Section 1 Basic principles

Chapter 1

Oxygen delivery, cardiac function and monitoring

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Oxygen delivery

The purpose of the circulatory system is ultimately the delivery of oxygen and nutrients to cells, with removal of waste and carbon dioxide. Oxygen delivery depends on blood flow (cardiac output) and the amount of oxygen in the blood.

Oxygen delivery = cardiac output × oxygen content in arterial blood

Oxygen is carried in the blood in two forms:

1. Bound to hemoglobin (the amount of oxygen bound to hemoglobin depends on oxygen saturation)
2. Dissolved in plasma (the amount of oxygen dissolved in plasma depends on the arterial partial pressure of oxygen (PaO_2) and the solubility of oxygen)

Arterial oxygen content = oxygen bound to hemoglobin + oxygen dissolved in plasma

Most of the oxygen in blood is carried bound to hemoglobin, and only a small fraction is dissolved. Clinically, this means that an arterial oxygen saturation of 90% (corresponding to a PaO_2 of ~60 mmHg) provides essentially normal arterial oxygen content. Oxygen saturation is measured noninvasively using pulse oximetry.

Arterial oxygen content = oxygen bound to hemoglobin + oxygen dissolved in plasma

$$\textbf{Arterial oxygen content } (CaO_2) = \textbf{(hemoglobin)(oxygen saturation) (1.34)} + \textbf{(}PaO_2\textbf{) (0.031)}$$

The usual arterial oxygen saturation is close to 100%, and PaO_2 is approximately 90 mmHg. Arterial blood normally contains approximately 200 mL of oxygen per liter of blood. If we assume a cardiac output of ~5 L/min then this is an oxygen delivery of ~1 L/min.

Oxygen consumption

Oxygen is carried to the tissues and delivered to cells via the capillaries, where oxygen is taken up (consumed) by cells, so that venous blood contains less oxygen (and more carbon dioxide) than arterial blood. The partial pressure of oxygen in the venous blood (PvO_2) is, on average, ~40 mmHg (this corresponds to an oxygen saturation of ~70–75% in the venous blood).

Handbook of ICU Therapy, third edition, ed. John Fuller, Jeff Granton and Ian McConachie. Published by Cambridge University Press.

The overall oxygen content of venous blood is ~150 mL of oxygen/liter of blood. Overall oxygen consumption is ~250 mL of oxygen per minute; if delivery is ~1 L/min this means we usually extract about 25% of the oxygen delivered.

- Oxygen consumption (demand) will increase with exercise or fever
- Sedation, paralysis and hypothermia decrease oxygen consumption.

Venous oxygen saturation

Venous oxygen saturation (SvO_2) reflects oxygen supply and demand; venous oxygen saturation will decrease if there is a decrease in oxygen delivery or an increase in oxygen consumption, because cells will extract more oxygen from the blood to meet demand [1].

Venous oxygen saturation can be monitored either:

- Intermittently, with blood gas sampling from a central venous catheter in the superior vena cava, or from the pulmonary artery using a pulmonary artery catheter.

Or

- Continuously, using a central venous or pulmonary artery catheter designed to continuously measure venous oxygen saturation.
- Note that measuring venous oxygen saturation from a femoral venous catheter is not reliable as an indicator of global perfusion since it reflects oxygen supply and demand only from the lower extremity [2].

A decrease in venous oxygen saturation below the usual value of ~70–75% suggests increased oxygen extraction and an oxygen supply/demand imbalance. Increasing oxygen delivery with inotropic support, or red blood cell transfusion if the hemoglobin is low, may improve patient outcomes in sepsis [3].

- A normal SvO_2, however, does not necessarily reflect normal oxygen delivery because venous oxygenation is a flow-weighted average of venous blood (no flow in means no flow out of tissues).
- In some clinical situations, in particular sepsis, there is maldistribution of flow at the microvascular level. A normal or high venous oxygen saturation may be associated with a worse prognosis in these patients [4].

Lactic acid is a by-product of anaerobic metabolism. Monitoring lactate levels as an indicator of tissue ischemia and anaerobic metabolism may also be used to monitor response to therapy [5–7].

