

Overview of Cardiac Pathophysiology

Six mechanisms that connect cardiovascular lesions to dysfunction

Mechanism → hemodynamic stress → functional consequence

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What a cardiac lesion can disrupt

- Effective contraction and relaxation of myocardium
- One-way movement of blood through valves and vessels
- Electrical sequencing of atrial and ventricular contractions
- Integrity of the vascular circuit and adequate coronary perfusion

Six routes to cardiovascular failure

Pump failure

Impaired ejection or filling

Obstruction

Resistance to forward flow

Regurgitation

Backward movement of
blood

Shunt

Inappropriate
communication

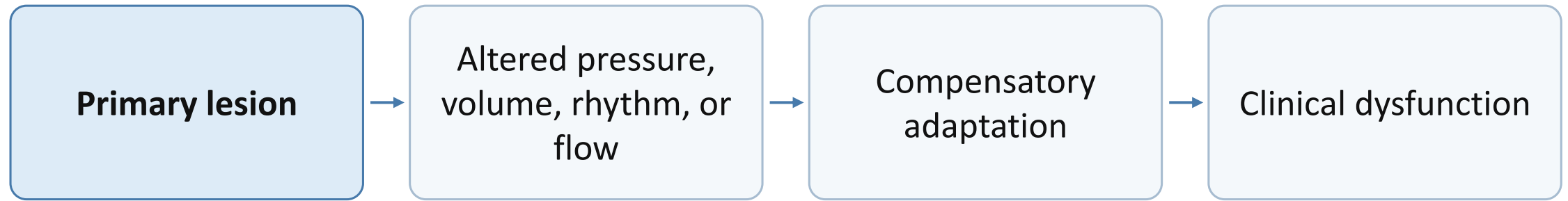
Conduction disorder

Ineffective electrical
coordination

Rupture

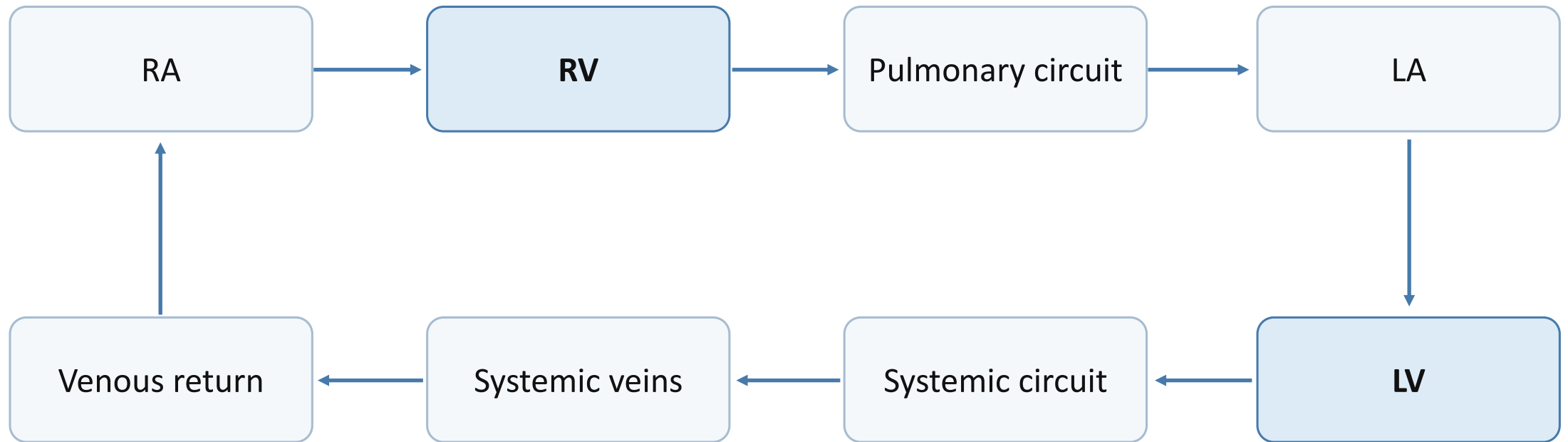
Loss of circulatory continuity

An abnormality can have several effects



- A structural lesion may disturb both loading conditions and effective cardiac output.
- Compensation can initially preserve perfusion yet become maladaptive.

The heart is two pumps in series



Schematic: The cardiovascular system is a closed circuit

Systole and diastole answer different demands

Systole

- Ventricular myocytes contract
- Effective chamber emptying
- Failure reduces forward ejection

Diastole

- Myocardium relaxes
- Ventricles accept filling blood
- Failure raises filling pressure

Myocardial fiber orientation supports pumping

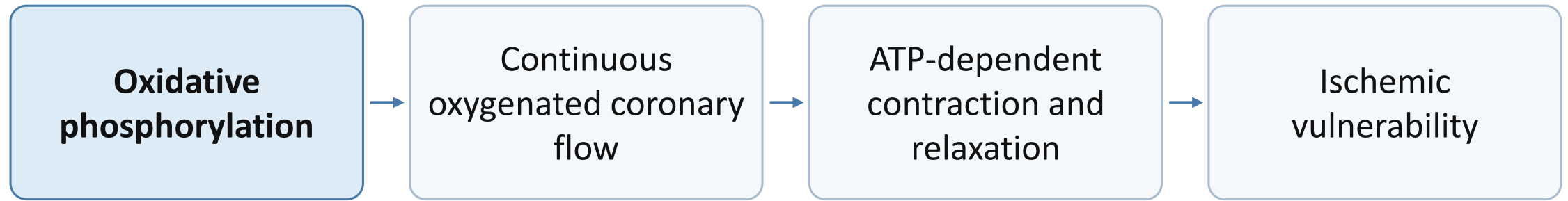
Left ventricle

- Spiral and circumferential fibers
- Coordinated apex-to-base contraction
- Supports high-pressure systemic output

Right ventricle

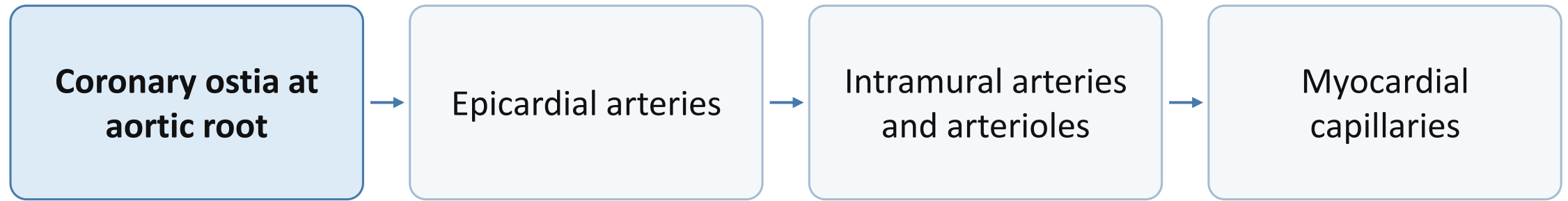
- Longitudinal shortening
- Inward free-wall movement
- Bellows-like ejection

The myocardium has high oxygen dependence



- Mitochondria occupy approximately 20%–30% of myocyte volume.
- Limited ability to regenerate myocytes magnifies the consequences of injury.

Coronary arteries supply contractile tissue



- Coronary arteries function physiologically as end arteries.
- Collateral anastomoses exist but do not eliminate ischemic susceptibility.

