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Hemodynamics in Sepsis

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ABSTRACT

Hemodynamics in sepsis change as sepsis develops. Initial hemodynamics of sepsis often are much different from later stages of sepsis, shifting from low cardiac output states to high cardiac output states. Tissue oxygenation also changes with initial mixed venous oxyhemoglobin (Svo_2) or central venous oxyhemoglobin ($Scvo_2$) levels below normal, with later stages reflecting high values. These changes occur as sepsis progresses, producing a marked disturbance in capillary flow and tissue oxygenation. Treatments for these changes in sepsis are different, making the identification of the hemodynamic state essential to optimally treat the patient. Fortunately, hemodynamic monitoring techniques are markedly improved from older techniques such as the pulmonary artery catheter. With noninvasive techniques such as esophageal and external Doppler for measuring hemodynamics, clinicians beyond the intensive care unit can make hemodynamic assessments that were not possible until just recently. This improved assessment should make it much easier to properly identify sepsis and initiate appropriate treatments in a timely manner.
Keywords: hemodynamic monitoring, mixed venous oxyhemoglobin, sepsis, stroke index

The hemodynamics of sepsis (ie, blood flow and tissue perfusion) is complicated because of the phasic nature of sepsis. The cardiovascular response in sepsis is probably the most complicated and difficult to treat all hemodynamic disturbances since it changes as the condition worsens, from an initial hypodynamic cardiac function to a hyperdynamic state. Treatments that work in one phase may not work in the next. In this article, a review of the types of hemodynamic alterations that occur in sepsis will be presented, along with case studies and treatment guidelines.

Hemodynamic Changes in Sepsis

Sepsis is not easily characterized in terms of hemodynamic changes. Initial stages of sepsis produce a hemodynamic effect due to immune system mediator release.[1] This mediator release is an attempt to combat a local infection. For example, mediators that change endothelial wall permeability to allow larger neutrophils into the area also allow for increased capillary permeability.[2] This increased permeability causes fluid shifts into the interstitial space, producing hypovolemia.[3] At this point, fluid replacement can aid in treating the hypovolemia of early sepsis.

However, as sepsis progresses, other mediator effects, such as vasodilation and microcapillary obstruction (eg, clotting), take place.[4] The clotting produces obstruction of blood supply even though cardiac output and blood flow are at or above normal levels. Obstruction of blood flow leads to worsening tissue hypoxia and a shock state known as distributive shock.[5] In addition, activation of mediators, such as oxygen free radicals, tissue factor, tumor necrosis factor-α (TNFA), interleukin 1

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(*IL1*), and *IL6*, normally effective mechanisms to contain and destroy antigens, is exaggerated and leads to the damage of normal cells, including endothelial walls. Resulting damage to capillary walls creates increased permeability in the endothelial wall, allowing large amounts of fluid to escape from the capillaries and into the interstitial space.

The inflammatory mediators also help increase blood flow to isolated areas under normal circumstances. However, in sepsis, the blood flow increase becomes systemic, increasing cardiac output/index and stroke volume/index, a shift between initial stages of sepsis to a more severe stage, one from a low blood flow state to high blood flow state.[6] The cellular mechanisms producing this change are significant, changing from an initial proinflammatory response to more of an antiinflammatory response.[7] The systemic response produces vasodilation with a decrease in resistance to the pumping ability of the heart. The decrease in afterload produces a drop in blood pressure that triggers an increase in cardiac output to maintain normal perfusion pressure.[8] The net result is a further increase in cardiac output and stroke volume.[9]

Unfortunately, the distributive shock state is unlikely to be as simple as a shunting of blood from tissues or a leaking of fluid from the capillaries. In addition, the change from initial sepsis with low cardiac output states to those with late sepsis and high cardiac output phases is difficult to detect from traditional assessments.[10]

Cellular dysoxia is likely present in sepsis, including mitochondrial dysfunction.[11] Cellular dysoxia may lead to "cell stunning," with a subsequent reduction in oxygen consumption at the cellular levels. This cell stunning may be similar to what is seen in myocardial infarction, where cardiac muscle cells are temporarily stunned. Whether the process of cell stunning or the activation of mediators and key proteins is the cause, in sepsis cells have a tendency to progress to apoptotic (preprogrammed) cell death.[12] Apoptosis may be one of the causes of death in patients with sepsis, rather than cell damage.

