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The Interface between Monitoring and Physiology at the bedside

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Abstract

Hemodynamic instability as a clinical state represents either a perfusion failure with clinical manifestations of circulatory shock and/or heart failure, or one or more out-of-threshold hemodynamic monitoring values, which may not necessarily be pathological. Different types of circulatory shock etiologies require different types of treatment modalities making these distinctions important. Diagnostic approaches or therapies based on data derived from hemodynamic monitoring assume that specific patterns of derangements reflect specific disease processes, which will respond to appropriate interventions. Hemodynamic monitoring at the bedside improves patient outcomes when used to make treatment decisions at the right time for patients experiencing hemodynamic instability.

Keywords

hemodynamic instability; circulatory shock; MAP; hemodynamic monitoring

Hemodynamic instability

Hemodynamic instability as a clinical state represents either a perfusion failure with clinical manifestations of circulatory shock and/or heart failure, or one or more out-of-threshold hemodynamic monitoring values, which may not necessarily be pathological. Circulatory shock can be produced by decreases in cardiac output relative to metabolic demands, such as decreased intravascular volume (hypovolemic), impaired ventricular pump function (cardiogenic), or mechanical obstruction to blood flow (obstructive) or by maldistribution of blood flow independent of cardiac output (distributive). The prompt identification and diagnosis of the probable cause of hemodynamic instability, coupled with appropriate resuscitation and (when possible) specific treatments, are the cornerstones of intensive care medicine.¹ Hemodynamic monitoring plays a pivotal role in the diagnosis and management of circulatory shock.

The management of the critically ill patient often requires continual monitoring of hemodynamic variables and the functional hemodynamic status owing to the level of cardiovascular instability the circulatory shock creates. Patterns of hemodynamic variables often suggest hypovolemic, cardiogenic, obstructive, or distributive shock processes as the

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primary etiologies of hemodynamic instability. Since these different types of circulatory shock etiologies usually require different types of treatment modalities, making these differential distinctions important. Diagnostic approaches or therapies based on data derived from hemodynamic monitoring in the critically ill patient assume that specific patterns of derangement reflect specific disease processes, which will respond to appropriate interventions.²

Mean arterial pressure as a measure of hemodynamic instability

Organ perfusion is dependent on input organ perfusion pressure and local vasomotor tone. Local vasomotor tone varies inversely with local tissue metabolic demand. For most organs except the kidneys and heart, independent changes in arterial pressure above some minimal value are associated with increased vasomotor tone to keep organ perfusion constant, and are therefore not entirely dependent on cardiac function and cardiac output. In such situations, cardiac output is only important to allow parallel circuits to maintain flow without inducing hypotension, and cardiac function is only important in sustaining cardiac output and a given output pressure without causing too high a back pressure in the venous circuits. Hypotension, on the other hand, will decrease blood flow to all organs. Operationally, mean arterial pressure (MAP) is the input pressure to all organs other than the heart. Diastolic aortic pressure is the input pressure for coronary blood flow. MAP is estimated to be equal to the diastolic pressure plus one-third the pulse pressure between diastole and systole. Over a wide range of MAP values, regional blood flow to the brain and other organs remains remarkably stable owing to autoregulation of local vasomotor tone to keep that local blood flow constant despite changing MAP. However, in a previously normotensive subject, once MAP decreases below ~60 mmHg, then tissue perfusion may decrease independent of metabolic demand and local autoregulatory processes. As tissue blood flow decreases independent of metabolic demand, then tissue O₂ extraction increases to keep local O₂ consumption and metabolic activity constant. This process occurs routinely in most individuals and is transient and is not pathological. However, if tissue blood flow decreases further than increased O₂ extraction can compensate for, then end-organ ischemic dysfunction follows. Despite the lack of sensitivity of a non-hypotensive MAP to reflect hemodynamic stability, measures of MAP to identify hypotension are essential in the assessment and management of hemodynamically unstable subjects, since hypotension must decrease autoregulatory control and increasing MAP in this setting will also increase organ perfusion pressure and organ blood flow.

Hypotension as a measure of hemodynamic instability

Hypotension directly reduces organ blood flow, is synonymous with hemodynamic instability and is a key manifestation in most types of circulatory shock. It also causes coronary hypoperfusion, impairing cardiac function and cardiac output. However, the assumption is often false that, because MAP is maintained in low cardiac output shock states by sympathetic tone mediated peripheral vasoconstriction, the patient is not unstable. Intra-organ vascular resistance and venous outflow pressure along with MAP are the two other determinants of organ blood flow, and therefore organ perfusion. The normal mechanism allowing autoregulation of blood flow distribution is local changes in organ inflow

resistance, such that organs with increased metabolic demand enact arterial dilation to increase their blood flow. If there is hypotension, then local arterial dilation will not result in increased blood flow because the lower inflow pressure will have minimal effect on the organ perfusion pressure. Thus, hypotension impairs autoregulation of blood flow distribution.³

In shock states, normal homeostatic mechanisms functioning through carotid body baroreceptors vary arterial vascular tone so as to maintain MAP relatively constant despite varying cardiac output and metabolic demand. Presumably, this vasoconstriction occurs in low cardiac output states to maintain cerebral and myocardial blood flow at the expense of the remainder of the body. In subjects with normal renal function, oliguria is the immediate manifestation of this adaptive response, reflecting marked reduction in renal blood flow and solute clearance despite persisting “normal” MAP. As such, normotension does not insure hemodynamic sufficiency of all organ systems simultaneously. Hence, indirect measures of sympathetic tone, such as heart rate, respiratory rate, peripheral capillary filling and peripheral cyanosis are more sensitive estimates of increases circulatory stress and hemodynamic instability than is MAP.⁴

Although systemic hypotension can be identified non-invasively using a sphygmomanometer, in the treatment of hypotension not readily responsive to simple maneuvers like recumbency and an initial fluid bolus, invasive arterial catheterization and continuous monitoring of arterial pressure is indicated. There is no consensus as to the absolute indication for invasive arterial pressure monitoring, but caution should be aired in favor of monitoring as opposed to its avoidance in the patient who cannot be rapidly resuscitated. Although peripheral radial arterial catheterization is the most common site for arterial access, femoral arterial catheterization is also available and has the advantage of greater likelihood of successful arterial cannulation in the setting of profound hypotension and shock. The femoral artery is also the preferred site if one specific minimally invasive arterial monitoring device (i.e. PiCCOplus) use is being considered. However, these issues are addressed in subsequent chapters in this volume on invasive monitoring and minimally invasive and non-invasive monitoring, respectively. Importantly, in conditions of marked vasoconstriction associated with profound hypovolemia and hypothermia, central arterial pressure may exceed peripheral arterial pressure because of increased arterial resistance between these two sites. Thus, assessing end-organ perfusion parameters like level of consciousness, urine output and vascular refill are important early measures of the effectiveness of blood flow. Finally, though early attention is appropriately focused on restoring MAP to some minimal threshold level, organ perfusion pressure is actually MAP minus output pressure. Thus, in the setting of increased intracranial or intra-abdominal pressures, cerebral and splanchnic/renal perfusion pressures will be less than MAP, respectively and these compartment pressures need to be directly measured so as to target an organ perfusion pressure of >60 mmHg.

