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The crashing patient: hemodynamic collapse

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Abstract

Purpose of review—Rapid restoration of tissue perfusion and oxygenation are the main goals in the resuscitation of a patient with circulatory collapse. This review will focus on providing an evidence based framework of the technological and conceptual advances in the evaluation and management of the patient with cardiovascular collapse.

Recent findings—The initial approach to the patient in cardiovascular collapse continues to be based on the Ventilate–Infuse–Pump rule. Point of care ultrasound is the preferred modality for the initial evaluation of undifferentiated shock, providing information to narrow the differential diagnosis, to assess fluid responsiveness and to evaluate the response to therapy. After the initial phase of resuscitative fluid administration, which focuses on re-establishing a mean arterial pressure to 65mmHg, the use of dynamic parameters to assess preload responsiveness such as the passive leg raise test, stroke volume variation, pulse pressure variation and collapsibility of the inferior vena cava in mechanically ventilated patients is recommended.

Summary—The crashing patient remains a clinical challenge. Using an integrated approach with bedside ultrasound, dynamic parameters for the evaluation of fluid responsiveness and surrogates of evaluation of tissue perfusion have made the assessment of the patient in shock faster, safer and more physiologic.

Keywords

cardiovascular; collapse; hemodynamic; lactate; shock

Introduction

Shock is a clinical syndrome characterized by circulatory failure that results in inadequate oxygen delivery to meet tissue metabolic demand [1]. Shock is common in the critically ill population, occurring in a third of patients admitted to the ICU [2] and is lethal if untreated. The cellular consequences of insufficient perfusion are a chain of events that impair oxidative metabolism, leading to energy failure, cell injury and death [1]. Clinically this manifests as multiple organ dysfunction, which often leads to death weeks or months after

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the initial shock episode occurred. However, shock is reversible if recognized and treated early, and therefore a prompt diagnosis coupled to appropriate treatment is fundamental to the patient's survival. Although clinical signs of hypoperfusion like altered mentation, oliguria and mottling of the skin; hypotension, defined as systolic or mean arterial pressure (MAP) below 90 or 60mmHg, respectively; or hyperlactatemia (lactate >2 mmol/l) constitute sufficient evidence for the diagnosis of shock and would justify initiating treatment, several challenges remain. First, the coexistence of distinct types of shock can make a differential diagnosis elusive and mislead treatment selection. Second, hemodynamic monitoring systems are limited in assessing important parameters like preload, sympathetic tone and effective circulating volume. Third, there are no organ-specific biomarkers of perfusion. Despite these challenges, the popularization of bedside ultrasonography, the use of dynamic parameters for the assessment of fluid responsiveness, and the critical assessment of surrogates of perfusion provides promising alternatives when approaching a patient in shock. This review will focus on providing an evidence-based framework of these advances, for the evaluation and management of the patient with hemodynamic or cardiovascular collapse.

Mechanistic Classification and Differential Diagnosis

Weil and Shubin [3] proposed a classification of circulatory shock based on the origin of the hemodynamic deficits, separating them in four categories: blood flow distribution, cardiac failure, obstruction to flow and hypovolemia. Distributive shock is associated with a vasodilatory state with an elevated cardiac output (*CO*), whereas the rest are associated with reduced *CO*.

Establishing a differential diagnosis of the type or types of shock is as important as initiating immediate supportive treatment to limit hypoperfusion. The differential diagnosis of shock states is done by analyzing information derived from the clinical assessment and hemodynamic monitoring in the appropriate context provided by a complete clinical history. The most common cause of shock in the adult critically ill patient is sepsis (62%), and thus, the most common mechanism is the alteration in blood flow distribution [4]. Sepsis is followed by cardiogenic and hypovolemic (16% both), other types of distributive (i.e. neurogenic or anaphylactic, 4%) and obstructive shock (2%) [4]. However, most frequently different types of shock will coexist, making the diagnosis and hence treatment, challenging.

