Commentary

Searching for non-invasive markers of tissue hypoxia

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Published: 23 February 2007
This article is online at http://ccforum.com/content/11/1/116

Critical Care 2007, **11:**116 (doi:10.1186/cc5691)

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Abstract

Tissue hypoxia is a common end product of circulatory shock and a primary target for resuscitation efforts. In this issue Podbregar and Mozina show that thenar tissue O_2 saturation (StO_2) and mixed venous O_2 saturation (SvO_2) co-vary in patients in left ventricular failure, but in patients with sepsis StO_2 was higher than SvO_2. Although StO_2 may co-vary with SvO_2 they have different determinants such that after shock StO_2 may increase well before SvO_2 as a result of increased O_2 demands to repay O_2 debt incurred during hypoperfusion. Thus, the use of StO_2 alone to define the endpoint of resuscitation may be misleading.

In this issue of the journal Podbregar and Mozina propose the use of tissue oxygen saturation (StO_2), monitored non-invasively with near-infrared spectroscopy of the thenar muscle, as a surrogate measurement of tissue perfusion [1]. They measured StO_2 in patients with left ventricular (LV) failure and with or without sepsis. They reasoned that StO_2 would discriminate between patients with low cardiac output and preserved or unimpaired O_2 extraction ratio (not present in septic patients) from those septic patients with poor ventricular function and low O_2 extraction ratio as assessed by SvO_2 [1]. Not unexpectedly, they found the lowest StO_2 values in patients with LV failure without sepsis. Interestingly, StO_2 was significantly higher in patients with both LV failure and sepsis than in normal volunteers. Unfortunately, the authors did not address the fundamental differences between peripheral StO_2 and SvO_2 even though they suggest that StO_2 may replace SvO_2 in the absence of sepsis. These issues deserve comment.

Severe shock is characterized by inadequate O_2 delivery relative to metabolic demands [2]. Unfortunately, present monitoring techniques for the assessment of O_2 delivery and O_2 utilization are invasive, impracticable, give an incomplete picture of the circulation, and may not be useful in guiding effective resuscitation, as documented by the poorer outcomes for SvO_2-guided therapy in patients with established shock [3,4]. Recently, however, early goal-directed therapy in patients with sepsis presenting to an emergency department improves outcome when central venous O_2 saturation is used as one of the endpoints of resuscitation [5]. Still, neither SvO_2 nor central venous O_2 provide any insight on the state of oxygen utilization in tissues.

The relationship between StO_2 and SvO_2 is not always predictable. Although StO_2 should decrease when tissues are starved of O_2 relative to their needs, the physiological events dictating changes in StO_2 and SvO_2 are different. Ischemic tissues initially sustain metabolism by anaerobic respiration, leading to an 'O_2 debt' shown by a transient increase in O_2 consumption during reoxygenation. Similarly, StO_2 must increase before SvO_2 increases because its increase is the cause of the increase in SvO_2. SvO_2 may therefore remain low for a while despite normalization of StO_2. Thus, with decreases in O_2 delivery one would expect both SvO_2 and StO_2 to decrease in parallel, but with resuscitation StO_2 should increase before SvO_2.

Shock is a complex process with neurovascular, metabolic and inflammatory responses occurring simultaneously. Changes in StO_2 capture the vasoconstriction associated with reduced cardiac output during progressive hypovolemia. In fact, StO_2 is as good a predictor of multiple organ dysfunction syndrome in trauma patients as base deficit, with the advantage that StO_2 is continuous and noninvasive [6]. Initially, the O_2 extraction ratio in hemorrhagic shock is high, and cellular metabolism is not compromised. However, as flow decreases, extremity flow usually decreases first; therefore decreases in thenar StO_2 should occur before significant visceral ischemia develops, and when thenar StO_2

LV = left ventricular; StO_2 = thenar tissue O_2 saturation; SvO_2 = mixed venous O_2 saturation.

has recovered after resuscitation most other organs should also show resolution of ischemia. Unfortunately, when shock progresses to generalized mitochondial dysfunction, tissue wellness will not be captured by StO_2 values alone. Therefore an ideal noninvasive monitoring platform for shock should indicate not only that O_2 delivery is impaired but also the extent to which this has affected cell metabolism. Such parameters may include tissue pH, partial pressure of CO_2, and ideally the levels of a mitochondrial function product such as NADH. Furthermore, many of these changes are dynamic and multidirectional depending on the integrity of the patient's compensatory response and the timeliness and effectiveness of the resuscitation.