Mixed venous oxygen saturation as a measure of hemodynamic instability

One cardinal sign of increased circulatory stress is an increased O₂ extraction ratio, which in the setting of an adequate arterial O₂ content manifests itself as a decreasing mixed venous

O₂ saturation (SvO₂) in the face of adequate oxygen uptake in the lungs. SvO₂ can only be sampled using a pulmonary artery catheter (PAC), while central venous (unmixed superior vena cava) O₂ saturation can be assessed using a central venous catheter. The choice of the type of monitoring to be used and how it is interpreted is the subject for the invasive monitoring chapter later in the volume. However, low SvO₂ values can also occur if arterial O₂ content is low, as is the case with anemia and hypoxemia or if O₂ consumption is increased as with muscular exercise.

Muscle activity effectively extracts O₂ from the blood because of the set-up of the microcirculatory flow patterns and the large concentration of mitochondria in these tissues. Thus, normal vigorous muscular activity can be associated with a marked decrease in SvO₂ despite adequate oxygen uptake and a normal circulatory system and metabolic demand.⁵ Muscular activities, such as moving in bed or being turned, “fighting the ventilator,” and labored breathing spontaneously increase O₂ consumption. In the patient with an intact and functioning cardiopulmonary apparatus, this will translate into an increase in both oxygen delivery (DO₂) and O₂ consumption and a decrease in SvO₂ only to the extent that the increased DO₂ cannot supply the needed O₂ for this increased demand. Under normal conditions of submaximal exercise, DO₂ is the parameter increasing most markedly, although some decrease in SvO₂ also occurs. However, in the sedated and mechanically ventilated patient, decreased SvO₂ is a very sensitive marker of diminished circulation. Although muscle activity is minimal, the diminished flow permits more time for oxygen extraction across the transversed tissue and organ capillary beds. Although there is no level of cardiac output which is ‘normal,’ there are DO₂ thresholds below which normal metabolism can no longer occur.⁶ Nevertheless, SvO₂ can be utilized as a sensitive but nonspecific marker of circulatory stress, with values less than 70% connoting circulatory stress, less than 60% identifying significant metabolic limitation, and values less than 50% indicating frank tissue ischemia.⁷

Principles of hemodynamic monitoring based on shock etiology

Weil and Shubin defined circulatory shock in 1968 as a decreased effectiveness of circulatory blood flow to meet the metabolic demands of the body.⁸ The heart, vascular integrity, vasomotor tone, and autonomic control all interact to sustain circulatory sufficiency. Circulatory shock reflects a failure of this system and results in an inadequate perfusion of the tissues to meet their metabolic demand, which can lead to cellular dysfunction and death.⁹

Four basic functional etiologies of circulatory shock can be defined: (1) hypovolemic, due to inadequate venous return (hemorrhage, dehydration [absolute hypovolemia]), (2) cardiogenic, due to inadequate ventricular pump function (myocardial infarction, valvulopathy), (3) obstructive, due to impingement on the central great vessels, (pulmonary embolism, tamponade), and (4) distributive, due to loss of vasoregulatory control (sepsis, anaphylaxis, neurogenic shock, adrenal insufficiency [relative hypovolemia])(Table 1).

Tissue hypoperfusion is common in all forms of shock, with the possible exception of hyperdynamic septic shock, and results in tissue hypoxia and a switch from aerobic to

anaerobic metabolism, inducing both hyperlactacidemia and metabolic acidosis. However, hyperlactacidemia is not a reliable marker of ongoing tissue hypoperfusion because lactate clearance is often delayed or impaired in shock states, and processes such as exercise (seizure activity) and inflammation can induce hyperlactacidemia without cardiovascular insufficiency.¹⁰ Sustained circulatory shock results in cellular damage, not from anaerobic metabolism alone, but also from an inability to sustain intermediary metabolism and enzyme production necessary to drive normal mitochondrial performance.¹¹ Metabolic failure due to sustained tissue hypoxia may explain why surgical preoptimization¹² and early goal-directed therapy¹³ improve outcome, whereas aggressive resuscitation after cellular injury has already occurred is not effective at reducing mortality from a variety of insults.¹⁴

Since most forms of hemodynamic monitoring measure global systemic blood flow parameters like arterial pressure, heart rate, other central vascular pressures and cardiac output, the assessment of the severity of shock and its initial response to therapy is often limited if monitoring is limited to these global variables alone. Since cellular respiration does not cease when tissue blood flow decreases until some very low level of blood flow occurs, tissue CO₂ production usually continues at a normal rate, resulting in an increased venous PCO₂. Potentially, measuring SvO₂, or alternatively the difference between tissue PCO₂ (PvCO₂) and arterial PCO₂ (PaCO₂), referred to as the Pv-aCO₂ gap, would allow one to assess effective tissue blood flow, since decreases in capillary blood flow initially causes CO₂ from aerobic metabolism to accumulate.¹⁵ Currently, global measures of circulatory function are being used to determine which of the four shock categories is the most likely cause of organ dysfunction by noting their characteristic patterns or groupings of abnormalities, referred to as hemodynamic profile analysis.¹⁶

Hypovolemic shock

Hypovolemia is the cardiovascular state in which the effective circulating blood volume is inadequate to sustain adequate venous return and thus cardiac output to support normal function without invoking supplemental sympathetic tone or postural changes to provide venous return assistance. It is a process of absolute hypovolemia, which can occur through loss of blood, such as with hemorrhage and trauma, or with fluid and electrolyte loss, as with diuresis, diarrhea, vomiting, or evaporation from large burn surfaces, or with severe fluid intake restriction resulting in dehydration.¹⁷ The normal reflex response to absolute hypovolemia is increased sympathetic tone causing selective vasoconstriction. Cardiac output is often sustained by this vasoconstrictive maneuver, and venous return is maintained by diverting blood away from the skin, resting muscles, and gut and into the central circulation. The cardinal sign of this circulatory stress is increased heart rate owing to increased sympathetic tone. If the hypovolemic state progresses, this vasoconstriction becomes inadequate to sustain venous return and cardiac output decreases. Under these conditions, heart rate increases but stroke volume decreases more such that cardiac output declines. With tissue hypoperfusion, increased O₂ extraction occurs across the capillary beds, but eventually even increased extraction fails to sustain aerobic metabolism, and lactic acidosis develops as a marker of tissue anaerobic metabolism.¹⁸ Thus, hypovolemia initiates tachycardia, reduced arterial pulse pressure, and (often) hypertension with a near normal

resting cardiac output, followed by signs of end-organ hypoperfusion (oliguria, confusion) as cardiac output decreases.