Left ventricular perfusion favors diastole

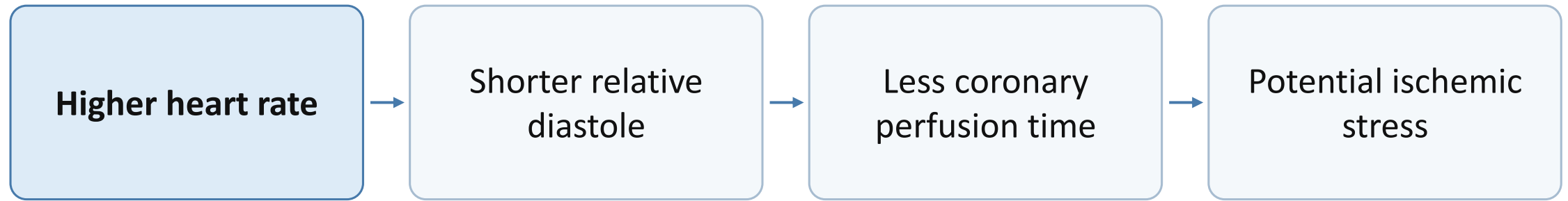
Ventricular systole

- Intramural microvessels compressed
- Coronary delivery constrained
- Myocardial force generated

Ventricular diastole

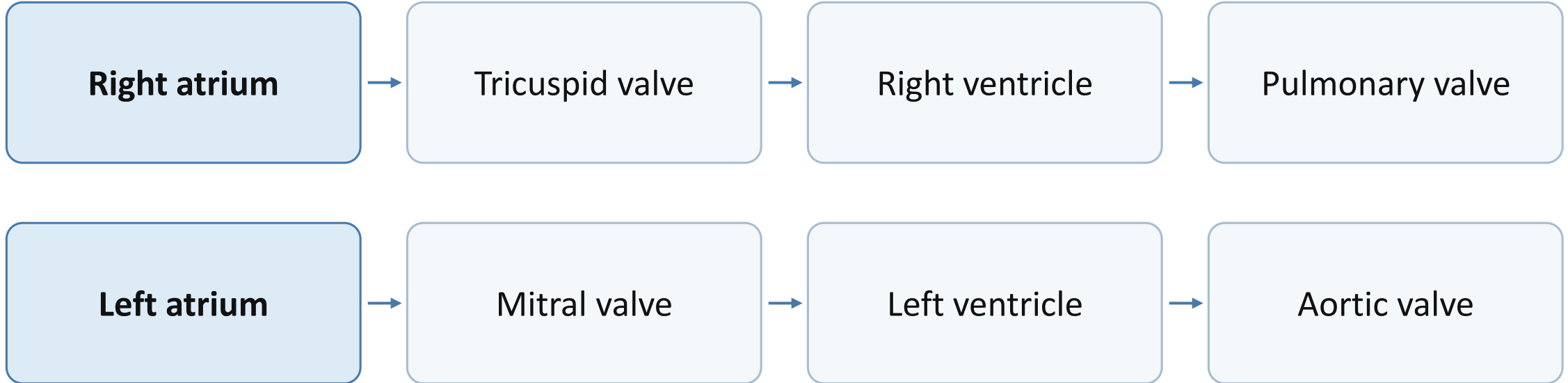
- Aortic valve closed
- Reduced myocardial compression
- Coronary flow permitted

Tachycardia shortens perfusion opportunity



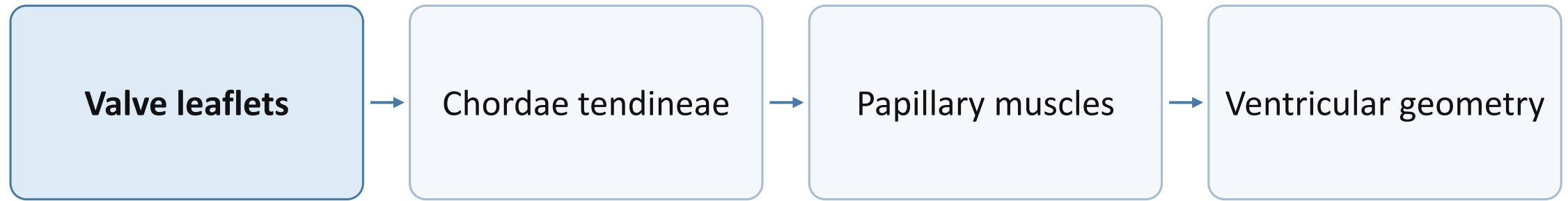
- Increased heart rate can coincide with increased myocardial oxygen demand.
- Shorter diastole is particularly important when coronary reserve is limited.

Four valves preserve unidirectional flow



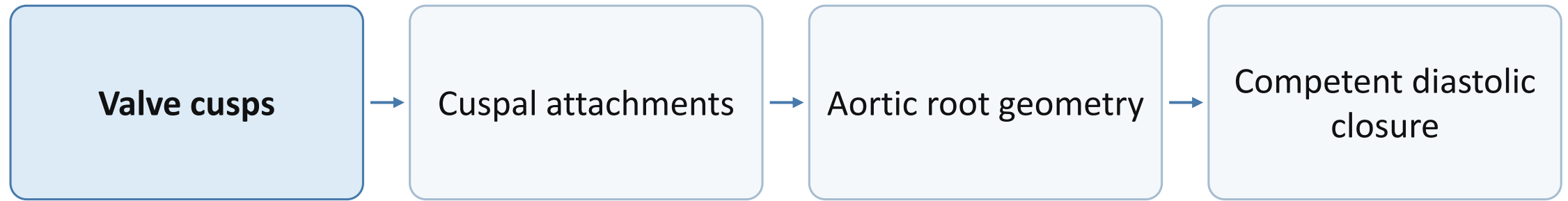
- Atrioventricular: Tricuspid and mitral
- Semilunar: Pulmonary and aortic
- Stenosis obstructs forward flow; Incompetence permits reverse flow.

Mitral and tricuspid competence requires support



- Failure of any element may prevent leaflet coaptation.
- Ventricular dilation can create insufficiency despite anatomically intact leaflets.

Semilunar valve competence needs intact geometry



- Dilation of the aortic root can produce aortic regurgitation.
- A valve need not have a primary cusp lesion to become incompetent.

Three connective-tissue layers support valve function

Fibrosa

Dense collagen

Spongiosa

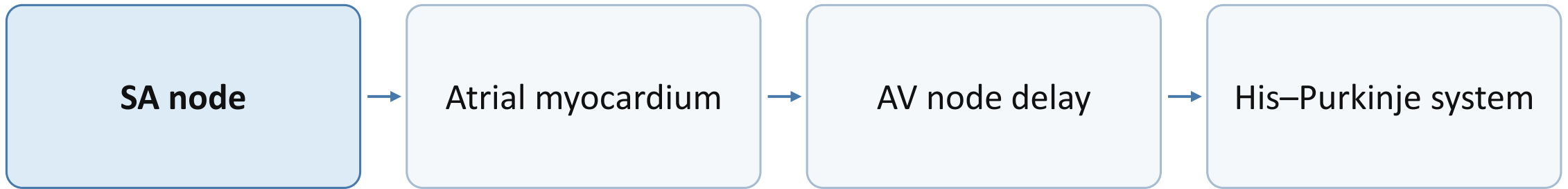
Loose connective tissue

Ventricularis / atrialis

Elastin-rich recoil

Schematic valve leaflet architecture; Not a histologic specimen

Normal electrical activation is ordered



- Sinoatrial node initiates the predominant rhythm.
- Atrioventricular node delays transfer to the ventricles.
- His–Purkinje network rapidly distributes ventricular activation.