The potential danger of hypoxia and apoptosis is the development of a systemic failure of multiple organs. Distributive shock is exceedingly difficult to treat and can affect all organs. Many, if not most, patients who die of septic shock do so because of multiple organ system failure, from either apoptosis or cell damage. Once enough cells from vital organs have been injured or initiated apoptosis, shock can become irreversible, and death can occur despite correction or elimination of the underlying process that started the septic cascade.

Evaluation of the Effect of Abnormal Hemodynamics on Tissue Oxygenation

The dominant practice in the assessment of the effectiveness of shock and preshock therapy centers around global physical measures, such as blood pressure, mean arterial blood pressure, altered cognition, and changes in urine output. These measures have been demonstrated to be slow to change or misleading in their accuracy.[13–16] The need for better evaluative measures for assessing the effectiveness of treatment in shock states is essential for better patient management.

Some centers attempt to better assess the impact of treatments on shock by utilizing hemodynamic monitoring to evaluate the effectiveness of treatment. Hemodynamic monitoring offers the benefit of evaluating changes in blood flow (ie, stroke volume and cardiac output). However, even with the understanding of general blood flow concepts such as stroke volume/index and cardiac output/index, the evaluation of what is occurring at the tissue level, from either a blood flow or nutrition/oxygenation perspective, is not possible. To understand whether tissue perfusion has reestablished tissue oxygenation, a measure of tissue oxygenation, not blood flow, must also be used.

Evaluation of tissue oxygenation includes parameters that reflect tissue utilization of nutrients. Some parameters that are commonly assessed include lactate/pH measurements and mixed venous oxyhemoglobin levels (SvO_2). Both of these parameters have value in assessing tissue oxygenation. Lactate levels, when associated with a metabolic acidosis, reflect tissue hypoxia. Hypoxia is reflected since lactate levels are increased during anaerobic metabolism. SvO_2 levels do not directly reflect hypoxia. However, SvO_2 levels reflect the amount of oxygen returning to the lungs after the tissues have removed the needed oxygen. If tissue oxygenation is threatened, venous oxygen levels will decrease to reflect the severity of the threat.

Both lactate and SvO_2 measurements, however, have limitations. For example, lactate levels give a good indication of tissue anaerobic metabolism but change slowly and cannot be measured continuously. SvO_2 is a very rapid reflector of a change in the oxygen reserve but requires a central venous catheter, does not reveal individual organ function, and does not clearly identify when hypoxia is present. Despite these limitations, both lactate and SvO_2 are good indicators of oxygenation in most clinical situations.

Use of SvO_2 and $ScvO_2$ in Assessing Adequacy of Hemodynamics

Of the parameters listed above, SvO_2 levels may hold the most promise as an indicator of therapy effectiveness. There are several methods to measure venous oxygenation saturations. The two most common are SvO_2 (obtained by measuring the oxyhemoglobin in the pulmonary artery) and the $ScvO_2$ (obtained by measuring a blood sample in the right atrium). $ScvO_2$ levels are slightly higher than SvO_2 levels, generally about 5% to 13% higher.[17] The higher $ScvO_2$ level in comparison with the SvO_2 level is due to incomplete mixing of inferior, superior, and coronary sinus blood in the right atrium.

$ScvO_2$ and SvO_2 levels do not equal each other. However, both values trend well enough to allow substitution of the $ScvO_2$ for the SvO_2.[18–20] Clinically, this is useful since it is more difficult to obtain a SvO_2 (due to the need for a pulmonary artery catheter). All that is needed for a $ScvO_2$ level is a central venous catheter, for example, a triple lumen catheter.

