Coronary blood flow
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The heart has the highest oxygen consumption per tissue mass of all human organs. The resting coronary blood flow is \(~250 \text{ ml min}^{-1} \text{ g}^{-1}\) of heart muscle; this represents 5% of cardiac output. Ischaemia results when oxygen demand outstrips supply.

Arterial oxygen extraction is 70–80%, compared with 25% for the rest of the body. Therefore, increased oxygen consumption must principally be met by an increase in coronary blood flow, which may increase fivefold during exercise. Supply usually closely matches any change in demand. However, an increase in coronary blood flow can independently increase myocardial oxygen consumption (Gregg effect). This may be explained by full coronary arteries splinting the heart and increasing the end-diastolic fibre length and contractility.

Anatomy
The two coronary ostia arise from the sinuses of Valsalva just above the aortic valve. The left coronary artery divides into the left anterior descending artery and circumflex artery. It supplies the lateral and anterior walls of the left ventricle, and the anterior two thirds of the interventricular septum. The right coronary artery supplies the right ventricle, the posterior wall of the left ventricle and posterior third of the septum. The major coronary arteries divide into epicardial arteries. Intramuscular arteries penetrate the myocardium perpendicularly to form subendocardial arterial plexuses.

Most of the blood from left ventricular muscle drains into the coronary sinus. The anterior cardiac vein receives blood from the right ventricular muscle. They both open into the right atrium. Thebesian veins drain a small proportion of coronary blood directly into the cardiac chambers and account for true shunt.

Determinants of coronary blood flow
Coronary perfusion pressure
During systole, intramuscular blood vessels are compressed and twisted by the contracting heart muscle and blood flow to the left ventricle is at its lowest. The force is greatest in the subendocardial layers where it approximates to intramyocardial pressure. In systole, intramyocardial blood is propelled forwards towards the coronary sinus and retrogradely into the epicardial vessels, which act as capacitors. Flow resumes during diastole when the muscle relaxes. The coronary perfusion pressure is the difference between the aortic diastolic pressure and left ventricular end-diastolic pressure (LVEDP). Phasic changes in blood flow to the right ventricle are less pronounced because of the lesser force of contraction. Central venous pressure may be a more appropriate choice for downstream pressure to calculate the right-sided coronary perfusion pressure.

Perfusion time
Any increase in heart rate impinges on diastolic time more than systolic time and reduces the perfusion time.

Vessel wall diameter
Vasomotor tone and deposits inside the vascular lumen determine the vessel wall diameter. The interplay of various mechanisms that regulate the coronary vasomotor tone usually favours vasodilatation (Fig. 1).

Factors influencing the vasomotor tone
Myocardial metabolism
Vasomotor tone is almost exclusively determined by local metabolic oxygen demand. Hypoxia causes coronary vasodilatation directly but also releases adenosine and opens ATP-sensitive potassium channels. Pre-capillary sphincters are relaxed and more capillaries recruited.

Autoregulation
Under resting conditions, coronary blood flow remains constant between mean arterial blood pressure and a middle fixed coronary perfusion pressure.

Key points
Blood flow to the heart occurs mainly during diastole.
Coronary blood flow is mainly determined by local oxygen demand.
The vascular endothelium is the final common pathway controlling vasomotor tone.
When anaesthetising patients with coronary artery disease, maintain coronary perfusion pressure and avoid tachycardia.
pressures of 60–140 mm Hg. Beyond this range, flow becomes pressure-dependent. Probable mechanisms include the myogenic response to intraluminal pressure changes (fast) and metabolic regulation (slow). The myocardial oxygen tension and presence of vasoconstrictors or vasodilators influence the range of coronary autoregulation.

Nervous control

Autonomic influences are generally weak. It is difficult to tease out the role of neural control on coronary blood flow, as the metabolic effects of any change in blood pressure, heart rate and contractility dominate the subsequent response. The epicardial blood vessels primarily have α receptors, stimulation of which produces vasoconstriction. Intramural and subendocardial blood vessels predominantly have β2 receptors (vasodilatation). Sympathetic stimulation increases myocardial blood flow through an increased metabolic demand and a predominance of β receptor activation.

