Hemodynamic Evaluation and Monitoring in the ICU

Michael R. Pinsky

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Hemodynamic monitoring, a cornerstone in the care of the critically ill patient in the ICU. The ICU provides a place for monitoring and care of patients with potentially severe physiologic instability requiring advanced artificial life support. Within this context, hemodynamic monitoring is used to identify hemodynamic instability and its cause and to monitor the response to therapy. We have witnessed an impressive number of medical technological advances, allowing monitoring, display, and assessment of physiologic variables not even imagined before, yet the utility of most hemodynamic monitoring is unproven. It is the commonly available technologies for which clinical studies have demonstrated relevance. Physiologic measures available from commonly available monitoring devices are given in Table 1. Despite the many options available, most ICUs monitor and display only BP, heart rate (HR)
and oxygen saturation by pulse oximetry (SpO₂), as they have done for the last 20 years. Furthermore, with few exceptions, such monitoring does not drive treatment protocols but rather serves as an automated vital signs record to trigger further attention. It is hard to validate the utility of monitoring when it is used in this fashion because no hemodynamic monitoring device will improve outcome useless coupled to a treatment that itself improves outcome. Thus, the effectiveness of hemodynamic monitoring to improve outcome is limited to specific patient groups and disease processes for which proven effective treatments exist. Although, like most of medicine, the utility of hemodynamic monitoring is not well documented, a primary rationale for the use of hemodynamic monitoring is to identify cardiovascular instability and its specific etiology, and to guide therapy.

Interestingly, physicians have developed a psychological dependence on feedback from continuous hemodynamic monitoring tools, independent of their utility. SpO₂ monitoring in low-risk patients is an example. One would presume that continual measure of SpO₂ should improve patient outcomes by identifying hypoxemia and brady/tachyarrhythmias, thus allowing for effective and rapid correction before the development of global tissue ischemia. However, Moller et al.² examined the benefit of intraoperative SpO₂ monitoring in low-risk surgery patients. They monitored 20,502 patients: 10,312 patients assigned to an oximetry group, and 10,490 patients assigned to a control group without oximetry. They found no numerical differences in cardiovascular, respiratory, neurologic, or infectious complications, duration of hospital stay, or number of in-hospital deaths between the two groups. When shown these results, 80% of the anesthesiologists replied by questionnaire that they still felt more secure in their practice when they used a pulse oximeter in these patients.³ In this article, I shall discuss the rationale for commonly available monitoring, the usefulness of static measured variables to assess specific disease states (hemodynamic profile analysis), and interactive monitoring to predict response to therapy (applied physiology), and monitoring-driven treatment protocols (functional hemodynamic monitoring) that improve outcomes.

**Rationale for Hemodynamic Monitoring**

Three progressive arguments can be made for using specific monitoring. At the basic level, one cites its common use. Here, prior experience has shown that such monitoring can identify disease states and/or known complications, even though the link between the monitoring and disease may not be known or even postulated. The second level of defense rests with an understanding of shock pathophysiology, the etiologies of which are usually categorized into four broad groups: hypovolemic, cardiogenic, obstructive, or distributive, all of which may have different causes and treatments.⁴ Since the primary goal of the cardiovascular system is to supply adequate amounts of oxygen to meet the metabolic demands of the body, calculation of systemic oxygen delivery (DO₂) and oxygen consumption (VO₂), identifying tissue ischemia (usually monitored by mixed venous oxygen saturation [SvO₂]) as well as measures of ventricular performance (stroke work) are often calculated from such primary variables. At this level,
Hemodynamic Profile Analysis

Circulatory shock causes tissue hypoperfusion. Cellular dysfunction, organ injury, and death may occur proportional to the degree and duration of tissue hypoperfusion as quantified by oxygen debt.8 The four pathophysiologic categories of shock are usually characterized by different specific hemodynamic variables, induced by the associated primary hemodynamic event and the autonomic response to it. These variables can be measured by a variety of noninvasive and invasive means (Table 1) and derived hemodynamic parameters calculated that reflect global cardiovascular status (Table 2).

