An Introduction to Cardiovascular Physiology

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Summary

This article aims to provide an overview of the physiology of the cardiovascular system and its response to anaesthesia. The next article in this section deals with myocardial physiology in greater detail.

INTRODUCTION

The cardiovascular system consists of the heart and two vascular systems, the systemic and pulmonary circulations. The heart pumps blood through these two vascular systems - the low pressure pulmonary circulation in which gas exchange occurs, and then the high pressure systemic circulation, which delivers blood to individual organs, matching supply to metabolic demand. Blood pressure and flow are largely controlled by the autonomic nervous system, and are also influenced by surgery and anaesthetic drugs.

THE HEART

The heart comprises four chambers, and is divided into a right and left side, each with an atrium and a ventricle. The atria act as reservoirs for venous blood, with some pumping action to assist ventricular filling. In contrast, the ventricles are the major pumping chambers, delivering blood to the pulmonary (right ventricle) and systemic (left ventricle) circulations. The left ventricle is conical in shape and has to generate greater pressures than the right ventricle, and so has a much thicker and more muscular wall. Four valves ensure that blood flows only one way, from atria to ventricle (tricuspid and mitral valves), and then to the arterial circulations (pulmonary and aortic valves). The myocardium consists of muscle cells, which can contract spontaneously and pacemaker and conducting cells, which have specialised functions.

ELECTROPHYSIOLOGY OF THE HEART

Myocardial contraction results from a change in voltage across the cell membrane (depolarisation), which leads to an action potential. Although contraction may happen spontaneously, it is normally in response to an electrical impulse. This impulse starts in the sinoatrial (SA) node, a collection of pacemaker cells located at the junction of the right atrium and superior vena cava. These specialised cells depolarise spontaneously, and cause a wave of contraction to pass across the atria. Following atrial contraction, the impulse is delayed at the atrioventricular (AV) node, located in the septal wall of the right atrium. From here His-Purkinje fibres allow rapid conduction of the electrical impulse via right and left branches, causing almost simultaneous depolarisation of both ventricles, approximately 0.2 seconds after the initial impulse has arisen in the sinoatrial node. Depolarisation of the myocardial cell membrane causes a large increase in the concentration of calcium within the cell, which in turn causes contraction by a temporary binding between two proteins, actin and myosin. The cardiac action potential is much longer than that of skeletal muscle, and during this time the myocardial cell is unresponsive to further excitation (the refractory period).

The electrocardiogram (ECG)

The ECG measures changes in skin electrical voltage/potential caused by electrical currents generated by the myocardium. The P wave reflects atrial depolarisation, the QRS complex ventricular depolarisation, and the T wave ventricular repolarisation. Repolarisation is a process that occurs in many cells where the electrical potential across the cell membrane returns from the value during the action potential to that of the resting state, the resting potential. Although the ECG shows heart rate and rhythm and can indicate myocardial damage, it gives no information on the adequacy of contraction. Normal electrical complexes can exist in the absence of cardiac output, a state known as **pulseless electrical activity**.

CARDIAC OUTPUT

Cardiac output (CO) is the product of heart rate (HR) and stroke volume (SV): **CO = HR x SV**

For a 70kg man normal values are HR=70min^{-1} and SV=70ml, giving a cardiac output of about 5l.min^{-1}. The cardiac index is the cardiac output per square metre of body surface area and normal values range from 2.5-4.0l.min^{-1}m^{-2}.

Heart rate is determined by the rate of spontaneous depolarisation at the sinoatrial node (see article on myocardial physiology), but can be modified by the autonomic nervous system. The vagus nerve acts on muscarinic receptors to slow the heart, whereas the cardiac sympathetic fibres stimulate beta-adrenergic receptors and increase heart rate.

Stroke volume is determined by three main factors: preload, afterload and contractility.

