Applied cardiovascular physiology

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Abstract

Maintaining an equilibrium between oxygen supply and demand is a principal function of the cardiovascular system. In times of altered metabolic demand mechanisms exist to maintain the balance between supply and demand. Exercise, haemorrhage and pregnancy all lead to changes in oxygen demand and subsequently modification of cardiac output. During isotonic exercise, metabolic demands of muscle are greatly increased. Sympathetic stimulation and inhibition of the parasympathetic system lead to increases in heart rate and venous return, increasing cardiac output. This allows a proportional increase in blood flow to the exercising muscle. Cardiac output increases throughout pregnancy. In the first and second trimesters this rise is mainly due to an increase in stroke volume, however during the later stages of pregnancy stroke volume reaches a plateau and further increase in cardiac output is mediated by a rising heart rate. In contrast, during haemorrhage, decreased venous return leads to a reduction in cardiac output, with a baroreceptor response due to the drop in arterial blood pressure. The tachycardia and vasoconstriction which follows are compensatory mechanisms in an attempt to preserve blood pressure. The Valsalva manoeuvre illustrates several aspects of reflex control of the cardiovascular system and allows non-invasive assessment and quantification of control mechanisms. Changes in stroke volume during the respiratory cycle can be used to predict fluid responsiveness and can be measured as pulse pressure variation or stroke volume variation.

Keywords Autonomic; baroreceptor; cardiac output; exercise; haemorrhage; pregnancy; Valsalva

Royal College of Anaesthetists CPD Matrix: 1A01

Learning objectives

After reading this article, you should be able to:

- explain the mechanisms controlling cardiac output during isotonic and isometric exercise
- describe the changes in cardiovascular physiology which occur during pregnancy
- discuss the cardiovascular response seen in acute haemorrhage
- contrast the physiological mechanisms used to increase cardiac output during haemorrhage and exercise
- explain the Valsalva manoeuvre and draw the physiological responses in heart rate and blood pressure corresponding to each phase
- understand how the heart and lungs interact during the respiratory cycle to change stroke volume and predict fluid responsiveness

The autonomic nervous system effects cardiac output, primarily via heart rate modulation. At rest, sympathetic and parasympathetic nervous systems are in balance. The vagus nerve originates in the medulla and innervates the SA and AV nodes. Acetylcholine acts as the neurotransmitter. Parasympathetic stimulation leads to decreased activity of the SA and AV nodes, decreasing heart rate, this baseline parasympathetic activity is known as vagal tone. The sympathetic nerves arise from the thoracolumbar spinal cord and innervate the SA node and ventricular muscle mass. The nerves release norepinephrine as the neurotransmitter. The response is an increase in heart rate and an increased force of contractility of the ventricles.

Stroke volume (SV) is governed by end-diastolic volume (preload), afterload, and the strength of ventricular contraction. When end-diastolic volume (the preload) increases, the stroke volume increases. With this increased end-diastolic volume, a slight stretching of the cardiac muscle fibres also occurs, which increases the force of contraction. This is the Frank-Starling Law.

Afterload is left ventricular wall stress during ejection, which in most circumstances is a measurement equivalent to the blood pressure in the aorta. The SV has an inversely proportional relationship to the aortic BP.

Exercise

During exercise there is an increased metabolic load in the exercising muscles. In order to maintain the balance between oxygen supply and demand, several physiological mechanisms exist and sympathetic activity predominates. Initially, in anticipation of increased physical activity, there is a cortically mediated 'central command' response. This causes activation of the sympathetic nervous system and decreased parasympathetic outflow leading to an increase in heart rate prior to commencement of exercise. The next phase of the cardiovascular response is dependent upon whether the exercise is isometric (static) or isotonic (dynamic). In isometric exercise (when muscle fibre length remains static, such as during weight lifting), there is minimal change in stroke volume. Muscle contraction is sustained causing occlusion of its own arterial supply and consequently, a marked increase in peripheral vascular resistance. This increase in vascular resistance raises both systolic and diastolic arterial blood pressures. Because BP is a major determinant of afterload, the left ventricular wall stress, and thus the cardiac workload, is significantly higher during static exercise compared with the cardiac workload achieved during dynamic exercise. In comparison, during isotonic exercise (when repeated shortening and lengthening of muscle occurs, for example in running or swimming), there is a marked increase in cardiac