Cardiac function

Cardiac output

Cardiac output (CO) is the volume the heart ejects over time (usually expressed as L/min), a normal cardiac output is about 5 L/min. Normal cardiac output varies with the size of a patient (you would expect a 200 kg patient to have a higher cardiac output than a 50 kg patient because of the increased body mass that must be perfused). In order to standardize measurements cardiac output is divided by a patient's body surface area (BSA) to calculate the cardiac index (CI). The normal CI is 2.5–4 L/min/m^2.

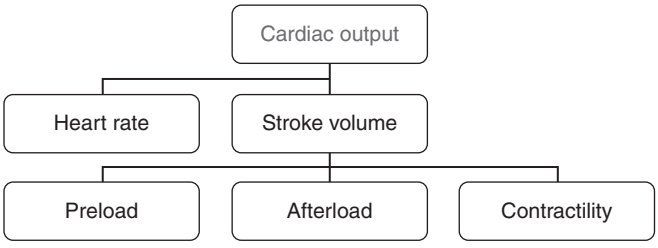
Cardiac index (CI) = CO/BSA

Stroke volume (SV) is the volume of blood ejected with a single contraction (because the right and left ventricle are in series, it follows that the stroke volume of the right ventricle must be the same as the left ventricle). Cardiac output over a minute therefore is the stroke volume multiplied by the number of beats per minute (or heart rate).

CO = SV × HR

Stroke volume is determined by:

1. Preload – the end-diastolic volume of the ventricle
2. Afterload – the wall tension the ventricle must develop to eject blood
3. Contractility (or inotropy) – the intrinsic performance of the heart at a given preload and afterload.



Heart rate

Since cardiac output depends on heart rate it follows that a low heart rate (bradycardia) can contribute to low cardiac output.

- An increase in heart rate increases the force of ventricular contraction (this is known as the treppe phenomenon). This effect, however, is minimal or absent in a failing ventricle with poor systolic function.
- An increase in heart rate increases myocardial oxygen demand, which may precipitate cardiac ischemia, and decreases the time available for diastolic filling.

Overall, the optimal heart rate is determined by a combination of the treppe phenomenon and the need for diastolic filling time, as well as other factors in individual patients such as intrinsic contractility, and valvular or ischemic heart disease.

Stroke volume

The normal ventricle ejects approximately 70 mL of blood with each beat – this is the stroke volume (SV). The ventricles do not empty completely with contraction, there is some residual volume remaining at the end of systole (end-systolic volume). During diastole the ventricles fill; a normal end-diastolic volume (EDV) is approximately 120 mL.

Ejection fraction

Ejection fraction is defined as the ratio of SV/EDV. A normal ejection fraction is 60–65%.

Preload

Preload is defined as the end-diastolic volume (EDV) of the left ventricle.

The determinants of preload include:

- Circulating blood volume – more volume increases preload.
- Venous tone – venoconstriction increases preload. Venous tone determines venous capacitance (the veins are the major reservoir for blood volume).
- Ventricular compliance – a more compliant ventricle can hold more blood at a given pressure than a noncompliant (stiff) ventricle.
- Afterload – if afterload is increased acutely, less blood is pumped out with ventricular contraction, which leaves more residual blood to add on to end-diastolic volume. Preload therefore is increased (this is one of the acute compensatory responses to an increase in afterload).
- Atrial contraction – especially in patients with stiff noncompliant ventricles, by forcing some additional blood into the ventricles from the atria during late diastole.
- Intrathoracic pressure – increased pressure in the thorax can reduce venous return to the heart; intrathoracic pressure is increased with positive-pressure ventilation and the use of positive end-expiratory pressure with mechanical ventilation. Hypovolemic patients may become hypotensive with intubation and positive-pressure ventilation because of the increased intrathoracic pressure and decreased venous return to the right ventricle.