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Preload is the ventricular volume at the end of diastole. An increased preload leads to an increased stroke volume. Preload is mainly dependent on the return of venous blood from the body and is influenced by changes in position, intra-thoracic pressure, blood volume and the balance of constriction and dilatation (tone) in the venous system. The relationship between ventricular end-diastolic volume and stroke volume is known as 'Starling's law', which states that the energy of contraction of the muscle is related/proportional to the initial length of the muscle fibre. This can be graphically illustrated by a series of 'Starling curves' (Figure 1). As volume at the end of diastole (end-diastolic volume) increases and stretches the muscle fibre, so the energy of contraction and stroke volume increase, until a point of over-stretching when stroke volume may actually decrease, as in the failing heart. Cardiac output will also increase or decrease in parallel with stroke volume if there is no change in heart rate. The curves show how the heart performs at different states of contractility, ranging from the normal heart to one in cardiogenic shock. This is a condition where the cardiac output is insufficient to maintain tissue perfusion. Also shown is the curve for an increasing level of physical activity, which requires a corresponding increase in cardiac output.
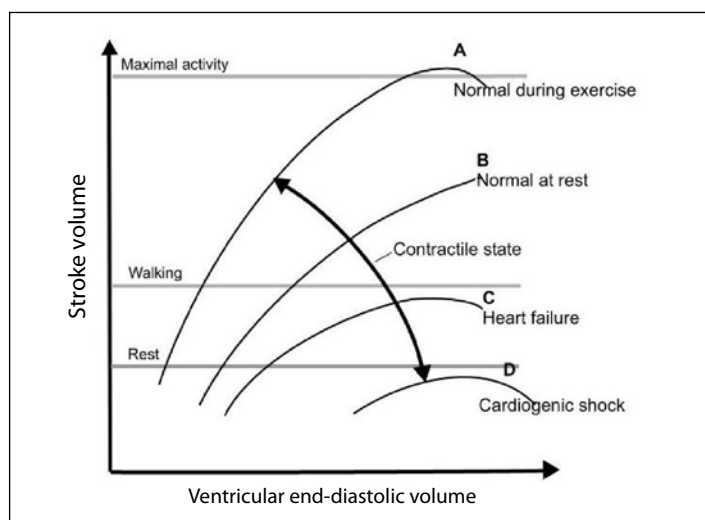

Figure 1. *Starling's Law* - *Curves A and B illustrate the rise in cardiac output with increases in ventricular end-diastolic volume (pre-load) in the normal heart. Note that with an increase in contractility there is a greater cardiac output for the same ventricular end-diastolic volume. In the diseased heart (C and D) cardiac output is less and falls if ventricular end diastolic volume rises to high levels, as in heart failure or overload*

Afterload is the resistance to ventricular ejection. Assuming the aortic valve is normal, this is caused by the resistance to flow in the systemic circulation and is the systemic vascular resistance (SVR). The resistance is determined by the diameter of the arterioles and pre-capillary sphincters; the narrower or more constricted, the higher the resistance. The level of SVR is controlled by the sympathetic system which controls the tone of the muscle in the wall of the arteriole, and hence the diameter. The resistance is measured in units of dyne.sec. cm^{-5}. A series of Starling curves with differing afterloads is shown in Figure 2, demonstrating a fall in stroke volume as afterload increases. The relationship between systemic vascular resistance and the control of arterial pressure is discussed below.
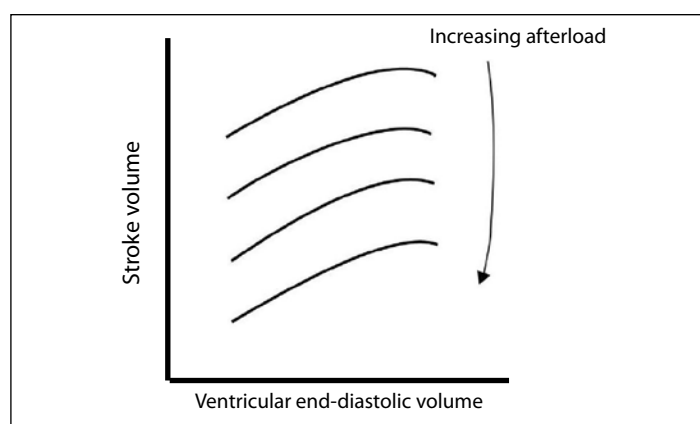

Figure 2. *The relationship between stoke volume and afterload. A series of curves illustrate the effects of increasing afterload on systemic vascular resistance. As afterload increases, the patient moves to a lower curve, with a lower stroke volume for the same ventricular end-diastolic volume (preload)*

Contractility describes the ability of the myocardium to contract in the absence of any changes in preload or afterload. In other words, it is the 'power' of the cardiac muscle. The most important influence on contractility is the sympathetic nervous system. Beta-adrenergic receptors are stimulated by norepinephrine (noradrenaline) released from nerve endings, and contractility increases. A similar effect is seen with circulating epinephrine (adrenaline) and drugs such as ephedrine, digoxin and calcium. Contractility is reduced by acidosis, myocardial ischaemia, and the use of beta-blocking and anti-arrhythmic agents.

