CHAPTER 5

Monitoring Organ Dysfunction in Critical Care

Michael R. Pinsky

OBJECTIVES

This chapter will:
1. Describe the principles of the assessment of organ function.
2. Explain the major aspects of hemodynamic monitoring.
3. List the key aspects of respiratory functional monitoring.
4. Describe the key aspects of neurologic monitoring.
5. Explain the key aspects of renal functional monitoring.

PRINCIPLES OF BIOMARKER ANALYSIS TO ASSESS ORGAN DYSFUNCTION

Critically ill patients often experience or develop acute organ dysfunction during their course of stay. Such parenchymal injury has profound outcome implications: the mortality rate exceeds 90% with three or more organ systems failing for 2 days or longer.[1] Various biomarkers, blood and bodily fluid levels of specific molecules, and physiologic measures or responses to stress have been developed to assess basal performance and organ system reserve. Importantly, these biomarkers usually do not define the cause of organ dysfunction, merely its presence. The assumption is that knowing organ dysfunction is present will alter therapy either to prevent further deterioration or to compensate for its presence in terms of treatments that depend on its function to be effective. However, few data support knowing that organ dysfunction is present improves outcome, other than by avoiding untoward effects primary to either the organ system toxicity or its lack of homeostatic support. Although every organ system can be monitored, primary assessment focuses on cardiovascular, respiratory, renal, neurologic, hepatic, endocrinologic, hemostatic, and immunologic function. Clearly, each of these topics could fill a chapter. Here we discuss them only in global terms of the utility of static variables, estimates of physiologic reserve, and the interpretation of biomarker changes over time.

Separating organ systems into separate units is arbitrary and overly simplistic. The organism's health and vitality is a function of the integrated performance of all organ systems combined. However, it is useful to compartmentalize bedside monitoring analysis, because treatments are often focused on one system.

Cardiovascular Function and Hemodynamic Monitoring

Circulatory insufficiency resulting from a variety of causes often occurs in critically ill patients, either as part of their initial presentation or over time as a result of disease progression and side effects of therapies. In general, hemodynamic monitoring is a cornerstone in the assessment of cardiovascular state. Usually, invasive, minimally invasive, and noninvasive measures of cardiovascular function are used to assess cardiovascular state and its reserve to handle increased stress. Box 5.1 lists the most commonly measured vascular pressures and their derived variables. Cardiovascular insufficiency causes can be grouped roughly into four general etiologic categories: cardiogenic, obstructive, hypovolemia, and distributive.[2] I have added a fifth, metabolic, only because its signs and causes are different (Table 5.1). Each group carries a specific profile of characteristics that help to make its bedside diagnosis. Serum biomarkers of cardiovascular insufficiency include brain natriuretic peptide (BNP) and troponin. BNP is useful in identifying disease processes associated with increased right atrial pressure, such as congestive heart failure and cor pulmonale (cardiogenic and obstructive shock), whereas troponin is useful in identifying cardiac myonecrosis (cardiogenic shock).

Although all forms of circulatory shock have cardiovascular insufficiency as defined by evidence of inadequate tissue perfusion, not all forms of shock are associated with a decreased cardiac output. After the initial resuscitation, distributive shock is associated with an increased cardiac output (CO), whereas the other three types of shock usually have a decreased CO. In assessment of the global severity of circulatory shock, inspection is the first line of analysis. Evidence of tissue hypoperfusion should be sought and quantified. Markers of impaired circulation include delayed capillary refill, skin mottling (especially over the knees), cool periphery with cyanosis, tachycardia, decreased urine output, altered sensorium, and ileus. The level of severity correlates well with the level of severity of the low CO circulatory shock causes. Blood biomarkers of tissue hypoperfusion include increased oxygen (O_2) extraction, slower carbon dioxide (CO_2) wash out, and evidence of anaerobic metabolism. Thus documenting low venous O_2

BOX 5.1

Physiologic Measures Derived From Invasive Monitoring and Their Physiologic Relevance

Arterial Pressure*
Mean arterial pressure (MAP)
Organ perfusion inflow pressure
Arterial pulse pressure and its variation during ventilation
  Left ventricular stroke volume changes and pulsus paradoxes
  Preload-responsiveness (if assessed during IPPV)
Arterial pressure waveform
  Aortic valvulopathy, input impedance, and arterial resistance
  Used to calculate stroke volume and cardiac output by pulse contour technique

