Chapter 14
Hypotension and Shock

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Key Points

- Shock is a life-threatening, generalised form of acute circulatory failure associated with inadequate oxygen utilisation by the cells.
- Shock may result in macrocirculatory and microcirculatory abnormalities.
- Management components include recognition of pattern of shock, selecting appropriate treatment, specific therapy for the underlying problem and monitoring clinical response.
- Resuscitation goals are based on 'VIP' rule: V for ventilate, I for infuse and P for pump.
- Lactate, mixed venous oxygen saturation and serial cardiac output measurements may help monitor response to therapy.

Introduction

Traditionally shock, or more precisely circulatory shock, was defined as an acute clinical syndrome initiated by ineffective perfusion resulting in severe dysfunction of organs vital to survival. More recently, the European Society of Intensive Care Medicine (ESICM) has defined shock as a life-threatening, generalised form of acute circulatory failure associated with inadequate oxygen utilisation by the cells [1]. The latter definition is more appropriate since inadequate cellular oxygen

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utilisation may be the result of either a low cardiac output state with reduced oxygen transport (e.g. cardiogenic shock) or altered oxygen extraction (e.g. mitochondrial dysfunction) with normal or increased cardiac output (e.g. septic shock). Inadequate cellular oxygen utilisation leads to cellular dysoxia with resultant increase in blood lactate levels.

Diagnosis of Shock

The diagnosis of shock is based on a triad of features [2] that include arterial hypotension (haemodynamic), evidence of tissue hypoperfusion (clinical) and hyperlactataemia (biochemical). Although clinically arterial hypotension has been considered a cardinal sign of shock, this may not be always present as hypotension can be masked by a sympathetic vasoconstriction response [3]. A systolic blood pressure of <90 mmHg is considered as an arbitrary value for hypotension. However younger patients may tolerate lower blood pressures without any clinical evidence of tissue hypoperfusion or hyperlactataemia. Conversely, in older patients, tissue hypoperfusion and hyperlactataemia may occur even with a higher blood pressure.

The clinical signs of tissue hypoperfusion have been described through three 'windows' [1–3]. The cutaneous window (the skin) responds to circulatory shock, in low-flow states, with sympathetic activation resulting in vasoconstriction and manifests as cold, clammy, pale or dusky-coloured skin. It is important to remember that the skin may be warm and appear well perfused in distributive shock (e.g. warm phase of septic shock), even in the presence of significant hypotension, tissue hypoperfusion and organ dysfunction. The second window, the neurological window, is characterised by drowsiness, disorientation or confusion. The renal window presents as reduced (typically <0.5 ml/kg/h) urine output (in the absence of tubular absorptive dysfunction).

The biochemical marker for hypoperfusion is hyperlactataemia, which indicates abnormal cellular oxygen metabolism (cellular dysoxia). The blood lactate level is increased (>1.5 mmol/l) in acute circulatory failure. Although hyperlactataemia is generally associated with anaerobic metabolism, regional hypoperfusion (e.g. limb ischaemia, bowel ischaemia), excessive aerobic glycolysis (e.g. seizures, hyperventilation), drugs (e.g. metformin, beta-adrenergic agents) or decreased utilisation (e.g. liver failure) may also increase lactate levels [3]. In the context of altered tissue perfusion, the severity of hyperlactataemia and changes in lactate concentration over time predict outcome [3].

Pathophysiology

Circulatory shock is associated with both macrocirculatory and microcirculatory changes. Macrocirculatory parameters are called *upstream parameters*, while microcirculatory parameters are called *downstream parameters*. The upstream

parameters are cardiac output and systemic vascular resistance. Cardiac output is the product of heart rate and stroke volume, while systemic vascular resistance is determined by mean arterial pressure (MAP), central venous pressure (CVP) and cardiac output (Fig. 14.1). Macrocirculatory failure may occur either due to low cardiac output or reduced systemic vascular resistance.