Hypovolemic shock represents a decrease in effective circulating blood volume and venous return. It can be due to primary intravascular volume loss (hemorrhage, capillary leak) or secondary intravascular volume loss (third-space loss, insensible loss through skin with burns, diarrhea, vomiting). The specific findings of hypovolemic shock are decreased cardiac filling pressures (low venous return manifested by low right atrial pressure [Pra] and low left atrial pressure [pulmonary artery occlusion pressure or Ppao]) accompanied by low cardiac output and high systemic vascular resistance (reflexive or sympathetically induced vasoconstriction manifested by high systemic vascular resistance index).² Systemic hypotension is the final presentation of hypovolemic shock¹⁹ and if the clinician waits for hypotension to identify circulatory shock before intervening, ischemic tissue injury is almost always already present.

Cardiogenic shock

Cardiac pump dysfunction can be due to left ventricle (LV), right ventricle (RV) failure, or both. LV failure is usually manifested by an increased LV end-diastolic pressure and left atrial pressure, which must exist to sustain an adequate LV stroke volume. Tachycardia is universal in the patient who is not β -blocked. The most common cause of isolated LV failure in the critically ill patient is acute myocardial infarction.²⁰ However, in post-operative cardiac surgery patients, myocardial stunning can also cause transient LV failure. In acute isolated LV failure, LV stroke work is reduced and heart rate increased. In chronic heart failure, cardiac output may be adequate, or the periphery may have adapted enough to increase O₂ extraction such that tissue hypoperfusion is not present, with the only sign of heart failure being peripheral edema and increased sympathetic tone. However, in acute LV failure cardiac output may be normal or even increased, owing to increased sympathetic tone. However, LV filling pressure becomes markedly elevated as the increased sympathetic tone decreases unstressed volume increasing mean systemic pressure and augmenting the pressure gradient for venous return. This causes a marked increase in intrathoracic blood volume which may induce flash hydrostatic pulmonary edema, also known as cardiogenic pulmonary edema. However, neither cardiac output nor systemic vascular resistance are sensitive markers of LV failure until after cardiogenic shock develops.²¹

The normal adaptive response of the patient to impaired LV contractile function and resulting low organ and tissue perfusion is to increase sympathetic tone, induce tachycardia, activate the renin-angiotensin system, retain sodium by the kidneys, and thus increase the circulating blood volume. In essence, the body does not differentiate its adaptive response to low tissue perfusion caused by either hypovolemic or cardiogenic shock. Fluid retention as a compensatory mechanism, if present, takes time to evolve, whereas acute impairments of LV contractility can occur over seconds in response to myocardial ischemia. Thus, the hemodynamic profile of acute and chronic LV failure can be different. Acute LV failure is manifest by increased sympathetic tone (tachycardia, hypertension), impaired LV function (increased left atrial filling pressure and reduced stroke volume), with minimal RV effects (normal central venous pressure, unless RV infarction also occurs), and increased oxygen

extraction manifested by a low SvO₂. Cardiac output may not be reduced and may actually be slightly elevated early on, owing to the release of catecholamines as part of the acute stress response.²² Vascular resistance, therefore, is increased. By contrast, in chronic heart failure, although sympathetic tone is elevated, the heart rate is rarely >105 beats/min, while filling pressures are elevated in both atria consistent with combined LV failure and fluid retention. Importantly, cardiac output is not reduced except in severe chronic heart failure states. Importantly, a cardinal finding of heart failure is the inability of the heart to increase cardiac output in response to a volume load or metabolic stress state (exercise). Furthermore, owing to the increased sympathetic tone, splanchnic and renal blood flows are reduced and can lead to splanchnic or renal ischemia.²³ Although acute heart failure may present with shock, more commonly patients with preexisting chronic heart failure develop a new illness, or acute exacerbation of their heart failure. Thus, their new pathology is superimposed upon the preexisting heart failure. Such mixed process shock states are often difficult to treat because of the limitations of the patient's cardiac response created by the prior heart failure, and it is quite easy to induce pulmonary and peripheral edema using routine fluid resuscitation.

Cardiogenic shock represents primary cardiac failure. It can be due to impaired myocardial contractility (myocardial ischemia/infarction, electrolyte imbalance, hypoxemia, hypothermia, endocrinologic diseases, metabolic poisoning, beta-blockers), pump function (valvulopathy, ventriculoseptal defect, dysrhythmias), or diastolic compliance (left ventricular hypertrophy, fibrosis, infiltrative cardiomyopathies, asymmetric septal hypertrophy, cor pulmonale). The specific cardinal findings of cardiogenic shock are increased back pressure to cardiac filling (increased right atrial pressure [Pra] and pulmonary artery occlusion pressure [Ppao]) and upstream edema owing to compensatory fluid retention (peripheral and pulmonary).⁵ The hemodynamic profile pattern therefore seen in cardiogenic shock is as it progresses is low cardiac output, high right atrial pressure [Pra] and pulmonary artery occlusion pressures [Ppao], and high systemic vascular resistance (reflexive or sympathetically induced vasoconstriction manifested by high systemic vascular resistance index).

Obstructive shock

Obstructive shock represents a blockage of blood flow in one of the heart's outflow tracts. It may be due to right ventricular (RV) outflow obstruction (pulmonary embolism, lung hyperinflation and pulmonary artery compression), LV outflow obstruction (aortic stenosis, dissecting aortic aneurysm) or cardiac tamponade (pericardial effusion, lung hyperinflation and atrial compression). The specific findings of obstructive shock are often difficult to separate from cardiogenic shock, and may be different relative to the ventricle with the obstructive pathophysiology.

The most common cause of obstructive shock is pulmonary embolism and RV outflow obstruction leading to acute RV failure²⁴. However, isolated RV dysfunction can occur in the setting of an acute inferior wall myocardial infarction, and also as a consequence of pulmonary vascular disease (chronic obstructive pulmonary disease, primary pulmonary hypertension) and hyperinflation. Neither pulmonary vascular resistance nor mean

pulmonary artery pressure need be grossly elevated for RV failure to be present. Indeed, and importantly, if pulmonary arterial pressures are greater than 30 to 35 mmHg, then pulmonary hypertension is probably chronic in nature because acute elevations of pulmonary arterial pressures above this level are physiologically tolerable. Elevations in central venous pressure of more than 12 mmHg also reflect fluid retention, suggesting further that RV decompensation or massive volume overload from LV failure has occurred. The most common hemodynamic monitoring pattern in acute pulmonary embolism is that of elevated central venous pressure, decreased pulmonary artery occlusion pressures [Ppao] relative to the CVP (since preload to the left ventricle is diminished but LV contractility remains normal), and low cardiac output accompanied by high systemic vascular resistance (reflexive or sympathetically induced vasoconstriction manifested by high systemic vascular resistance index). However, in severe cor pulmonale, RV and LV diastolic pressure equalization occurs and it is indistinguishable from pericardial tamponade, as indeed acute RV dilation will induce tamponade physiology. Echocardiography is extremely useful in making the diagnosis of acute cor pulmonale because it can be performed immediately at the bedside and is non-invasive. Echocardiographic studies will reveal RV diameters greater than LV diameters and a paradoxical intraventricular septal shift. These points are discussed in detail in the chapter on ultrasonography.