Clinical History and Physical Examination

The clinical history provides the framework within which the rest of the data must be interpreted. The physical examination involves a quick, focused examination including but not limited to the 'three windows' to organ perfusion: the brain (i.e. altered mental status), urine output (i.e. oliguria) and the skin (i.e. mottled, cold and clammy vs. flushed skin, capillary refill) [1]. A systematic review [5] showed that estimation of the *CO* using three clinical signs including capillary refill time, mottling and skin temperature had a sensitivity of 12% and a specificity of 98%, suggesting a good performance to rule in the presence of low flow states [6]. The information from this clinical assessment often will guide the targeted expansion of the diagnostic workup.

Hemodynamic Monitoring

The primary goal of hemodynamic monitoring is to assess the adequacy of cardiopulmonary function, blood flow distribution and oxygen delivery relative to tissue demand.

Hemodynamic monitoring provides information necessary to establish a mechanistic diagnosis (i.e. cardiogenic vs. obstructive shock), to choose the appropriate treatment, and to assess the response to such treatment. Most often, information about the cardiac function beyond that provided by basic hemodynamic assessment (i.e. vital signs, physical exam) is required to establish a diagnosis, and thus escalation to advanced hemodynamic monitoring techniques that continuously assess cardiac function and blood oxygenation is necessary and recommended [7]. Further cardiac evaluation can include the use of non invasive technology such as point of care ultrasonography (POCUS) and pulse plethysmography, minimally invasive systems that calculate CO from the analysis of the arterial pressure waveform derived from an indwelling arterial catheter, and invasive monitoring systems like the pulmonary artery catheter (PAC).

Critical care ultrasound

Point of care ultrasound is the preferred modality for the initial evaluation of undifferentiated shock [7,8]. The use of POCUS provides information to narrow the differential diagnosis, to assess fluid responsiveness and to evaluate the response to therapy. Common to all ultrasonography-based shock-assessment protocols is that first, the exam is done at the bedside; second, the ultrasonographic findings are correlated with the clinical context in real time; third, the assessment can be repeated as often as necessary [9].

Several protocols have been developed for the assessment of different systems in isolation or combined in the context of shock and trauma, with variable diagnostic performances. A description of these protocols goes beyond the scope of this review, but some of the most commonly used are the following: focused cardiac ultrasound [10], focus assessed transthoracic echocardiography [11], focused assessment with sonography in trauma [12], rapid ultrasound for shock and hypotension [13] and HeartScan [14]. Regardless of the protocol used, as POCUS provides the clinician with valuable, rapid and reliable information to diagnose and treat the patient, there is strong support for the use of ultrasonography in the acute care setting (see [8,15], and Table 1). The caveat is that the assessment and interpretation of ultrasonographic images requires training and is operator dependent.

Hemodynamic monitoring systems

Hemodynamic monitoring systems have evolved with the introduction of minimally invasive and noninvasive devices, that are capable of calculating stroke volume (SV) and CO using pulse contour waveform analysis (PCA). These devices can provide real-time, beat-by-beat arterial blood pressure and SV (and CO) monitoring, and provide parameters that have been validated for the assessment of preload responsiveness such as the pulse pressure variation (PPV) and SV variation (SVV) [21].

Pulse contour analysis-derived CO is more accurate in calibrated (PiCCO and Volumeview systems) than in noncalibrated devices (FlowTrac; Edwards LifeSciences, Irvine, California,

USA) [22]. The most common calibration system uses transpulmonary thermodilution which calculates the CO from the reciprocal of the integral of the area under the curve that describes the change in temperature in blood induced by a bolus of cold saline (Stewart–Hamilton equation) [23]. Because SVV and PPV are calculated relative to mean values of SVV and PPV (Table 1), these parameters are not affected by the lack of calibration. However, SVV and PPV will only predict fluid responsiveness if certain conditions are met (Table 1). The accuracy of the CO , and potentially SVV and PPV decrease in the context of profound circulatory collapse, limiting the utility of PCA devices in the initial management of the patient in shock. In addition, calibration is recommended every time there are significant hemodynamic changes (i.e. starting a vasopressor, an episode of vasodilatation, etc.) and ideally every hour if the CO is essential to interpret the hemodynamic profile of the patient [20,23]. Therefore, the use of PCA devices is most helpful after the initial ‘salvage’ phase of resuscitation.

