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Near infrared spectroscopy for evaluation of skeletal muscle tissue oxygenation in different types of shock

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Abstract

Clinical examination is non-invasive, but has well-recognized limitations in detecting compensated and uncompensated low flow states and their severity.

This paper describes the principles of near infra-red spectroscopy (NIRS) and the basis for its proposed use, in hypovolaemic, cardiogenic and septic shock, for assessing global and regional tissue oxygenation. The vascular occlusion test is explained. Limitations of NIRS, current controversies, and what is necessary in the future to make this technology a part of the initial and ongoing assessment of a patient, are discussed as well. The ultimate goal of such techniques is to prevent miss-assessment and inadequate resuscitation of patients, two major initiators in the development of multisystem organ failure and death.

Key words: shock, skeletal muscle, near-infrared spectroscopy

Introduction

Oxygen delivery (DO2) is acutely reduced in all types of shock. Consequently, tissue hypoxia occurs. Sustained tissue hypoxia is one of the most important factors in the pathophysiology of organ dysfunction. (1) Maintenance of DO2 is essential to preserve organ function, and sustained low DO2 is a path to organ failure and death. (2,3) Monitoring of global systemic and tissue oxygenation in critically ill patients appears indispensable for their treatment. (4) Cardiogenic, hypovolaemic and obstructive types of shock are characterized by decreased DO2, but a preserved oxygen extraction ratio. In septic shock, tissue oxygen extraction capability is altered so that the critical oxygen extraction ratio is typically decreased. (2,3)

Clinical signs of tissue perfusion adequacy (capillary refill, mottling of the skin, mental status, heart rate, pulse pressure, systemic blood pressure and urine output) are not sufficiently sensitive indicators of tissue perfusion. (5-7) Normalisation of these traditional clinical indices, after initial resuscitation, does not exclude on-going inadequate tissue perfusion. (8) The search for a more sensitive monitoring technology continues. (9) The ideal monitoring method should perform as a sensitive, early index of altered state of oxygen delivery and should also provide a goal for the treatment of low flow states, even before clinical signs are evident.

Mixed venous oxygen saturation (SvO2) was traditionally used to estimate global tissue oxygenation (oxygen delivery/oxygen consumption (VO2) ratio). But catheterization of the pulmonary artery is costly, has inherent risks and its usefulness remains under debate. (10-12) Not surprisingly, the monitoring of central venous oxygen saturation (ScvO2) was suggested as a simpler and cheaper assessment of global DO2 to VO2 ratio, (13) and was used successfully as a hemodynamic goal in the treatment of patients with septic shock and severe sepsis. (14) ScvO2 of 70% was subsequently included in the international guidelines as a hemodynamic goal for the management of severe sepsis and septic shock. (15)

Although the relationship between systemic and peripheral circulation is not always well defined, the assessment of peripheral perfusion during peripheral cooling-induced vasoconstriction in healthy volunteers has shown that profound changes in peripheral circulation can occur independently of systemic haemodynamic parameters, such as blood pressure and cardiac output. (16) Regional perfusion changes can occur significantly earlier than traditional global indices. (17) The rationale of peripheral perfusion monitoring is based on a concept that peripheral tissues are the first to reflect hypoperfusion during shock and the last to reperfuse during resuscitation. (18) Examples of technologies which may take advantage of regional changes and which may help identify these states, include transcutaneous partial pressure of oxygen (pO2) and carbon dioxide partial pressure (pCO_2), subcutaneous and interstitial pH, pCO_2, and pO_2 measurements, gastric and sublingual tonometry, and near-infrared absorption spectroscopy (NIRS). (9)

Principles of NIRS

The concept of NIRS has already been available during the second half of 20th century. (19) Visible light (450—700 nm) penetrates tissue only short distances because of strong attenuation by various tissue components. However, in the near infra-red (NIR) spectrum (700—1100 nm) photons are capable of deeper penetration (several centimetres or more), even through bone. Metalloproteins (haemoglobin, myoglobin and mitochondrial cytochrome oxidase) act as chromophores and absorb NIR radiation differently based on their concentration and interaction with oxygen. The Beer—Lambert law provides the physical and mathematical basis for NIRS. This law states that light passing through a solution of a coloured compound (chromophore) is absorbed by the compound resulting in a reduction in the intensity of the emerging light. (20) A probe with a near infrared light source is placed on the skin where it transilluminates tissues and detects reflected light.