Microcirculatory failure occurs either as a consequence of macrocirculatory failure (e.g. cardiogenic shock) or due to a systemic process that initiates microcirculatory abnormalities (e.g. sepsis, pancreatitis, acute liver failure). Unlike the macrocirculation which can be more easily measured (cardiac output, vascular resistance) and manipulated, it is more difficult to assess and treat microcirculatory abnormalities. Surrogate markers such as lactate, mixed venous oxygen saturation ($ScvO_2$), veno-arterial carbon dioxide ($vaCO_2$) difference and gastric tonometry have been used to study the adequacy of the microcirculation. Although microcirculatory changes in circulatory shock are global, regional vascular beds may respond differently by either shunting blood or vasodilatation. For example, regions such as the skin, muscle and splanchnic circulation may typically respond to the early phases of hypovolaemic shock by vasoconstriction in order to increase mean systemic filling pressure and maintain blood flow to more essential organs.

At a cellular level, several changes have been noted in shock. This includes endothelial dysfunction, leucocyte activation, changes in the haemorheological

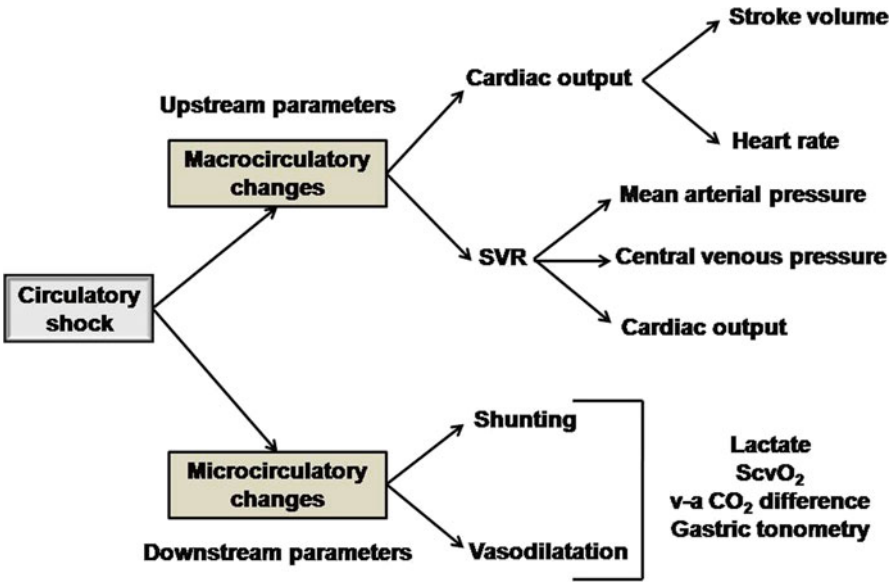

Fig. 14.1 Macrocirculatory and macrocirculatory changes. Circulatory shock is associated with macrocirculatory (upstream) and microcirculatory (downstream) changes. Macrocirculatory changes include alterations in cardiac output, reflected by stroke volume and heart rate and systemic vascular resistance reflected by changes in mean arterial pressure, central venous pressure and cardiac output. Microcirculatory changes of shunting and vasodilatation are reflected by downstream parameters such as lactate levels, mixed venous saturation (ScvO2) and veno-arterial CO2 ($vaCO_2$) difference

Table 14.1 Different types of shock

Type of shock	Pathophysiology	Haemodynamic changes		
		Central venous pressure	Cardiac output	Systemic vascular resistance
Cardiogenic	Pump failure	High	Low	High
Distributive	Vasodilatation	Low	High	Low
Hypovolaemic	Loss of volume	Low	Low	High
Obstructive	Obstruction	Variable	Low	High

The highlighted box is the primary changes. Compensatory mechanisms are the unshaded boxes

properties of red cells, coagulation abnormalities, vascular smooth muscle changes and mitochondrial dysfunction [3]. These changes result in cellular oedema, microvascular (capillary) obstruction with shunting and leaky capillaries with interstitial oedema, all of which contribute to patchy heterogeneous areas of hypoxia and microcirculatory changes, characteristic in human sepsis [3]. Technology is still being developed and evaluated to directly assess the microcirculation, and hopefully these will translate in the future to better monitoring and treatment of microcirculatory abnormalities.

Shock may result from four pathophysiological mechanisms – hypovolaemic, cardiogenic, obstructive and distributive. Mixed forms of shock may occur in the same patient. The primary pathophysiological mechanisms and compensation are outlined in Table 14.1.

