CHAPTER 19 ■ MONITORING TISSUE PERFUSION AND OXYGENATION

KENNETH WAXMAN

Shock occurs when tissue oxygen delivery is inadequate to meet metabolic demands, and cellular dysfunction results. Since a primary goal of treating shock is elimination of cellular hypoxia, it logically follows that detecting and treating shock would best be monitored by measuring the state of tissue perfusion and cellular oxygenation. To this end, many devices that have the capability of monitoring tissue perfusion and oxygenation have been developed. However, to date, none of these devices has gained widespread acceptance in clinical practice. Why is this? This chapter will outline underlying principles of tissue perfusion and oxygenation and review the complexities of making clinically useful measurements with existing monitoring approaches.

There are multiple components of the circulation that contribute to cellular oxygenation, each of which is related to monitoring of tissue perfusion and oxygenation. As shown in Figure 19.1, tissue perfusion is determined by cardiac output, the distribution of cardiac output to regional tissue beds, and the state of the microcirculation. Tissue oxygenation is determined by perfusion as well as by arterial oxygenation, nutritional blood flow, and cellular extraction of oxygen. This is a complex system, which is highly dynamic: Alteration of any component has physiologic impact upon other components. Moreover, there is enormous heterogeneity within the circulation, both between organs and within organs. Hence tissue perfusion and oxygenation is never uniform between organs, nor even in particular tissue beds. Nonetheless, despite these complexities, there are several principles that allow useful monitoring to occur:

1. Peripheral perfusion and oxygenation monitors are not replacements for other commonly used monitors, but instead provide unique physiologic information.
2. A measured decrease in peripheral tissue perfusion may provide a significant and early warning of circulatory insufficiency.
3. In low-flow shock states (such as hemorrhagic or cardiacogenic shock); there is a characteristic redistribution of regional blood flow, such that blood flow to the heart and brain is preserved, while peripheral blood flow is decreased. Blood flow to the skin decreases very early in this process; hence, monitoring skin perfusion is a very sensitive indicator of circulatory shock. Blood flow to other tissues such as the intestinal tract also decreases relatively early in shock, making the gut an alternative sensitive monitoring site. Unfortunately, in high-flow shock states (such as septic shock), the distribution of regional blood flow is less predictable, and interpretation of peripheral perfusion data becomes more complex.
4. A measured decrease in peripheral tissue oxygenation may be a significant warning of decreased tissue perfusion, decreased hemoglobin concentration, arterial oxygenation, or increased cellular utilization of oxygen. Sorting out these alternative explanations for abnormal tissue oxygenation can lead to prompt diagnosis and treatment of the underlying problem.
5. Monitors of tissue perfusion and oxygenation can be used in several ways. They can serve as early sensitive but nonspecific warning devices to alarm when decreases of blood flow or oxygenation occur. In addition, these monitoring approaches can be used as components of a system of monitoring, such that their specificity is enhanced. For example, combining tissue oxygen monitoring with pulse oximetry can indicate that a decreased tissue oxygen value is not due to arterial hypoxemia.
6. Monitoring changes of tissue oxygenation in response to changes in cardiac output or arterial oxygen may provide meaningful clinical information. The use of these devices in response to physiologic challenges adds another dimension to their potential value.

MONITORING TECHNIQUES

Pulse Oximetry

Pulse oximeters are designed to monitor arterial oxygen saturation, not tissue perfusion or oxygenation. In fact, the technology of pulse oximetry is precisely designed to detect oxyhemoglobin saturation, even when blood flow is greatly reduced. Estimation of arterial oxygen saturation is thus of great benefit in monitoring arterial oxygenation, but of little value in assessing the circulation. A patient in shock may have 100% arterial oxygen saturation, and pulse oximetry will reflect this regardless of the state of the circulation, as long as the probe can detect pulsation. When pulsations can no longer be detected, the monitor ceases to function. Hence, it is only the absence of a signal that indicates very low flow, and this absence is both insensitive and nonspecific. Pulse oximetry is, however, useful in combination with tissue oxygen monitors to indicate whether low tissue oxygenation is due to arterial hypoxemia or to inadequate circulation.