SvO_2 and $ScvO_2$ levels have been shown to correlate with outcome, respond rapidly to changes in blood flow and oxygenation, and better predict response to treatment.[21,22] Used along with key therapies in sepsis, for example, components of early goal-directed therapy, SvO_2 and $ScvO_2$ have been shown to substantially aid in mortality and cost reduction.[23–25]

When a threat to tissue oxygenation, such as a decrease in blood flow, occurs, tissues extract more oxygen than normal from hemoglobin. This drop in the SvO_2 level indicates the severity of the threat to tissue oxygenation. The lower the SvO_2, the more severe the threat to tissue oxygenation. In early sepsis, which presents as hypovolemia, the SvO_2 and $ScvO_2$ levels are low.

The exact SvO_2 level is less significant than understanding whether the value is abnormal or not. If the SvO_2 is abnormal, a therapy to correct the value is needed. The lower the SvO_2, for example, less than 60%, the more aggressive the therapy required to return the oxygen reserves and tissue oxygenation to near-normal levels, for example, 70%. Treatment is particularly important when the SvO_2 acutely drops. In patients with chronically low SvO_2 levels due to conditions such as congestive heart failure or cardiomyopathy, there may be limited ability to raise the SvO_2 levels.

As sepsis progresses, a dangerous change in SvO_2 levels occurs. As sepsis worsens, SvO_2 levels do not fall but increase. The increase in SvO_2 levels occurs only in septic shock, not in cardiogenic and hypovolemic shock. Several reasons for an increase in the SvO_2 levels are likely, including reduction in cellular oxygen consumption (cellular dysoxia) and obstruction of blood flow due to disturbances in fibrinolysis and coagulation.[26]

Regardless of the shock state, a normalization of SvO_2 level reflects a reestablishment of blood flow to the tissues and a rebuilding of the body's oxygen reserve. The use of SvO_2 offers the potential to have a more effective measure of assessing tissue oxygenation over current parameters.

Use of Blood Lactate Values in Assessing Oxygenation

In sepsis, elevated blood lactate concentrations reflect anaerobic metabolism due to reduced blood flow, capillary obstruction, or cellular dysoxia. However, caution should be exercised when interpreting lactate levels. An elevated lactate level (>4 mmoL) in the presence of an acidosis is highly suggestive of type A (hypoxic) acidosis. However, lactate levels can change for other reasons, such as glyconeogenesis. While lactate concentrations may not be a perfect indicator of tissue hypoxia, the prognostic value of elevations of blood lactate has been well established in septic shock patients.[27,28] Similar to SvO_2 values, the trend of lactate concentrations is a better indicator of tissue oxygenation than single lactate values. If a lactate level is elevated for a brief period of time (eg, exercise or postseizure), the danger of a high lactate level is lower. If a lactate level is elevated and remains elevated for hours or longer, the threat is much more dangerous.

Indices of Regional Perfusion

There are few reliable measures of perfusion of each organ. Venous blood samples from each organ are possible, but often are technically difficult. For example, cerebral assessment of venous oxyhemoglobin levels in blood samples from the jugular bulb ($SjvO_2$) can provide useful information regarding cerebral oxygenation.[29] While $SjvO_2$ is an example of a technology that can yield useful information, its use has normally been associated with specialized units.

Because of limitations such as the technical difficulty, as seen with the $SjvO_2$, the adequacy of perfusion to individual organs is more difficult to assess than global evaluation. Each organ can show symptoms of hypoperfusion but these changes may be due to causes other than sepsis. For example, the following organs show signs of sepsis involvement through a variety of clinical presentations.