The relation between specific hemodynamic variables is complex is health, and even more complex is disease. However, a solid understanding of the cardiovascular underpinnings of blood flow homeostasis is required to interpret hemodynamic variables effectively. If disease causes cardiac output and DO2 to decrease, mean arterial pressure (MAP) decreases as well. Baroreceptors in the aortic arch and carotid body alter vasomotor tone through modulation of sympathetic tone to maintain cerebral perfusion pressure (eg, MAP > 65 mm Hg).9 The hemodynamic effects of this increased sympathetic tone are tachycardia and restoration of MAP toward normal values by reducing unstressed circulatory blood volume and increased arterial vasomotor tone. Thus, hypotension reflects failure of the sympathetic nervous system to compensate for circulatory shock, while normotension does not insure hemodynamic stability.10 Since regulation of blood flow distribution occurs by regional vasodilation of arterial resistance vessels, hypotension impairs autoregulated blood flow distribution.11,12 Except in conditions of severe hypoxemia and anemia, the primary means by which DO2 is varied to match metabolic requirements is by varying cardiac output and tissue oxygen extraction. Since metabolic demands can vary widely, there is no normal cardiac output or DO2 value, but rather minimal thresholds for resting conditions and potentially adequate higher levels during stress. Operationally, it is better to access cardiac output as being either adequate or inadequate to meet the metabolic demands of the body. Inadequate DO2 is presumed to occur if tissue oxygen extraction is markedly increased, as manifest by a decrease in S\text{\textit{V}}\text{O}_{2} < 70%.13

<table>
<thead>
<tr>
<th>Table 2—Derived Hemodynamic Parameters From Hemodynamic Monitoring*</th>
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<tr>
<td>Primary hemodynamic variables</td>
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<tr>
<td>HR, beats/min</td>
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<tr>
<td>MAP, mm Hg</td>
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<tr>
<td>P\text{ra}, mm Hg</td>
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<tr>
<td>MPAP, mm Hg</td>
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<td>P\text{pao}, mm Hg</td>
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<td>CO, L/min</td>
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<td>S\text{ao}_{2}, %</td>
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<tr>
<td>S\text{p}O\text{\textsubscript{2}} as an estimate of S\text{ao}_{2}, %</td>
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<tr>
<td>S\text{v}O_{2}, %</td>
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<tr>
<td>Hb, g/dL</td>
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<tr>
<td>Height and weight needed to calculate BSA, m²</td>
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<tr>
<td>Calculated hemodynamic parameters</td>
</tr>
<tr>
<td>CI = CO/BSA, L/min/m²</td>
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<tr>
<td>Stroke volume = CO/HR × 1,000, mL/L/min</td>
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<tr>
<td>Stroke index = stroke volume/BSA, mL/m²</td>
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<tr>
<td>LV stroke work = stroke volume × (MAP – P\text{pao}), mL·mm Hg</td>
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<tr>
<td>LV stroke work index = LV stroke work/BSA, mL·mm Hg/m²</td>
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<tr>
<td>Total peripheral resistance = (MAP/CO) × 80, dyne·s/cm²</td>
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<tr>
<td>Systemic vascular resistance = ([MAP – P\text{ra}]/CO) × 80,</td>
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<td>dyne·s/cm²</td>
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<tr>
<td>RV stroke work = stroke volume × (MPAP – P\text{ra}), mL·mm Hg</td>
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<tr>
<td>RV stroke work index = RV stroke work/BSA, mL·mm Hg/m²</td>
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<tr>
<td>Pulmonary vascular resistance = ([MPAP – P\text{pao}]/CO) × 80,</td>
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<td>dyne·s/cm²</td>
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<td>Global DO2\textsuperscript{\textit{\textdagger}} = CO × (S\text{ao}<em>{2} – S\text{v}O</em>{2}) × Hb × 1.36 × 1,000, mL</td>
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<tr>
<td>oxygen/min</td>
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<tr>
<td>Global DO2 index\textsuperscript{\textit{\textdagger}} = CI × (S\text{ao}<em>{2} – S\text{v}O</em>{2}) Hb × 1.36, mL</td>
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<td>oxygen/min</td>
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<tr>
<td>Global V\text{O}<em>{2}\textsuperscript{\textit{\textdagger}} = CO × S\text{ao}</em>{2} × Hb × 1.36 × 1,000, mL oxygen/</td>
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<td>Global V\text{O}<em>{2} index\textsuperscript{\textit{\textdagger}} = CI × S\text{ao}</em>{2} × Hb × 1.36 × 1,000, mL oxygen/</td>
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*CO = cardiac output; CI = cardiac index; BSA = body surface area; S\text{ao}_{2} = arterial oxygen saturation; MPAP = mean pulmonary artery pressure; Hb = hemoglobin. \textdagger}S\text{p}O\text{\textsubscript{2}} can be substituted for arterial oxygen saturation in these calculations.
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.4 Thus, cardiac output, stroke work, DO2, and SvO2 are decreased in cardiogenic, hypovolemic, and obstructive shock but may be normal or even increased in distributive shock. However, in all conditions, HR increases associated with an increased sympathetic tone. Cardiogenic shock represents primary cardiac failure. It can be due to impaired contractility (myocardial ischemia/infarction, electrolyte imbalance, hypoxemia, hypothermia, endocrinologic diseases, metabolic poisoning, β-blockers), pump function (valvulopathy, ventriculoseptal defect, dysrhythmias), or diastolic compliance (fibrosis, infiltrative cardiomyopathies, hypertrophy). The specific cardinal findings of cardiogenic shock are increased back pressure to cardiac filling (right atrial pressure [Pra] and pulmonary artery occlusion pressure [Ppao]) and upstream edema (peripheral and pulmonary). 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), secondary intravascular volume loss (third-space loss, insensible loss through skin with burns, diarrhea, vomiting), and increased unstressed vascular volume (loss of sympathetic tone, spinal cord injury, vasodilating drugs). The specific findings of hypovolemic shock are decreased filling pressures. Obstructive shock represents a blockade of blood flow. It may be due to right ventricular (RV) outflow obstruction (pulmonary embolism, hyperinflation), tamponade (pericardial effusion, hyperinflation), or left ventricular (LV) outflow obstruction (aortic stenosis, dissecting aortic aneurysm). The specific findings of obstructive shock are often more subtle but include decreased LV diastolic compliance (small LV volume with increased Ppao) and signs of cor pulmonale (Pra greater than Ppao, tricuspid regurgitation). Distributive shock represents loss of normal sympathetic responsiveness resulting in decreased vasomotor tone. In the nonresuscitated subject, this presents as hypovolemic shock,14 but with fluid resuscitation BP does not increase despite an increase in cardiac output. It can be due to loss of vascular responsiveness (sepsis, spinal shock, vasodilating drugs, metabolic poisons). The specific findings of distributive shock are an increased cardiac output, DO2, and SvO2 despite persistent hypotension. Hemodynamic monitoring can aid in determining circulatory shock etiology.