When RV dysfunction predominates and is induced by pulmonary parenchymal disease, it is referred to as cor pulmonale, which is associated with signs of backward failure, elevated RV volume and pressures, systemic venous hypertension, low cardiac output, as well as reduced renal and hepatic blood flow.²⁵ LV diastolic compliance decreases as the right ventricle dilates due to ventricular interdependence, either from intraventricular septal shift or absolute limitation of biventricular volume due to pericardial restraint. Thus, Ppao is often elevated for a specific LV stroke work, giving the erroneous appearance of impaired LV contractility.²⁶

Cardiac tamponade, another cause of obstructive shock, can occur from either (1) biventricular dilation limiting biventricular filling due to pericardial volume limitation, (2) acute pericardial fluid accumulation due to either effusion fluid (inflammation, severe uremia) or blood (hemorrhage), which needs not be great in quantity, and (3) lung hyperinflation resulting in mechanical compression of the heart from without, which acts like pericardial tamponade to limit biventricular filling.²⁷ The first two etiologies are rarely seen, whereas hyperinflation commonly occurs. The cardinal sign of tamponade is diastolic equalization of all intrathoracic vascular pressures (CVP, pulmonary arterial diastolic pressure, and Ppao).²⁸ Since RV compliance is greater than LV compliance early on in tamponade, there may be selective reduction in RV filling.²⁹

Distributive shock

Loss of blood flow regulation occurs as the end-stage of all forms of circulatory shock owing to hypotension, but is one of the initial presenting processes seen in sepsis, neurogenic shock, and adrenal insufficiency. The hemodynamic profile of sepsis is one of increased cardiac index, low right and left filling pressures, elevated SvO₂, low mean arterial pressure, and low systemic vascular resistance consistent with loss of peripheral

vasomotor tone and pooling of blood in the vascular system manifesting as a relative hypovolemia.

Sepsis is a systemic process characterized by activation of the intravascular inflammatory mediators resulting in generalized vascular endothelial injury, but it is not clear that tissue ischemia is an early aspect of this process.³⁰ Acute septicemia is associated with increased sympathetic activity (tachycardia, diaphoresis) and increased capillary leak with secondary loss of intravascular volume, and inappropriate clotting in the microcirculation. Before fluid resuscitation, this combination of processes resembles simple hypovolemia, with decreased cardiac output, normal to increased peripheral vasomotor tone, and very low SvO₂, reflecting systemic hypoperfusion. LV function is often impaired, but usually in parallel with depression of other organs, and this effect of sepsis is usually masked by the associated hypotension that maintains low LV afterload.³¹ Initially, decreased adrenergic responsiveness and impaired diastolic relaxation characterize septic cardiomyopathy. If sepsis remains ongoing, impaired LV contractile function also occurs. However, most patients with such a clinical presentation receive initial volume expansion therapy such that the clinical picture of sepsis reflects a hyperdynamic state rather than hypovolemia, which has been referred to as 'warm shock' in contrast to all other forms of shock.³²

Neurogenic shock results from an acute spinal injury above the upper thoracic level, spinal anesthesia, general anesthesia, neurotoxic poisoning and central nervous system catastrophe. All of these states induce a profound loss of sympathetic tone and pooling of blood in the vascular compartment causing a relative hypovolemic state. In neurogenic shock, the resulting hypotension is often not associated with compensatory tachycardia, hence systemic hypotension can be severe and precipitate cerebral vascular insufficiency and myocardial ischemia.³³ Since neurogenic shock reduces sympathetic tone, the biventricular filling pressures, arterial pressure and cardiac output are all decreased. Treatment consists of reversing the primary process and supporting the circulation with volume loading and an infusion of an α -adrenergic agonist, such as norepinephrine, dopamine or phenylephrine to induce vasoconstriction and reverse vascular pooling of blood.³⁴

Acute adrenal insufficiency can present with hyperpyrexia and circulatory collapse. This is more common than might be realized based on the epidemiology of adrenal cortical disease, because many patients in the community are receiving chronic corticosteroid therapy for the management of chronic systemic and localized inflammatory states, such as asthma or rheumatoid arthritis. In such cases the added stress of trauma, surgery, or infection can precipitate secondary adrenal insufficiency, as can the discontinuation of long-term steroid treatment.³⁵ Patients typically present with nausea and vomiting, diarrhea, confusion, hypotension, and tachycardia. Cardiovascular collapse is similar to that seen in neurogenic shock, except that the vasculature is not as responsive to sympathomimetic support.³⁶ Since systemic hypotension is a profound stimulus of the adreno-cortical axis, measures of random cortisol levels in a patient with systemic hypotension will show low values in patients with adrenal insufficiency, and an ACTH-stimulation test is not needed to make the diagnosis. Accordingly, failure to respond to vasoactive pharmacological support in a patient who is hypotensive should suggest the diagnosis of adrenal insufficiency, while giving stress doses of corticosteroids usually reverses the unresponsive nature of the shock process.³⁷ Since

there is little detrimental effect of providing adrenal replacement levels of hydrocortisone in the short term, it is reasonable to start low dose hydrocortisone (60–80 mg intravenously every eight hours) while awaiting the response to resuscitation, and results of the plasma cortisol test.

Circulatory support of the patient with hemodynamic instability

A brief summary of the four main shock states has been provided in Table 1. Of the four categories of shock, only distributive shock states following intravascular volume resuscitation are associated with an increased cardiac output but decreased vasomotor tone. Thus, cardiac output, stroke work, DO_2 , and SvO_2 are decreased in cardiogenic, hypovolemic, and obstructive shock, but may be normal or even increased in distributive shock. However, in all conditions, heart rate increases associated with an increased sympathetic tone (except in neurogenic shock and sympathetic impairment). Hemodynamic monitoring can aid in determining circulatory shock etiology and in assessing response to therapy. Since most forms of circulatory shock reflect inadequate tissue DO_2 , a primary goal of resuscitation is to increase DO_2 .³⁸