A decrease in urine output or elevation in creatinine level or serum urea nitrogen may be reflective of either prerenal azotemia (loss of perfusion) or acute tubular necrosis (renal injury). Hepatic injury can be manifested by several factors (eg, increased serum concentrations of transaminases, lactic dehydrogenase, and bilirubin). Injury to the liver can also be seen with reduction in hepatocyte synthesis capability through a reduced albumin and clotting factors. Gastrointestinal injury in sepsis is common. Gastrointestinal injury can be manifested by stress ulceration, ileus, and malabsorption. Pulmonary function can be impaired because of infections (pneumonia), inability to clear secretions (chronic obstructive pulmonary disease), or sepsis-induced neutrophil injury. Reduced pulmonary function can be seen through increased intrapulmonary shunting, for example, PaO_2/FIO_2 (P/F) ratios less than 200. Cardiovascular involvement can be seen through the development of hypotension and abnormal blood flow (either high or low cardiac outputs) and reduced or normal cardiac filling pressures.

Systemic indicators of perfusion are used to guide treatment of systemic oxygen and hemodynamic instability, and regional perfusion indicators should be evaluated on the basis of specific treatments of that region. For example, a patient with normal $SvO_2/ScvO_2$ but low $SjvO_2$ (jugular oxygen) would illustrate that the brain might be hypoxic although systemic oxygenation is adequate.

The Clinical Presentation of Hemodynamic Changes in Sepsis

Early sepsis presents much like hypovolemia. Blood flow indicators are reduced, and tissue oxygenation begins to worsen (Table 1). The indicators that are most likely to produce clinically useful numbers in sepsis are SvO_2 and stroke index (SI). Cardiac index (CI) is useful but CI can be maintained at a normal level due to a compensating tachycardia. A compensating tachycardia can keep the CI normal while the SI is low. Therefore, SI is a better indicator of initial low flow states since it is less affected by heart rate changes. As sepsis progresses to more severe stages, SI, CI, and SvO_2 levels increase.

Table 1: Hemodynamic Characteristics of Sepsis*

	Normal	Early Sepsis	Late Sepsis
SvO_2	60%–75%	Low	High
$ScvO_2$	65%–80%	Low	High
Stroke index	25–45 mL/m^2	Low	High
Cardiac index	2.5–4 L/m^2	Low	High
Peak velocity	50–120 cm/s	Normal	Low or normal
Flow time	330–360 ms	Low	Low or normal
Pulmonary artery occlusive pressure	8–12 mm Hg	Low or normal	Low or normal
Central venous pressure	2–6 mm Hg	Low or normal	Low or normal

*SvO_2 indicates mixed venous oxygen saturation; $ScvO_2$, central venous oxygen saturation.

Other hemodynamic parameters are not as simple to assess as blood flow (SI and CI) and $ScvO_2$ levels. Parameters such as filling pressures (pulmonary artery occlusive pressure [PAOP] and central venous pressure [CVP]) and contractility can be either normal or low, reflecting the impact of sepsis on the cardiovascular system in sepsis. When considering indicators of cardiovascular volume, for example, filling pressures, such as the CVP, PAOP, and right ventricular end diastolic pressure, these parameters tend to be normal or low, reflecting the hypovolemia secondary to vasodilation and leakage of fluid from damaged capillaries. The same can be said for measures of volume such as flow time (FTc) and right ventricular end diastolic volume. Contractility measures, such as peak velocity (PV), tend to be normal or reduced, reflecting myocardial hibernation in sepsis.[30]

The parameters that are most accurate and easiest to use and obtain in sepsis are indicators of tissue oxygenation (SvO_2 and $ScvO_2$) and blood flow (SI and CI). Most clinical decisions start with evaluating these parameters first and referring to other indicators, such as pressures, volume, or FTc, primarily if the SvO_2 and/or SI are abnormal.

How to Measure Hemodynamics in Sepsis

The measurement of hemodynamics has traditionally been performed with techniques ranging from blood pressure to the pulmonary artery catheter. However, it is much easier to measure hemodynamics with less invasive devices. A brief review of the current practices will help illustrate the value in the newer forms of hemodynamic measurement.