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output via increases in heart rate and stroke volume (Figure 1). Activation of the muscle pump greatly enhances venous return to the heart, which compensates for the reduced diastolic filling time resulting from the rise in heart rate. A decrease in oxygen concentration sensed by chemoreceptors located in the arch of the aorta and the carotid arteries and escalation of temperature leads to further sympathoactivation to allow increased oxygen delivery and reduction of internal core temperature. Epinephrine and norepinephrine released during exercise increase contractility via increased calcium influx through calcium channels in cardiac muscle membranes. This allows for greater myosin and actin interaction, increasing inotropy. During exercise, the afterload is reduced, which allows for an increase in SV and therefore increased cardiac output.

Active skeletal muscle releases locally vasoactive substances such as adenosine, K^+ and acid metabolites which cause vasodilatation, capillary recruitment and redistribution of blood flow. Blood flow to the exercising muscle may increase more than tenfold. The resultant reduction in muscle vascular resistance is offset by an increased sympathetic drive to other vascular beds. Splanchnic, renal and initially skin blood flow are all decreased. As exercise progresses, cutaneous blood flow increases in order to facilitate heat loss and then falls again as exhaustion is approached. Blood flow to the myocardium is also increased to match metabolic demands[1] (Table 1).

Effects of different levels of isotonic exercise on cardiovascular function

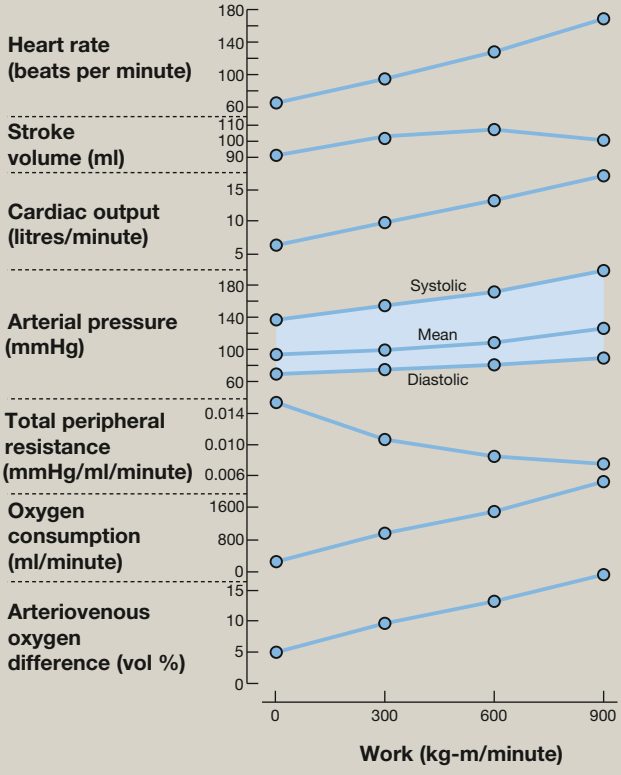

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Figure 1

Cardiopulmonary exercise testing

As work load increases, oxygen consumption (VO_2) will eventually exceed oxygen supply. The point at which the rate of VO_2 exceeds aerobic capacity is called the Anaerobic Threshold (AT). ATP required for continued exercise is then generated anaerobically producing an increase in lactic acid and subsequently CO_2 production which can be detected by cardiopulmonary exercise testing (CPET). CO_2 production increases in comparison to O_2 consumption and the respiratory exchange ratio exceeds 1.