The basis for the use of NIRS to monitor changes in haemoglobin (Hb) and oxyhaemoglobin (HbO_2), and to monitor states of tissue oxygenation, lies in the tissue compartmentalisation of blood volume, which in most organ systems is believed to be proportioned among the arteriolar, capillary, and venular compartments in a ratio of 10:20:70% respectively. (21,22) Consequently, the majority of the NIRS signal, reflects the venous or post-extraction compartment of any particular tissue. This phenomenon provides valuable information on tissue oxygen consumption or extraction in much the same way as mixed venous haemoglobin oximetry is used from the pulmonary artery catheter. The NIR value of haemoglobin oxygen saturation from the tissue (StO_2) thus represents spatially integrated information from arterioles, capillaries, and venules, which are normally weighted towards the venous compartment. Larger vessels (>1mm) are assumed to be excluded from StO_2 determination. (23)

Clinical and technical considerations in NIRS measurements

Microcirculatory perfusion and tissue oxygen utilization are affected by sepsis and shock. (24,25) These derangements can be studied non-invasively using NIRS, a technique that is able to determine the oxygenation status of tissue haemoglobin. Decreased StO2 reflects the presence of hypoperfusion and has been used clinically to guide resuscitation during hypovolaemic shock. (26) Thus, determination of regional StO2 might provide an early warning index of global hypoperfusion prior to significant alterations in vital signs or critical DO2 and help the clinician to verify that oxygen delivery to the tissue had been restored to a desired level.

Measurements of StO2 are noninvasive, continuous, bedside and simple. NIRS equipment is becoming light and easy to handle – all these characteristics make this method fit for emergency and critical care use.

The anatomical advantages of the thenar eminence are: the easy bedside approach; the thenar eminence can be easily subjected to the vascular occlusion test; has relatively thin skin and fat tissue over the muscle; and fibrous strands in its subcutaneous tissue limit oedema formation. All these characteristics make the thenar eminence the best possible setting for StO2 measurements, even in critically ill or obese patients.

In a human validation study, a significant correlation between NIRS measured StO2 and venous oxygen saturation ($r=0.92$, $p < 0.05$) was reported, where the venous effluent was obtained from a deep forearm vein that drained the exercising muscle. (27) StO2 was minimally affected by skin blood flow. Changes of limb perfusion affect StO2: skeletal muscle StO2 decreases during norepinephrine and increases during nitroprusside infusion.

Choosing the right probe is crucial. The distance between the source of NIR light and the receiver of reflected light defines the depth and the volume of the transilluminated tissues under the probe. If one uses a 15 mm probe, penetration is only 7,5 mm, thus the measurements will be importantly influenced by the skin and subcutaneous tissue oxygenation and will not represent skeletal muscle oxygenation. At our department we use deep penetrating probes (25 mm probes) and probes with filtering of superficial structures. (28)

The discriminatory power and predictive ability of StO2 can be improved by measuring the response to an ischaemic challenge. The vascular occlusion test (VOT) is a provocative test in which StO2 is measured at a peripheral site (such as the thenar eminence) whilst a transient rapid vascular occlusion is performed (above elbow cuff inflation to 260 mmHg) for either a defined time interval or until a pre-defined StO2 value is reached. During the vascular occlusion test, several StO2 parameters can be studied: average StO2 before arterial cuffing/occlusion; StO2 downslope during cuffing- the deoxygenation rate (Δdown StO2)/sec); StO2 upslope (Δup StO2)/sec); hyperaemia (overshoot of StO2 above baseline) (figure 1). The deoxygenation rate is a surrogate for tissue oxygen consumption. (25) StO2 and arterial oxygen saturation measured by transcutaneous pulse oxymetry can be used to calculate fractional tissue oxygen extraction according to the formula: (SaO2 – rStO2)/SaO2. (29)

NIRS for evaluation of skeletal muscle tissue oxygenation in hypovolaemic shock

During hypovolaemic shock, blood flow is diverted from less important tissues to vital organs leading to decreased blood flow in muscles. Activation of the sympathetic nervous system should decrease thenar muscle blood flow, with increased oxygen extraction and decreased tissue haemoglobin content. (18,30) In this setting, NIRS may thus act as a sensor of the vascular response to hypovolaemia. This hypothesis was tested in trauma patients and the perioperative period.