Alpha stimulation may play a role in the distribution of blood flow within the myocardium by restricting metabolically mediated flow increase and exerting an anti-steal affect. Parasympathetic influences are minor and weakly vasodilatory. The vasodilatory effect of acetylcholine depends on an intact endothelium.

Humoral control

Most vasoactive hormones require an intact vascular endothelium. The peptide hormones include antidiuretic hormone, atrial natriuretic peptide, vasoactive intestinal peptide, and calcitonin gene-related peptide. Antidiuretic hormone in physiological concentration has little effect on the coronary circulation but causes vasoconstriction in stressed patients. The other peptides cause endothelium-mediated vasodilatation.

Angiotensin II causes coronary vasoconstriction independent of sympathetic innervation. It also enhances calcium influx and releases endothelin, the strongest vasoconstrictor peptide yet identified in humans. Angiotensin-converting enzyme inactivates bradykinin, a vasodilator.

Vascular endothelium

The vascular endothelium is the final common pathway regulating vasomotor tone. It modulates the contractile activity of the underlying smooth muscle through synthesis and secretion of vasoactive substances in response to blood flow, circulating hormones and chemical substances. Vasorelaxants are endothelium-derived relaxing factor, nitric oxide, prostacyclin and bradykinin. Vasocostrictors include endothelin and thromboxane A2. The net response depends on the balance between the two opposing groups.

Myocardial oxygen balance

Oxygen delivery is the product of arterial oxygen carrying capacity and myocardial blood flow. The diastolic pressure time index (DPTI) is a useful measure of coronary blood supply and is the product of the coronary perfusion pressure and diastolic time. Similarly, oxygen demand can be represented by the tension time index (TTI), the product of systolic pressure and systolic time.

The ratio DPTI/TTI is the endocardial viability ratio (EVR) and represents the myocardial oxygen supply-demand balance. The EVR is normally 1 or more. A ratio <0.7 is associated with subendocardial ischaemia.

Such a value may be reached in a patient with the following physiological data:

- Blood pressure = 180/95 mm Hg
- Heart rate = 120 min⁻¹
- LVEDP = 15 mm Hg
- DPTI = 80 mm Hg × (60 s/heart rate − 0.2 s) = 24 s mm Hg
- TTI = 180 mm Hg × 0.2 s = 36 s mm Hg
- EVR = 0.67

Note that systolic time is typically fixed at 200 ms, with diastole occupying the remaining time.

Diseases affecting the coronary blood flow

The coronary circulation functions in a state of active vasodilatation. Abnormal endothelial nitric oxide production may play a role in diabetes, atherosclerosis and hypertension.

Coronary artery disease

Deposits of lipids, smooth muscle proliferation and endothelial dysfunction reduce the luminal diameter. Critical stenosis occurs when coronary blood flow is unable to respond to an increase in
metabolic demand, usually when the diameter is reduced by 50%. Resting flow becomes affected if the diameter is reduced by 80%.

With increasing stenosis, distal arterioles dilate maximally to preserve flow up to the point where the vascular bed is maximally dilated. Further stenosis leads to a drop in flow and flow becomes pressure dependent. Flow diverted into a dilated parallel bed proximal to a stenosis is called coronary steal and can aggravate ischemia. Flow in collaterals is also often pressure dependent.

**Hypertension**

The left ventricle undergoes hypertrophy in response to raised afterload. The myofibrillar growth outstrips the capillary network, resulting in decreased capillary density. Raised intramyocardial pressure lowers the subendocardial blood flow. The pressure load increases myocardial work and oxygen demand. There is also an impaired vasomotor response to hypoxia in hypertrophied tissue that makes it susceptible to ischaemia.

**Heart failure**

Impaired ejection results in larger diastolic volumes, raised LVEDP and lower coronary perfusion pressure. Sympathetic-mediated systemic vasoconstriction may help to improve the myocardial perfusion but increases pressure load and oxygen demand.