If the cause of hypotension is diminished intravascular volume, either absolute or relative, then cerebral and coronary perfusion pressures must be maintained while fluid resuscitation is begun, otherwise cerebral ischemia and cardiac pump failure may develop and limit the effectiveness of fluid resuscitation.³⁹ Infusions of vasoactive agents with both α and β -1 adrenergic agonist properties will increase both MAP and cardiac output at the expense of the remaining vascular beds, hence fluid resuscitation to achieve an adequate intravascular blood volume is an essential co-therapy for sustaining organ perfusion pressure. Isolated vasopressor therapy in the setting of systemic hypotension causes worsening hypoperfusion of the periphery and organs excluding the heart and brain. Thus, though giving vasopressor therapy in the setting of acute hypotension is often indicated, it is essential to assess volume status as well, because the pathologic ischemic effects of hypovolemia will be heightened by isolated vasopressor therapy. Many pathological states and acute stress conditions are associated with either adrenergic exhaustion or blunted responsiveness to otherwise adequate circulating levels of catecholamines (e.g. diabetes, adrenal insufficiency, hypothermia, hypoglycemia, and hypothyroidism). Furthermore, acute sepsis and systemic inflammation are associated with reduced adrenergic responsiveness or relative adrenal insufficiency.^{40,41} Thus, even if the patient produces an otherwise adequate sympathetic response, the vasomotor and inotropic response may be inadequate, requiring transient use of potent sympathomimetic agents to sustain hemodynamic stability, and adrenocortical hormone replacement to support relative adrenal insufficiency is also often needed.

Pharmacotherapies for hemodynamic instability

Pharmacotherapies for hemodynamic instability are directed at the pathophysiological processes that either induce or compound it. Hemodynamic monitoring plays a central role in assessing the effectiveness of these therapies in an iterative fashion. These therapies can be loosely grouped into one of three processes: (1) those that increase vascular smooth

muscle tone (vasopressor therapy), (2) those that increase cardiac contractility (inotropic support), and (3) those that decrease smooth muscle tone (vasodilator therapy).

Infusion of vasopressor agents are indicated to sustain a MAP greater than 60 mmHg to prevent coronary or cerebral ischemia while other resuscitative measures like volume resuscitation and specific treatments of the underlying condition are initiated. This level of MAP is clearly arbitrary since some patients maintain adequate coronary and cerebral blood flow at lower MAP levels, whereas others, notably those with either pre-existent systemic hypertension or atherosclerotic cerebrovascular disease, may not tolerate MAP decreasing more than 30 mmHg below their baseline value.⁴² Once an “adequate” MAP has been achieved and intravascular volume losses corrected, care shifts toward maintaining adequate blood flow to perfuse metabolically active tissues in order to sustain organ performance while minimizing the detrimental effects of these vasoactive therapies.

Vasopressor agents for hemodynamic instability

Vasopressor therapy can reverse systemic hypotension, but at a price: the only means whereby it can increase systemic MAP is by reducing blood flow through vasoconstriction. Importantly, cerebral vascular circuits have no α -adrenergic receptors, and coronary vascular circuits have minimal α -adrenergic receptors, and therefore their vascular beds will not constrict in the presence of exogenous α -adrenergic stimulation. Unfortunately, in hypovolemic states vasopressor support may transiently improve both global blood flow and MAP, but at the expense of worsening local non-vital blood flow and hastening tissue ischemia. Initial resuscitative efforts should therefore always include an initial volume expansion component and fluid challenge while diagnostic approaches that identify shock states ensue, before relying on vasopressors alone to support the hemodynamically unstable patient.⁴³

Phenylephrine

The only non-catecholamine sympathomimetic used, phenylephrine differs chemically from other sympathomimetics by the absence of a hydroxyl group on position 4 of the benzene ring. This deletion reduces its potency relative to other sympathomimetics. It acts as a moderately potent α_1 -agonist and is used in those patients in whom hypotension is due to decreased arterial elastance (it only activates β -adrenoreceptors at high doses). A modest direct coronary vasoconstrictor effect appears to be offset by autoregulatory mechanisms in the absence of flow-limiting coronary disease. It is not metabolized by catecholamine O-methyltransferase (COMT), which metabolizes catecholamines, and therefore its absolute half-life is considerably longer than catecholamine sympathomimetics.⁴⁴ Thus, if phenylephrine is used to treat hypotension, it universally causes cardiac output to decrease. This is because α_1 -agonist activity results in an MAP increase purely on the basis of the associated increase in vascular resistance and therefore increased left ventricular afterload, but without β_1 stimulation to assist with improved contractility. Accordingly, its prolonged use is potentially detrimental to tissue blood flow, though its acute use may reverse hypotension and transiently sustain cerebral and coronary blood flow.

Norepinephrine

Norepinephrine has significant activity at α and β 1-adrenoreceptors, resulting in a positive vasoconstrictor and inotropic effect. Its accompanying β 1 activity makes it the α 1-agonist of choice in the patient with hypotension and known LV dysfunction.⁴⁵ Its positive vasopressor effect may enhance renal perfusion and indices of renal function in hemodynamically stable patients and this effect may also be seen at higher doses when norepinephrine is used as a vasopressor in those patients with sepsis. Both effects are likely related to elevation of MAP, the input pressure for organ perfusion. If norepinephrine is used to treat hypotension and decreased vasomotor tone, then one usually sees MAP increase with minimal changes in cardiac output because the increase in afterload is balanced by the associated increased contractility. However, this balance is also dependent on the LV being responsive to adrenergic stimulation. Maas et al. demonstrated that when post-operative cardiac surgery patients had their MAP increased by 20 mmHg by norepinephrine infusion, cardiac output increased in those with normal cardiac reserve and decreased in those with impaired cardiac reserve.⁴⁶ Thus, the cardiac output response to increasing MAP with norepinephrine is variable and dependent on baseline cardiac contractile reserve.

Epinephrine

Epinephrine is a very potent catecholamine sympathomimetic that has markedly increased β 2-adrenoreceptor activity compared with its molecular substrate, noradrenaline. Adrenaline has potent chronotropic, inotropic, β 2-vasodilatory, and α 1-vasoconstrictor properties. Its net vasopressor effect is the end result of the balance between adrenaline-mediated β 2 and α 1 adrenoreceptors stimulation. At low doses this balance may result in no net pressor effect, with a fall in the diastolic blood pressure. Thus, the effects of epinephrine on hemodynamics will be variable and dependent on dosage, perhaps more so than other sympathomimetic agents. Epinephrine, like norepinephrine, is known to have potent renovascular and splanchnic vasoconstrictor properties.³⁹ Clearance rates are variable and mediated by both the COMT and monoamine oxidase systems.