Already in the late 1990s, at the University of Texas Houston Medical School, a team of surgical intensivists collaborated with bioengineers and health information experts to improve traumatic shock resuscitation. They tested the utility of various monitors in this process of care. One such monitor was StO2. Throughout resuscitation, skeletal muscle StO2 appeared to be quite responsive to changes in systemic DO2. SvO2 derived from the pulmonary artery (PA) catheter showed only a small rise from roughly 70 to 78% during the resuscitation process, changes in StO2 showed a strong correlation with changes in DO2, base deficit, and lactate (r = 0.95 vs. 0.83 vs. 0.82, respectively) but only modest correlation with SvO2 (r = 0.55). (26)

Furthermore, trauma patients who develop multiorgan dysfunction (MODS) or die, have a lower StO2 within 1 hour of admission, and StO2 is a stronger predictor of MODS or death than other diagnostic modalities. (31,32) A low StO2 within 1 hour of admission identifies trauma patients who will require blood transfusion within the next 24 hours. (33)

An area of central interest in anaesthesia is the ability of NIRS measurements in the thenar muscle to detect blood loss. Data are conflicting. A 500-ml blood loss at blood donation in awake volunteers did not lead to changes in StO2. (34) A possible explanation could be that tissue haemoglobin and oxygenation at the thenar eminence are not affected by blood loss within the capacity of the compensatory mechanisms of hypovolaemia. However, StO2 during the perioperative period in cardiac surgery is lower in patients who develop certain postoperative complications. (35)

NIRS for evaluation of skeletal muscle tissue oxygenation in cardiogenic shock

Measurement of mixed venous oxygen saturation (SvO2) from the pulmonary artery is used for calculations of oxygen consumption and has been advocated as an indirect index of tissue oxygenation and prognostic predictor in critically ill patients. (36-39) We studied skeletal muscle StO2 in severe left heart failure with or without additional severe sepsis, and compared it with SvO2. (40) The hypothesis was that skeletal muscle StO2 could estimate SvO2 in patients with severe left heart failure and preserved oxygen extraction capability (without severe sepsis/septic shock).

In patients with severe left heart failure ($n = 24$) StO2 was lower than in healthy volunteers (58 ± 13% and 84 ± 4%, respectively; $p < 0.001$). There was a good correlation between StO2 and SvO2 (figure 2), and between SvO2 and plasma lactate ($r = 0.689$, $p = 0.002$, $r = -0.522$, $p = 0.009$, respectively). StO2 and SvO2 tracked well with each other over time, although StO2 overestimated SvO2 with a bias of – 2.3% and a precision 4.6%.

The result confirmed the hypothesis that skeletal muscle StO2 values in patients with severe left heart failure could be used for fast non-invasive SvO2 estimation; and the trend of StO2 may be substituted for the trend of SvO2. StO2 overestimated SvO2 (bias -2.5%). (40) Overestimation may be due to the NIRS method, which does not discriminate between compartments. It provides a global assessment of oxygenation in all vascular compartments (arterial, venous and capillary) in the sample volume of underlying tissue.

Our data in patients with severe heart failure/ cardiogenic shock without severe sepsis/ septic shock are supported by previous work from Boekstegers et al. who measured the oxygen partial pressure distribution in the biceps muscle. (41) They found low peripheral oxygen availability in cardiogenic shock compared to sepsis. In cardiogenic shock, skeletal muscle oxygen partial pressure correlated with systemic oxygen delivery ($r=0.59$, $p < 0.001$) and systemic vascular resistance ($r=0.74$, $p < 0.001$). In a recently published study in patients experiencing cardiogenic shock, significant correlations between StO_2 values and cardiac index (CI) (Spearman $r=0.81$; $p < .0001$), systemic vascular resistance index ($r=-0.45$; $p < .0001$), and mean arterial pressure ($r=0.58$; $p < .0001$) were found. Linear regression analysis revealed that CI could be calculated using the following equation: $CI = StO_2/24.0$. (42)

NIRS for evaluation of skeletal muscle tissue oxygenation in septic shock

In sepsis, StO_2 values can be at the higher end of the normal spectrum (40,43,44) or markedly low. (45,46) In early stage septic shock, low StO_2 values (i.e., $StO_2 < 75\%$), when measured on the thenar eminence, specifically predict extremely low $ScvO_2$ values and higher mortality. (46,47)