Cardiogenic shock, hypovolaemic shock and obstructive shock are characterised by a low cardiac output state. Cardiogenic shock is the result of 'pump failure' either due to a myocardial pathology, valvular heart disease or cardiac arrhythmias. Hypovolaemic shock is due to volume loss (relative or absolute). Obstructive shock occurs because of obstruction to flow. In distributive shock, the primary pathophysiological process is vasodilatation as a result of many mediators including cytokines. Vasodilatation results in a compensatory increase in cardiac output, although in the later stages of shock, myocardial depression may occur due to microcirculatory abnormalities and cellular dysfunction, resulting in a fall in cardiac output. In addition, microvascular obstruction impairs blood flow and results in tissue hypoperfusion. Altered mitochondrial function with impaired oxygen extraction further compounds the problem, resulting in cellular dysoxia. The various aetiologies of the different types of shock are summarised in Table 14.2.

Management of Shock

The management of shock comprises of the following principles that include recognition of the pattern of shock, selecting appropriate treatment (resuscitation), specific therapy for the underlying problem and monitoring clinical response. Early and adequate haemodynamic support of patients in shock is essential to prevent

Table 14.2 Aetiology of shock

Type of shock	Site	Causes
Cardiogenic	Myocardial pathology	Myocardial infarction
		Myocarditis
		Cardiomyopathy
		Acute ventricular septal defect
	Valvular heart disease	Papillary muscle dysfunction
		Ruptured chordae tendineae
		Acute mitral regurgitation
		Acute aortic regurgitation
		Severe forms of valvular heart disease
	Conduction system	Arrhythmia (ventricular, supraventricular)
Distributive	–	Sepsis
		Anaphylaxis
		Multi-trauma
		Pancreatitis
		Acute liver failure
		Adrenal crisis
		Beriberi
Hypovolaemic	–	Internal haemorrhage (ruptured aneurysm)
		External haemorrhage (trauma, GI bleed)
		Fluid loss (e.g. diarrhoea, heat stroke)
		Third space loss (e.g. burns)
Obstructive	Pulmonary	Pulmonary embolism
		Tension pneumothorax
		Massive hydro-/haemothorax
		High levels of PEEP
	Cardiac	Pericardial tamponade
		Ball valve thrombus/atrial myxoma
	Abdomen	Tense ascites
		Abdominal compartment syndrome

GI gastrointestinal, *PEEP* positive end-expiratory pressure

worsening organ dysfunction and organ failure. Resuscitation and evaluation should go hand in hand with focus on rapid restoration of tissue perfusion.

Recognition of Pattern of Shock

The recognition of the pattern of shock is dependent on a careful history, thorough clinical examination and appropriate investigations. History and physical examination may provide a clue to the aetiology of shock (Fig. 14.2). For example, in a patient presenting with a diarrhoeal illness, the cause of shock is likely to be hypovolaemic. In a diabetic patient with retrosternal chest pain with hypotension, shock