Transcutaneous Oxygen

In 1956 Clark developed a practical polarographic electrode to measure oxygen tension, using a semipermeable polyethylene membrane-covered platinum cathode (1). The Clark electrode has become the standard for blood gas analysis. Subsequently,
the Clark electrode was placed into a heated probe, and utilized for transcutaneous oxygen monitoring. Heating of the skin by the transcutaneous electrode is necessary to allow diffusion of oxygen across the stratum corneum. This occurs because heating the skin to 44°C or higher rapidly (over minutes) melts the lipoprotein barrier to oxygen diffusion. Heating the skin, however, also affects thin tissue, dilating the underlying vessels and increasing local blood flow. In addition, heating decreases oxygen solubility, shifting the oxyhemoglobin dissociation curve to the right (2). Initial measurements must be delayed for up to 5 minutes for the skin to heat. Moreover, transcutaneous oxygen tension (PtcO$_2$) values may be site specific, sometimes with lower values in the extremities of patients with peripheral vascular disease. For critical care monitoring, most studies utilize the torso. Despite these confounding issues, transcutaneous oxygen monitoring provides useful physiologic data that are meaningfully related to tissue oxygenation.

Experimental studies have shown that transcutaneous oxygen monitoring is sensitive to arterial oxygen tension during normal cardiac output, but is more sensitive to perfusion in low-flow shock (3). In adult patients, PtcO$_2$ is approximately 80% of the arterial oxygen tension (PaO$_2$) during normal hemodynamic conditions. However, when blood flow is diminished, PtcO$_2$ also decreases. PtcO$_2$ is therefore related to both perfusion and oxygenation. When perfusion is normal, PtcO$_2$ varies with arterial oxygenation. When perfusion is inadequate, PtcO$_2$ varies with cardiac output. Hence, a normal PtcO$_2$ value indicates that both oxygenation and perfusion are relatively normal. A low PtcO$_2$ indicates that either oxygenation and/or cardiac output are inadequate. If arterial oxygenation is normal (as indicated by blood gases or pulse oximetry), low PtcO$_2$ indicates low-flow shock (4).

The relationship between PtcO$_2$ and PaO$_2$ can be quantitated, utilizing the PaCO$_2$ index, which is simply defined as PaCO$_2$/PtcO$_2$. In a study that simultaneously measured cardiac index, PtcO$_2$, and PaO$_2$ in a large number of critically ill surgical patients, it was found that when cardiac output was relatively normal (cardiac index >2.2 L/minute/m$^2$), the PtcO$_2$ index averaged 0.79 ± 0.12. In individual patients with these normal cardiac outputs, PtcO$_2$ varied linearly with PaO$_2$. When cardiac output decreased, however, the PtcO$_2$ index decreased as well. For patients with a cardiac index between 1.5 and 2.2 L/minute/m$^2$, the PtcO$_2$ index averaged 0.48 ± 0.07. For patients with a cardiac index below 1.5 L/minute/m$^2$, the PtcO$_2$ index was 0.12 ± 0.12 (4). These data confirm that when blood flow is relatively normal, PtcO$_2$ varies with arterial oxygenation. However, with low-flow shock, PtcO$_2$ becomes very sensitive to changes in cardiac output.

Clinical studies have demonstrated the usefulness of transcutaneous oxygen monitoring in detecting shock. When PtcO$_2$ monitors are placed during acute emergency resuscitation, low PtcO$_2$ values detect both hypoxemia and hemorrhagic shock. Moreover, the response of PtcO$_2$ during fluid infusion is a sensitive indicator of the efficacy of shock resuscitation (5,6).

Transcutaneous oxygen monitoring thus has benefit both as an early detector of shock and as a monitor to titrate resuscitation to a physiologic end point. It is noninvasive and inexpensive, and is therefore widely applicable for patients at risk, such as during emergency resuscitation of trauma and acute surgical emergencies, in the perioperative and postanesthesia period, and in the intensive care unit (ICU). However, while end points of successful resuscitation utilizing transcutaneous oxygen monitoring have been suggested, such values have not been validated in large prospective studies. The only risk of transcutaneous oxygen monitoring is minor skin burn beneath the probe if probe temperatures exceed 44°C or if the device is left in place for excessive periods of time.

**Tissue Oxygen Monitors**

In addition to transcutaneous oxygen probes, alternative direct tissue oxygen monitoring techniques have been developed. An advantage of such tissue probes is that heating of the skin is not necessary. In addition, specific tissues can be monitored to provide organ-specific information. Probes may be placed into the subcutaneous tissue, which is very sensitive to low flow. They may also be placed into muscle, which is perhaps less sensitive to low flow, but more rapidly responsive to resuscitation. Probes may also be placed directly into organs. For example, specific probes are now available for placement in the brain to provide a measure of cerebral oxygenation.