Since most forms of circulatory shock reflect inadequate tissue DO2, a primary goal of resuscitation is to increase DO2. Three important functional questions are usually asked of the hemodynamically unstable patient. First, will cardiac output increase with fluid resuscitation and, if so, by how much? Physiologically speaking, this equates to preload responsiveness. Second, in the hypotensive patient is arterial vasomotor tone increased, decreased, or normal? Finally, is the heart capable of sustaining an effective cardiac output once arterial pressure is restored without going into failure? Clearly, patient-specific hemodynamic questions are also asked but, in general, these are the fundamental questions addressed by most effective treatment algorithms. Unfortunately, although specific patterns of hemodynamic values, as described above, reflect specific types of disease, they do not predict individual patient response to therapy.

APPLIED PHYSIOLOGY APPLIED TO HEMODYNAMIC MONITORING

To address the question of preload responsiveness, physicians usually attempt to measure intravascular volume status, either by indirect measures (skin turgor, mucus membrane wetness and venous congestion, or vascular pedicle diameter of the chest radiograph)15 or by attempting to estimate RV and LV end-diastolic volumes. Importantly, the published clinical literature does not support the use of direct or indirect measures of end-diastolic volume as a means to predict preload responsiveness. Readers are referred to the metaanalysis by Michard and Teboul16 published in CHEST for further discussion. Although general trends in filling pressures and volumes define patient populations, their use in clinical decision making is poor. Specifically neither absolute values for Pra, Ppao, RV end-diastolic volume, or LV end-diastolic area predict preload responsiveness. Furthermore, the changes in either Pra or Ppao do not reflect changes in either cardiac output or stroke volume in hemodynamically unstable patients.17 Although increases in either RV or LV end-diastolic volumes do increase stroke volume, knowing ventricular pressures or volumes at a single point in time is not useful in making this prediction. Although the reasons for such inaccuracies of using Pra or Ppao to estimate preload may reflect inaccuracies in measures,18 or in understanding what Ppao reflects even when these values are measured accurately,19 even when measured accurately they do not predict preload responsiveness.20 Thus, the lack of the ability of measures of Pra or Ppao to predict preload responsiveness may explain the lack of difference in outcome from Pra- vs Ppao-guided fluid resuscitation therapies in the two published articles on the ARDS Clinical Trials Network Fluid and