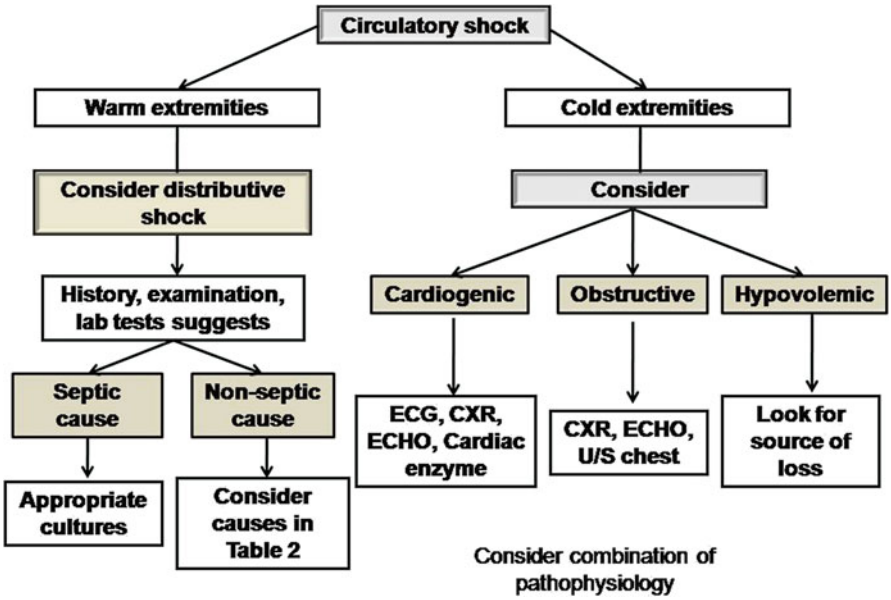

Fig. 14.2 Clinical approach to circulatory shock. The first step is to ascertain if the extremities are cold or warm. Warm shock is likely to be distributive. Detailed history, examination and appropriate laboratory tests would help differentiate between septic and non-septic causes of distributive shock. Cold shock may be due to cardiogenic or obstructive shock or due to hypovolaemia. The distinction between cardiogenic and obstructive shock can be made on the basis of test such as chest X-ray and ECHO. In hypovolaemic shock, the source of blood/fluid loss should be identified

may be due to an acute coronary syndrome. Presentation with fever and localising symptoms (e.g. cough, dysuria) may suggest distributive shock due to sepsis, while acute onset breathlessness in the setting of a venous thrombus may suggest obstructive shock due to pulmonary embolism. More than one pattern of shock may coexist in the same patient. For example, in a patient with trauma, shock may be due to hypovolaemia due to blood loss coupled with a tension pneumothorax. In sepsis, shock may be distributive and cardiogenic (due to myocardial depression).

Clinical examination should include, in addition to vital signs (pulse, respiration, temperature, blood pressure), skin colour, extremities (warm or cold, presence of oedema), jugular venous pressure and systemic examination (cardiovascular, respiratory, abdomen) looking for a focus of infection or other causes for hypotension. Appropriate investigations should be done to rule in or rule out cardiogenic (e.g. ECG, ECHO), distributive (imaging, cultures), hypovolaemic (haemoglobin, electrolytes, renal function) or obstructive (chest X-ray, ECHO) shock. Point-of-care echocardiographic evaluation has enabled the rapid assessment and diagnosis of the aetiology of shock. Focused assessment with sonography in trauma (FAST) may help localise the site of bleed and cause of shock in patients with trauma. Ultrasound examination of the chest may show absence of lung sliding suggesting a pneumothorax, while echocardiography may help diagnose pericardial disease or myocardial

disease (right or left ventricular) as the reason for circulatory shock. In hypovolaemic shock, variations in vena cava dimensions with respiration, ventricular cavity size and dynamic assessment of volume status may help assess the severity of hypovolaemia. An algorithm for the assessment of patients with shock is presented in Fig. 14.2.

The first step in the approach to circulatory shock is to ascertain if tissue hypoperfusion is present in terms of organ dysfunction with hyperlactataemia. If arterial hypotension is present without organ dysfunction or hyperlactataemia, the possibility of chronic hypotension should be considered (Fig. 14.3). If tissue hypoperfusion is evident, then assessment of cardiac output helps differentiate between high cardiac output states with shock (distributive shock) and low cardiac output states with shock (cardiogenic, hypovolaemic or distributive). Measurement of central venous pressure (CVP) helps differentiate between hypovolaemic (low CVP) and cardiogenic or obstructive shock (high CVP). An echocardiogram would help further distinguish cardiogenic from obstructive shock.