Dopamine

Dopamine is the most controversial of the clinically utilized catecholamine sympathomimetics. This stems largely from claims for selective, dose-dependent, splanchnic and renovascular vasodilatory properties. Its dopaminergic properties do not reduce the incidence of renal failure in patients with shock when compared to noradrenaline.⁴⁷ Dopamine stimulates the release of norepinephrine from sympathetic nerve terminals in a dose-dependent manner, with this indirect norepinephrine effect accounting for up to half of dopamine's clinically observed physiological activity.⁴⁸ Cardiomyocyte norepinephrine stores are finite, accounting for tachyphylaxis to the positive inotropic effects of dopamine observed after approximately 24 h in patients with acute myocardial infarction.⁴⁹

Recent clinical trials showing norepinephrine beneficial effects over dopamine

Consensus guidelines and expert recommendations suggest that either norepinephrine or dopamine may be used as a first-choice vasopressor in patients with shock.^{50–52} However, observational studies have shown that the administration of dopamine may be associated

with mortality rates that are higher than those associated with the administration of norepinephrine in patients with septic shock.^{53–55} The Sepsis Occurrence in Acutely Ill Patients (SOAP) study, which involved 1058 patients with shock, demonstrated that administration of dopamine was an independent risk factor for death in the intensive care unit. In a recent multicenter, randomized, blinded trial comparing dopamine and norepinephrine as the initial vasopressor therapy in the treatment of shock,⁵⁶ there was no significant difference in mortality at 28 days between patients who received dopamine and those who received norepinephrine, although dopamine was associated with more severe arrhythmic events than was norepinephrine. Other studies in patients with cardiogenic shock have shown that the mortality rate was significantly higher in the dopamine group than in the norepinephrine group,^{57–59} with higher heart rates in patients who received dopamine as a potential contributor to the occurrence of ischemic events. Clinical trials in critically ill patients at risk for renal failure have also shown no renal vascular saving-effect of low dose dopamine.^{60,61} In summary, recent clinical trials have raised serious concerns about the safety and efficacy of dopamine therapy in the treatment of hypotensive circulatory shock.

Inotropic agents

Dobutamine

Dobutamine is a synthetic analogue of dopamine. It is utilized by continuous infusion as a positive inotrope, with the improvement in cardiac output noted to potentially increase renal blood flow, creatinine clearance, and urine output. Dobutamine also induces vasodilation that can cause profound hypotension in the hypovolemic patient. As a β_1 -agonist it increases myocardial oxygen consumption, although autoregulatory increases in coronary blood flow usually fully compensate in the absence of flow-limiting coronary artery disease. A noted problem with dobutamine is the development of tachyphylaxis with prolonged (as little as 72 hours) infusions, suggested to be due to the down-regulation of β_1 -adrenoreceptors.^{62–64} A recent randomized, double blind, placebo-controlled clinical trial in septic shock patients with low cardiac output and persistent hypoperfusion showed that dobutamine failed to improve sublingual microcirculatory, metabolic, hepatosplanchnic or peripheral perfusion parameters despite inducing a significant increase in systemic hemodynamic variables.⁶⁵ Thus, changes in measures of macrocirculatory flow may not be translated into changes in microcirculatory tissue blood flow. This unfortunate potential dissociation between macrocirculatory and microcirculatory is not unique to dobutamine, but may be seen in response to volume resuscitation and both vasopressor and vasodilator therapies.

Dopexamine

Dopexamine is a synthetic dopamine analogue with significant β_2 -adrenoreceptor agonist activity. Its splanchnic blood flow effects and positive inotropic activity have led to enthusiasm for potential utility outside its primary indication—decrease of afterload in acute heart failure syndromes with hypertension and oliguria. Randomized controlled clinical investigations have demonstrated improvement in morbidity and mortality outcomes when dopexamine was utilized as the pharmaceutical of choice in achieving goal-oriented oxygen delivery values in perioperative critically ill patients.^{66,67} Though widely utilized outside of North America, it is not licensed for use in North America.

Phosphodiesterase inhibitors

Although these agents are not widely used in the management of circulatory shock, but the two most commonly employed agents in this class are amrinone and milrinone. Both are bipyridines, and the class of drugs is otherwise known as ‘inodilators’ with reference to the two predominant dose-dependent modes of action—inotropy and vasodilation.⁶⁸ Milrinone has a shorter half-life and is a more potent (10–15-fold) inotropic agent than amrinone, but from all other aspects they are similar agents.^{69,70} Both are eliminated by conjugation, with amrinone’s biological half-life known to be extended in the presence of congestive heart failure. Their mechanism of action is not precisely known, but at least part of their activity is related to inhibition of phosphodiesterase type 3, found in high concentrations in cardiomyocytes and smooth muscle cells, and they may activate a sodium-dependent calcium channel. The end result is an increase in intracellular cAMP and calcium, with the physiological effect being an improvement in diastolic myocardial function, and for this reason these agents are felt to be positive lusiotropes.⁷¹ Clinically, they are used as positive inotropes, given by continuous intravenous infusion following a loading dose, with their catecholamine-independent mechanism of action making them theoretically attractive as an inotropic support of choice in patients with potential β 1-adrenoreceptor down-regulation.

Levosimendan

Levosimendan, as a pharmacological agent, exerts positive inotropic effects by binding to cardiac troponin C, thus sensitizing the myofilaments to calcium^{72,73} and increasing the effects of calcium during systole, thereby improving contraction. During diastole, it causes calcium concentration to decline, allowing normal or improved diastolic relaxation.⁷⁴ Levosimendan also has vasodilatory properties due to its facilitation of an adenosine triphosphate-dependent potassium channel opening⁷⁵ as well as anti-ischemic effects.⁷⁶ In clinical studies, levosimendan increased cardiac output and lowered cardiac filling pressures and was associated with reduced cardiac symptoms, risk of death, and hospitalization in patients.^{77–79} Unlike other positive inotropic agents, the primary actions of levosimendan are independent of interactions with β -adrenergic receptors.⁸⁰ In the Levosimendan Infusion versus Dobutamine (LIDO) study⁷⁴, levosimendan was shown to exert superior hemodynamic effects compared with the β -adrenergic agonist dobutamine, and in secondary and post hoc analyses was associated with a lower risk of death after 31 and 180 days.

Vasodilators

Afterload reducing vasodilators act via vascular smooth muscle relaxation. Vascular dilatation is mediated by both nitric oxide (NO) and non-NO-based mechanisms, NO being a powerful, locally acting vascular smooth muscle relaxant. Among commonly used vasodilators in hemodynamically unstable patients, both sodium nitroprusside and glyceryl trinitrate (nitroglycerine) function as NO donors. Numerous other non-NO donor vasodilating agents are available, with hydralazine, clonidine, and inhibitors of the renin-angiotensin system being the most commonly employed non-NO-based vasodilators in patients with hemodynamic instability. Although uncommonly needed in the management of circulatory shock, their use in combination with vasopressor therapy has recently been advocated to increase microcirculatory flow since nitrate releasing agents cause

microcirculatory flow to increase even in the setting of vasopressor-induced arteriolar vasoconstriction.⁸¹ However, this is an approach still under investigation and not ready yet for general clinical use.⁸²

Ventricular Assist Devices

Ventricular assist devices (VADs) are artificial pumps that take over the function of the damaged ventricle so as to restore hemodynamic stability and end-organ blood flow. These devices are useful in two groups of patients. The first group consists of patients who require ventricular assistance to allow the heart to rest and recover its function. In such situations, it is critical to obtain complete drainage of the ventricle so as to unload the ventricle, diminish myocardial work, and maximize subendocardial perfusion.⁸³ The second group consists of patients with myocardial infarction, acute myocarditis, or end-stage heart disease who are not expected to recover to adequate cardiac function and who require mechanical support as a bridge to transplantation.^{84,85} Patients on VAD support often require hemodynamic monitoring to assess their cardiovascular state both in the perioperative state and afterward.