Cardiac output will change to match changing metabolic demands of the body. The outputs of both ventricles must be identical, and also equal the venous return of blood from the body. The balancing of cardiac output and venous return is illustrated during the response to exercise. Blood vessels dilate in exercising muscle groups because of increased metabolism, and blood flow increases. This increases venous return and right ventricular preload. Consequently more blood is delivered to the left ventricle and cardiac output increases. There will also be increased contractility and heart rate from the sympathetic activity associated with exercise, further increasing cardiac output to meet tissue requirements.

CONTROL OF HEART RATE

The heart will beat independently of any nervous or hormonal influences. This spontaneous rhythm of the heart (called intrinsic automaticity) can be altered by nervous impulses or by circulatory substances, like epinephrine. The muscle fibres of the heart are excitable cells like other muscle or nerve cells, but have a unique property. Each cell in the heart will spontaneously contract at a regular rate because the electrical properties of the cell membrane spontaneously alter with time and regularly "depolarise". Depolarisation means that the electrical gradient across the cell membrane becomes less negative and then reverses, causing muscle contraction or passage of a nervous impulse. Muscle fibres from different parts of the heart have different rates of spontaneous depolarisation; the cells from the ventricle are the slowest, and those from the atria are faster.

The coordinated contraction of the heart is produced because the cells with the fastest rate of depolarisation "capture" the rest of the heart

muscle cells. These cells with the fastest rate of depolarisation are in the sinoatrial node (SA node), the "pacemaker" of the heart, found in the right atrium. As the SA node depolarises, a wave of electrical activity spreads out across the atria to produce atrial contraction. Electrical activity then passes through the atrioventricular node (AV node) and through into the ventricles via the Purkinje fibres in the Bundle of His to produce a ventricular contraction. If there is any disease of the conducting system of the heart, then this process may be interfered with and the heart rate altered. If, for example, there is disease of the AV node, then there is an electrical block between the atria and the ventricles. The ventricles will beat with their own inherent rhythm, which is much slower, usually 30-50 beats per minute.

Anaesthetic drugs, like halothane, may depress the rate of depolarisation of the SA node, and the AV node may become the pacemaker of the heart. When this occurs it is frequently termed nodal or junctional rhythm. This automatic rhythm of the heart can be altered by the autonomic nervous system. The sympathetic nervous system supply to the heart leaves the spinal cord at the first four thoracic vertebra, and supplies most of the muscle of the heart. Stimulation via the cardiac beta-1 receptors causes the heart rate to increase and beat more forcefully. The vagus nerve also supplies the atria, and stimulation causes the heart rate to decrease (bradycardia). Surgical procedures can cause vagal stimulation and produce severe bradycardia. Examples include pulling on the mesentery of the bowel, anal dilatation or pulling on the external muscles of the eye. Under normal conditions the vagus nerve is the more important influence on the heart. This is especially noticeable in athletes who have slow heart rates.

There are nervous reflexes that effect heart rate. The afferents (i.e. going to the brain) are nerves in the wall of the atria or aorta that respond to stretch. The aorta contains high pressure receptors. When the blood pressure is high these cause reflex slowing of the heart to reduce the cardiac output and the blood pressure. Similarly, when the blood pressure is low, the heart rate increases, as in shock. Similar pressure receptors are found in the atria. When the atria distend, as in heart failure or overtransfusion, there is a reflex increase in the heart rate to pump the extra blood returning to the heart. When there is a sudden reduction in the pressure in the atria the heart slows. This is called the Bainbridge Reflex and is the cause for the marked bradycardia sometimes seen during spinal anaesthesia. It is best treated by raising the legs to increase the venous return. Early administration of a cardioaccelerator such as ephedrine or epinephrine is recommended if there is no immediate response to this manoeuvre.

Circulatory substances can also affect the heart rate. Catecholamines, like epinephrine, are released during stress, and will cause an increase in heart rate. Drugs are another common cause of change in the heart rate and most anaesthetic drugs can do this. Halothane affects the SA node and will also depress the force of contraction of the heart. Isoflurane, by contrast has little direct affect on the heart, but causes peripheral vasodilation of the blood vessels. This will then decrease the blood pressure, and hence produce a reflex tachycardia as explained above. Administration of greater than 1 MAC of desflurane or isoflurane may increase sympathetic outflow and so increase heart rate transiently and acutely; this does not happen with sevoflurane. Ketamine causes stimulation of the sympathetic nervous system, and therefore produces a tachycardia. Other circulating substances may also affect the heart rate, acting indirectly through the autonomic nervous system. For example, increased blood concentrations of carbon dioxide will cause stimulation of the sympathetic nervous system and tachycardia, and this is an important sign of respiratory failure.