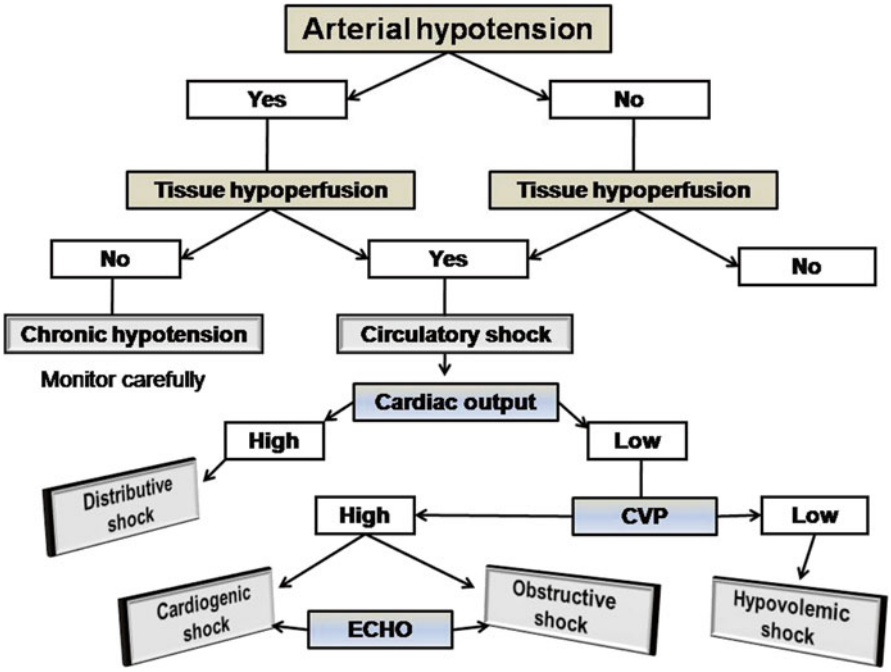

Fig. 14.3 Algorithm for approach to arterial hypotension. If arterial hypotension is not associated with tissue hypotension or hyperlactataemia, chronic hypotension should be suspected. If tissue hypoperfusion is present (even in the absence of arterial hypotension), then circulatory shock should be diagnosed. A high cardiac output (on ECHO) would suggest distributive shock, while a low cardiac output may be due to cardiogenic or obstructive shock where the central venous pressure would be high or due to hypovolaemic shock where the central venous pressure would be low

Selecting Appropriate Therapy and Resuscitation Goals

Early, appropriate and adequate management of shock is vital to limit organ dysfunction and failure. As mentioned earlier, assessment of aetiology and resuscitation should go on parallel. Resuscitation goals are focused on the 'VIP' rule; V for ventilate, I for infuse and P for pump [1, 3].

The *ventilation component* involves measures to improve oxygen delivery. Supplemental oxygen by face mask may be considered in mild shock. If shock is severe or associated with marked dyspnea, persistent hypoxaemia or worsening acidosis, endotracheal intubation and invasive mechanical ventilation must be considered. Since respiratory failure can be perpetuated by shock (see chapter on acute respiratory failure) as a result of hypoperfusion of the respiratory muscles, invasive mechanical ventilation would help by decreasing the work of breathing, reducing oxygen demand and decreasing left ventricular afterload. Improvement in oxygenation improves acidosis. It must be kept in mind that the actual process of intubation and ventilation may result in a further drop in blood pressure due to the use of sedative agents, an underfilled state (e.g. hypovolaemic shock) or increased intrathoracic pressure (e.g. use of high level of PEEP) with worsening right ventricular dysfunction

Infusion involves appropriate fluid therapy to improve cardiac output and microvascular blood flow. Three aspects are important, namely, the choice of fluid, the quantum to be administered and the end points of fluid resuscitation. Generally it is agreed that although colloids may be associated with smaller resuscitation volumes, there is no clear advantage of colloids over crystalloids. Further, colloids such as hydroxyl ethyl starch (HES) may be associated with increased need for renal replacement therapy when compared with saline. The use of albumin is precluded by cost and availability. Thus saline may be an appropriate choice for a resuscitation fluid. There is however some concern that large-volume saline resuscitation may worsen metabolic acidosis (hyperchloraemic acidosis) [3]. Suitable alternatives are balanced fluids such as lactated Ringer's or Plasmalyte® that have electrolyte compositions close to plasma and do not worsen metabolic acidosis. However it must be noted that these solutions contain potassium and so must be used with caution in the setting of renal failure.

The quantum of fluid administration is dependent on the type of shock. In hypovolaemic or distributive shock, initial fluid therapy involves the rapid administration of 20–30 ml/kg of crystalloid (see section on severe sepsis) with about 300–500 ml infused over 20–30 min. Further therapy is guided by end points of resuscitation (see below). In patients with cardiogenic shock with pulmonary oedema, fluid boluses are generally avoided. However a subset of patients with acute oedema may still benefit with cautious administration of fluids (in small aliquots, e.g. 100 ml at a time) since there may be a decrease in the effective intravascular volume. This should be done with close monitoring since oxygenation may worsen due to worsening pulmonary oedema. Patients with right ventricular myocardial infarction with shock may benefit with fluid administration.