Our research group confirmed De Blasi group's findings (48) that thenar muscle tissue deoxygenation during stagnant ischaemia at admission and after haemodynamic stabilisation is significantly slower in septic shock patients compared to severe sepsis, localized infection and healthy controls. (44) The rate of StO_2 decrease correlated tightly with severity of septic shock (Sequential Organ Failure Assessment score) and weakly with norepinephrine requirement, plasma lactate and C-reactive protein concentrations. The muscle tissue deoxygenation rate increased with improvement of sepsis in the septic shock and severe sepsis group. (44) These results are in accordance with those reported in a baboon septic shock model. (49) These data were interpreted as being consistent with the presence of a defect in the ability of the enzyme to accept electrons from oxygen or a limitation in the availability of the reducing equivalent. Similar results were reported in the dog gracilis muscle preparation after treating the animals with endotoxin. (50)

This local oxygen consumption limitation may be due to two different but cumulative mechanisms: first – a local dependency on low flow or inadequate flow conditions (46) or second – a low oxygen extraction due to mitochondrial dysfunction and/or alteration of oxygen diffusion (interstitial oedema). (25,46,48) Although the mechanism involved in sepsis resuscitation is not yet fully understood, it is clear that the persistence of impaired peripheral perfusion is associated with worse patient outcomes. (51)

In the previously described study of patients with severe left heart failure, with or without additional severe sepsis/septic shock (40), we hypothesized a disagreement between StO_2 and SvO_2 in the group of patients with sepsis, because in patients with decreased oxygen extraction capability (with severe sepsis/septic shock), blood flowing through upper limb muscles could importantly contribute to higher venous oxygen saturation in the superior vena cava. The results confirmed the hypothesis (figure 2). StO_2 correlated neither with SvO_2 nor with serum lactate.

The high StO_2 / low SvO_2 seen in severe sepsis and septic shock, suggest blood flow redistribution. StO_2 probably correlates with $ScvO_2$ which is measured in the mixture of blood from head and both arms. (52) In healthy resting individuals $ScvO_2$ is slightly lower than SvO_2. (53) This relationship changes in periods of cardiovascular instability. Scheinman and co-workers performed the earliest comparison of $ScvO_2$ and SvO_2 in both haemodynamically stable and shocked patients . (54) In stable patients, $ScvO_2$ was similar to SvO_2. In patients with a failing heart, $ScvO_2$ was slightly higher than SvO_2 and in shock patients the difference between SvO_2 to $ScvO_2$ was even more expressed (47.5% ± 15.11% vs. 58.0% ± 13.05%, respectively, $p < 0.001$). Lee and co-workers described similar findings. (55) Other more detailed studies in mixed groups of critically-ill patients designed to test if the $ScvO_2$ measurements could substitute the SvO_2 showed problematically large confidence limits (56) and poor correlation between the two values. (57)

The hypothesis that the slower skeletal muscle StO_2 deoxygenation rate (more disturbed tissue oxygen extraction) is proportional to the $ScvO_2$-SvO_2 difference in patients with severe heart failure with additional sepsis/septic shock, was confirmed by our more recent study. (58) We showed that these patients had a clinically considerable $ScvO_2$-SvO_2 discrepancy. Monitoring $ScvO_2$ is a simpler and cheaper assessment of global DO_2 to oxygen consumption ratio, but its use as a treatment goal in patients with severe heart failure, with additional sepsis/septic shock, is questionable. Higher levels of ScvO2 in patients in the latter stages of septic shock were found in the non-survivors. (59) These findings raise concerns about high levels of ScvO2 in patients with septic shock. Consequently, ScvO2 or probably StO2, as a treatment goal, provides a false favourable impression of adequate body perfusion. Future studies that implement NIRS into treatment algorithms are ongoing.

Summary

The present review provides a foundation for understanding the potential value and limitations of NIRS as a tool in the assessment of patients with different types of shock. Despite continuous controversies, skeletal muscle NIRS clearly takes monitoring from a global to a local level, from invasive to non-invasive, and closer to the entrance to the hospital.

In low cardiac output states, with preserved oxygen extraction ratio (cardiogenic, hypovolaemic types of shock), StO2 measurements correlate well with invasive global indexes of oxygen delivery and consumption. In hypovolaemic shock and in the perioperative period, StO2 is a good prognostic tool. In septic shock the oxygen extraction capability is altered, and StO2 correlates better with ScvO2 than with SvO2, however, correlation coefficients are relatively low. In patients with severe sepsis and severe heart failure StO2 did not estimate SvO2, but, in the end, data suggest that in patients in early phase of septic shock low StO2 predicts low ScvO2 and higher mortality.