Two techniques for direct tissue oxygen monitoring are available. Polarographic electrodes incorporated into needles have been most widely utilized. In addition, a technique utilizing the phenomenon of fluorescence quenching is available. Tissue oxygen probes contain a fluorescent compound that is O$_2$ sensitive, such that its fluorescent emission is diminished in direct proportion to the amount of O$_2$ present. Energy from the monitor is transmitted through fiberoptic elements to the fluorescent compound in the probe, resulting in the emission of light, which is then measured by sensors in the tissue probe. The intensity of the emitted light is inversely proportional to the tissue pO$_2$ (7).

Another method of tissue oxygen monitoring is transconjunctival. The conjunctiva of the eye does not have a stratum corneum, so oxygen is freely diffusible. Transconjunctival probes are placed against the eye, and allow continuous tissue oxygen monitoring without heating; the technology has been utilized both during anesthesia and shock (8).
Chapter 19: Monitoring Tissue Perfusion and Oxygenation

Direct tissue oxygen monitoring devices offer alternatives to transcutaneous monitoring, with the potential advantages of more rapid initial readings, a variety of monitoring sites, and no heating necessary. However, there are little clinical data to determine the relative sensitivities and specificities of these various techniques.

Near-infrared Spectroscopy
Near-infrared spectroscopy (NIS) has been developed as a non-invasive measure of tissue oxygenation (9–12). NIS measures the ratio of oxygenated hemoglobin to total hemoglobin (S\textsubscript{O\textsubscript{2}}) in the microcirculation of the underlying muscle by measuring the absorption and reflectance of light. Using cutaneous probes placed upon the thenar eminence, values of 87% ± 6% have been measured in normal volunteers. Early clinical experience suggests that S\textsubscript{O\textsubscript{2}} values decrease during shock and increase with successful resuscitation. A recent multicenter trial in trauma patients suggested that a S\textsubscript{O\textsubscript{2}} value of 73% may be a therapeutic goal. This monitoring approach has potential value, as it provides convenient, continuous, noninvasive measurements. However, clinical data are limited. Tissue edema may be a confounding factor, as the distance between the probe and the underlying muscle affects measurements. Again, the sensitivity and specificity of this device compared to other tissue oxygen monitoring devices has not been studied. NIS has been demonstrated to have a close relationship to base deficit in critically injured patients (13) as well as predicting development of organ failure in traumatic shock patients (14).

NIS has also been utilized as a cerebral oximeter. By passing light through the scalp and skull, this technology provides a noninvasive measure of cerebral oxygenation.

Gastric Tonometry
The mesenteric circulatory bed, particularly the gut mucosa, is prone to hyperperfusion and ischemia during shock. Tonometry has been developed as a technique to detect adequacy of gastrointestinal mucosal perfusion (14). The technique is based upon calculation of the gastrointestinal intramucosal pH (pHi). The basis of this measurement is that the gastrointestinal mucosal pH (pHi) is equilibrated with the gastric luminal pCO\textsubscript{2}. Measurement of luminal pCO\textsubscript{2} was originally accomplished by placing a tube with an attached balloon into the stomach, allowing time for the CO\textsubscript{2} to diffuse; measuring pCO\textsubscript{2} in the balloon, assuming that luminal pCO\textsubscript{2} equals mucosal pCO\textsubscript{2}; and then calculating pHi by the Henderson-Hasselbalch equation as follows:

\[ pHi = 6.1 + \log \left( \frac{HCO_3^-}{pCO_2} \right) \times 0.031 \]

Gastric pHi monitoring has recently been improved by utilizing gas tonometry without the need for balloons, utilizing capnography. This improvement decreases the lag time necessary for equilibration of carbon dioxide, and allows for more continuous measurements.

The potential usefulness of gastric tonometry has been suggested in clinical studies, in which pHi has been reported to reflect the severity of shock and to increase during successful resuscitation (14). However, the technique has not gained widespread acceptance, in part because the accuracy of the pHi measurement has been questioned. Utilization of arterial bicarbonate as an estimate of mucosal bicarbonate concentrations may be inaccurate. Measurements can be also be altered by gastric acid secretion, because buffering of gastric acid by bicarbonate can produce CO\textsubscript{2} in the gastric lumina, which will confound the estimate of mucosal pCO\textsubscript{2}. Enteral feeding may also affect pHi, although this effect is variable. To minimize these errors, it has been suggested that gastric feeding be withheld and antacid medication given prior to pHi monitoring. However, the variation and inaccuracies of gastric tonometry have limited its widespread application. Moreover, clear treatment endpoints have not been validated.