The end points for fluid resuscitation have been the subject of much discussion. The objective of fluid resuscitation is to optimise preload in order to maximise cardiac output. Traditionally, static parameters such as a target MAP and CVP were used to guide fluid therapy. However it is well known that the targets for these parameters need to be individualised. In septic shock, although a MAP of 65 mmHg is generally recommended, in patients with a history of hypertension, maintaining a higher MAP (around 75 mmHg) is associated with a lower incidence of acute kidney injury [1]. A lower MAP may be acceptable in patients with acute bleeding in the absence of major neurological symptoms, till the source of bleeding is dealt with (permissive hypotension). In haemodynamically unstable patients and those who require vasoactive agents, it may be prudent to have an arterial line and central line for continuous haemodynamic monitoring and to administer vasoactive drugs.

More recently, dynamic parameters have been used, particularly in mechanically ventilated patients (with minimal or no spontaneous breaths), to assess fluid responsiveness. These include the assessment of pulse-pressure variation (in an arterial tracing), stroke-volume variation (using cardiac output monitors), inferior vena cava variability with respiration (using ultrasound) or increment in blood pressure or stroke volume (using ECHO) following a passive leg raise test. A fluid challenge may also be administered to assess the actual blood pressure response to the fluids.

The pump refers to the use of vasoactive agents. Three categories of vasoactive agents are available – vasoconstrictors, inotropes and vasodilators (Table 14.3). The choice of the agent depends on the cause of shock and the volume status of the patient. For example, adrenaline is the agent of choice in anaphylactic shock and cardiopulmonary resuscitation, while inotropes (e.g. dobutamine) are preferred in cardiogenic shock and vasoconstrictors (e.g. noradrenaline) in distributive shock. Adrenergic agents such as noradrenaline or adrenaline as well as dopamine and vasopressin are the commonly available vasoconstrictors. Noradrenaline is preferred since it is less arrhythmogenic when compared to adrenaline or dopamine. Noradrenaline can however reduce cardiac output due to increase in vascular tone, while adrenaline can increase myocardial oxygen demand, increase lactate levels and reduce splanchnic blood flow. However noradrenaline may also improve myocardial performance by increasing diastolic blood pressure and improving coronary perfusion. In clinical trials, dopamine has been shown to be associated with more adverse events when compared with noradrenaline and hence not generally recommended. In septic shock, noradrenaline and adrenaline were found to be equally effective. Recent trials have also shown that the addition of vasopressin to noradrenaline improved outcome in milder forms of septic shock.

In cardiogenic shock, inotropes should be used. Dobutamine is considered the agent of choice in cardiogenic shock [2]. Since dobutamine, in addition to improving cardiac contractility, causes vasodilatation, it is often combined with noradrenaline to counteract the vasodilatory effects. The vasodilatory effects of dobutamine on the peripheral circulation may help improve capillary perfusion in septic shock. In cardiogenic shock, if the patient is hypotensive, the blood pressure must be increased before initiating dobutamine therapy. Phosphodiesterase inhibitors such as milrinone and calcium-channel-sensitising drugs such as levosimendan may also

Table 14.3 Summary of vasoactive agents used in shock

Medication	Category	Action on[a]	Effect	Indication	Dose
Noradrenaline	Vasoconstrictor	Alpha	↑ SVR	Septic shock Spinal shock	0.01–0.1 mcg/kg/min
	Inotrope	Beta			
Adrenaline	Inotrope	Beta	↑ CO	Anaphylaxis	10–500 mcg bolus for anaphylaxis
	Vasodilator	Alpha	↓ SVR low dose	CPR	*Infusion*: 0.1–0.4 mcg/kg/min
	Vasoconstrictor		↑ SVR high dose	Septic shock	
Dopamine	Vasoconstrictor	Dopamine	↑ CO	Cardiogenic	0.5–2 mcg/kg/min
	Inotrope	Beta	Dose-dependent changes in SVR	Septic	2–5 mcg/kg/min – β
		Alpha			5–20 mcg/kg/min – α
Dobutamine	Inotrope	Beta	↑ CO	Cardiogenic Septic	2.5–20 mcg/kg/min
	Vasodilator		↓ SVR		
Vasopressin	Vasoconstrictor	V Receptor	↑ SVR	Septic shock	Sepsis: 0.01–0.06 U/min
				Variceal bleed	Asystole: 40 units
Isoprenaline	Chronotropic	Beta	↑ Heart rate	Heart block	0.01–0.1 mcg/kg/min
Nitroglycerin	Vasodilator	Nitric oxide	↓ SVR	Heart failure	5 mcg/min – increase based on response
Milrinone	Inotrope	PDI	↑ CO	Heart failure	*Bolus*: 50 mcg/kg bolus over
	Vasodilator				10–30 min
			↓ SVR		*Infusion*: 0.375–0.75 mcg/kg/min
Levosimendan	Inotrope	Ca-channel-sensitising drug	↑ CO	Heart failure	*Loading dose*: 12–24 mcg/kg over 10 min; *Infusion*: 0.05–0.2 mcg/kg/min
	Vasodilator		↓ SVR		