Left Ventricular Assist Device (LVAD)

Left ventricular assist devices (LVADs), which are rapidly evolving, are used to treat patients with advanced stages of heart failure. While the main goals of LVAD therapy are to improve symptoms of heart failure and quality of life, they also reverse pulmonary vascular hypertension in the setting of venous back-pressure induced increased pulmonary vasomotor tone, thus reversing right ventricular dysfunction.⁸⁶

Patient selection is a crucial consideration that determines the ultimate outcome of patients who receive a LVAD. In general, patients who receive LVADs have end-stage heart disease without irreversible end-organ failure. For patients who are too ill to undergo heart transplantation, such as those who cannot be weaned from cardiopulmonary bypass, use of a short-term extracorporeal LVAD is a first-line therapy. For patients who are suitable candidates to receive a heart transplant but are unlikely to survive the wait required before transplantation, LVADs are an effective bridge to transplantation.⁸⁷

Complications that could occur in the post-implant period include infection, thromboembolism and failure of the device. The most common causes of early morbidity and mortality after placement of a LVAD include air embolism, bleeding, right-sided heart failure, and progressive multisystem organ failure.⁸⁸ In general, complications are less with the smaller pumps and drivelines, and in those that use axial rather than pulsatile flow. Pump thrombosis, a complication with high mortality or one requiring a pump change, can occur causing an obstruction of the pump,^{85,86} but can be treated with tirofiban/tissue plasminogen activator. Since 60–70% of RV systolic power comes from LV contraction,⁸⁹ acute cor pulmonale can occur post LVAD insertion. This can be corrected by applying therapies aimed at sustaining coronary blood flow (i.e. increased MAP) and minimizing any increased pulmonary vasomotor tone (i.e. intravenous prostacyclin or inhaled nitric oxide). Hemodynamic monitoring often requires echocardiographic support, as described later in this volume. Importantly, the unsupported right ventricle will be minimally responsive to positive inotropic drug infusion since most of the beneficial effects of increased inotropy on

the right ventricle are derived from increased LV contraction. Thus, volume overload and acute RV dilation are serious concerns and need to be closely monitored using echocardiographic techniques.

Right ventricular assist device (RVAD)

Right ventricular (RV) dysfunction occurs in clinical scenarios such as RV pressure overload due to increased pulmonary vascular resistance, cardiomyopathies, arrhythmias, RV ischemia, congenital or valvular heart diseases, and sepsis.⁹⁰ The most common cause of increased pulmonary vascular resistance is pulmonary arterial hypertension (PAH), which is defined as the mean pulmonary artery pressure > 25 mmHg with a Ppao, left atrial pressure or LV end-diastolic pressure $\geq$ 15 mmHg.⁹¹ The critical determinant of patient outcomes in PAH is the functioning of the right ventricle, and has been recognized as an important avenue for further research.⁹² Historically, long-term outcomes for patients with PAH are poor. Progressively increasing PAH results in severe RV failure, since the RV, in an attempt to adapt to the pressure overload, becomes hypertrophied and eventually dilated, with diminished systolic and diastolic function. RV failure is the end result of PAH and the cause of at least 70% of all PAH deaths.⁹³ Mechanical support for the RV may be appropriate in etiologies where it is likely to be reversed (i.e. acute vasospastic disease) or as a bridge to definitive treatment (i.e. lung transplantation). RVADs may be used in primary RV dysfunction⁹⁴ and have been used with coexisting PAH.^{95,96} In patients with PAH, however, there is concern that pulsatile devices may cause pulmonary microcirculatory damage.⁹⁷

Although theoretically an RVAD may be beneficial for decreasing right-side atrial and ventricular filling pressures, decongesting the liver, and increasing LVAD flow, the RVAD itself has complications, with the current RVAD technologies requiring external pumps with a cumbersome drive system, making hospital discharge difficult to achieve.^{98,99} Furthermore, it is difficult to assess volume status in RVAD patients because the RV is the primary balance in between volume and volume response. Thus, no clear guidelines as to minimal CVP values can be made even when individualized to a given patient's cardiac output, since unstressed intravascular volume can vary widely.

BiVentricular Assist Device (BiVAD)

The rationale for the use of a BiVAD in patients with heart failure is still controversial. These patients are typically more severely ill preoperatively, have a higher serum creatinine, and a greater proportion of them are ventilator dependent before VAD insertion.^{99,100} While the selection of patients for BiVAD support is crucial to obtaining successful outcomes, criteria for predicting the need for a BiVAD have not been well established and remain a major focus for future research. While rates of survival to discharge have been shown to be similar to LVAD when used post transplantation,¹⁰⁰ patient survival to transplantation is much lower with BiVAD than LVAD.⁹⁹ Patients on BiVAD therapy are at a greater risk of complications with higher incidences of infection, thromboembolism and failure of the device due to twice as many cannulae and pumps.¹⁰¹ As may be expected, BiVAD patients are monitored more by their VAD-displayed cardiac output estimates and measures of MAP than central venous O₂ saturation. Volume status and need for vasopressor therapy are

usually accomplished through therapeutic trials to observe if changes in cardiac output and MAP occur, rather than on predefined physiological conditions.

Acute Kidney Injury

Fluid resuscitation together with attention to DO_2 are the cornerstones of resuscitation in all critically ill patients.¹ However, acute kidney injury (AKI) is a common complication of circulatory shock, and is associated with high mortality.^{102,103} Circulating fluid deficits can occur as a result of absolute or relative hypovolemia, resulting in inadequate blood flow to meet the metabolic requirements of the kidneys. Low cardiac output, either as a primary mechanism in cardiogenic shock or a secondary mechanism in the other forms of shock also decreases kidney perfusion. Both of these volume and flow problems must be treated urgently if AKI is to be avoided.^{104,105} Although the importance of fluid management is generally recognized, the choice and amount of fluid, and fluid status end-points are controversial,^{29,106,107} requiring special attention to monitoring hemodynamic patterns of fluid resuscitation in patients at risk for AKI.

