defect

Left-to-right shunt

Acute hemodynamic burden

Papillary rupture

Acute structural valve failure

Severe mitral regurgitation

Rapid clinical deterioration

Why rupture risk peaks during days 3–7

- Inflammatory digestion weakens necrotic myocardial architecture.
- Early granulation tissue is soft and mechanically fragile.
- Wall rupture is most common during the interval of peak necrotic tissue removal.

Tissue repair has a vulnerable interval before collagen stabilizes the infarct.

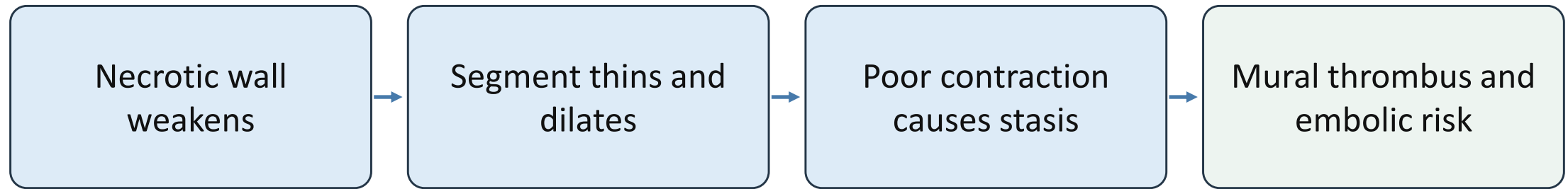
Arrhythmias occur early and may be lethal

- Ischemic myocardium develops irritability and conduction disturbances.
- Manifestations range from bradyarrhythmias and heart block to ventricular fibrillation.
- Risk of serious arrhythmia is greatest during the first hour after MI.

Postinfarct pericarditis

- Transmural necrosis may trigger fibrinohemorrhagic pericardial inflammation.
- Chest pain and a friction rub may emerge around days 2–3.
- A later immune-associated pericarditis is described as Dressler syndrome.

Wall dilation can promote mural thrombosis



Stasis combines with endocardial damage to create a thrombogenic surface.

Ventricular aneurysm is a late scar complication

- A large healed transmural infarct may leave a thin fibrous ventricular wall.
- Ventricular aneurysm predisposes to mural thrombi, arrhythmias, and failure.
- The scarred aneurysm described here does not rupture.

Distinguish early rupture of friable myocardium from a late fibrous aneurysm.

Complication patterns depend on infarct topography

Infarct pattern	Complications emphasized by Robbins
Large transmural	Cardiogenic shock, arrhythmia, later heart failure
Anterior transmural	Free-wall rupture, dilation, mural thrombus, aneurysm
Posterior transmural	Conduction block, RV involvement
Subendocardial	Rupture, pericarditis, and aneurysm are uncommon

Ventricular remodeling: Adaptive, then harmful

- Noninfarcted myocardial segments hypertrophy and dilate after MI.
- Compensatory hypertrophy can initially maintain hemodynamic performance.
- Excess dilation increases oxygen demand and can aggravate ischemia.
- Scar and hypertrophy may stiffen or distort the ventricle, limiting output.

Long-term outcome and prevention

- Residual LV function strongly influences long-term prognosis.
- Persistent coronary obstruction in remaining viable myocardium is also important.
- Risk-factor control before an initial MI is primary prevention.
- Preventing reinfarction in survivors is secondary prevention.

Clinicopathologic integration: A time sequence

- Minutes: Contractile dysfunction can precede myocyte necrosis.
- Hours: Sarcolemmal disruption precedes detectable biochemical markers.
- Days 1–3: Neutrophilic inflammation becomes prominent.
- Days 3–7: Weakening during macrophage clearance predisposes to rupture.
- Weeks: Collagenous replacement produces a permanent scar.

Core distinctions to retain

- Reversible ischemic dysfunction versus irreversible myocyte necrosis.
- Transmural versus subendocardial versus multifocal microinfarction.
- Restored epicardial flow versus inadequate microvascular reperfusion.
- Early rupture of softened myocardium versus late scar aneurysm.