Measurement of Arterial Blood Flow

Arterial blood pressure measurement has been a mainstay in hemodynamic evaluation for decades. This is true despite the clear limitations of blood pressure in terms of reflecting blood flow and tissue oxygenation. Controversy exists over what type of blood pressure to use in clinical situations, for example, cuff methods or direct arterial measurement through an arterial catheter and when using the cuff, where to measure.[31] Clinicians often use arterial catheters for patients who are hypotensive. However, blood pressure measurement runs a real danger of misleading the clinician. Blood pressure does not always correlate with blood flow and tissue oxygenation. For example, a low blood pressure could be present in both hypovolemia (low cardiac output) and the hyperdynamic state of sepsis (high cardiac output). More significantly, blood pressure can be maintained at normal levels by compensatory mechanisms, even though blood flow and tissue oxygenation are abnormally affected. Blood pressure should be a secondary monitoring parameter, not a replacement for tissue oxygenation and blood flow measurements.

Measurement of SvO_2 and $ScvO_2$

SvO_2 and $ScvO_2$ can be measured by drawing a blood sample from the distal tip of a pulmonary artery or triple lumen catheter, respectively. With the incorporation of oximetry capability into triple lumen catheters, continuous monitoring of $ScvO_2$ is now possible. Continuous monitoring of $ScvO_2$ allows for precise titration of drugs and fluids, allowing for an improvement in patient treatment.

Measurement of Blood Flow

Multiple techniques exist to measure hemodynamics besides the pulmonary artery catheter (Table 2). Ideal technologies would be those that are noninvasive or minimally invasive, safe, easy to use, easy to learn, and accurate (see Figure 1 for an example). Cost is considered as a factor when technologies are similar. While none of the existing technologies meet all criteria in a wide array of patients, of the available technologies, one or two will tend to dominate practice.[32] Less invasive or noninvasive devices, for example, external or esophageal Doppler, are likely to dominate practice because of ease of use; they are relatively inexpensive, rapid, and accurate.

The newer technologies such as Doppler represent excellent tools for use of assessing hemodynamic disturbances, including those associated with sepsis. However, technologies by themselves do not change patient outcomes. Clinicians' skill and knowledge in interpreting the information and applying appropriate therapies is the key to improving patient outcomes.

Using Hemodynamic Monitoring to Aid in the Treatment of Sepsis

The treatment of hemodynamic alterations in sepsis has not changed markedly until the last

Table 2: Comparison of Technology for Measuring Cardiac Output

	Is the Technology Noninvasive?*	Is the Cost <$25/Patient?	Can the Technology Be Used on Any Patient?
External Doppler	Yes	Yes	Yes
Esophageal Doppler	Yes	Yes	No, the patient must be sedated.
Thoracic bioimpedance	Yes	Yes	No, the patient must have normal anatomy and access to the neck.
Exhaled CO_2 Fick method	Yes	No	No, the patient must be on a ventilator.
Pulse contour	No	No	No, the patient must have at least an arterial line in place.
Pulmonary artery catheter	No	No	No, the patient must have a central line in place.

*That is, does not require arterial or venous access.

few years. For the past 50 years, treatment for altered hemodynamics in sepsis has included the administration of fluids, vasopressors or inotropes, appropriate antibiotics, and source control of the infection. One key advancement in the treatment of severe sepsis is the recent introduction of drotrecogin alfa (activated). While the drug is designed to improve depleted levels of activated protein C, it has other effects that can improve blood pressure and blood flow.[33] While drotrecogin alfa (activated) is not a hemodynamic drug, it should be considered for use in patients who have severe sepsis and a high risk of death.[34]

In an effort to save the lives of patients who are in preseptic shock states, or even in shock, aggressive resuscitative therapies are applied.