Despite its vilification after several studies concluding no improvement in outcomes [24–26], the PAC continues to have a place in the management of patients with complex hemodynamic pictures, and is recommended in the context of refractory shock, severe acute respiratory distress syndrome, pulmonary artery hypertension or right ventricular dysfunction [7■,21■,27].

The initial approach

Weil and Shubin [28] proposed the initial approach to the patient in circulatory collapse, as the ventilate, infuse and pump rule that is discussed below.

Ventilation

Supporting ventilation is a rational first step in the management of the patient to optimize cellular oxygenation in circulatory shock. Mechanical ventilation reduces oxygen consumption by unloading respiratory muscles that otherwise would consume a significant proportion of the CO and oxygen delivered peripherally in the context of respiratory failure. In addition, positive pressure ventilation can decrease left ventricular afterload, which decreases myocardial oxygen consumption and can benefit the ejection of a failing ventricle [29]. However, invasive or noninvasive positive pressure ventilation can have detrimental effects on cardiopulmonary circulation in patients who are intravascularly depleted, and thus fluid resuscitation should be concurrently initiated.

Infusion

Intravenous fluids are the first-line agents for the treatment of patients with circulatory collapse. Repletion of the intravascular volume to increase CO is necessary to improve tissue perfusion in most types of shock. However, fluid administration should be carefully guided by the assessment of preload responsiveness, because volume overload is also associated with poor outcomes [30,31].

Traditional, static parameters such as pulmonary artery occlusion pressure, central venous pressure or the size of the inferior vena cava measured by ultrasonography have been shown to be poor predictors of preload responsiveness [32]. Dynamic parameters such as SVV,

PPV, collapsibility of the inferior vena cava in mechanically ventilated patients and the change in CO with passive leg raising, outperform static parameters and thus, are recommended for the assessment of preload responsiveness [21,33], which is defined as the likelihood that the infusion of a bolus of 500 ml will increase CO by 10–15%. This assessment is based on the concept of functional hemodynamic monitoring [34] and supported on the physiologic principle described by the Frank–Starling curve of the heart. Patients that are preload responsive have their biventricular function in the steep portion, whereas patients that are nonresponsive, will be in the flat portion of the Frank–Starling curve (Fig. 1).

Crystalloids are the fluid of choice for resuscitation of the patient in circulatory collapse. There is no survival benefit with the use of albumin as resuscitative fluid when compared with crystalloids [35,36]. Although the ALBIOS trial suggested a decrease in mortality with albumin in the subgroup of patients with sepsis, this is only hypothesis generating [36]. Conversely, synthetic colloids have been associated with acute kidney injury and with an increase in the use of renal replacement therapy [37,38], and should not be used in this setting. Between crystalloids, 0.9% normal saline is associated with a higher risk of hyperchloremia, acidosis [39] and acute kidney injury when compared with balanced crystalloids (i.e. Lactate Ringers or Plasmalyte) [40–42]. Although not based on randomized trials, the observational data favor the use of balance crystalloids over normal saline.

Pump

The use of a vasoactive agent is necessary when volume resuscitation results insufficient to reestablish MAP. The goal is to restore and maintain a MAP above 65mmHg, with the exception of patients known to have hypertension and who may benefit of higher MAP [43–45]. Increasing vascular tone through pure alpha adrenergic stimulation in isolation can increase MAP effectively, but may result in a decrease in CO and further peripheral hypoperfusion. Table 2 summarizes the mechanisms of action, dose, effects on the heart and peripheral vasculature, and common clinical use of the most frequently used inotropes and vasopressors. Norepinephrine is the most commonly used vasoactive medication and is considered the first-line agent for the treatment of circulatory shock [7,46]. However, the differences in the activity of each of these agents over cardiac contractility, chronotropy and vasomotor tone provides the clinician with a wide range of options to manage the patient according to the four pathophysiologic diagnosis, and their combinations.