Central Venous Pressure (CVP)
Mean central venous pressure
If elevated, that effective circulating blood volume is not reduced
Central venous pressure variations during ventilation
Tricuspid insufficiency, tamponade physiology
  Preload-responsiveness (if assessed during spontaneous breathing)

Pulmonary Arterial Pressure (Ppa)
Mean Ppa
  Pulmonary inflow pressure
Systolic pulmonary artery pressure
  Right ventricular pressure load
Diastolic pulmonary artery pressure and pulse pressure and their variations during ventilation
Right ventricular stroke volume, pulmonary vascular resistance
  Diastolic pressure tract changes in intrathoracic pressure during ventilation

Pulmonary Artery Occlusion Pressure (Ppao)
Mean Ppao
  Left atrial and left ventricular intraluminal pressure and by inference, left ventricular preload
  Backpressure to pulmonary blood flow
Ppao waveform and its variation during occlusion and ventilation
Mitral valvulopathy, atrial or ventricular cause of arrhythmia, accuracy of mean Ppao to measure intraluminal LV pressure, and pulmonary capillary pressure (Ppc)

*Arterial pressure also can be measured noninvasively and derive all the listed parameters in most patients.
IPPV, intermittent positive-pressure ventilation.

saturation (<70%), increased venoarterial CO_2 gradient (> 6 mm Hg), hyperlactecemia (>1.5 mmol/dL), and metabolic acidosis correlates well with the degree of global tissue hypoperfusion.[3] Cardiogenic shock reflects primary myocardial pump failure and is characterized by systemic hypotension and tachycardia with decreased pulse pressure despite an increase in ventricular filling pressure and biventricular end-diastolic volumes. Left ventricular (LV) failure secondary to myocardial infarction is the most common cause of cardiogenic shock. In general, these failing hearts need higher filling pressures and end-diastolic volumes than normal hearts to sustain even a small stroke volume and thus uniformly display compensatory tachycardia. If the LV filling pressure rises enough, hydrostatic pulmonary edema can develop (i.e., cardiogenic pulmonary edema), causing impaired gas exchange in the lungs and creating arterial hypoxemia, which may further complicate O_2 delivery to the tissues. Furthermore, the reflex increased sympathetic tone usually sustains mean arterial pressure by preventing diastolic arterial pressure from decreasing but usually is associated with a marked decrease in systolic pressure and pulse pressure. Because the primary cause of cardiogenic shock is the heart, most patients will not increase their stroke volume in response to a fluid bolus, a concept referred to as not being volume responsive. Dynamic measures of volume responsiveness also will display minimal changes. These functional measures include observing the dynamic changes in LV output during positive-pressure breathing, such as arterial pulse pressure variation (PPV) and LV stroke volume variation assessed from arterial catheterization; the dynamic changes in central venous conduits during spontaneous breathing, such as inferior vena caval or internal jugular vein diameter changes assessed by ultrasonography; or changes in CO in response to a small bolus fluid infusion, passive leg raising, or an end-expiratory occlusion maneuver if on positive-pressure ventilation.[4,5] Echocardiographic assessment is extremely useful in defining the cause of cardiogenic shock and in guiding therapy. Obstructive shock resembles cardiogenic shock from outside the perspective of the heart, in that central venous pressure is increased, stroke volume decreased decreasing arterial pulse pressure, but diastolic pressure is preserved. Massive pulmonary embolism, tamponade, tension pneumothorax, and lung hyperinflation during exacerbations of chronic obstructive lung disease are the most common causes of obstructive shock. Here echocardiography is usually diagnostic. However, unlike cardiogenic shock, PPV and SVV may be elevated owing to acute cor pulmonale. However, the mechanisms by which PPV and SVV increase in cor pulmonale is through right ventricular (RV) compression during positive pressure inspiration increasing LV diastolic compliance and thus LV end-diastolic volume. Importantly, fluid infusions may exacerbate RV dilation and precipitate fatal acute cor pulmonale.