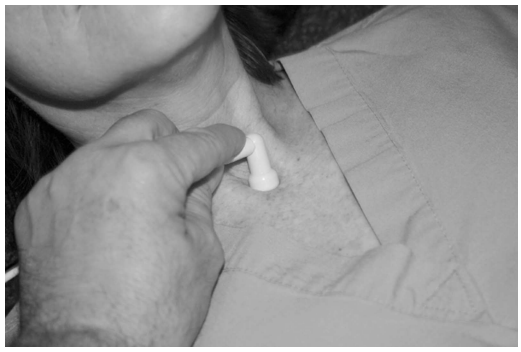

Figure 1: Suprasternal notch Doppler technique for measuring cardiac output/index and stroke volume/index.

These therapies usually center on a few key categories, for example, inotropes, fluid replacement, and vasopressors. However, any therapy aimed at treating shock, regardless of the type, is designed to improve perfusion to tissues and reestablish adequate nutrient supply to the tissues.

As described earlier, traditional measures of assessing the adequacy of perfusion to the tissues are limited, that is, blood pressure, urine output, and cardiac pressures. Because of the limited measures for assessing the reestablishment of adequate blood flow, it is often unclear how effective treatments are in the patient in shock. It is possible that the limited accuracy of traditional assessment of tissue perfusion and oxygenation misleads clinicians in their treatment choices. The inadequacy of traditional monitoring is why use of specific hemodynamic goals, such as $ScvO_2$ and SI, is the key to improving patient outcomes.

Goals and Monitoring of Fluid Resuscitation

The goal of hemodynamic treatments is to return SvO_2, or $ScvO_2$ and SI to normal (SvO_2 65%; $ScvO_2$ 70%; and SI above 25 mL/m^2). When administering fluids, the choice of fluids usually starts with a crystalloid such as sodium chloride. A colloidal agent such as albumin or Hetastarch could be used but evidence suggests that the less expensive crystalloid achieves similar outcomes.[35,36] The amount of fluid to give is not clear but one

approach is to give a set amount of fluid, for example, 500 mL bolus of sodium chloride, and observe the Scv_{O_2} and SI response, continuing to titrate until the values return to normal.

Case Studies in Goals and Monitoring of Treatments for Sepsis

Four case studies are presented to illustrate the assessment and treatment of the hemodynamics associated with sepsis. Included in the treatment of abnormal hemodynamics associated with sepsis is the titration of fluids and drugs to specific hemodynamic end points. In each of the 4 cases, both PAOP and PV are provided. Normally, only 1 of these would be present since the values are obtained from different technologies. However, both the PAOP and PV are provided in an illustration of bridging the older (pulmonary artery catheter) and newer (Doppler) technology for measuring hemodynamics.

Case Study 1: Hypovolemia Associated With Sepsis

For the patient with hypovolemia (Table 3), notice that the Scv_{O_2} and SI are low. The low Scv_{O_2} suggests a threat to tissue oxygenation due to poor blood flow (low SI). The PAOP is slightly low while the PV is normal. The low PAOP suggests hypovolemia and is confirmed by the normal PV, which indicates adequate contractility. The fluid therapy that is initiated at 5:00 AM produces an initial, small increase in Scv_{O_2} and SI. Keep in mind that the Scv_{O_2} and SI are the main parameters to improve, not the PAOP. Since the fluid bolus did not return Scv_{O_2} (and SI) back to normal, further fluid is needed. Notice that it takes 2 additional fluid boluses to return the Scv_{O_2} back to normal. SI, PAOP, and PV are all normal as well. However, only when Scv_{O_2} has returned to normal can the goal of the fluid therapy be considered achieved.