It is necessary to understand the hysteresis of the StO_2 response throughout the continuum of shock and resuscitation. Such information is lacking in the report by Podbregar and Mozina. However, a physiologic perturbation such as inducing a brief episode of forearm ischemia as a circulatory stress test, to note the rapidity of re-oxygenation upon release, may be more revealing about the physiologic reserve of the patient and the metabolic activity of the muscle. We have used this approach in a fashion similar to that of De Blasi and colleagues [7]. Our preliminary study [8] supports previously published findings that resting StO_2 levels in both normal volunteers and patients with sustained circulatory shock are not dissimilar and thus cannot be used for early monitoring of tissue hypoperfusion [9]. However, by inducing an occlusion stress, emergent parameters can be defined that allow one to assess local metabolic demand and reperfusion reserve. Potentially, this approach might prove useful in clinical decision making. We are still searching for measures of circulatory adequacy, and non-invasive measures of StO_2 reflect one exciting avenue of exploration. Let us use it to define the adequacy of resuscitation therapy in those in circulatory shock. Whether its value may or may not track SvO_2 is less of an issue than its potential to define circulatory sufficiency.

Competing interests

The authors declare that they have no competing interests.

References

1. Podbregar M, Mozina H: **Skeletal muscle oxygen saturation dose not estimate mixed venous oxygen saturation in patients with severe left heart failure and additional severe sepsis or septic shock.** *Crit Care* 2007, **11:**R6.
2. Moore FA, McKinley BA, Moore EE: **The next generation in shock resuscitation.** *Lancet* 2004, **363:**1988-1996.
3. Hayes MA, Timmins AC, Yau EH, Palazzo M, Hinds CJ, Watson D: **Elevation of systemic oxygen delivery in the treatment of critically ill patients.** *N Engl J Med* 1994, **330:**1717-1722.
4. Gattinoni L, Brazzi L, Pelosi P, Latini R, Tognoni G, Pesenti A, Fumagalli R: **A trial of goal-oriented hemodynamic therapy in critically ill patients. SvO2 Collaborative Group.** *N Engl J Med* 1995, **333:**1025-1032.
5. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M; Early Goal-Directed Therapy Collaborative Group: **Early goal-directed therapy in the treatment of severe sepsis and septic shock.** *N Engl J Med* 2001, **345:**1368-1377.
6. Cohn SM, Nathens AB, Moore FA, Rhee P, Puyana JC, Moore EE, Beilman GJ; StO_2 in Trauma Patients Trial Investigators: **Tissue oxygen saturation predicts the development of organ dysfunction during traumatic shock resuscitation.** *J Trauma* 2007, **62:**44-54.
7. De Blasi RA, Palmisani S, Alampi D, Mercieri M, Romano R, Collini S, Pinto G: **Microvascular dysfunction and skeletal muscle oxygenation assessed by phase-modulation near-infrared spectroscopy in patients with septic shock.** *Intensive Care Med* 2005, **31:**1661-1668.
8. Torres A KH, Polanco P, Pinsky MR, Puyana JC: **Non-invasive real-time quantification of cardiovascular reserve in human circulatory shock [abstract].** *J Surg Res* 2006, **130:**279.
9. Crookes BA, Cohn SM, Bloch S, Amortegui J, Manning R, Li P, Proctor MS, Hallal A, Blackbourne LH, Benjamin R, Soffer D, Habib F, Schulman CI, Duncan R, Proctor KG: **Can near-infrared spectroscopy identify the severity of shock in trauma patients?** *J Trauma* 2005, **58:**806-813.