The fastest normal pacemaker governs rhythm

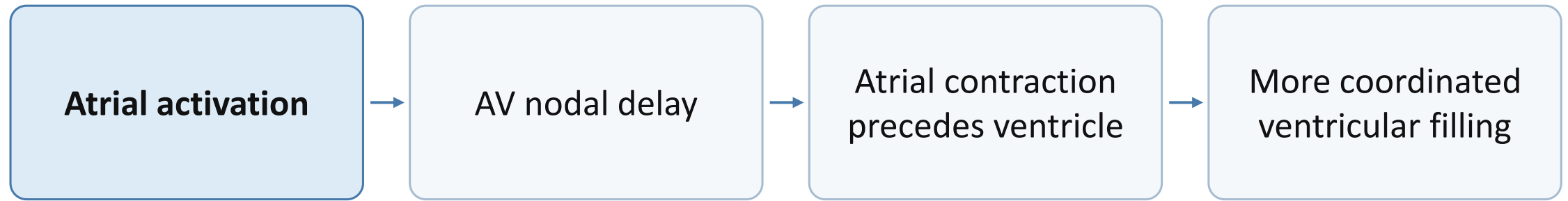
Sinoatrial node

- Normally 60–100 beats/min
- Outpaces subsidiary pacing sites
- Initiates usual sinus rhythm

Escape pacemakers

- May take over when SA node fails
- Typically slower spontaneous rate
- Can preserve limited cardiac activity

Atrioventricular delay protects filling sequence



- AV nodal conduction is physiologically delayed.
- Loss of proper sequencing can impair effective pumping.

Electrical function responds to physiology

Neural input

Vagal stimulation

Adrenergic drive

Circulating adrenaline

Oxygenation

Hypoxia

Electrolytes

Potassium disturbances; Hyperkalemia may block transmission

Pump failure has two fundamental modes

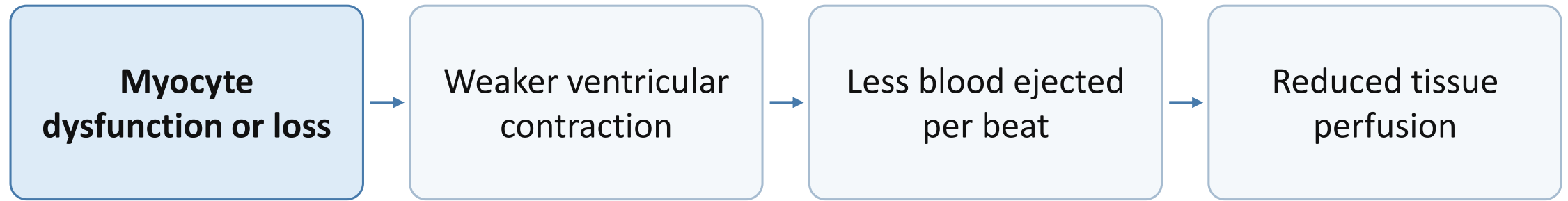
Systolic dysfunction

- Weak ventricular contraction
- Incomplete chamber emptying
- Reduced ejection

Diastolic dysfunction

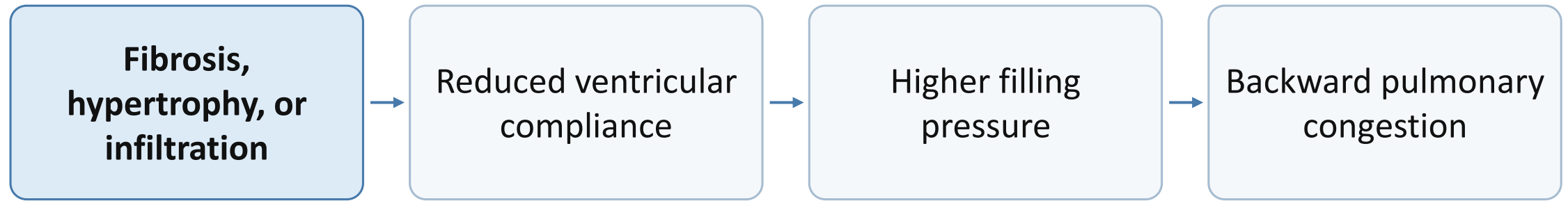
- Impaired ventricular relaxation
- Restricted filling
- Elevated filling pressures

Contractile impairment reduces forward output



- Ischemic injury and chronic overload are examples.
- Compensatory systems may initially mask inadequate myocardial performance.

Diastolic stiffness raises upstream pressure



- Diastolic failure can occur without marked impairment of ejection fraction.
- Amyloid deposition and constrictive pericarditis are identified contributors or mimics.

Ejection fraction measures relative ejection

$$\text{LVEF (\%)} = 100 \times (\text{end-diastolic volume} - \text{end-systolic volume}) / \text{end-diastolic volume}$$

- Normal LVEF is approximately 50%–70%.
- A reduced LVEF supports systolic impairment but does not characterize every form of cardiac dysfunction.

Reduced and preserved EF identify different patterns

HFrEF

- LVEF $\leq 40\%$
- Systolic dysfunction predominates
- Reduced ejection fraction

HFpEF

- LVEF $\geq 50\%$
- Diastolic dysfunction is prominent
- Adequate EF does not exclude failure

Forward and backward failure coexist

Forward failure

- Inadequate tissue perfusion
- Reduced downstream oxygen delivery
- Organ hypoperfusion

Backward failure

- Raised venous pressure
- Pulmonary congestion or systemic edema
- Fluid accumulation

Acute stresses may overwhelm reserve

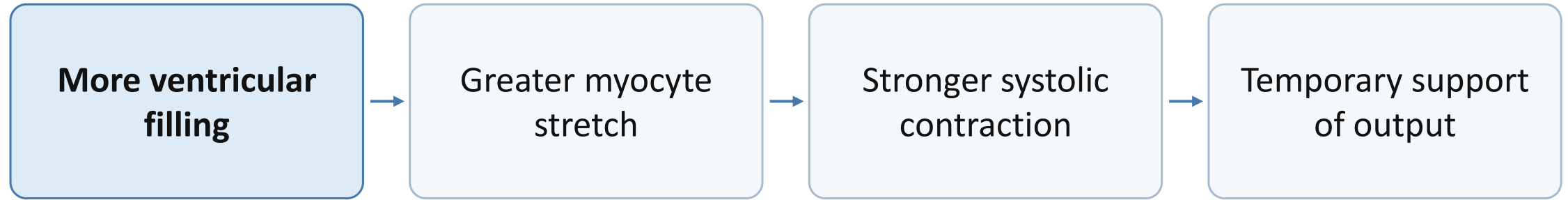
Abrupt perturbation

- Myocardial infarction
- Sudden valvular failure
- Acute fluid overload

Chronic workload

- Systemic hypertension
- Longstanding valve disease
- Progressive ischemic myocardial damage

Frank–Starling compensation has a limit



- Increased filling volume can support stroke output early.
- Persistent overload may eventually exceed this compensatory capacity.