Case Study 2: Use of Inotropic Therapy

In the second case, the use of inotropic therapy is illustrated (Table 4). Administration of an inotrope, such as dobutamine or milrinone, is acceptable when an assessment of reduced contractility has been determined. The goal is the same as with fluids, that is, return Scv_{O_2} and SI to normal. In case study 2, note that fluids have already been given but the Scv_{O_2} and SI are still low. In addition, the heart appears weak due to the reduced PV. The inotrope (in this case dobutamine) should be administered until either Sv_{O_2} and SI return to normal, no improvement has been seen, or a side effect (such as tachycardia) occurs. In this case, notice that the initial dose of dobutamine at

Table 3: Case Study 1: Fluid Therapy for Treatment of Hypovolemia in Sepsis*

	Scv_{O_2}, %	Stroke Index, mL/m²	Pulmonary Artery Occlusive Pressure, mm Hg	Peak, Velocity cm/s	Treatment
5:00 AM—Treatment is initiated.	45	19	7	73	Start 500 mL sodium chloride
5:30 AM—Improvement but not return to normal. More fluid needed.	48	20	7	74	500 mL sodium chloride
6:00 AM—Improvement but not a return to normal. More fluid needed.	58	25	8	76	500 mL sodium chloride
6:30 AM—Return to normal, and treatment can be stopped.	70	31	9	75	

*Scv_{O_2} indicates central venous oxygen saturation.

Table 4: Case Study 2: Inotropic Therapy for Treatment of Sepsis*

	$ScvO_2$, %	Stroke Index, mL/m^2	Pulmonary Artery Occlusive Pressure, mm Hg	Peak, Velocity cm/s	Treatment
4 Liters of sodium chloride given.					
9:30 PM–treatment is initiated.	42	16	11	49	Start dobutamine 2.5 mcg kg^{-1} min^{-1}
10:00 PM–Improvement but not a return to normal. Continue inotrope.	47	19	10	57	Increase dobutamine to 5 mcg kg^{-1} min^{-1}
10:30 PM–Improvement but not a return to normal. Continue inotrope.	59	23	9	64	Increase dobutamine to 7.5 mcg kg^{-1} min^{-1}
11:00 PM–Return to normal, and treatment can be stopped.	73	34	12	72	

*$ScvO_2$ indicates central venous oxygen saturation.

9:30 PM has not produced a return to normal of $ScvO_2$ by 10:00 PM. despite an increase in dobutamine to 5 mcg kg^{-1} min^{-1} at 10:00 PM, the $ScvO_2$ has improved but remains below 70%. Only after an increase in dobutamine to 7.5 mcg kg^{-1} min^{-1} does the $ScvO_2$ return to normal ($ScvO_2$ is 73%). At this time, no further increase in the dose is needed.

Case Study 3: Use of Vasopressor Therapy

The third case study represents how vasopressors are used to treat the hemodynamic profile (Table 5). Vasopressors are traditionally given when the blood pressure is low. Unfortunately, the blood pressure may change much later than $ScvO_2$ and SI. Therefore, blood pressure is not a direct indicator of tissue oxygenation and is not an ideal hemodynamic measurement. However, despite this limitation, blood pressure is still a standard of care and current practice mandates its use. In this example, the incorporation of the blood pressure with $ScvO_2$ end points is provided.

In this case study, notice that the blood pressure is low (82/48) with a very low $ScvO_2$ (36%), SI (20 mL/m^2), and normal PV (71 cm/s) and PAOP.[13] These values indicate normal contractility (normal PV) and adequate volume (normal PAOP) but poor perfusion (low $ScvO_2$ and SI). In this case, vasopressor therapy might be useful. The initial therapy, norepinephrine (Levophed), is started at 2:30 PM. Over the following 90 minutes, the norepinephrine must be increased because of the inability to return $ScvO_2$ to normal. Note that 30 minutes into the therapy, the blood pressure has returned to a normal level (100/54). However, $ScvO_2$ was still low (45%), indicating that tissue oxygenation was not returned to normal. This example illustrates how $ScvO_2$ should be used along with blood pressure when applying vasopressor therapy. Without using the $ScvO_2$ value, vasopressor therapy would have been stopped before tissue oxygenation had improved.