Preoperative measurement of the AT has important clinical significance as there is elevated postoperative mortality risk following major surgery when AT is <11 ml/kg/min.[2]

Pregnancy

By 5 weeks post conception cardiac output increases. This occurs from a combination of increased stroke volume, increased heart rate and a decrease in total peripheral resistance. Cardiac output is increased by approximately 40% at the end of the first trimester. Anatomically, the heart is displaced upward and to the left by the gravid uterus. Flow murmurs are quite common due to increases in plasma volume and cardiac output. The ECG reflects these changes with left axis deviation, ST segment depression and T wave flattening often seen.

A decrease in systemic vascular resistance (SVR) occurs due to the vasodilatory effects of progesterone and the proliferation of low resistance vascular beds in the inter-villous spaces of the placenta. Blood flow to the uterus increases to about 700ml/min by term. Blood flow to the kidneys and skin also increase but the brain and liver blood flow remains constant. Despite

Blood flow to organ systems during exercise and at rest

Organ system	Blood flow (ml min^{-1})	
	Exercise	Rest
Brain	750	750
Heart	750	750
Skeletal muscle	12,500	1200
Skin	1900	500
Abdominal viscera	600	1400
Kidneys	600	1100
Other	400	600
Total	17,500	5800

In trained athletes cardiac output can be increased up to seven times its baseline, but stroke volume rarely rises above twice its resting state. With endurance training, there can be an elevation in resting stroke volume and drop in resting heart rate, with increased left ventricular muscle mass. In addition, there is an increase in resting blood volume and red cell count to enhance cardiac reserve. These changes are similar to those mechanisms evident in pregnancy.

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Table 1

the increase in cardiac output, there is a fall in BP, due to the significant drop in SVR. Diastolic pressure may fall as much as 20 % and systolic by around 8 %. By 13 weeks, the gravid uterus can compress the inferior vena cava when the woman is supine, impeding venous return and therefore leading to a fall in cardiac output. Venous blood is diverted via collaterals, particularly the vertebral venous plexus to drain via the azygous system. Obstruction of the aorta occurs to a lesser degree but can result in decreased placental blood flow. Aortocaval compression is of great importance when positioning a pregnant patient on the operating table, particularly following a neuroaxial blockade. During regional anaesthesia, sympathetic blockade occurs, so there will be a lack of physiological compensation. This can lead to profound hypotension. It is usual to use either a wedge under the patient's right flank, or to tilt the operating table to the left to counteract these effects. In extreme hypotension (or foetal compromise such as a bradycardia) the patient can be turned to the full left lateral position.[3]

Haemorrhage

The physiological response to haemorrhage involves reflex compensatory mechanisms of the cardiovascular and neurohormonal systems. These macrovascular, renal and microvascular changes divert blood away from non-vital organs and preserve the function of vital organs during haemorrhage.

Acute blood loss of greater than 5% of total blood volume will trigger an immediate physiological response. The decrease in preload reduces stroke volume and cardiac output which in turn reduces baroreceptor discharge in the aortic arch and carotid sinus. Afferent nerve fibres via the vagus to the cardio-inhibitory centre reduce parasympathetic outflow to the heart while stimulation of the vasomotor centre via the carotid sinus nerve simultaneously increase sympathetic activity. The result is a compensatory increase in heart rate and systemic vascular resistance in an attempt to maintain blood pressure.

The microvascular circulation responds to haemorrhage by minimizing fluid escape into the interstitial space. As capillary hydrostatic pressure reduces the shift in Starling's forces promote intravascular fluid retention.

A reduction in renal blood flow detected in the juxtaglomerular apparatus of the renal afferent arterioles leads to activation of the renin-angiotensin-aldosterone system. Renin converts plasma angiotensinogen to angiotensin which is subsequently converted in the lungs by ACE to angiotensin II. The result is release of aldosterone from the adrenal cortex, antidiuretic hormone (ADH) production and profound vasoconstriction. Aldosterone acts on the distal convoluted tubules to cause salt and water retention.