Neurohumoral adaptation maintains perfusion

Adrenergic activation

Increases rate and contractility

RAAS activation

Retains salt/water and increases tone

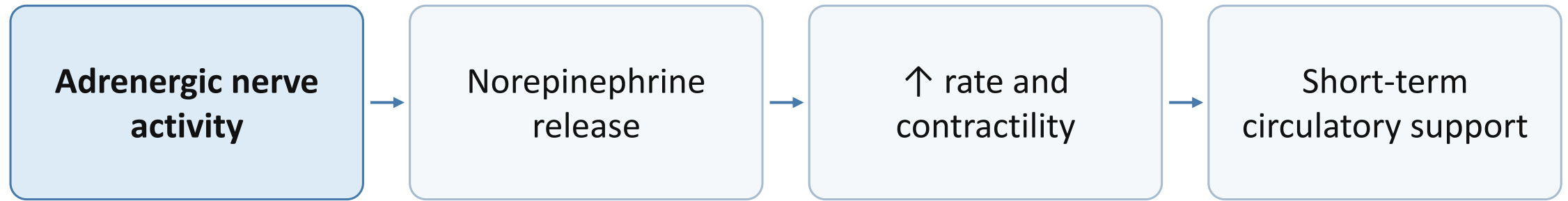
Natriuretic peptides

Promote natriuresis and vasodilation

Myocardial remodeling

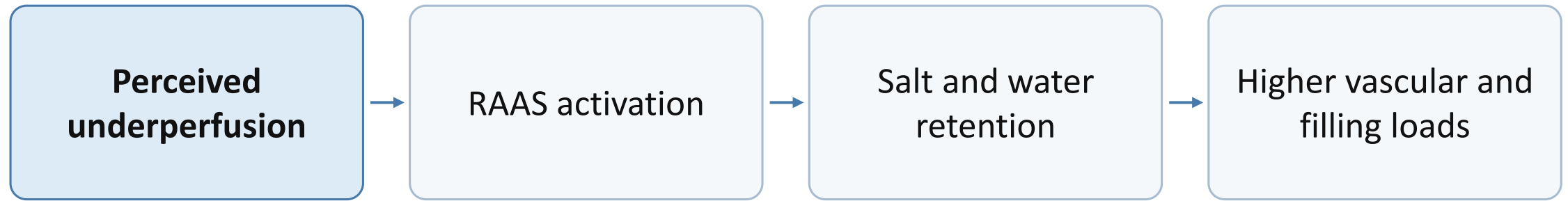
Adapts structure to workload

Sympathetic signaling supports output acutely



- Adrenergic stimulation also raises vascular resistance.
- Persistent neurohumoral activation contributes to the burden of heart failure.

Renin–angiotensin–aldosterone activation raises load



- Volume expansion can temporarily support perfusion.
- Ongoing fluid retention can aggravate edema and congestion.

Natriuretic peptides oppose salt retention

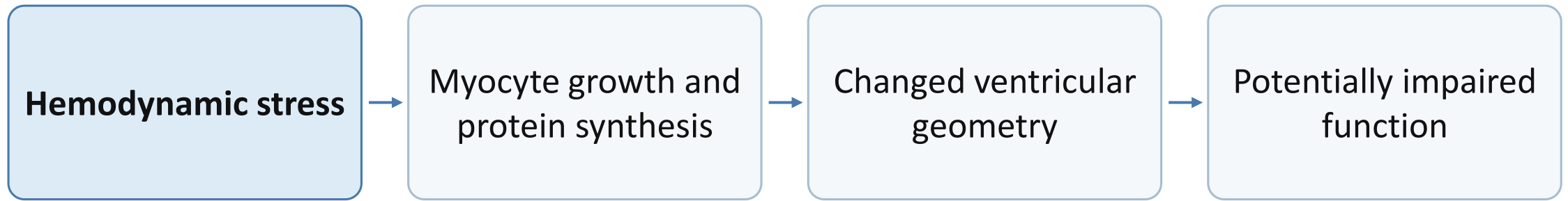
ANP

- Granules in atrial myocytes
- Released with stretch
- Promotes diuresis and vasodilation

BNP

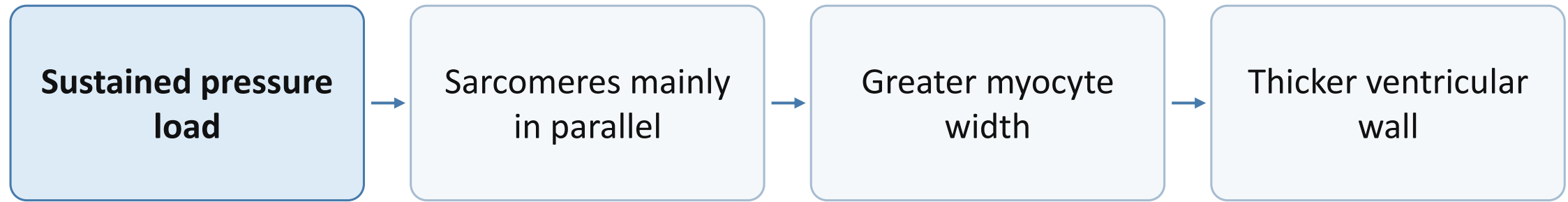
- Found in ventricular myocytes
- Related to myocardial stretch
- Promotes natriuresis and vasodilation

Remodeling begins as an adaptive response



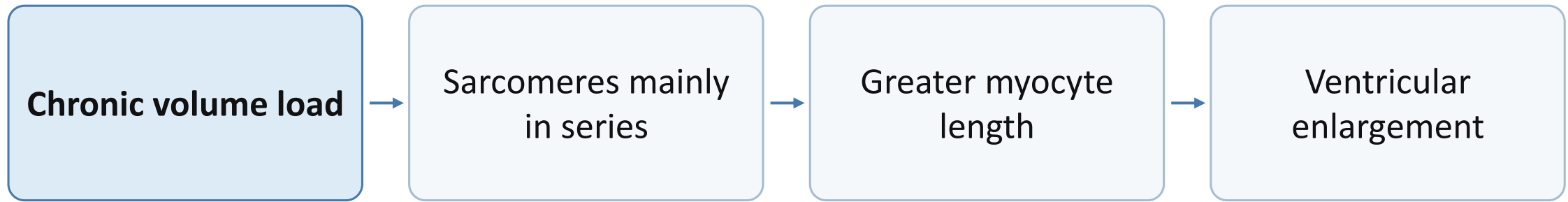
- Ventricular remodeling includes molecular, cellular, and structural changes.
- Increased workload may be due to pressure loading, volume loading, or regional injury.

Pressure overload favors concentric hypertrophy



- Hypertension and aortic stenosis exemplify pressure loading.
- Compensatory myocardial growth can create increased oxygen demand.

Volume overload favors chamber dilation



- Regurgitant valves are a typical volume-load stimulus.
- Wall thickness alone can underestimate hypertrophy in a dilated heart.

Cardiomegaly includes distinct structural changes

Hypertrophy

- Increase in myocardial mass
- Often accompanies sustained workload
- Myocytes become enlarged

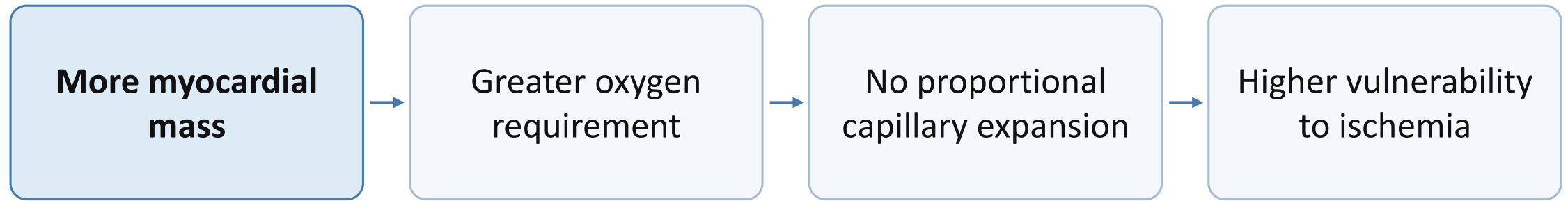
Dilation

- Increase in chamber dimensions
- Reflects altered loading or failure
- May coexist with hypertrophy

Hypertrophic myocytes change microscopically

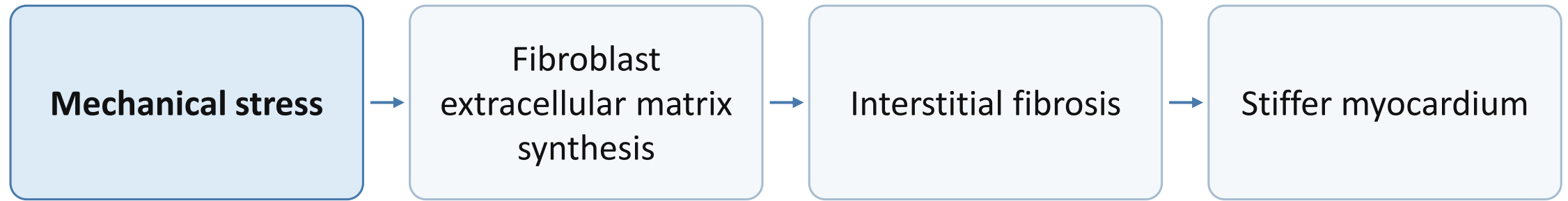
- Myocytes enlarge and synthesize additional contractile proteins.
- Cardiomyocyte nuclei may be enlarged or multiple.
- DNA replication without cell division contributes to nuclear ploidy.
- Associated interstitial fibrosis reflects fibroblast matrix synthesis.