THE SYSTEMIC CIRCULATION

The systemic blood vessels are divided into arteries, arterioles, capillaries and veins. Arteries supply blood to the organs at high pressure, whereas arterioles are smaller vessels with muscular walls, which allow direct control of flow through each capillary bed. Capillaries consist of a single layer of endothelial cells, and the thin walls allow exchange of nutrients between blood and tissue. Veins return blood from the capillary beds to the heart, and contain 70% of the circulating blood volume, in contrast to 15% in the arterial system. Veins act as a reservoir, and venous tone is important in maintaining the return of blood to the heart, for example in severe haemorrhage, when sympathetic stimulation causes venoconstriction.

BLOOD FLOW

The relationship between flow and driving pressure is given by the Hagen-Poisseuille formula. This states that flow rate in a tube is proportional to:

$$\frac{\text{driving pressure} \times \text{radius}^4}{\text{length} \times \text{viscosity}}$$

In blood vessels flow is pulsatile rather than continuous, and viscosity varies with flow rate, so the formula is not strictly applicable. However, it illustrates an important point; small changes in radius result in large changes in flow rate. In both arterioles and capillaries changes in flow rate are brought about by changes in tone and therefore vessel radius.

Viscosity describes the tendency of a fluid to resist flow. At low flow rates the red blood cells stick together, increasing viscosity, and remain in the centre of the vessel. The blood closest to the vessel wall (which supplies side branches) therefore has a lower haematocrit. This process is known as 'plasma skimming'. Viscosity is reduced in the presence of anaemia, and the resulting increased flow rate helps maintain oxygen delivery to the tissues.

CONTROL OF THE SYSTEMIC CIRCULATION

Arteriolar tone determines blood flow to the capillary beds. A number of factors influence arteriolar tone, including autonomic control, circulating hormones, endothelium derived factors and the local concentration of metabolites.

Autonomic control is largely by the sympathetic nervous system, which supplies all vessels except the capillaries. Sympathetic fibres arise from the thoracic and lumbar segments of the spinal cord. These are under the control of the vasomotor centre in the medulla, which has distinct vasoconstrictor and vasodilator areas. Although there is a baseline sympathetic discharge to maintain vascular tone, increased stimulation affects some organs more than others (Figure 3). This tends to redistribute blood from skin, muscle and gut to brain, heart

and kidney. Increased sympathetic discharge is one of the responses to hypovolaemia, for example in severe blood loss, with the effect of protecting blood supply to the vital organs. The predominant sympathetic influence is vasoconstriction via alpha-adrenergic receptors. However, the sympathetic system also causes vasodilation via beta-adrenergic and cholinergic receptor stimulation, but only in skeletal muscle. This increased blood flow to muscle is an important part of the 'fight or flight' reaction, when exercise is anticipated.
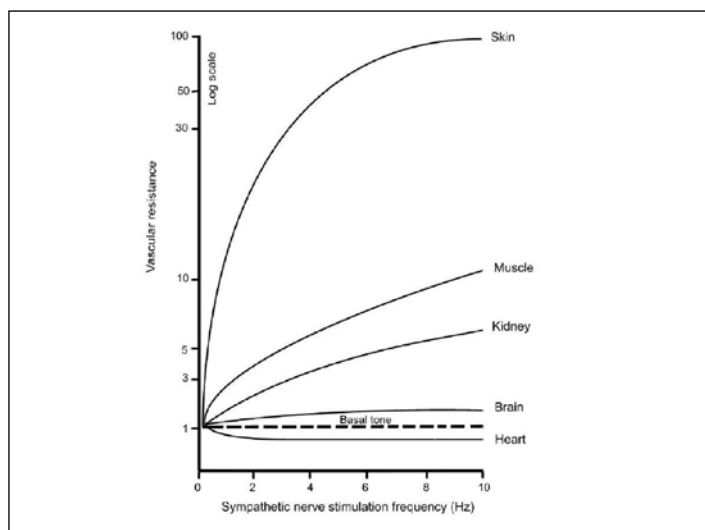

Figure 3. *The effects of sympathetic nervous stimulation on vascular resistance in different organs. Note that for the same sympathetic stimulation, the resistance is higher in skin*

Circulating hormones such as epinephrine and angiotensin II are potent vasoconstrictors, but they probably have little effect on acute cardiovascular control. In contrast, endothelium derived factors play an important role in controlling local blood flow. These substances are either produced or modified in the vascular endothelium, and include prostacyclin and nitric oxide, both potent vasodilators. An accumulation of metabolites such as CO_2, K^+, H^+, adenosine and lactate causes vasodilation. This response is probably an important mechanism of autoregulation, the process whereby blood flow through an organ is controlled locally, and remains constant over a wide range of perfusion pressure. Autoregulation is a particular feature of the cerebral and renal circulations.