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CO cardiac output, *SVR* systemic vascular resistance, *PDI* phosphodiesterase inhibitor, *CPR* cardiopulmonary resuscitation

[a]Mechanism of action or action on specific receptor

be used in cardiogenic shock. Vasodilators such as nitrates may be used cautiously in patients with cardiogenic shock to reduce afterload. However such agents have the potential to reduce blood pressure and worsen haemodynamics.

Specific Therapy for the Underlying Problem

Investigation of the cause of shock and definitive treatment is vital for shock reversal. This may involve the rapid control of bleeding in a patient with trauma, fluid replacement in a diarrheal illness, use of thrombolytic therapy for pulmonary embolism, thrombolytic therapy or percutaneous coronary intervention and revascularisation for an acute coronary event or appropriate and early administration of antibiotic therapy (within 1 h) and source control in a patient with septic shock.

Monitoring Clinical Response

The clinical response to treatment in shock may be assessed by shock reversal, improvement of organ dysfunction and failure and by currently measurable downstream parameters. Shock reversal is characterised by improving haemodynamics with the need for reducing doses of vasoactive agents and normalisation of upstream parameters such as heart rate and blood pressure. Cardiac output can be measured serially and trends observed over time. Cardiac output response to therapy (e.g. fluid boluses) is more important than a pre-targeted cardiac output. Reversal of organ dysfunction can be clinically assessed through the three windows – the skin (improvement in peripheral perfusion), neurological system (conscious state) and the renal window (urine output) as well as through laboratory parameters (oxygenation, renal function).

Downstream parameters have also been used recently to monitor clinical response. Shock reversal is associated with a reduction in lactate level. Serial lactate levels correlate with mortality. However it must be remembered that when circulation is restored, there may be an initial paradoxical increase in lactate level despite improvement in haemodynamics. This 'lactate washout', which is a temporary state, must be distinguished from worsening hyperlactataemia due to persistent or ongoing microcirculatory abnormalities.

$ScvO_2$ monitoring, both continuous as well as intermittent, has been used extensively in studies on shock. A decrease in $ScvO_2$ may occur either due to a decrease in oxygen delivery or increase in tissue oxygen consumption or both. A low $ScvO_2$ has been used as a surrogate marker of reduced cardiac output [4] with resuscitation protocols such as the early goal-directed therapy (EGDT), focusing on improving cardiac output with a view to normalising $ScvO_2$. However in a subset of patients, although resuscitation results in normalisation of $ScvO_2$ (>70 %), some patients continue to manifest features of tissue hypoperfusion, characterised by an increase in the $vaCO_2$ difference of >6 mmHg. These patients with a $vaCO_2$ 'gap' of >6 mmHg may indicate a subset of patients who continue to remain inadequately resuscitated [5]. On the other hand, in situations such as sepsis, which is characterised by impaired mitochondrial respiration with non-utilisation of oxygen by the cell, CO_2 production may be reduced resulting in a 'narrow' $vaCO_2$ gap. These

patients are likely to have cytopathic dysoxia or regional microcirculatory abnormality [6]. The value of these downstream parameters ($ScvO_2$, $vaCO_2$) in monitoring response to therapy is still unclear.

Conclusion

Circulatory shock is associated with a high mortality. A careful history, examination and appropriate investigations would help ascertain the cause of shock. The management of shock should focus on early recognition of the pattern of shock, appropriate treatment to reverse shock, specific therapy of the underlying problem, organ support and monitoring clinical response.

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Further Reading

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