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Catheter Treatment Trial comparing central venous catheters (Pra guided) to pulmonary arterial catheters (Ppao guided)\textsuperscript{21} and liberal vs restricted fluid resuscitation (high Pra or Ppao vs low Pra or Ppao), other than length of stay being slightly shorter in the conservative fluids arm\textsuperscript{22} because neither measure correlates with DO\textsubscript{2}, although both tend to parallel changes in effective circulating blood volume. Furthermore, the Surviving Sepsis Campaign recommendations\textsuperscript{23} for targeted values of Pra and Ppao are not supported by the existing evidence. Fluid responsiveness was documented to be unrelated to the recommended Pra and Ppao values.\textsuperscript{24} Such negative findings based on a treatment protocol targeting specific Pra or Ppao values are not surprising. In essence, preload is not preload responsiveness. Clearly, as numerous previous studies\textsuperscript{25–28} have demonstrated, preload is not preload responsiveness. Clearly, as numerous previous studies\textsuperscript{25–28} have underscored, just inserting a catheter to make measurements without a defined and effective treatment protocol requiring such information is unlikely to result in improved patient outcomes. What clinicians need to know is the latter, and what static measurers estimate is the former. Clearly, as intravascular volume increases, Pra may also increase, especially in patients with impaired RV function. Still, one can have an expanded intravascular volume and a low Pra, as is the case in hyperdynamic hepatic cirrhosis patients. Similarly, Ppao also tends to be higher with hypervolemia and tends to track intrathoracic blood volume especially in heart failure patients. However, as was shown previously by Michard and Teboul,\textsuperscript{16} absolute Pra or Ppao values are no better than a random chance at predicting preload responsiveness. There are few relative truths in the assessment of single, fixed hemodynamic variables, but Table 3 lists those I have come to realize when considering acute resuscitation of the critically ill.

In the assessment of preload responsiveness, one needs to measure other parameters than filling pressures and ventricular volumes. The time-honored method of assessing preload responsiveness is the intravascular fluid challenge, wherein a bolus of fluid is rapidly infused and the subsequent changes in specific flow-dependent variables (cardiac output, MAP, HR, $\text{SvO}_2$, Pra, Ppao) are measured. The problems with performing a fluid challenge for clinical decision making are multiple. First, only half the hemodynamically unstable patients administered a volume challenge will have increased cardiac output.\textsuperscript{16} Thus, the correct management may have been delayed in half the patients. Second, in the half of those patients who are not preload responsive, volume loading may be directly injurious. For example, both acute cor pulmonale (pulmonary embolism, COPD) or LV failure may deteriorate further with volume loading. Two alternative methods of performing a reversible fluid challenge have recently gained interest in the acute care setting. These include the use of positive pressure ventilation-induced changes in arterial pressure and LV stroke volume to cyclically varying venous return, and by performing a passive leg raising (PLR) maneuver to transiently increase venous return and noting the change in mean blood flow.