Risk of starches to cause AKI

Hydroxyethyl starches (HES) are identified by three numbers corresponding to concentration, molecular weight, and molar substitution (e.g.: 6% HES, 130/0.4). According to the number of hydroxyethylations at carbon positions C2, C3, or C6 (degree of substitution), the HES are more or less resistant to degradation by plasma α -amylase. Molar substitution is the most clinically significant number since it relates to the rate of enzymatic degradation of the starch polymer.¹⁰⁸ Pharmacokinetic characteristics of HES solutions are based upon the molecular weight, and degree of substitution and C2/C6 hydroxyethylation ratio.¹⁰⁹ Renal toxicity of HES depends on the level of molar substitution, although a meta-analysis of randomized clinical trials in surgical patients failed to show any difference in the incidence of renal impairment between patients who received low substituted HES and other forms of fluid therapy.¹¹⁰ However, in the intensive care units, renal toxicity has been reported even with low substituted HES, due to concurrent sepsis and distributive shock,¹¹¹ with the initiation of renal replacement therapies significantly greater in patients who received HES than those who received saline for fluid management.¹¹²

Continuous Renal Replacement Therapies

In general, critically ill patients receive high daily amounts of volume infusions: continuous infusions, vasopressors, blood or fresh frozen plasma. Patients with renal failure and in septic shock continue to receive large amounts of fluid resuscitation thus leading to fluid overload. The consequent positive fluid balance necessitates water removal, with a major consequence of rapid fluid removal being hemodynamic instability.¹¹³

Daily or every other day conventional hemodialysis (HD) is the standard dialysis regimen for hemodynamically stable patients with renal failure. However, hypotension during HD due to rapid fluid and solute removal is the most common complication of this therapy, and can prolong renal insufficiency in critically ill AKI patients. The rapid rate of solute removal during HD results in an abrupt fall in plasma osmolality which induces further extracellular

volume depletion by promoting osmotic water movement into the cells. This reduction in plasma osmolality may contribute to the development of hypotension. Severe hypotension still accompanies 20–30% of HD sessions in patients with AKI.¹¹⁴ It was for that reason that continuous renal replacement therapy (CRRT) was developed. With CRRT, volume control is more gently continuous and immediately adaptable to changing circumstances (e.g. the immediate need for blood or blood products in a patient at risk for ARDS). Because of this adaptability, volume overload can be immediately treated or prevented, and volume depletion avoided.

The ideal renal replacement therapy would be one that achieves slow yet adjustable fluid removal, in order to easily meet the highly variable required daily fluid balance. At the present time, by mimicking urine output, CRRT slowly and continuously removes a patient's plasma water. It must be emphasized, however, that the protection afforded by CRRT is relative and not absolute, since hypotension can still occur if too much fluid is removed or if fluid is removed too quickly, irrespective of the therapy name. Studies comparing CRRT to HD in patients with AKI have not shown a survival benefit for one approach versus the other.¹¹⁵ It remains a controversial matter as to which clinical parameter (dry weight, MAP, Ppao, SvO₂, etc.) or currently available invasive monitoring (central venous catheter, pulmonary artery catheter, etc.) should be utilized in order to define the concept of 'fluid overload' and subsequent therapies thereof to be employed for fluid removal.¹¹⁶

Conclusion

Hemodynamic monitoring at the bedside improves patient outcomes when used to make treatment decisions at the right time for patients experiencing hemodynamic instability. For monitoring to provide any benefit, the clinician must be able to use the information to guide management within the context of known physiological principles and an understanding of the pathological processes that may be in play. Three basic guiding principles could be used to effectively manage patients with hemodynamic instability associated with signs and symptoms of tissue hypoperfusion. If blood flow to the body increases with fluid resuscitation, then treatment must include volume expansion. If the patient is also hypotensive and has reduced vasomotor tone, then vasopressor therapy might be initiated simultaneously. If the patient is neither preload responsive nor exhibiting reduced vasomotor tone and is hypotensive, then the problem is the heart, and both diagnostic and therapeutic actions must be initiated to address these specific problems. Protocolized management, based on existing hemodynamic monitoring technologies at the bedside, is both pluripotential (different monitoring devices can drive the same protocol) and scalable (can alter the resuscitation intensity) and thus lends itself to automation.

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Key points

1. Bedside measures of hemodynamic instability include mean arterial pressure (MAP), hypotension and mixed venous oxygen saturation.
2. Circulatory shock etiologies can be divided into hypovolemic, cardiogenic, obstructive and distributive shock, and the hemodynamic patterns are characteristic for each etiology.
3. The different etiologies of circulatory shock usually require different types of treatment modalities, making the correct etiologic diagnosis important.
4. Pharmacotherapies for hemodynamic instability include vasopressors, inotropes and vasodilators.
5. Technological advances to restore hemodynamic instability include the use of ventricular assist devices and continuous renal replacement therapies.

Table 1Categorization of Shock States based on the Weil and Shubin⁸ Nosology

Shock state	Pathophysiology	Disease States	Hemodynamic Monitoring Pattern
Hypovolemic	Decrease in effective circulating blood volume and venous return	Primary intravascular volume loss (hemorrhage, capillary leak) Secondary intravascular volume loss (third-space loss, burns, diarrhea, vomiting)	↓ filling pressures (↓Pra and Ppao) ↓ CO ↑ SVR
Cardiogenic	Primary cardiac failure	Impaired contractility (myocardial ischemia/infarction, electrolyte imbalance, hypoxemia, hypothermia, endocrinologic diseases, metabolic poisoning, beta-blockers) Pump function (valvulopathy, ventriculoseptal defect, dysrhythmias) Diastolic compliance (left ventricular hypertrophy, fibrosis, infiltrative cardiomyopathies, asymmetric septal hypertrophy, cor pulmonale)	↑ back pressure to cardiac filling (↑Pra and Ppao) ↓ CO ↑ SVR
Obstructive	Blockage of blood flow in heart's outflow tracts	RV outflow obstruction (pulmonary embolism, lung hyperinflation and pulmonary artery compression) LV outflow obstruction (aortic stenosis, dissecting aortic aneurysm) Cardiac Tamponade (pericardial effusion, lung hyperinflation and atrial compression)	↑CVP ↓ Ppao relative to CVP ↓ CO ↑ SVR
Distributive	Loss of blood flow regulation	Sepsis (increased capillary leak with secondary loss of intravascular volume, and inappropriate clotting in the microcirculation) Neurogenic shock (acute spinal injury above the upper thoracic level, spinal anesthesia, general anesthesia, neurotoxic poisoning and central nervous system catastrophe) Acute adrenal insufficiency (hyperpyrexia and circulatory collapse)	↓CVP ↓ filling pressures (↓Pra and Ppao) ↑ SvO ₂ ↓ MAP

Abbreviations: right atrial pressure, Pra; pulmonary artery occlusion pressure, Ppao; cardiac output, CO; systemic vascular resistance, SVR; mean arterial pressure, MAP, central venous pressure, CVP, venous oxygen saturation, SvO₂.