Resuscitation goals

During the ‘salvage’ phase [48] of resuscitation, efforts are focused on re-establishing MAP and CO to sustain autoregulation, and on performing life saving measures. Once the patient is rescued from immediate life-threatening risk, the ‘optimization’ phase focuses on improving oxygen delivery to the tissues and re-establishing organ perfusion. The goals of resuscitation or perfusion goals within these phases of the management of the patient with cardiovascular collapse are described below.

Mean arterial pressure

The goal of resuscitation must always be tissue perfusion. During normal conditions, microcirculatory blood flow distribution is driven by metabolic demand of the tissue, a mechanism known as autoregulation. However, autoregulation can only occur if there is sufficient input pressure to the arterioles that feed microcirculatory beds, and this input pressure is dependent on MAP. Therefore, with the exception of patients with active hemorrhage requiring surgical control, the first step in re-establishing tissue perfusion in a patient with circulatory failure is to re-establish a MAP to 65mmHg, or higher if the patient has a history of hypertension [48].

Cardiac output and mixed venous O₂ saturation

The *CO* is the vehicle to achieve the goal of resuscitation, which must always be tissue perfusion. Regardless of the nominal value, the *CO* will be adequate or inadequate to meet the metabolic demand of tissues, and thus, increasing the *CO* will only be important if it improves MAP, and if it improves oxygen consumption. The mixed venous [mixed venous O₂ saturation (SvO₂), measured in the pulmonary artery] is a reasonable indicator of the adequacy of the *CO*, because a low SvO₂ will always signify inadequacy of *CO* to meet systemic metabolic demand. The central venous oxygen saturation (ScvO₂, measured in the atriocaval junction) may be used as a surrogate of SvO₂, albeit representing only the venous oxygenation of the upper half of the body, and usually being slightly higher than the SvO₂ in critically ill patients [48]. Based on the results of three multicenter studies that showed that a resuscitation protocol targeting a specific value of ScvO₂ does not offer a survival advantage over a nonprotocolized strategy [49], the surviving sepsis campaign guidelines no longer recommend the use of ScvO₂ in the management of the patient with septic shock. We believe this is unfortunate, because monitoring the ScvO₂ provides the clinician with a valuable tool for the interpretation of the adequacy of the *CO* and with a monitor of systemic oxygen consumption, and because in the context of persistent hyperlactatemia, a low ScvO₂ suggests ongoing hypoperfusion [50,51].

Lactate

Although induction of glycolysis by catecholamines and decreased hepatic clearance are important causes of hyperlactatemia during sepsis [52], inadequate tissue perfusion is an important cause of lactate elevation during circulatory shock and therefore, a useful biomarker in the diagnosis of shock. However, several misconceptions have lead to the improper interpretation of hyperlactatemia in this context. Because of its association with outcome and with acidosis, lactate is unfairly regarded as a deleterious molecule. Lactate is a fundamental metabolic defense mechanism during shock. During shock lactate is consumed by the heart and brain as energy substrate, lactate increases contractility of the cardiac myofibers and is shuttled from skeletal muscle to the liver and kidneys as a carbon source for the biosynthesis of glucose. In the clinical context, an elevated lactate on presentation (i.e. >4mmol/l) is associated with increased mortality [53–55]. Although a decline in lactate in response to initial resuscitation has been associated with improved outcome, the clinician must exercise caution not to interpret the response of lactate levels to therapeutic maneuvers only in the context of hypoperfusion. It is important to couple lactate to other measures of

perfusion like ScvO₂, physical exam, or the partial pressure of CO₂ (PCO₂) gap (see below) to understand when increasing forward flow will result in improved tissue perfusion, and when hyperlactatemia is an indicator of metabolic stress rather than hypoperfusion.