Positive pressure ventilation when applied to a patient at rest and with no spontaneous respiratory effort is associated with a cyclic increase in Pra in phase with inspiration. Since Pra is the back-pressure to venous return, if upstream venous pressures do not simultaneously increase then RV filling will also decrease in a cyclic fashion. This cyclic variation in RV filling will induce a cyclic variation in LV filling if both RV and LV are preload responsive.\textsuperscript{30} This cyclic variation in LV filling will induce a cyclic variation in LV stroke volume and arterial pulse pressure if the patient is preload responsive. Several studies\textsuperscript{31–33} have documented that the associated variations in LV stroke volume, referred to as stroke volume variation (SVV)\textsuperscript{34–36} since the primary determinant of arterial pulse pressure is stroke volume, pulse pressure variation (PPV), calculated in the same manner as SVV, has also been shown to predict preload responsiveness. For a tidal volume of 6 mL/kg, a SVV $\geq 10\%$ predicts a $\geq 15\%$ increase in cardiac output for a 500-mL fluid bolus.\textsuperscript{34–36} Since the primary determinant of arterial pulse pressure is stroke volume, pulse pressure variation (PPV), calculated in the same manner as SVV, has also been shown to predict preload responsiveness well. Here however, a $\geq 13\%$ PPV predicts a $\geq 15\%$ increase in cardiac output for a 500-mL volume bolus. Presently, PPV is easier to measure than SVV because it only requires inspection of the arterial pressure waveform over time,\textsuperscript{37} whereas SVV can be assessed by either esophageal Doppler echocardiography\textsuperscript{38} or echocardiographic measures of aortic velocity.\textsuperscript{39} Several commercially available technologies have evolved based on arterial waveform analysis that can estimate stroke volume from the pulse pressure waveform. Furthermore, only quantifying systolic pressure variation (SPV) over the ventilatory cycle has been proposed.\textsuperscript{40} This measured, also known as pulse paradoxus, has the advantage of being easier to monitor but also has de-

### Table 3—Hemodynamic Monitoring Truths

<table>
<thead>
<tr>
<th>Truth</th>
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<tr>
<td>Tachycardia is never a good thing.</td>
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<tr>
<td>Hypotension is always pathologic.</td>
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<tr>
<td>There is no such thing as normal cardiac output.</td>
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<tr>
<td>Central venous pressure is only elevated in disease.</td>
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<tr>
<td>Peripheral edema is of cosmetic concern.</td>
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creased sensitivity because it does not quantify the varying diastolic arterial pressure component of the PPV. Finally, studies suggest that the Spo2 plethysmographic waveform amplitude co-varies with arterial pulse pressure, and this plethysmographic signal variation predicts fluid responsiveness in hypotensive patients. If validated to predict preload responsiveness in the broader group of hemodynamically unstable patients, then such noninvasive techniques could expand the application of this applied physiologic approach at the bedside.

Like all hemodynamic monitoring approaches, the use of SVV, PPV, or SPV to assess preload responsiveness requires an understanding of its physiologic underpinnings. SVV, PPV, and SPV are created by tidal volume-induced changes in venous return. They assume a constant R-R interval and are measured from diastole to systole, not vice versa, such that SVV, PPV, and SPV reflect only changes in venous return and not diastolic filling time. Thus, these parameters will lose their predictive value under conditions of varying R-R intervals (atrial fibrillation), and they may also lose accuracy if tidal volume varies from breath to breath as may occur with assisted and spontaneous ventilation. Thus, these approaches are limited to only a small percentage of critically ill patients. Furthermore, since the ratio of PPV to SVV reflects central arterial compliance, if arterial tone varies, PPV and SVV may vary in disproportionate ways. However, potentially one can monitor the PPV/SVV ratio to identify changing central arterial vasoconstrictor tone. Finally, preload responsiveness does not mean that the patient requires volume resuscitation because normal subjects are also preload responsive.

More advanced monitoring using transthoracic ultrasound and transesophageal ultrasound (echo) imaging of the vena cava collapse during positive pressure ventilation has also been shown to predict Pra > 10 mm Hg. If venal caval diameter is decreased below a threshold value, the Pra is < 10 mm Hg; otherwise, it is > 10 mm Hg. This Pra threshold value is important in a limited way because patients with a Pra < 10 mm Hg invariably have decreased cardiac output if additional positive end-expiratory pressure is applied during positive pressure ventilation. However, if Pra is > 10 mm Hg, no predictions can be made as to the change in cardiac output in response to increasing levels of positive end-expiratory pressure.

To simplify these approaches, the clinically validated PLR method can be used as a transient and reversible increase in venous return. The PLR method requires that the legs be raised 30° above the chest and held there for 1 min. PLR causes an approximate 300-mL blood bolus in a 70-kg man that persists for about 2 to 3 min before resulting in intravascular volume redistribution. The immediate hemodynamic response from before to during the PLR is taken to reflect preload response. To minimize the need for a constant HR and tidal volume, measures of mean aortic flow averaged over 20 to 30 s can be measured and are actually superior to SVV and PPV measures in the same subjects.