An increase in preload (end-diastolic volume of the ventricle) and hence muscle-fiber length increases resting tension, velocity of tension development and peak tension:

- This allows for greater stroke volume and therefore cardiac output. This is the Frank–Starling relationship.
- Excessive ventricular volume, however, will eventually overwhelm the ventricle's capacity to pump blood forward, and lead to decompensation. As well, a ventricle with poor systolic function has less capacity to improve contractility with an increase in preload.

Clinically we cannot easily measure preload. Central venous pressure or pulmonary capillary wedge pressure measurements provide information about ventricular filling pressures; however, correlation with intravascular and intraventricular volume depends on many factors, such as vascular tone and ventricular compliance.

Afterload

Afterload is the wall tension or stress the ventricle must develop to eject blood. The law of Laplace states that tension is proportional to both the pressure and radius of a sphere, divided by twice the wall thickness. This equation assumes that the ventricles are spheres. Although the ventricles are not true spheres, pressure, radius and wall thickness contribute to ventricular afterload.

Tension ~ (pressure × radius)/(wall thickness × 2)

- Afterload will therefore be increased if the ventricle generates higher pressures or becomes larger (dilates). This means that the afterload for the left ventricle is normally higher than for the right ventricle – it is larger and develops much higher pressures. This is offset somewhat by the fact that the left ventricle is more muscular, with a thicker wall than the right ventricle.

- Afterload to the ventricle includes a component of preload (ventricular size or radius), therefore afterload and preload are interdependent.
- In a normal heart, changes in afterload do not impact stroke volume until extreme values are reached; however, a ventricle with decreased contractility (a "failing ventricle") is very sensitive to an increase in afterload.

Clinically, we often simplify the concept of afterload to refer to the pressure the ventricle generates; we can measure blood pressure quite easily, but it is much more difficult to quantify the size of a ventricle or its wall thickness.

- Typical conditions that will increase the afterload of the left ventricle are hypertension and aortic stenosis (aortic stenosis produces a pressure gradient between the left ventricle and aorta).
- Examples of diseases that increase afterload to the right ventricle include pulmonary hypertension and pulmonary embolism.
- A chronic increase in afterload leads to compensatory ventricular hypertrophy. An acute increase in afterload can cause acute cardiac dilatation.
- A clinical example is acute massive pulmonary embolism leading to increased pulmonary artery pressures and acute right ventricular dilatation seen on echocardiography.

Compliance

Compliance is the relationship between volume and pressure.

Compliance = Δ volume/Δ pressure

The concept of compliance applies to the heart and diastolic function.

- Ventricular volume can be increased in the normal ventricle with little change in pressure, but as ventricular end-diastolic volume increases further, the diastolic intraventricular pressure will increase.
- With a less compliant (stiffer or less distensible) ventricle, the same end-diastolic volume is associated with a higher left-ventricular diastolic pressure.

Contractility

Inotropy or contractility is the intrinsic ability of cardiac muscle cells to shorten in response to a stimulus (the stimulus is an action potential); shortening of cardiac muscle tissue results in ejection of blood. An increase in contractility results in a higher stroke volume.

Inotropy can be acutely (myocardial infarction) or chronically (systolic heart failure) reduced. Clinically this is seen as a reduction in ejection fraction of the left ventricle. The autonomic nervous system is responsible for controlling the inotropic state of the heart.

- Increased levels of circulating catecholamines result in greater contractility and an increase in heart rate (mediated by the adrenergic β-receptors), as well as increased vascular resistance (vasoconstriction mediated by the adrenergic α-receptors).
- Inotropic medications (such as dopamine, dobutamine or epinephrine) can be given as intravenous infusions to increase cardiac contractility.
- These medications, however, may cause tachycardia, arrhythmias and increased myocardial oxygen consumption predisposing to myocardial ischemia [8].

The right and left ventricles: similar but different

The right ventricle (RV) pumps blood to the relatively low-pressure, low-resistance pulmonary system. Pulmonary hypertension is defined as a mean pulmonary artery pressure of >25 mmHg, or a pulmonary vascular resistance of >3 Wood's units); the left ventricle generates higher pressures (the normal systemic mean arterial pressure is ~65 mmHg or more).