ADH is released from the posterior pituitary in response to angiotensin II, trauma, hypovolaemia and an increase in serum osmolality detected in the hypothalamus. ADH causes peripheral vasoconstriction and acts on the collecting ducts of the kidney to retain water.

The net effect is intravascular volume expansion, peripheral vasoconstriction and reflex tachycardia in an attempt to preserve blood pressure. If blood loss continues clinical signs of hypoperfusion become evident including oliguria, confusion and cold, clammy peripheries with a prolonged capillary refill time. Once blood loss exceeds 30% the compensatory mechanisms are overwhelmed and hypotension is inevitable.

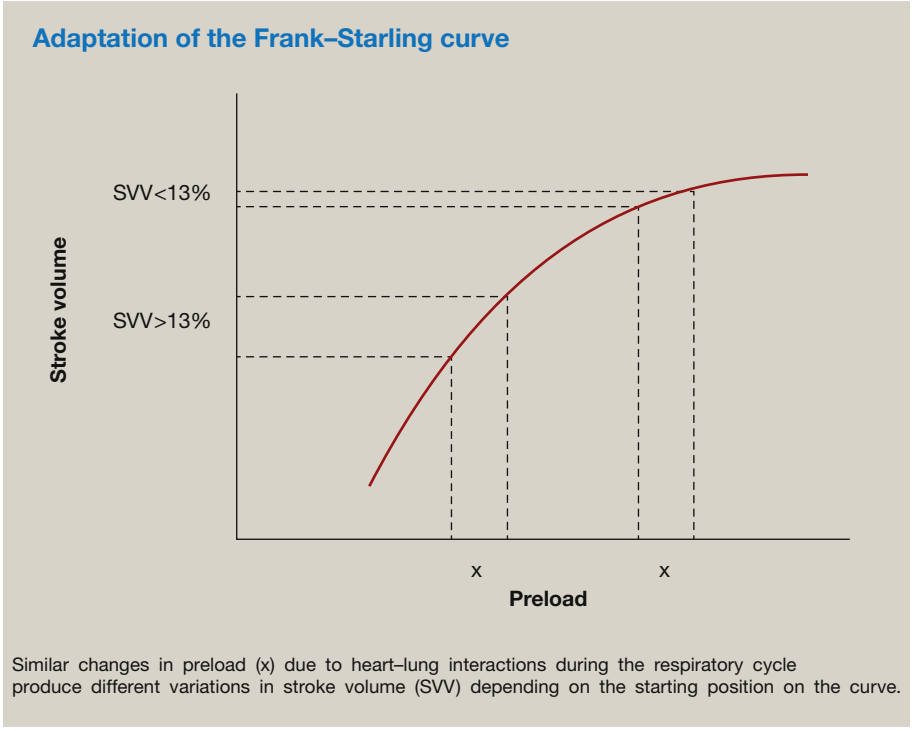

Figure 2

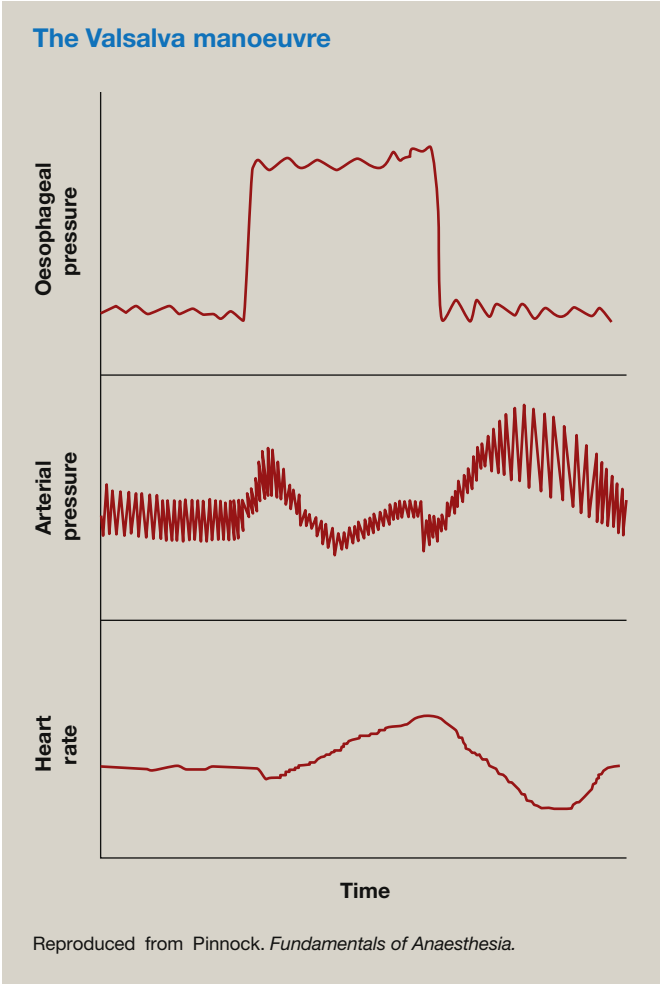

Figure 3

Fluid responsiveness

The Frank-Starling mechanism describes the ability of the heart to increase its force of contraction, and therefore the stroke volume in response to increases in venous return. An increase in stroke volume by >10% following a 500ml fluid challenge is termed fluid responsiveness. If preload is then increased beyond the flat part of the Frank-Starling curve, any further increase will not increase stroke volume any further and may be detrimental.

During normal physiological conditions the heart operates on the ascending part of the Frank-Starling curve and small changes in preload will affect the stroke volume (Figure 2). Such changes can be seen due to the dynamic interactions between the heart and lungs during the respiratory cycle and can be used to predict fluid responsiveness during mechanical ventilation.[4]

Positive pressure ventilation produces an increase in alveolar pressure that subsequently increases right ventricular afterload and reduces venous return to the right ventricle. There is a simultaneous increase in left ventricular preload as blood is squeezed from the pulmonary capillary bed into the left ventricle. The result is an increase in stroke volume and therefore elevation in pulse pressure that is greatest at end inspiration and lowest during expiration.