Partial pressure of CO₂ gap

An increase in venous PCO₂, which in the context of a constant arterial PCO₂ will result in an increased venous to arterial PCO₂ gap, is an indication of inadequate venous flow and thus inadequate CO [56]. After MAP has been re-established and ScvO₂ is within normal limits, a PCO₂ gap more than 6 mmHg suggests residual hypoperfusion that will benefit from further increasing CO and oxygen delivery [57]. Furthermore, an increased PCO₂ gap/(a-v) O₂ content ratio more than 1.8 can identify patients that will respond to an increase in CO with an oxygen consumption with a sensitivity and specificity of 86 and 91%, respectively [58].

Microcirculation

Sublingual microcirculation has enabled the assessment of microcirculatory flow in the context of shock. Persistent microcirculatory abnormalities in the context of sepsis predicts the development of multiple organ dysfunction and higher mortality. However, there are no specific therapeutic strategies to alter the microcirculation. Furthermore, analysis of microcirculatory videos takes time, and it's not possible in real time, which makes it a limitation for the use of this technology to drive resuscitation, and thus, this technology remains experimental.

Conclusion

Circulatory collapse continues to be common and lethal in the critically ill population. Although the initial care of these patients continues to honor the 'Ventilation–Infusion–Pump' paradigm, the integration of bedside ultrasound, the use of dynamic parameters for the evaluation of fluid responsiveness, and the renewed understanding of surrogates of tissue perfusion have made the assessment of the patient in shock faster, safer and more physiologic. Despite outstanding limitations, the conjunction of these powerful tools and current evidence based interventions for the initial management of the crashing patient represents a solid framework that can hopefully assist the clinician in navigating the never-ending uncertainties of caring for the critically ill and provide a platform to move the field forward.

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- of special interest
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Key Points

- Establishing a differential diagnosis of the type or types of shock with the clinical history and a focused physical examination is an important step in initiating immediate supportive treatment to limit hypoperfusion.
- Bedside ultrasonography is the recommended modality for the initial evaluation of undifferentiated shock, as it provides key information to characterize the type of shock, to choosing the appropriate therapeutic intervention and to assess the response to resuscitation.
- The use of dynamic parameters such as passive leg raising, pulse pressure and stroke volume variation, and collapsibility of the inferior vena cava is recommended for the assessment of preload responsiveness and guiding fluid therapy, and is preferred over unrestricted fluid administration.
- The goal of resuscitation is always tissue perfusion. The initial 'salvage phase' focuses on performing life saving measures and restoring autoregulation by reestablishing mean arterial pressure; the 'optimization' phase focuses on re-establishing organ perfusion which should be assessed using goals such as SvO₂, lactate, partial pressure of CO₂ gap, partial pressure of CO₂ gap/C(a-v)O₂ and hopefully in the near future, microcirculatory flow.

Figure 1.

The concept of preload responsiveness represented on the cardiac function curve describing the Frank–Starling law of the heart. The increment in enddiastolic volume or preload by administration of a bolus of fluid will result in a significant increase in stroke volume (* on Y axis) and cardiac output only if the ventricular function is in the steep portion of the Frank–Starling curve of the heart (gray, thick line). The magnitude of the increase in cardiac output that is considered significant is most frequently set between 10 and 15%. Conversely, a bolus of fluid (same volume), which expands the end-diastolic volume in the same proportion as the previous example, will not result in an increment of more than 10–15% (# on Y axis) of the cardiac output if the ventricle is operating in the flat portion of the Frank–Starling curve (black, thick line).