There are two important implications of these findings. First, since measures of changing mean blood flow during PLR accurately predict preload responsiveness during both spontaneous and positive pressure ventilation and with or without arrhythmias, this approach can be applied in all hemodynamically unstable patients. Second, since measures of mean blood flow can be ascertained at the bedside using many commercially available devices, including esophageal Doppler flow-measuring devices and arterial pressure waveform estimates of flow, most ICUs are capable of making these measures today.

Unfortunately, although SVV, PPV, and SPV have been described for several years, and recently the change in mean blood flow with PLR, none of these techniques has been used to drive treatment protocols. Clearly, this application of these simple monitoring approaches is the next step in the evolution of functional hemodynamic monitoring.

**Functional Hemodynamic Monitoring: Goal-Directed Therapy**

Numerous clinical trials have attempted to document improved patient outcome when resuscitation strategies were driven by measured hemodynamic variables. Early on, the results were either mixed or negative. However, with increased understanding of the pathophysiology of shock and a heightened awareness of the need to prevent tissue ischemia, clinical trials in the emergency department by Rivers et al and the operating room have clearly documented improved outcome. Clearly, intraoperative volume expansion improves organ perfusion and reduces gastric ischemia as assessed by tonometric measures of gastric PCO2. Importantly, in the study by Rivers et al, the total amount of resuscitation fluids administered was similar in the treatment and control groups, but the treatment group received more additional early fluid when the control group protocol did not require it because traditional hemodynamic measures such as Pra and MAP were at their target levels. The benefits realized from these studies have recently filtered into the ICU environment, where two prospective clinical trials have shown that goal-directed therapy improves outcome. All these studies follow the same approach.
theme: the earlier treatment is begun and tissue ischemia resolved, the better the outcome.

For example, the greatest outcome benefit of goal-directed therapy appears to exist in the field of high-risk surgery or, speaking from a physiologic perspective, scheduled trauma. This form of resuscitation has been termed preoptimization because the resuscitation starts prior to the cardiovascular stress and surgical trauma. In essence, resuscitation occurs before tissue injury. Shoemaker et al60 documented improved outcome and reduced cost when high-risk surgery patients were resuscitated to high DO$_2$ values ($>600$ mL/min/m$^2$) prior to surgery. These findings were duplicated by Boyd et al69 and Lobo et al.70 Importantly, Lobo et al70 showed that the improved patient outcomes were realized across the entire treatment group of elderly patients, even in those patients who did not achieve the target DO$_2$ levels. One need not target DO$_2$ to see improved outcome. Goepfert et al71 measured the sum end-diastolic volume of the heart (eg, right and left atrial and ventricular volumes at end diastole) and targeted global end-diastolic volume in cardiac surgery patients and documented reduced need for catecholamines and less time on the ventilator but an increase in net fluid balance of approximately 500 mL.

Studies72 in critically ill ICU patients using goal-directed therapy presumed that if DO$_2$ were increased to supranormal levels (as references to resting DO$_2$ values), as was done in the preoptimization studies above, patients would have improved survival. This approach is referred to as postoptimization in distinction to the intraoperative preoptimization protocols because it is started after the patient presents in shock. However, neither Tuchschmidt et al73 norGattinoni et al74 were able to document any improved outcome when critically ill patients were enrolled 12 to 36 h after presenting with shock.75 In fact, Hayes et al76 saw increased mortality in their treatment group presumably because of overly aggressive attempts to reach target DO$_2$ values. However, Rivers et al60 underscored the importance of immediate (emergency department at presentation) and appropriate (adequate level of DO$_2$ as defined by the central venous oxygen saturation as a surrogate of SVO$_2$)77 resuscitation of critically ill patients to improve outcome.78 These authors79 also reported that proinflammatory cytokine levels were reduced in treatment patients, suggesting that early goal-directed therapy also reduces the systemic inflammatory response. Their study79 validated the principal of immediate restoration of cardiovascular stability as the primary treatment for circulatory shock and focused the issue on rapid triage and management. Clearly, allowing patients to remain in shock for hours before starting aggressive resuscitation is a major cause of increased morbidity and mortality. One prior study80 documented improved outcome and reduced cost when resuscitation was targeted to a minimal SVO$_2$; however, these studies were not followed up using defined treatment protocols until recently. If one delays resuscitation further, the benefits of that activity diminish. For example, McKendry et al66 used esophageal Doppler monitoring of mean blood flow to maximize preload in the immediate postoperative resuscitation of cardiac surgery patients. Their nurse-driven protocol targeted DO$_2$ values for only the first 6 postoperative hours. They observed a reduced length of hospital stay and a markedly reduced incidence of complications, most notably postoperative wound infections. Similarly, Pearce et al67 followed that up with a similar study design in postoperative high-risk patients. They targeted a postoperative DO$_2$ of 600 mL/kg/min using arterial pressure-derived estimates of cardiac output. Importantly, the treatment group received more colloid and dopexamine infusions but had similar stroke volumes, Pra, and blood lactate levels with the control groups. They found similar reductions in hospital length of stay primarily because of a reduced incidence of postoperative complications.