This swing during the respiratory cycle is exaggerated during hypovolaemia and can be measured as stroke volume variation (SVV) derived from pulse contour analysis or as pulse pressure variation (PPV) derived from analysis of the arterial waveform. In the absence of arrhythmias or spontaneous breathing, a PPV/SVV of greater than 12–13% reliably predicts fluid responsiveness.[5]

Valsalva manoeuvre

(Figure 3) The Valsalva manoeuvre is a good bedside indicator of autonomic function. It is defined as a forced expiration against a closed glottis following a full inspiration, at a pressure of 40 mmHg, held for 10 seconds.

It consists of four phases. Phase I is the initial part of the manoeuvre, during which there is a rise in intrathoracic pressure. This leads to expulsion of blood from thoracic vessels. During phase II, the sustained high intrathoracic pressure impedes venous return and therefore preload is decreased, dropping the systemic blood pressure. Hypotension activates baroreceptor reflexes causing tachycardia and vasoconstriction to normalize blood pressure. Phase III begins as the intrathoracic pressure falls suddenly, a further drop in BP occurs due to pooling of blood within the pulmonary vessels. Phase IV is signalled by an overshoot in BP as despite the restoration of venous return, compensatory mechanisms are ongoing. This leads to a baroreceptor mediated bradycardia. In autonomic dysfunction the initial fall in blood pressure is maintained until intrathoracic pressure is normalized. There are no reflex changes in heart rate and no overshoot. An abnormal response is also seen in patients with cardiac failure, tamponade, and constrictive pericarditis. In these populations, a square wave response occurs. There is an initial rise in blood pressure which remains constant throughout and only returns to baseline at the end of the manoeuvre.[6] ◆

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