Several alternatives to gastric tonometry have been studied. Sublingual capnography is a less invasive technique, which shows promise as a sensitive indicator of tissue acidosis in shock models and in early clinical reports (15). This device was recalled in 2004 for infectious complications and may be reinstated in the future. Alternative luminal monitoring sites, such as the small intestine, rectum, and bladder, have also been proposed as monitoring sites for pHi monitoring (16).

Transcutaneous and End-tidal Carbon Dioxide
Transcutaneous carbon dioxide may be measured using the Severinghaus carbon dioxide electrode. Because CO\textsubscript{2} is more diffusible than is O\textsubscript{2}, heating of the probe is not necessary. In analogy with PtcO\textsubscript{2} monitoring, transcutaneous CO\textsubscript{2} parallels arterial values when cardiac output is relatively normal, although transcutaneous values are normally 10 to 30 mm Hg higher than arterial. During low-flow shock, transcutaneous pCO\textsubscript{2} is increased, due to accumulation of carbon dioxide in the tissues due to inadequate perfusion (2). Increased transcutaneous pCO\textsubscript{2} may thus be utilized as an indicator of inadequate circulation, particularly if arterial pCO\textsubscript{2} is normal. In combination with low PtcO\textsubscript{2}, increased transcutaneous pCO\textsubscript{2} gives additional evidence of circulatory shock. End-tidal CO\textsubscript{2} may also be utilized as a measure of perfusion; end-tidal CO\textsubscript{2} is decreased during low-flow states due to decreased pulmonary flow (17). Decreased end-tidal CO\textsubscript{2} values in combination with increased transcutaneous pCO\textsubscript{2} and normal arterial pCO\textsubscript{2} values are strong evidence of circulatory shock. This is an example of how combining noninvasive monitoring data can provide additional information.

Tissue Blood Flow
Measuring tissue blood flow can provide an indication of the adequacy of both cardiac output and regional blood flow. In critical illness, blood flow measurement has the particular potential to be combined with tissue oxygen monitoring to help determine if inadequate tissue oxygenation is due to perfusion deficits. Hence, a reliable tissue perfusion monitor has great appeal.

Many technologies have been developed to measure tissue perfusion. The best studied of these is laser Doppler. Laser Doppler utilizes analysis of scattering of light to determine quantitative blood flow in a small area around the probe (18). A variety of probes have been developed, which can be placed noninvasively onto the skin, or into tissues with needle probes. Laser Doppler measurements have been shown to be useful in detecting changes in blood flow under many experimental conditions.
conditions. However, clinical utility has been limited due to the large variation in blood flow within tissues (19). Because of these limitations, no normal values, no optimal values, and no therapeutic goal values for blood flow have been determined.

Numerous alternative approaches to monitoring tissue perfusion have also been developed. Measurement of local blood flow by thermal diffusion has been developed as an alternative to light scattering, and implantable probes using this technology are available. In addition, magnetic resonance imaging, positron emission tomography, and contrast-enhanced ultrasonography have been used to measure tissue perfusion, although these are not available as continuous monitoring devices. Fluorescence microangiography has also been developed to provide both visual imaging of the microcirculation and measurements of local blood flow (20,21). As with laser Doppler monitoring, validated clinical applications for these technologies have yet to be defined.