Dynamic StO2 monitoring, with vascular occlusion test, is a promising technique with the potential of insight into microvascular and mitochondrial function. Used in conjunction with global measures of oxygen delivery, it could provide an integrated approach to haemodynamic resuscitation in different types and phases of shock.

Figure 1. Vascular occlusion test: An original thenar saturation from the tissue (StO2) recording after arterial upper arm cuffing, and cuffing release (upper arm ischaemia reperfusion test). During the upper arm ischaemia reperfusion test, several StO2 parameters can be studied: average StO2 before arterial cuffing/occlusion; StO2 downslope during cuffing-the deoxygenation rate (Δdown StO2)/sec); StO2 upslope (Δup StO2)/sec); hyperaemia (overshoot of StO2 above baseline). Reproduced from Mozina and Podbregar. (25)

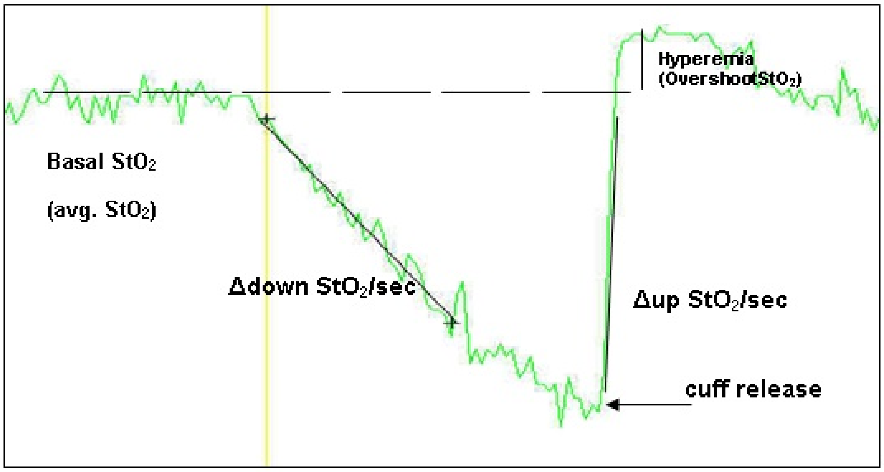
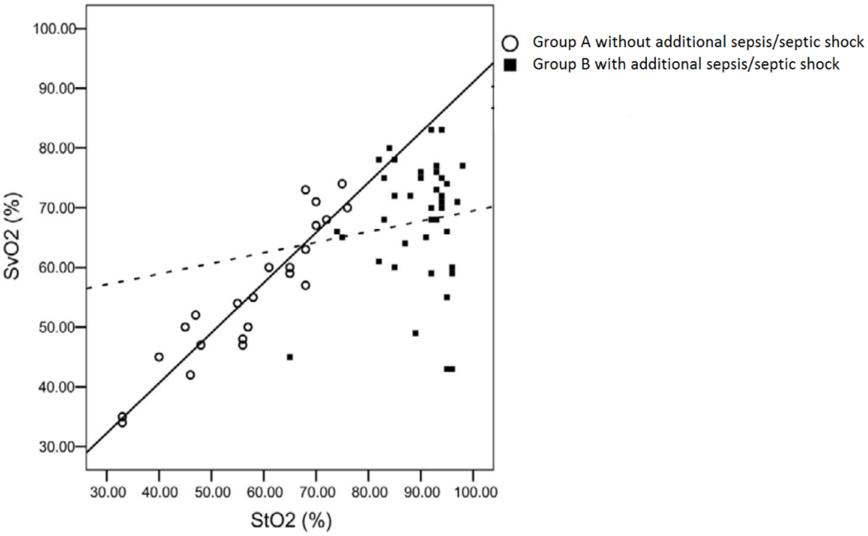


Figure 2. Correlation between skeletal muscle saturation from tissue (StO2) and mixed venous oxygen saturation (SvO2). Group A includes patients with severe left heart failure without severe sepsis/septic shock, and group B includes patients with primary heart disease and additional severe sepsis/septic shock. A statistically significant correlation was found in group A (r = 0.689, p = 0.002) but not in group B (r = -0.091, p = 0.60). StO2, tissue oxygenation; SvO2, mixed venous oxygen saturation. Modified from Podbregar and Mozina. (40)



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