CONTROL OF ARTERIAL PRESSURE
Systemic arterial pressure is controlled closely in order to maintain tissue perfusion. The mean arterial pressure (MAP) takes account of pulsatile blood flow in the arteries, and is the best measure of perfusion pressure to an organ. MAP is defined as diastolic arterial pressure plus one third of the pulse pressure, where pulse pressure is the difference between systolic and diastolic arterial pressure. MAP is the product of cardiac output (CO) and systemic vascular resistance (SVR) and can be thought of as analogous to Ohm's law (V=IR):

$$MAP = CO \times SVR$$

If cardiac output falls, for example when venous return decreases in hypovolaemia, MAP will also fall unless there is a compensatory rise in SVR by vasoconstriction of the arterioles. This response is mediated by **baroreceptors**, which are specialised sensors of pressure

located in the carotid sinus and aortic arch, and connected to the vasomotor centre in the brainstem. A fall in blood pressure causes reduced stimulation of the baroreceptors, and consequent reduced discharge from the baroreceptors to the vasomotor centre. This causes an increase in sympathetic discharge leading to vasoconstriction, increased heart rate and contractility, and secretion of epinephrine. Conversely, rises in blood pressure stimulate the baroreceptors, which leads to increased parasympathetic outflow to the heart via branches of the vagus nerve, causing slowing of the heart. There is also reduced sympathetic stimulation to the peripheral vessels causing vasodilation. Baroreceptor responses provide immediate control of blood pressure; if hypotension is prolonged, other mechanisms start to operate, such as the release of angiotensin II and aldosterone from the kidneys and adrenal glands, which leads to salt and water being retained in the circulation.

The Valsalva manoeuvre is a simple test of the baroreceptor reflex. The patient tries to breathe out forcefully against a closed larynx resulting in an increased intrathoracic pressure. This causes decreased venous return, cardiac output and a fall in blood pressure leading to reduced baroreceptor discharge to the vasomotor centre. This then causes peripheral vasoconstriction, and an increase in heart rate, which is the normal response. This has the effect of maintaining systolic pressure, although the pulse pressure is reduced due to vasoconstriction.

CARDIOVASCULAR RESPONSES TO ANAESTHESIA
All anaesthetic agents have a direct depressant effect on the myocardium. Therefore they reduce myocardial contractility, and many also reduce sympathetic stimulation of the vascular system. The result is a decreased cardiac output accompanied by vasodilation, causing hypotension. This fall in blood pressure can compromise perfusion of vital organs, especially at induction of anaesthesia in the hypovolaemic patient. In contrast, agents such as ketamine and ether increase sympathetic activity, which opposes the direct depressant effect. Thus cardiac output and blood pressure are maintained despite the direct myocardial depressant action. Volatile anaesthetic agents reduce discharge from the sinoatrial node. This can lead to junctional rhythms, when the atrioventricular node takes over as pacemaker, associated with an absent P wave on the ECG. Local anaesthetic agents depress conduction of the cardiac impulse. This effect can be therapeutic, for example in the treatment of ventricular arrhythmias with lidocaine.

Controlled ventilation in a paralysed patient has many effects on the cardiovascular system. Firstly it increases intrathoracic pressure, which reduces venous return and preload, causing a fall in cardiac output. Secondly, changes in the partial pressure of carbon dioxide ($PaCO_2$) resulting from changes in ventilation will also have cardiovascular effects. A low $PaCO_2$, which commonly occurs during controlled ventilation, causes peripheral vasoconstriction by a direct effect. This increases systemic vascular resistance, increases afterload and can result in a fall in cardiac output. It also causes cerebral vasoconstriction, reducing cerebral blood volume. A high $PaCO_2$ usually occurs in the anaesthetised patient during spontaneous breathing, and causes vasodilation and increased sympathetic activity, leading to increased cardiac output. However, the heart will be more likely to develop arrhythmias, particularly when using volatile agents.

Spinal and epidural anaesthesia blocks sympathetic nerves as well as sensory and motor fibres. This can lead to marked hypotension due to arteriolar and venous dilation because the sympathetic nerves to the lower extremities are blocked. Cardiac sympathetic nerve fibres, which arise from the high thoracic spinal cord, may also be blocked, allowing an unopposed vagal action on the heart. In this case there will not be an appropriate increase in heart rate, and blood pressure will fall further.