Hypovolemic shock is the most common type of cardiovascular insufficiency and is due to decreased effective circulating blood volume, causing the pressure gradient for venous return to decrease decreasing ventricular filling and CO. Intrathoracic blood volume, like peripheral blood volume, is decreased. With loss of intravascular volume, fluids shift from the interstitial and cellular compartments into the intravascular space, such that hypovolemic shock usually is associated with a decreased total body water relative to its prior stable state. Although ventricular volumes are reduced, there is no relation between end-diastolic volume or its change and either RV or LV filling pressures. The reflex increased sympathetic tone usually caused myocardial contractility to increase. Mean arterial pressure often is sustained by the associated increase in arterial vascular tone keeping diastolic arterial pressure elevated. These subjects are highly volume responsive with high PPV, SVV, and vena caval diameter change values with respiration.

Operationally, in the management of circulatory shock, the priorities are to first restore mean arterial pressure to more than 65 mm Hg to sustain cerebral and coronary blood flow, then to simultaneously address the primary cause of shock while giving therapies to ensure adequate total blood flow and oxygen delivery to sustain normal tissue viability and organ system function.[3,4,6] A simple initial resuscitation algorithm to achieve these immediate goals based on functional hemodynamic monitoring principles is described in Fig. 5.1. It is not the goal of this chapter to go into management principle, but these functional parameters

TABLE 5.1

Nosology of Circulatory Shock Causes

ETIOLOGIC GROUP	SIGNS	CARDIAC OUTPUT	EXAMPLES (IN ORDER OF LIKELIHOOD)
Cardiogenic	Tachycardia, systolic hypotension, decreased pulse pressure, increased filling pressures, decreased capillary refill	Decreased CO, decreased venous O_2, increased v-a CO_2 gradient, lactic acidosis	Myocardial infarction, cardiomyopathies, arrhythmias, valvulopathy
Obstructive			Tension pneumothorax, hyperinflation, tamponade
Hypovolemic	Tachycardia, systolic hypotension, decreased pulse pressure, decreased filling pressures, decreased capillary refill		Hemorrhage, dehydration (insensible loss: burns), massive GI fluid loss (vomiting, diarrhea), polyuria
Distributive	Tachycardia, diastolic hypotension, warm periphery, normal capillary refill	Increased CO (if fluid resuscitated), normal or increased venous O_2, lactic acidosis	Infection-sepsis, severe burns, pancreatitis, immune response, adrenal insufficiency
Metabolic	Bradycardia, hypotension	Decreased CO	Hypothermia, hypoglycemia, adrenal insufficiency, electrolyte imbalance

CO, Cardiac output; *CO_2,* carbon dioxide; *GI,* gastrointestinal; *O_2,* oxygen.

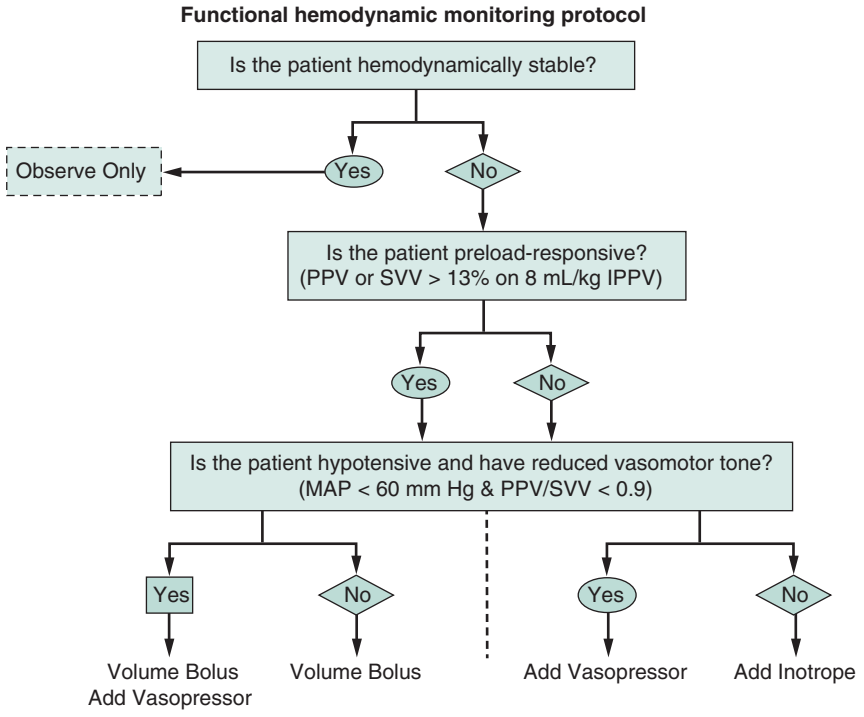

FIGURE 5.1 Schematic diagram of the logic tree for resuscitating potentially unstable patients in circulatory shock. (Modified from Pinsky MR. Protocolized care. In Pinsky MR, Payen D, eds. *Functional Hemodynamic Monitoring.* Berlin: Springer, 2004; 381–395.)