These data demonstrate two important things. First, that in high-risk surgical populations, preoptimization applied prior to surgery and postoptimization therapies applied in the ICU in a protocolized fashion improves outcomes and reduce cost. Second, the longer one delays aggressive metabolic targeted resuscitation, the less the observed benefit. It is not clear how long the therapeutic window remains open before such aggressive therapies worsen outcome, as exemplified by Hayes et al.70 Furthermore, it is not clear that similar metabolically targeted therapies will also be beneficial in other ICU patient populations, such as those with septic shock or single-organ failures such as primary ARDS and trauma. Furthermore, none of the above-mentioned clinical trials used the newly established SVV, PPV, or SPV methods of assessing preload responsiveness for clinical decision making. Clearly, prospective clinical trials of these proven treatment strategies and novel robust decision-support parameters used in different patient populations are needed. Still, the results of studies that have been completed using functional measures in targeted high-risk populations early in their disease have all been positive, whereas those studies using more traditional measures or using similar functional measures but applied later in the course of shock have been unsuccessful. The theme therefore appears to be clear: target patients at risk for tissue ischemia prior to severe organ injury using titrated therapies that monitoring circulatory sufficiency, and administer that therapy as soon as possible.
However, these consistent findings across studies, although promising, still reflect single-center trials using one proprietary blood flow-monitoring device (eg, esophageal Doppler, arterial pulse contour) in highly selected high-risk patient groups. What is needed is a large multicenter clinical trial aimed at early goal-directed treatment of all patients in shock from various etiologies for which the goals of therapy and the rapidity of treatment rather than the means to access treatment are the primary operative variables, while any within study comparison of monitoring device differences would be of secondary importance. If such studies documented improved patient outcomes, then the choice of which monitoring devices one uses would be subject more to issues of cost, convenience, and complications.

**Future Monitoring Approaches**

The future of hemodynamic monitoring is already here and can be summarized as focusing on measuring tissue wellness using continuous, noninvasive, and metabolic markers. Examples of these devices include sublingual $\text{PCO}_2$, tissue oxygen saturation, and capillary blood flow measured under the tongue. The above continuous noninvasive measures describe metabolic effects of circulatory function. Potentially, they may be used to identify compensated shock and to define functional end points of resuscitation. When applied using the above-mentioned titration of resuscitation to restore and sustain tissue blood flow, such novel monitoring devices may add an extra dimension to our monitoring options by allowing real-time assessment of response to therapy and potentially when to stop. Since no prospective outcomes clinical trials have been done, the use of these novel monitoring approaches is speculative.

**Conclusion**

Enough clinical data have accumulated over the past 30 years to defend abolishing the use of static hemodynamic values, such as Pra and Ppa0, as markers of preload responsiveness. Dynamic responses, to either a volume challenge or a physiologic reversible volume challenge using either positive pressure ventilation or PLR are highly sensitive and specific for preload responsiveness. Numerous prospective clinical trials have documented improved outcome and reduced cost when early goal-directed therapies are applied in a protocolized fashion in high-risk patients, whereas no benefit and even harm may occur when aggressive resuscitation is applied late (> 12 h) in the course of circulatory shock.

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