Table 1
Summary of selected evidence supporting the use of dynamic parameters to predict
preload responsiveness

Assessment tool	Performance to predict preload responsiveness	Threshold	Limitations
IVC distensibility (dIVC) in mechanically ventilated patients ($dIVC = \frac{MaxIVC_{insp} - MinIVC_{exp}}{MinIVC_{exp}}$)	Sensitivity: 90% [16] Specificity: 90%	dIVC > 18%	Validated in mechanically ventilated in volume control mode without ventilator dyssynchrony
IVC Collapsibility in spontaneously breathing patients ($cIVC = \frac{MaxIVC_{insp} - MinIVC_{exp}}{MaxIVC_{exp}}$)	Sensitivity: 31% [17] Specificity: 97%	cIVC > 42%	Significant or shallow breathing efforts may induce respectively falsely high or low changes in IVC diameter with respiration in the absence of fluid responsiveness
Passive leg raise (PLR) test	Using the change in <i>CO</i> [18] Pooled sensitivity: 85% Pooled specificity: 91%	Increase in <i>CO</i> 15%	Change in BP with PLR does not predict fluid responsiveness. Must use a measure of <i>CO</i> or SV. Unclear validity in patients with IAH
Pulse pressure variation (PPV) ($PPV = \frac{PP_{Max} - PP_{Min}}{PP_{mean}}$)	Pooled sensitivity: 89% [19] Pooled specificity: 88%	PPV > 12–13% Alternatively, a PLR test can be performed and change in PPV noted.	Arrhythmias, severe ARDS, open chest, ventilation with <8 ml/kg, intra-abdominal hypertension, profound circulatory shock, dampened arterial waveform
Stroke volume variation (SVV) ($SVV = \frac{SV_{Max} - SV_{Min}}{SV_{mean}}$)	Pooled sensitivity: 82% [20] Pooled specificity: 86%	SVV > 10% Alternatively, a PLR test can be performed and change in SVV noted	Arrhythmias, severe ARDS, open chest, ventilation with <8 ml/kg, intra-abdominal hypertension, profound circulatory shock, dampened arterial waveform

ARDS, acute respiratory distress syndrome; BP, blood pressure; cIVC, IVC Collapsibility; *CO*, cardiac output; IAH, intra-abdominal hypertension; IVC, inferior vena cava; PP, pulse pressure; SV, stroke volume.

Adapted from [16–19].

Table 2
Summary of inotropes and vasopressors used in the treatment of the patient in shock

Group	Agent	Site of action	Dose	Effect				Usual clinical application
				Cardiac		Vasculature		
				Contractility	Heart rate	Constriction	Dilatation	
Inotropes/vasopressors	Epinephrine	$\beta_1, \beta_2, \text{Ca}, \text{Pa}$ Increasing IC Ca^{++}	0.01–0.2 $\mu\text{g/kg/min}$	4+	4+	3+	0	Refractory, anaphylactic shock
	Dopamine	$\alpha, \beta_1, \text{DA1}, \text{DA2}$	1–20 $\mu\text{g/kg/min}$	3+	2+	2–3+	0	All types of shock
	Dobutamine	β_1 Increasing IC Ca^{++}	1–20 $\mu\text{g/kg/min}$	3+	2+	0	2+	Cardiogenic, obstructive
	Milrinone	PDE inhibitor, inhibits cAMP degradation and increases IC Ca^{++}	Bolus: 37.5–75 $\mu\text{g/kg}$ infusion: 0.125–0.75 $\mu\text{g/kg/min}$	3+	1+	0	2+	Cardiogenic
Pure vasopressors	Norepinephrine	$\text{Ca}, \beta_1, \text{Pa}$ Increasing IC Ca^{++}	0.01–0.3 $\mu\text{g/kg/min}$	2+	2+	4+	0	Septic shock, cardiogenic shock
	Phenylephrine	Pa	20–200 $\mu\text{g/min}$	0	0	4+	0	Septic shock, neurogenic shock
	Vasopressin	V1, V2	0.04 U/min	0	0	4+	0	Septic shock

α and β , alpha and beta adrenergic receptors; Pa , alpha adrenergic receptor in the peripheral vasculature; Ca , cardiac alpha adrenergic receptor; IC Ca^{++} , calcium; V1 and V2, vasopressin receptors 1 and 2, respectively. Grading of the effect is arbitrary. Modified from [47].