Case Study 4: Use of Drotrecogin Alfa (Activated)

Case study 4 illustrates the situation where traditional therapies for improving hemodynamics are attempted but are not effective (Table 6). In situations like this, where aggressive care is to be continued, a potential option is drotrecogin alfa (activated). Case study 4 offers a situation where drotrecogin alfa (activated) is a viable therapy to help

Table 5: Case Study 3: Vasopressor Therapy for Treatment of Sepsis*

	$Scvo_2$, %	Stroke Index, mL/m²	Pulmonary Artery Occlusive Pressure, mm Hg	Peak, Velocity cm/s	Treatment
4 liters of sodium chloride given.					
2:30 PM—treatment is initiated because of hemodynamics and BP level of 82/48.	36	20	13	71	Start norepinephrine 5 mcg/min
3:00 PM—improvement but not a return to normal. BP level is 100/54. An increase in the vasopressor is still needed.	45	22	10	68	Increase norepinephrine to 10 mcg/min
3:30 PM—improvement but not a return to normal. BP level is 110/62. An increase in the vasopressor is still needed.	62	25	14	70	Increase norepinephrine to 20 mcg/min
4:00 PM—return to normal, and treatment can be stopped.	74	29	13	72	

*$Scvo_2$ indicates central venous oxygen saturation.

improve the abnormal hemodynamics resulting from severe sepsis.

In this case, a 54-year-old woman was admitted from home with the diagnosis of bilateral pneumonia, possible Pneumocystis Carinii Pneumonia. After 4 days in the intensive care unit, her pneumonia did not respond to antibiotic therapy and she developed sepsis. She received fluids (6 L of sodium chloride) and vasopressors (norepinephrine at 100 mcg/min). Her hemoglobin level was adequate as was her heart strength (contractility was adequate as evidenced by a PV of 70). Despite the current hemodynamic treatments, she was still hypotensive. In addition, she developed renal failure. As part of her sepsis management, she was receiving tight glycemic control as well as replacement dose steroids.

Her hemodynamics showed several key abnormalities. Both her $Scvo_2$ and SI were higher

Table 6: Case Study 4: Activated Protein C Therapy for Treatment of Sepsis

	$Scvo_2$*, %	Stroke Index, mL/m²	Pulmonary Artery Occlusive Pressure, mm Hg	Peak Velocity, cm/s	Treatment
6 L of sodium chloride given					
7:30 AM—BP level is 76/42	85	51	14	70	Levophed at 100 mcg/min

*$Scvo_2$ indicates central venous oxygen saturation; BP, blood pressure.

than normal. The elevated Scv_{O_2} and SI represented a later, more severe stage of sepsis. In addition, her blood pressure was low. The use of fluids and vasopressors had not helped her hemodynamics return to normal.

At this point all therapies for sepsis were given, except drotrecogin alfa (activated). Since drotrecogin alfa (activated) is indicated only when a high risk of death is present (eg, APACHE II $>$ 25 or multiple organ failure), the clinician must evaluate if a high risk of death is present. In this case, there are multiple organs involved unrelated to the pneumonia, that is, cardiovascular and renal. The failure of these organs would represent a high risk of death and would also demonstrate that drotrecogin alfa (activated) would be indicated. If drotrecogin alfa (activated) therapy is effective, an improvement in hemodynamics could be expected, including a return to normal of the Scv_{O_2}, SI, and blood pressure. While not a hemodynamic therapy, drotrecogin alfa (activated) use may return hemodynamics to normal through its immune system effect.

Summary

Hemodynamics in sepsis change with the course of the condition. Understanding how the changes occur helps the clinician understand which treatments are best for each phase of sepsis. Helping the clinician evaluate the hemodynamics changes seen in sepsis is new technologies, for example, noninvasive Doppler, that allow hemodynamic monitoring to be performed on more patients, with greater ease and increased safety. As hemodynamic monitoring improves, improved assessment of patients with all forms of hemodynamic disturbances, including sepsis is possible. Improved monitoring will lead to more precise assessment and administration of treatments, holding the promise of improving patient outcome and reducing resource utilization.

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