Hypertrophy creates supply–demand mismatch



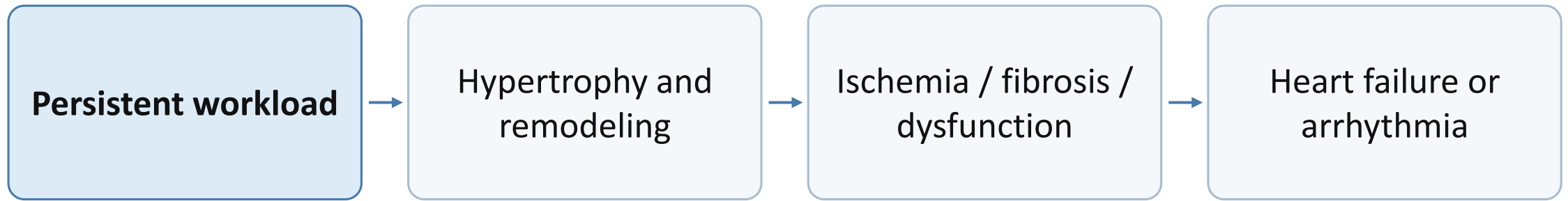
- Pressure-overloaded hearts are especially vulnerable to inadequate perfusion.
- Reduced coronary reserve can contribute to decompensation.

Fibrosis compounds filling impairment



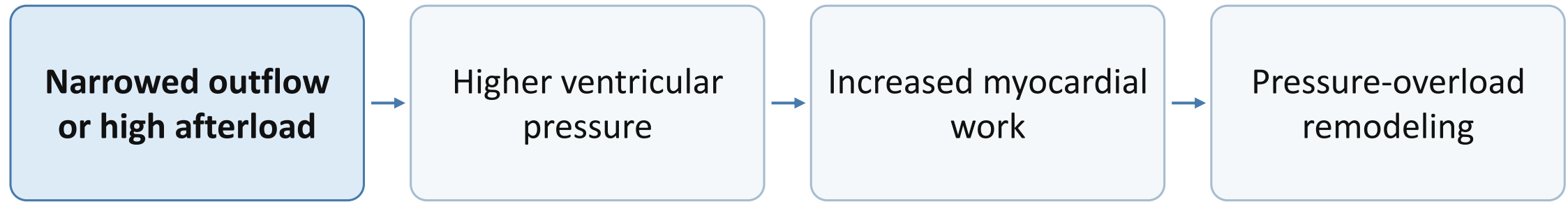
- Fibrosis increases resistance to diastolic filling.
- Functional impairment may be greater than gross morphology suggests.

Adaptation may become decompensation



- Initial compensatory growth is not indefinitely protective.
- Gross size alone does not explain the full burden of functional impairment.

Obstructive lesions impose pressure work



- Valve opening restriction and elevated systemic pressure are distinct causes.
- Maintaining flow across resistance increases chamber workload.

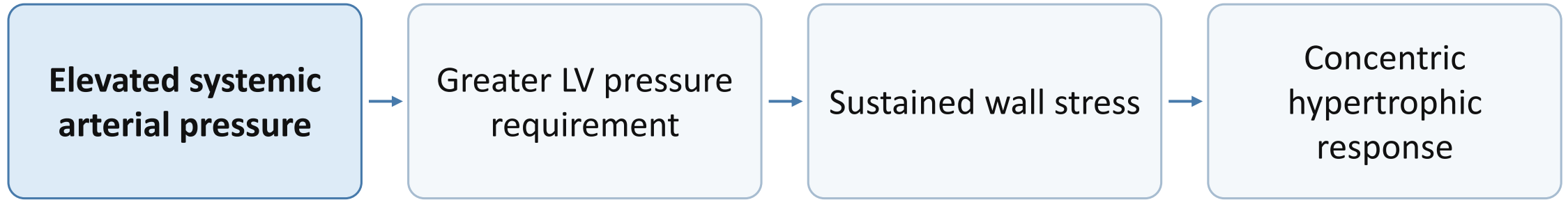
Aortic valve stenosis obstructs ejection

Stenosis: Opening restriction



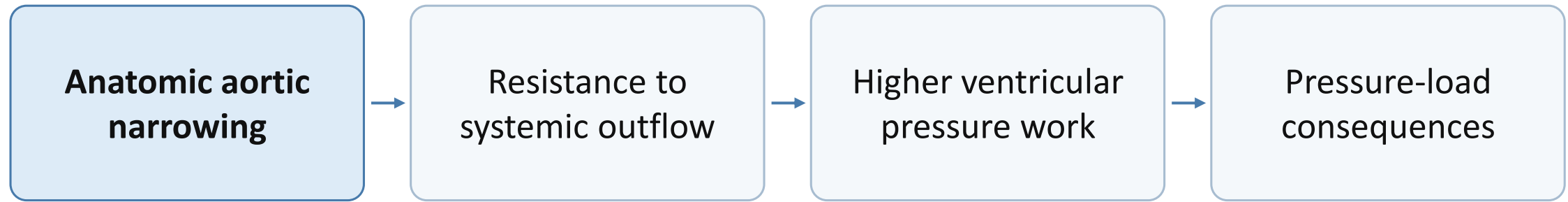
- Calcific aortic valve stenosis restricts valve opening.
- The left ventricle works against increased outflow resistance.
- Sustained pressure stress may promote ventricular hypertrophy.

Systemic hypertension raises ventricular afterload



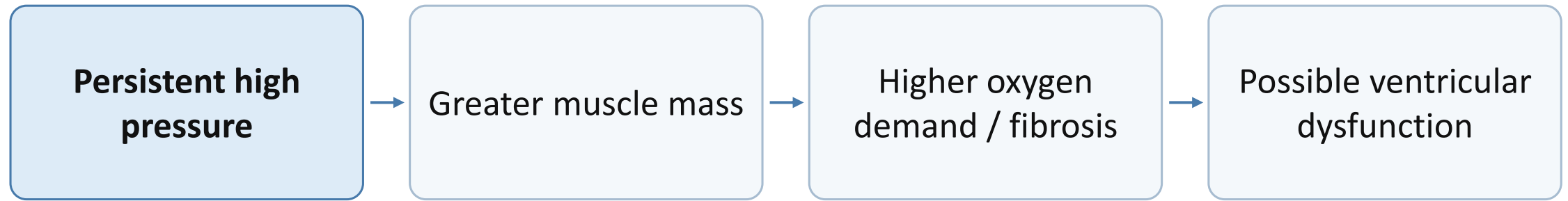
- This mechanism does not require an anatomic valve obstruction.
- Hypertension also appears among common causes of heart failure.