- The normal right ventricle is less muscular than the left ventricle (LV) anatomically. The right ventricle may hypertrophy over time (for example in patients with chronic pulmonary hypertension), just as the left ventricle may hypertrophy when faced with an increase in afterload.
- The right ventricle may acutely dilate with a sudden increase in afterload. For example, in a patient with acute pulmonary embolism a sudden increase in pulmonary artery pressure can lead to acute right ventricular dilation and RV failure.
- With severe RV dilation the RV may "push" the interventricular septum over toward the LV, impacting left ventricular diastolic filling, compliance and systolic function. This phenomenon is known as "ventricular interdependence" [9].

Coronary blood flow to the right ventricle occurs throughout the cardiac cycle – during both systole and diastole – because the right ventricle systolic pressures are not high enough to compress the coronary blood vessels. Maximal coronary blood flow to the left ventricle, however, occurs during early diastole. With the left ventricle there is actually a brief reversal of coronary flow during systole, as the muscular left ventricle contracts and generates high systolic pressures.

- Right heart failure is associated with an increase in right-sided pressures – clinically this is seen as elevated jugular venous pressure or central venous pressure – this pressure may be transmitted downstream causing congestion of the liver, ascites formation and peripheral edema.
- Patients can have biventricular failure (both right and left ventricular failure), pure right-sided heart failure (for example, with chronic pulmonary hypertension), or left-sided failure.
- Note, however, that with chronic left-heart failure the left-sided pressures will be increased, and the right ventricle will have to pump against these higher pressures, eventually causing the right ventricle to fail also; in fact the most common cause of right-sided failure is chronic left-heart failure.

Monitoring

Monitoring may be described as the intermittent or continuous observation of a patient using clinical examination and appropriate equipment to assess progress of the condition:

- The most useful and reproducible monitor remains a thorough and repeated clinical examination by the doctor.
- Not all critical care environments are the same, and all models of monitoring equipment are slightly different. The clinician must take time to become familiar with the equipment in his or her own hospital.

Monitoring may allow us to:

- intervene therapeutically in emergency situations,
- guide and plan future therapy,

- establish diagnoses,
- establish prognosis.

Monitoring, however, is not a therapy in itself; in order for monitoring to improve outcome it must be correctly interpreted and acted upon, and done with the minimum of complications.

Oxygen saturation monitoring (pulse oximetry)

Oxygen saturation monitors (pulse oximetry) use two different wavelengths of light in the red and infrared spectrum, which are absorbed differentially by oxyhemoglobin and deoxyhemoglobin. The pulse oximeter separates the pulsatile component of the absorption signal from the nonpulsatile component – the assumption being that the pulsatile component represents arterial blood.

- If a patient is hypotensive or severely vasoconstricted, the pulse oximeter may not be able to detect an accurate signal.
- The pulse oximeter shines the light through tissue (usually a finger, but earlobe, nose etc. can be used) and then determines how much of each wavelength was absorbed – and calculates the oxygen saturation.
- Since the absorption spectrum of carboxyhemoglobin (COHb) and oxyhemoglobin with the light wavelengths used in pulse oximetry are similar, the oximeter will give a falsely high oxygen saturation reading with carbon monoxide poisoning. Similarly methemoglobinemia may interfere with accurate pulse oximetry [10].

Noninvasive blood pressure monitoring

NIBP stands for noninvasive blood pressure and uses a blood pressure cuff, with a machine that automatically inflates and deflates the cuff. Noninvasive blood pressure devices provide systolic, diastolic and mean arterial pressure, as well as an audible alarm system, and can be programmed to measure BP as often as required clinically (as often as every minute in an unstable patient). The measurement is based on oscillometry; variations in the pressure in the BP cuff due to arterial pulsations are sensed by the monitor (if you take a blood pressure manually you will note these oscillations yourself as small deflections in the sphygmomanometer as you deflate the cuff). The pressure at which oscillations are maximal correlates with mean arterial pressure; systolic and diastolic pressures are calculated using a formula based on the peak of the oscillations.