also can be used to assess cardiovascular state. If everything is otherwise kept constant in terms of ventilatory status and fluids, increasing PPV and SVV connote volume loss and usually signal occult hemorrhage. Similarly, with fluid resuscitation, one would expect PPV and SVV to decrease if cardiac output increases. If patients are in circulatory shock and their PPV and SVV are low, they have primary heart failure of either cardiogenic or obstructive causes. Finally, the ratio of PPV to SVV decreases central arterial tone. If it is increasing, then there is increased sympathetic tone; that is a common finding associated with increased circulatory stress. Similarly, a decreasing PPV/SVV is expected in response to effective fluid resuscitation. When coupled with the metabolic measures of venous O_2 saturation venoarterial PCO_2 difference, metabolic acidosis and hyperlactecemia, a reasonably accurate measure of circulatory stress can be made. When these measures are combined further with estimates of end-organ function, such as urine output, skin mottling and temperature, sensorium, and bowel sounds, typically this provides a very good understanding of the level of circulatory shock present. Regrettably, none of these metabolic or organ-system parameters can assess the level of organ injury induced by circulatory shock or other pathogenic processes. Those may be discussed in later chapters.

Respiratory Functional Assessment

Respiratory symptoms are the most common presenting complaints in critically ill patients, either as increasing or unresolving dyspnea, chest pain, and tachypnea. Indeed,

one of the cardinal signs of developing sepsis is tachypnea. Although all forms of respiratory failure must result in inadequate gas exchange, owing to increased work of breathing, the causes are widespread and include increased airway resistance (asthma, chronic obstructive lung disease), inefficient ventilation (hyperinflation, chronic obstructive lung disease), impaired gas exchange (pneumonia, pulmonary embolism, acute lung injury, chronic obstructive lung disease), and loss of mechanical function (pneumothorax, upper airway obstruction).

The primary biosignals used to assess respiratory function are respiratory frequency, tidal volume, pulse oximeter-derived O_2 saturation (SpO_2), and arterial blood gas analysis. Respiratory frequency often is estimated indirectly: the phasic changes in electrocardiographic signal via impedance monitoring. Minute ventilation is the product of respiratory frequency and tidal volume, and frequency alone cannot assess the adequacy of minute ventilation. Tidal volume is further divided into (1) the gas volume needed to ventilate the airways and other nonperfused lung regions and (2) alveolar ventilation, that volume of gas that is involved in gas exchange. Patients with pulmonary vascular injury, as may occur with pulmonary embolism, asthma, and chronic obstructive lung disease) often have a marked increased dead space owing to pulmonary capillary hypoperfusion. These patients usually increase their tidal volume to maintain an adequate alveolar ventilation. Although increasing respiratory frequency also will increase alveolar minute ventilation, if the patient has increased airway resistance, air-trapping with its associated hyperinflation will occur. Hyperinflation makes the respiratory muscle less effective and also compromises cardiovascular function by passively increasing right atrial pressure, owing to the increase in intrathoracic pressure, and pulmonary vascular resistance, owing to lung overdistention.

Acute lung injury often causes alveolar flooding or interstitial edema, both of which act as an intrapulmonary shunt. The hallmark of this is a low arterial oxygenation that does not increase as expected in response to supplemental O_2. Although respiratory frequency and SpO_2 are the common default respiratory biosensor monitors, they do not assess alveolar ventilation or its efficiency. Respiratory inductance tomography and respiratory impedance tomography can assess tidal volume noninvasively. However, they are used infrequently outside of the sleep laboratory. In the intubated patient, measures of airway CO_2 by infrared spectroscopy can be extremely valuable to assess changes in cardiac output and alveolar ventilation. In a volume-responsive patient, performing a passive leg-raising maneuver will cause end-tidal CO_2 to transiently increase. Similarly, acute pulmonary emboli will result in an immediate decrease in end-tidal CO_2. Because all forms of respiratory insufficiency induce tachypnea, measures of respiratory frequency become sensitive but nonspecific measures of respiratory distress. Low SpO_2 values that easily increase with low levels of supplemental O_2 (e.g., <35% O_2) usually reflect ventilation-perfusion mismatch, as commonly occurs in patients with obstructive lung disease, whereas hypoxemia not responsive to supplemental O_2 usually reflects an intrathoracic venoarterial shunt. In most patients that shunt is at the perialveolar level.