Aortic coarctation increases upstream pressure



- Coarctation as an obstruction-to-flow example.
- The key mechanism is increased work needed to maintain output.

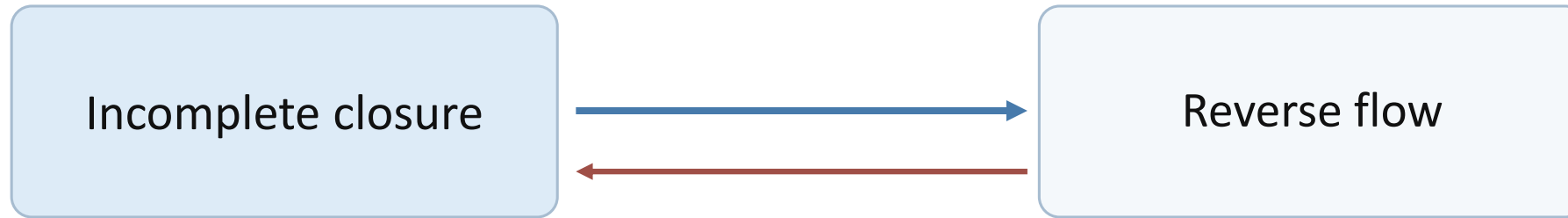
Pressure loading remodels without guaranteeing output



- Hypertrophy can restore wall performance transiently.
- Structural compensation can eventually reduce diastolic compliance.

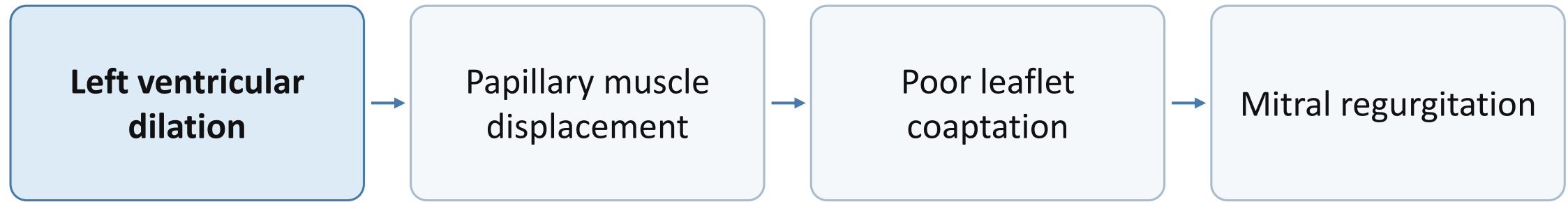
Regurgitant valves add volume workload

Regurgitation: Closing failure



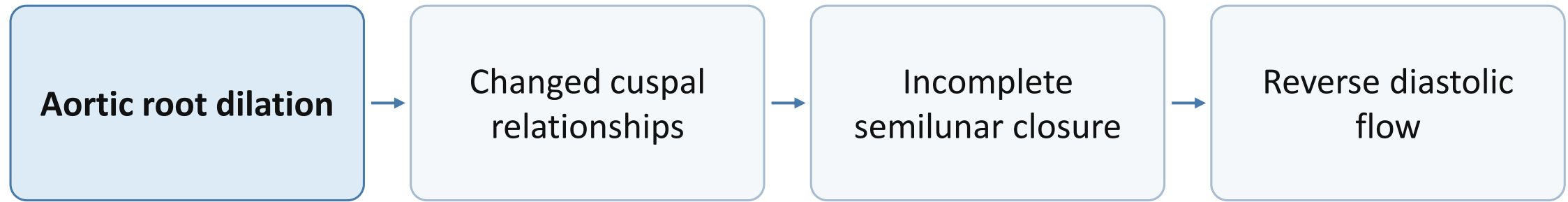
- Incomplete valve closure permits backward flow.
- The involved chambers handle recirculated blood volume.
- Sustained overload can overwhelm contractile reserve.

Mitral regurgitation can follow chamber dilation



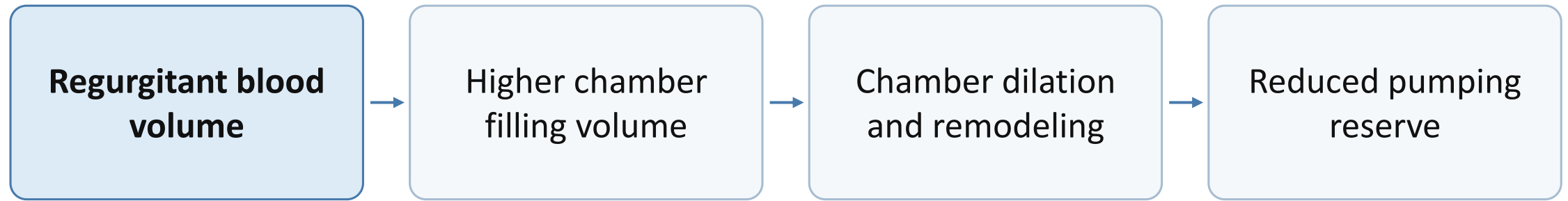
- A torn chord or papillary muscle dysfunction can also cause incompetence.
- Regurgitation may result from a damaged supporting apparatus.

Aortic regurgitation may arise from root dilation



- Leaflet motion and attachment geometry together determine competence.
- Structural failure outside the valve cusp can cause insufficiency.

Volume overload can amplify dysfunction



- Added volume workload is different from pressure-obstruction workload.
- Dilation and regurgitation can reinforce one another.

Pressure load and volume load produce different patterns

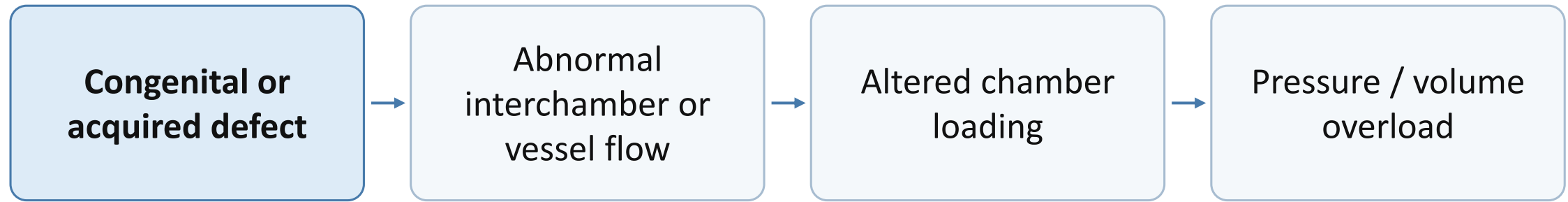
Pressure overload

- Resistance to ejection
- Sarcomeres predominantly in parallel
- Greater wall thickness

Volume overload

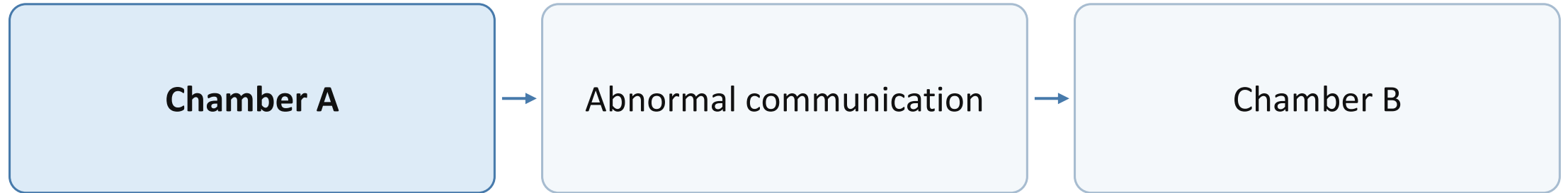
- Excess circulating chamber volume
- Sarcomeres predominantly in series
- Greater chamber dilation