- Automated NIBP measurements correlate closely with directly measured BP (standards require that error be less than 5 ± 8 mmHg with respect to reference standard); in severely hypotensive patients it may be impossible to measure BP using NIBP.
- Noninvasive blood pressure measurements will be less accurate (just as manual BP measurement is) if the BP cuff is the incorrect size.
- Complications of NIBP measurement that have been described include petechiae, bruising, and neuropathy (if the cuff compresses a nerve).

Direct arterial blood pressure measurement

- The insertion of a small (common sizes are 20 or 22 gauge) teflon-coated catheter into an artery (usually the radial, ulnar, brachial, dorsalis pedis or femoral are used) allows

direct beat-to-beat assessment of the systemic BP [11]. This may be required in patients with hemodynamic instability, or with the use of inotrope or vasopressor infusions.

- The presence of an arterial line also provides access for the measurement of arterial blood gas samples.
- Complications include local bleeding and infection. Serious complications include thrombosis and development of arterio-venous (AV) fistulas.
- Accurate pressure measurement requires zeroing of the transducer (opening the transducer to atmospheric pressure and identifying that as a pressure of "zero").
- In addition, the height of the transducer relative to the patient is important – the transducer should be positioned at the level of the mid-axillary line, 4th intercostal space of the patient (at the level of the heart). If the transducer was inadvertently raised to 14 cm above the patient, for example, the pressure reading would be ~ 10 mmHg lower than the true reading.
- Other reasons for inaccuracy of invasive pressure monitoring include damping or under-damping of the pressure trace. The pressure waveform may be "damped" if the catheter is kinked, or with blood or air within the catheter. It is also possible for the pressure waveform to be "under-damped" – typically recognized as a rapid, spiked upstroke in the waveform with a systolic pressure overshoot. This occurs when the pressure waveform in the catheter causes the transducer to reverberate at its own harmonic frequency. Typically, mean pressures are more accurate in the presence of under-damped system.

Central venous pressure (CVP) monitoring

Central venous catheters may be used to:

- Monitor central venous pressure.
- Provide central venous access for infusions of potent vasoconstrictors or hypersosmolar solutions such as total parenteral nutrition or both.
- Central venous pressure (pressure in the superior vena cava) may be monitored with jugular, subclavian or peripherally inserted central venous catheters [12].
- Femoral venous catheters are not useful for monitoring of central venous pressure.
- Accurate measurement of CVP requires that the catheter be zeroed, and the transducer leveled at the mid-axillary fourth intercostal space (as for arterial catheters) [13].

In addition CVP will fluctuate with changes in intrathoracic pressure:

- In a spontaneously breathing patient the CVP will decrease on inspiration as intrathoracic pressure decreases; with positive-pressure ventilation the CVP will increase on inspiration due to increased intrathoracic pressure.
- The actual filling pressure (transmural pressure) for the right ventricle is the CVP measured when intrathoracic pressure is zero – this will tend to be at end-expiration.
- For patients on positive end-expiratory pressure (PEEP), particularly levels over 10 cm H_2O, the CVP will be increased relative to the true filling pressure; the actual amount of increase can only be measured using a measurement of intrathoracic pressure (such as a pleural or esophageal pressure manometer).

CVP is often used as a guide for fluid management:

- A protocol for therapy in patients with early sepsis (within 6 hours), which included a goal of CVP of 8–12 mmHg, and additional fluid resuscitation to meet the target CVP, was associated with improved outcome [3].
- Ongoing aggressive fluid resuscitation after the initial early resuscitation, however, may not be beneficial [14, 15].

CVP is not an accurate surrogate for intravascular volume. The CVP depends on many factors:

- Patients may have a low CVP with a normal intravascular volume (for example with vasodilation, or a compliant right ventricle).
- Patients may have a higher than normal CVP and have a low intravascular volume, or benefit from additional fluid challenge (for example, with vasoconstriction, high intrathoracic pressure due to positive end-expiratory pressure, cardiac tamponade, or pulmonary hypertension and right-heart failure).