Finally, most patients with respiratory symptoms will have chest imaging studies, which usually include a chest radiograph, chest computed tomography, and, more recently, bedside thoracic echocardiogram. These imaging approaches have been traditionally the cornerstone of diagnosis of lung disease, and their description and use is beyond the scope of this introductory chapter.

NEUROLOGIC FUNCTIONAL ASSESSMENT

Altered sensorium is a highly sensitive but nonspecific marker of systemic stress. However, severe neurologic injury from nontrauma or nonischemic insults are rare and, if present, often reverse if the underlying pathologic process reverses. The bedside neurologic examination has not been replaced by any biomarkers as the best tool to assess neurologic function. Relevant to that, pupillary reflexes, eye movements, voluntary coordination, muscle tone, reflexes, sensation, confusion assessment, and response to pain reflect the main measures usually assessed at the bedside. In recent years, increased interest in processed electroencephalographic (EEG) signals has become popular. Independent of a full EEG examination, the bispectral monitor (BIS) assesses level of consciousness, and other recent commercial offerings allow one to assess left-right dyssynchrony and level of neuroactivity. Finally, recent studies suggest that specific fatty acid breakdown products present in the cerebrospinal fluid can detect neuronal injury.[7] Still, all these measures are ancillary to the bedside neurologic examination.

Renal Functional Assessment

Acute kidney injury (AKI) commonly occurs in the critically ill patient and affects survival.[8] Presently the major scoring systems rely on functional measures, such as urine output, creatinine, and creatinine clearance, to define AKI. No new measures have been shown to be superior to these assessing global renal function. However, they reflect present status, not future risk. Because AKI usually evolved over time, if patients are at increased risk of AKI, preventative measures, such as avoiding nephrotoxins and sustaining a higher renal perfusion pressure, may be indicated.

New biomarkers aim to detect AKI before overt loss of renal function. Increased serum and urine levels of neutrophil gelatinase-associated lipocalin (NGAL) predict subsequent renal impairment.[9] Similarly, lower levels of urinary cell cycle arrest biomarkers (tissue inhibitor of metalloproteinase-2 [TIMP-2] and insulin-like growth factor binding protein -7 [IGFBP-7]) can be used to rule out impending AKI.[10] The Kidney Disease: Improving Global Outcomes (KDIGO) scoring system uses these and other measures to stratify AKI risk.[11] These points are be addressed in greater detail later in this text.

CONCLUSION

Monitoring of organ system function in the critically ill patient is important to predict disease severity and mortality risk. For the cardiovascular system, such monitoring is central in the cardiovascular resuscitation and stabilization of these patients. For the brain, lungs, and kidney, such monitoring is useful not only to quantify the degree of organ injury but also to alert the clinicians that increased risk is present and avoid further organ specific insults that may occur for specific therapies while noting improvement when targeted resuscitation is given.

It is not clear if any monitoring or management approaches other than the rapid reversal of tissue hypoperfusion before initial organ injury improve outcome. Aggressive therapies once organ injury has occurred do not improve outcome. However, persistent excess therapy in an unresponsive

patient will be associated with all the complications of that therapy without any benefits. To the extent that monitoring identifies the at-risk patients to minimize untoward effects, monitoring of organ system function is valuable and should improve outcomes when compared with strategies that ignore these warning signs.

Key Points

1. Monitoring of organ system function in the critically ill patient is a key aspect of management.
2. Systemic cardiovascular monitoring is central to cardiovascular resuscitation and stabilization of acutely ill patients.
3. Brain, lung, and kidney monitoring alerts clinicians that increased risk is present and helps avoid further organ-specific insults.
4. It is not clear if any monitoring or management approaches other than the rapid reversal of tissue hypoperfusion before initial organ injury improves outcome, because aggressive therapies once organ injury has occurred do not improve outcome.
5. Persistent excess therapy in an unresponsive patient will be associated with all the complications of that therapy without any benefits, and monitoring of organ system function may prevent such iatrogenic injury.

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A complete reference list can be found online at ExpertConsult.com.

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