A shunt reroutes blood across an abnormal connection



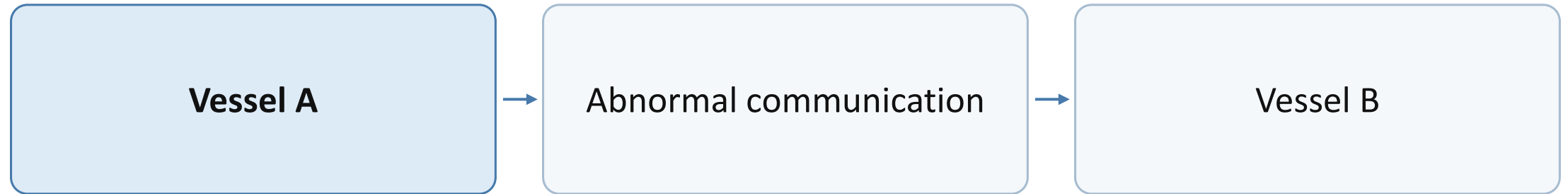
- A shunt is not synonymous with simple valve regurgitation.
- The hemodynamic burden depends on the communication and resulting flow.

Interchamber shunts bypass intended pathways



- Blood crosses an inappropriate cardiac connection.
- Receiving and upstream chambers may experience abnormal loading.
- The overview identifies both pressure and volume overload as possible outcomes.

Vessel-to-vessel shunts alter the closed circuit



- Pathologic communication may occur between major vessels.
- Flow is diverted away from its intended pathway.
- Downstream loading consequences depend on shunt physiology.

Shunts can impose coupled hemodynamic stresses

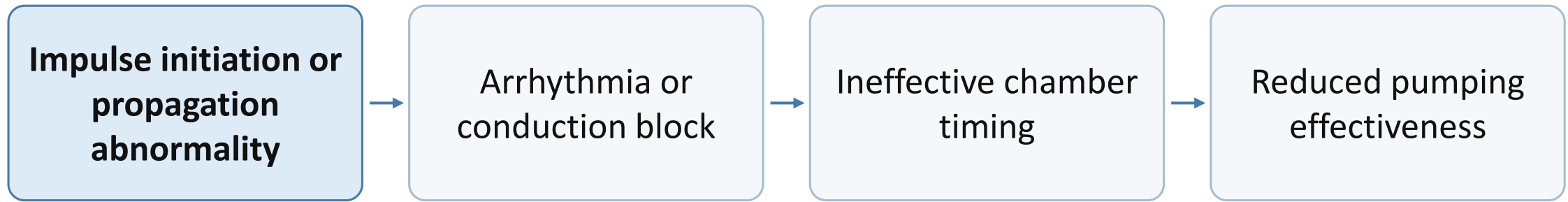
Volume component

- Extra flow through involved chambers
- Increased filling burden
- Potential chamber dilation

Pressure component

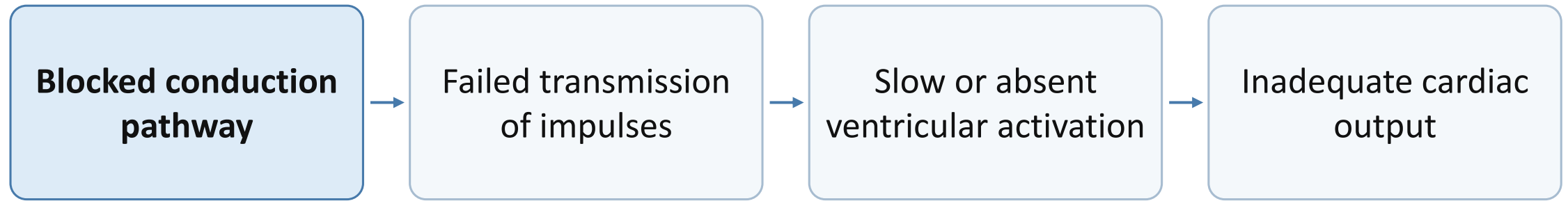
- Abnormal load or resistance
- Higher pressure work
- Potential hypertrophic response

Conduction disorders disrupt coordinated contraction



- Disorganized impulses can compromise effective ejection.
- A conduction defect may be hemodynamically important without valve damage.

Conduction block can slow ventricular activity



- Subsidiary pacemakers may provide slower escape activity.
- Severe interruption can prevent effective pumping.

Uncoordinated activation impairs flow

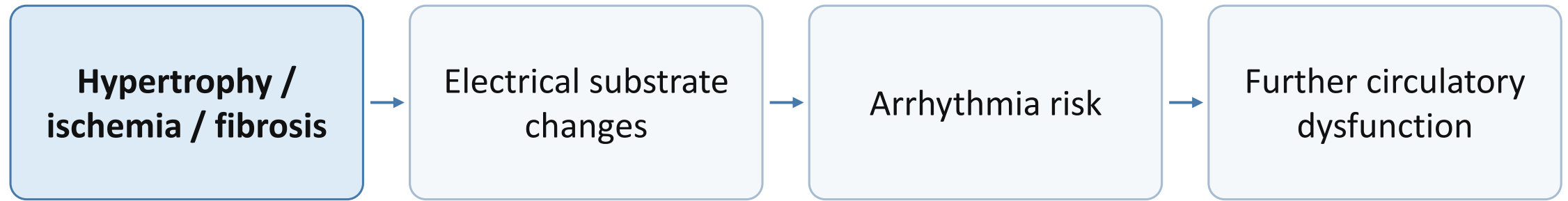
Coordinated sequence

- Atrial contraction precedes ventricular systole
- Ventricular activation is organized
- Effective pressure generation

Disorganized impulses

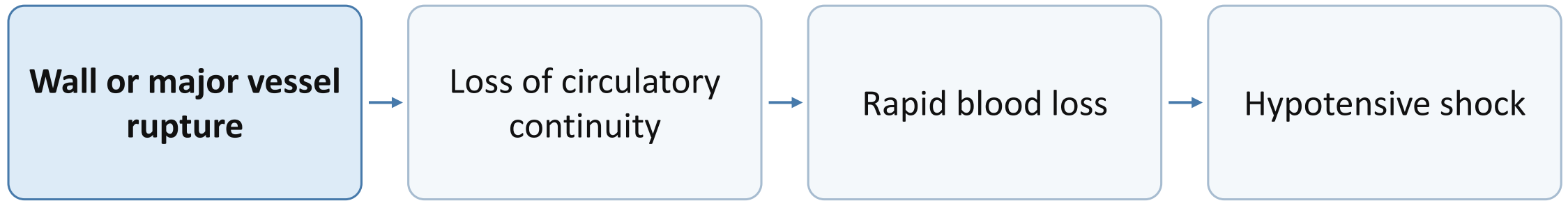
- Abnormal contraction sequence
- Reduced mechanical efficiency
- Risk of impaired output

Electrophysiology and structure interact



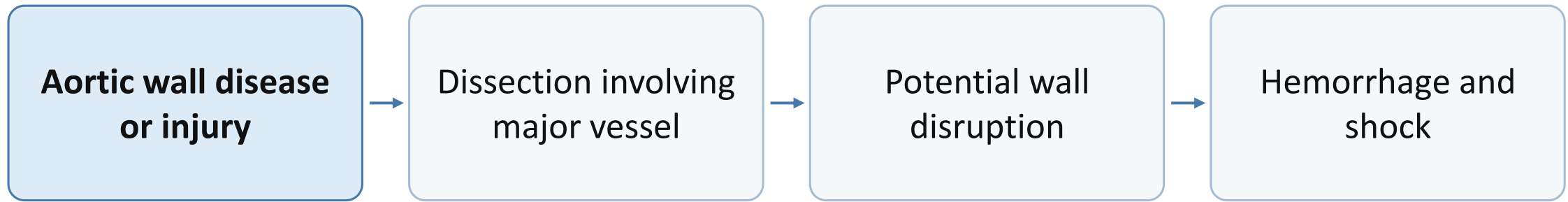
- Myocardial remodeling may culminate in arrhythmias.
- Pump failure and conduction problems can therefore coexist.