The Oxygen Challenge Test

An approach to utilize tissue oxygen monitoring in a more dynamic manner was proposed by Dr. Hunt’s group in San Francisco (22). Endeavoring to assess adequacy of tissue perfusion in postoperative patients, they measured subcutaneous PO2 before and after patients breathed high inspired O2 concentrations. The expected response in well-perfused patients was a rapid increase in tissue PO2. Many postoperative patients failed to demonstrate this response, which was, however, restored with intravenous fluid infusion. A physiologic explanation for the response of tissue PO2 to inspired O2 is interesting. If there is no cellular O2 deficit, then additional dissolved O2 supplied after breathing O2 is not required nor utilized by cells, and therefore results in increased tissue PO2. However, if there is a cellular O2 deficit (shock), then any additional dissolved O2 would be rapidly utilized, and would thus not result in increased tissue PO2. The tissue PO2 response to inspired O2 may then be a relatively rapid and minimally invasive method to detect cellular hypoxia. This approach, named the oxygen challenge test, was evaluated in trauma patients (22,23) (Table 19.1). The O2 challenge test had 100% sensitivity and specificity in detecting flow-dependent O2 consumption in invasively monitored patients in the intensive care unit. It also appeared to be a very sensitive indicator of shock during acute resuscitation. This method, utilizing either transcutaneous or direct tissue O2 monitors, has potential to detect which patients require fluid resuscitation, to provide a physiologic end point for resuscitation, and to detect the patients in whom initial resuscitation is inadequate and who therefore require additional monitoring and therapy. Using a noninvasive transcutaneous (PtcO2) monitor, Yu et al. have studied the O2 challenge test in patients in the intensive care unit and have validated the sensitivity and specificity of the test in identifying patients in occult shock. In addition, their data has defined an increase in PtcO2 of greater than 20 to 25 mm Hg in response to a FiO2 of 1.0 as a therapeutic endpoint (24,25). In a prospective randomized trial using the oxygen challenge test as an end point of resuscitation compared to the oxygen delivery variables from the pulmonary artery catheter, an improved survival was reported (25). The skin is the first to vasoconstrict (even before the gastrointestinal tract) and the last to perfuse in shock states, and the use of the PtcO2 monitor may give an early warning signal of occult shock. The same authors used the oxygen challenge test to identify patients who may benefit from activated protein C (26). Monitoring and treating the peripheral tissue oxygenation state does not exclude utilization of central hemodynamic parameters such as cardiac output and oxygen delivery (DO2), but does allow manipulation of DO2 to reach a specific goal of tissue perfusion rather than aiming for a general DO2 value.

### SUMMARY

Monitoring tissue perfusion and oxygenation provides important physiologic information. However, there is currently no consensus on how to utilize these devices. Great potential exists to develop noninvasive systems utilizing these devices, which will provide sensitive and specific indications both of the severity of shock and end points for resuscitation. Such systems would provide a minimally invasive approach to improve the treatment of shock. To achieve acceptance and application of such systems will require quality clinical studies to determine and validate optimal treatment goals.

### PEARLS

1. A decreased transcutaneous oxygen value may be an early warning of decreased arterial oxygenation, decreased hemoglobin, or decreased cardiac output.

2. The ratio of transcutaneous oxygen to arterial oxygen may be utilized as an end point of resuscitation, with a goal of 0.8.

3. Near-infrared spectroscopy devices placed on the thenar eminence provide a measure of tissue oxygenation, with a normal value of 87% ± 6% saturation. Values less than 75% may indicate shock.

---

**TABLE 19.1**

**OXYGEN CHALLENGE TEST**

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Select patients who have baseline arterial O2 saturation over 90% on FiO2 of 0.6–0.8.</td>
</tr>
<tr>
<td>2.</td>
<td>Obtain baseline transcutaneous (or tissue) PO2 value.</td>
</tr>
<tr>
<td>3.</td>
<td>Increase FiO2 to 1.0.</td>
</tr>
<tr>
<td>4.</td>
<td>After 5 min, repeat transcutaneous (or tissue) PO2 measurement.</td>
</tr>
<tr>
<td>5.</td>
<td>If transcutaneous (or tissue) PO2 increases &gt;20–25 torr, patient can be assumed to have no flow-dependent oxygen consumption.</td>
</tr>
<tr>
<td>6.</td>
<td>If transcutaneous (or tissue) PO2 increases &lt;20 torr, provide therapy to increase oxygen delivery until step 5 is met.</td>
</tr>
</tbody>
</table>

4. Sublingual tonometry is a less invasive alternative to gastric tonometry, but this technology needs to be reinstated since it has been recalled.

5. Increased transcutaneous pCO₂ is an indicator of tissue acidosis.

6. The presence of decreased end-tidal pCO₂ in the face of normal arterial pCO₂ is an indicator of low cardiac output.

7. The response of transcutaneous or tissue oxygen monitors to an increased FiO₂ is an indication of the presence or absence of flow-dependent oxygen consumption. An increase in tissue oxygen of greater than 24 torr may be utilized as an end point of resuscitation.

References