**Drugs and coronary blood flow**

**Antplatelet drugs, anticoagulants and lipid lowering drugs**

These agents act inside the lumen to prevent further reduction in the vessel diameter. Statins inhibit HMG CoA reductase, an enzyme involved in cholesterol synthesis. Antiplatelet drugs prevent platelet aggregation, often the initial step in the formation of an occlusive thrombus. Antithrombin agents act at various sites in the coagulation cascade to inhibit thrombin formation.

**Nitrates**

Nitrates produce vasodilatation in all vascular beds, mediated by nitric oxide release. They relieve coronary vasospasm but their main benefit is to reduce preload, afterload and to increase maximal coronary dilatation. Benefits may be offset by reflex tachycardia. Regional blood flow is improved due to dilatation of collaterals and a lower LVEDP.

**Calcium channel blockers**

Compared to the non-dihydropyridines (verapamil and diltiazem) the dihydropyridines (nifedipine) produce more vasodilatation, less inhibition of the sinus and atrioventricular nodes, and less negative inotropy. The myocardial oxygen supply improves due to coronary dilatation and lower LVEDP. The oxygen demand is lessened because of decreases in contractility and pressure load.

**Drugs acting on angiotensin**

Angiotensin-converting enzyme inhibitors reduce conversion of angiotensin I to angiotensin II. These drugs reduce angiotensin-mediated vasoconstriction and enhance myocardial perfusion by vasodilatation without reflex tachycardia. Over time, it also regulates fibrous tissue formation after tissue injury.3 Drugs such as losartan are angiotensin receptor antagonists and enhance endothelial nitric oxide release.

**Potassium channel openers**

Nicorandil is a novel anti-anginal agent. Increased potassium efflux results in reduced intracellular calcium and muscle relaxation. It dilates both normal and stenotic segments of the coronary arteries.

**β-Blockers**

Coronary blood vessels contain β₂ receptors. Chronotropy and inotropy depends on β₁ stimulation. Recent investigations in patients with coronary heart disease suggest that β-blockers do not depress the cardiac output as much as originally thought. The reduction in the heart rate prolongs the diastolic perfusion time and they inhibit stress-induced rises in myocardial contractility. In patients on cardioselective β₁-blockers, unopposed systemic β₂ stimulation reduces the afterload, improves ejection fraction, and exerts a ‘positive inotropic effect’.4

**Vasopressors and inotropes**

These drugs restore coronary perfusion pressure in hypotensive patients and may be especially beneficial in those patients heading towards the lower end of the autoregulation range. Any increase in aortic diastolic pressure may be offset by an increase in myocardial oxygen demand related to higher workload, contractility and heart rate. In the failing heart, inotropes also reduce the LVEDP.

**Anaesthesia and myocardial oxygen balance**

Halogenated anaesthetic agents activate ATP-sensitive potassium channels and lower intracellular calcium. This results in negative inotropy and mimic the protective effect of discrete episodes of myocardial ischaemia before a sustained ischaemic insult, so-called ‘ischaemic preconditioning’. In addition, coronary vasodilation and reduced afterload generally results in a favourable myocardial oxygen supply–demand ratio.

Isoflurane in particular causes coronary vasodilatation. Arterioles (resistance vessels) are dilated more than epicardial (conductance) vessels. Theoretically, coronary steal may occur
in a distinct anatomical pattern of coronary artery disease but this has not been borne out in practice. Isoflurane however, can provoke ischaemia in patients with coronary artery disease if tachycardia and hypotension is permitted. Sevoflurane and halothane do not cause tachycardia or maldistribution of myocardial perfusion.5

Perioperative stress results in sympathetically mediated tachycardia, hypertension, increase in shear forces and increased myocardial oxygen demand. Central neuraxial block obounds this potentially harmful response but any substantial fall in blood pressure will lower the coronary perfusion pressure. Thoracic epidural analgesia also blocks sympathetic outflow to the heart. Sympathetic stimulation produces coronary vasodilatation in healthy individuals but vasoconstriction in patients with coronary artery disease.6

References


See multiple choice questions 48–53.