Rupture causes immediate circuit failure



- Unlike slow myocardial remodeling, major rupture may be immediately lethal.
- Thoracic aortic injury and dissection as examples.

Aortic dissection is a rupture-related threat



- The overview refers to aortic dissection in its discussion of rupture.
- Its detailed vascular pathology belongs to the preceding chapter.

Mechanism dictates tempo of deterioration

Typically progressive

- Chronic pressure overload
- Progressive regurgitation
- Compensated remodeling → failure

Potentially sudden

- Abrupt myocardial injury
- Conduction interruption
- Rupture with hemorrhagic shock

Aging changes myocardial filling and valves

Chambers

Smaller LV cavity; Larger LA

Myocardium

Myocyte attrition; More connective tissue

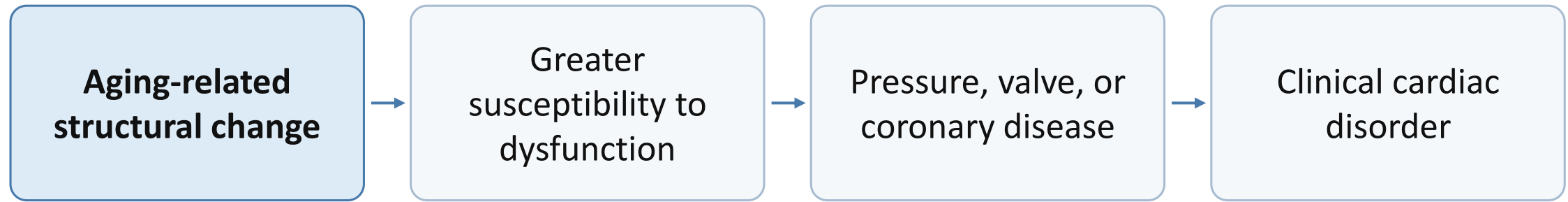
Valves

Calcification and fibrous thickening

Coronary arteries

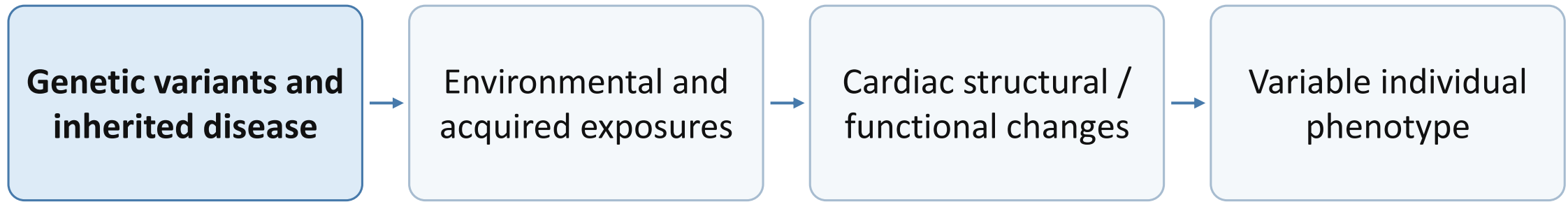
Tortuosity, atherosclerosis, reduced compliance

Aging provides a substrate—not one mechanism



- Amyloid deposits in older hearts can increase stiffness and impair filling.
- Several six-mechanism pathways may operate together in one patient.

Inherited susceptibility and environment interact



- Genetic and environmental contributions across heart disorders.
- Molecular diagnostics can help investigate selected cardiac diseases.

The six mechanisms can be distinguished clinically

Mechanism	Primary disturbance	Typical burden
Pump failure	Contraction or relaxation	Low flow / high filling pressure
Obstruction	Resistance to forward flow	Pressure work
Regurgitation	Reverse valve flow	Volume work
Shunt	Inappropriate flow route	Pressure $\pm$ volume work
Conduction disorder	Abnormal electrical timing	Ineffective pumping
Rupture	Loss of circuit integrity	Hemorrhage / shock

Case: Aortic stenosis and wall thickening

Teaching scenario

A patient has restricted aortic cusp opening and a thickened left ventricular wall. Which primary mechanism accounts for the remodeling?

Which explanation is most consistent with the mechanism?

- Obstruction → pressure overload
- Regurgitation → volume overload
- Rupture → loss of continuity

Case: Ventricular enlargement with mitral leak

Teaching scenario

A dilated left ventricle displaces papillary muscles and produces incomplete mitral valve closure. Identify the causal sequence.

Which explanation is most consistent with the mechanism?

- Dilation → altered apparatus → regurgitation
- Regurgitation → primary conduction block
- Rupture → chronic coronary insufficiency

Case: Congestion despite preserved EF

Teaching scenario

A patient has ventricular stiffness, elevated filling pressure, pulmonary congestion, and a preserved ejection fraction. Which pump defect predominates?

Which explanation is most consistent with the mechanism?

- Diastolic filling dysfunction
- Ventricular rupture
- Isolated forward-flow obstruction

Case: Loss of normal ventricular sequencing

Teaching scenario

A conduction pathway is interrupted; Ventricular activation slows despite no stated valve lesion. Why can circulatory output fall?

Which explanation is most consistent with the mechanism?

- Abnormal timing reduces effective pumping
- Valves must be stenotic
- A shunt must be present

Case: Abrupt hypotension after aortic injury

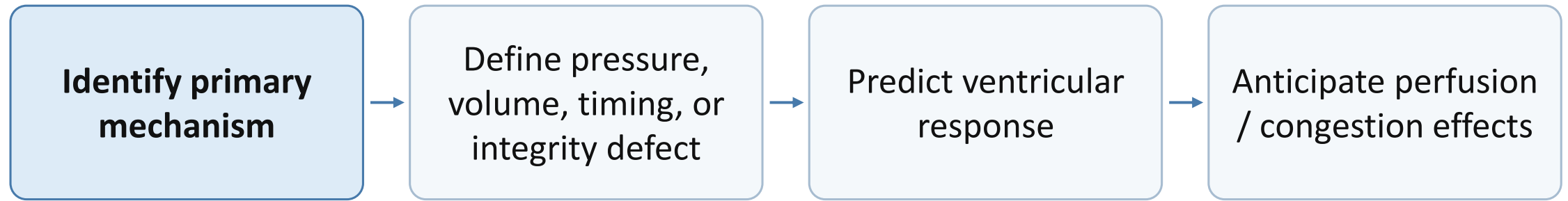
Teaching scenario

After major thoracic aortic injury, a patient develops rapid blood loss and profound hypotension. Which failure pathway is operating?

Which explanation is most consistent with the mechanism?

- Rupture and loss of circuit integrity
- Slow pressure hypertrophy
- Chronic diastolic stiffening

Link lesion to load, adaptation, and failure



- One patient may show more than one of the six mechanisms.
- Mechanical and electrical disturbances often converge on impaired tissue delivery.

Reference and source boundary

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).
- Core sections: “Cardiac Structure and Specializations” and “Overview of Cardiac Pathophysiology.”
- Adjacent explanatory context: “Heart Failure” and “Pathophysiology and Progression to Heart Failure.”