Clinically, patient assessment for intravascular volume status should include heart rate, blood pressure, capillary refill, urine output, response to previous fluid challenges, inotrope and vasopressor requirements, and overall fluid balance, venous oxygen saturation, lactate levels etc., as well as any trends in monitored parameters.

Other ways to assess cardiac function and intravascular volume

Pulse pressure variation (PPV)

- Pulse pressure variation is the cyclic variation in pulse pressure and systolic blood pressure with respiration due to changes in intrathoracic pressure; pulse pressure will be maximal at the end of inspiration and minimal during exhalation (in a mechanically ventilated patient); the PPV response is exaggerated in patients with "preload reserve" [16, 17].
- Pulse pressure variation can be used to predict response to fluid challenge (volume responsiveness).

Limitations of PPV monitoring include:

- Requires patients to be on positive-pressure ventilation; spontaneous breathing attempts (including triggering) will lead to changes in venous return and make PPV analysis inaccurate.
- Patients must be in sinus rhythm.
- PPV may be less accurate in patients with elevated filling pressures [17].
- Tidal volume is important – a small tidal volume (resulting in smaller changes in intrathoracic pressure) will make PPV inaccurate; a tidal volume of at least 8 mL/kg PBW is required [17].

Echocardiogram

- Echocardiography can provide information about ventricular size, ejection fraction and also identify pericardial fluid.

- Visualization of the inferior vena cava (IVC) as it enters the right atrium provides information about the size of the IVC, and in spontaneously breathing patients "collapse" of the IVC (or a decrease in diameter of over 30%) on inspiration suggests preload responsiveness.
- Cyclic variation in IVC volume/diameter may predict fluid responsiveness in a mechanically ventilated patient; however, large tidal volumes (at least 8 mL/kg PBW are required, even temporarily) and spontaneous breathing attempts are required for this assessment [18].

Pulmonary artery catheters

Pulmonary artery catheters (PAC) are catheters that use a distal balloon filled with 1.5 mL of air to "float" the catheter:

- from the central vein into the **right atrium** (pressure measured from the tip of the catheter will show a typical venous waveform), then
- across the **tricuspid valve** and into
- the **right ventricle** (as the catheter enters the right ventricle the waveform will show an increase in systolic pressure with the diastolic pressure approximately equal to the venous and atrial pressure). Typical RV pressure, in the absence of pulmonary hypertension is ~ 20–25 mmHg/0–8 mmHg. The catheter will then float across the pulmonic valve and into
- the **pulmonary artery**. As the catheter crosses the pulmonic valve the waveform of the systolic pressure will be unchanged, but the diastolic pressure will increase – typically to 10–15 mmHg. If the balloon is left inflated the catheter will continue to float along the pulmonary artery until it "wedges" and cannot float any further distally. At this point the pressure monitored from the tip of the catheter will be
- the **pulmonary wedge pressure** – this pressure reflects left atrial pressure (since there is an uninterrupted column of blood from the tip of the catheter to the left atrium, and a zero flow state since the catheter is occluding flow). This pressure is sometimes also called pulmonary artery occlusion pressure.

Pulmonary artery catheters have the ability to measure CVP (from the CVP port which is ~ 30 cm proximal to the catheter tip) as well as pulmonary artery pressure and the pulmonary wedge pressure.

Pulmonary artery catheters can also measure cardiac output using a principle known as thermodilution. There is a thermistor (temperature monitor) at the tip of the PAC. If a known quantity of fluid (typically 10 mL) at a known temperature (typically room temperature or ice-cold saline is used) is injected proximal to the thermistor (through the CVP port) the distal thermistor will detect a decrease in temperature relative to the baseline pulmonary artery temperature. In patients with a high cardiac output the relatively cold bolus of saline will be "diluted" by the large volume of blood flowing by and the temperature change will be small and short-lived. In a patient with a low cardiac output the temperature decrease will be larger and last longer. A computer is used to integrate the area under the temperature change curve and calculate the cardiac output.

Note that cardiac output measurements will not be accurate in patients with tricuspid regurgitation; other causes of cardiac output measurement error include: malpositioning of the catheter, rapid infusion of cold solutions (for example blood products) at the time of