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How I use skeletal muscle Near Infrared Spectroscopy to non-invasively assess hemodynamic status of the critically ill

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ABSTRACT

The major goal of hemodynamic treatment is to reach adequate flow. Near infrared spectroscopy (NIRS) allows non-invasive assessment of skeletal muscle tissue oxygenation during rest and also during vascular occlusion test (VOT). VOT allows estimation of tissue oxygen extraction capability, which could be preserved (i.e. hypovolemic, obstructive and cardiogenic shock) or inappropriate (i.e. sepsis/septic shock). By using ultrasound to estimate cardiac output, arterial hemoglobin oxygen saturation, skeletal muscle NIRS, arterial lactate and hemoglobin, therapeutic goals in critically ill patients with preserved oxygen extraction capability can easily be targeted. Current controversies of NIRS technology and approach to patients with impaired oxygen extraction are discussed as well.

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

INTRODUCTION

Clinical examination (capillary refill, mottling of the skin, mental status, heart rate, pulse pressure, systemic blood pressure and urine output) is non-invasive but has well-recognized limitations in detecting compensated and uncompensated low flow states and their severity (1-3). 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 (4). Maintenance of DO2 is essential to preserve organ function and sustained low DO2 is a path to organ failure and death (5, 6). Monitoring of global systemic and tissue oxygenation in critically ill patients appears indispensable for their treatment (7). Cardiogenic, hypovolemic and obstructive types of shock are characterized by a decreased DO2 but preserved oxygen extraction ratio. In septic shock, the tissue oxygen extraction capability is altered so that the critical oxygen extraction ratio is typically decreased (5, 6).

Mixed venous oxygen saturation (SvO2) was traditionally used to estimate global tissue oxygenation (oxygen delivery/oxygen consumption (VO2) ratio). However, pulmonary artery catheterization is costly, has inherent risks and its usefulness remains under debate (8-10). Not surprisingly, the monitoring of central venous oxygen saturation (ScvO2) was suggested as a simpler and cheaper assessment of global DO2 to VO2 ratio (11). It was used successfully as a hemodynamic goal in treatment of patients with septic shock and severe sepsis (12). ScvO2 of 70% was subsequently included in the international guidelines as a hemodynamic goal for management of severe sepsis and septic shock.

Regional perfusion changes can occur significantly earlier than traditional global indices (13). 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 (14).

Clinical approach to the critically ill

In critically ill patients, the time to definitive diagnosis and adequate treatment saves lives (Figure1). There are two major focuses in clinical workflow. The first major focus is to make definitive diagnosis, which allows us to proceed with specific treatment. The second major focus is to provide adequate oxygen delivery. It is essential to always consider the equation of oxygen consumption divided by oxygen delivery (Figure 2). We can manipulate the oxygenation, metabolism, blood oxygen content and flow. Point of care ultrasound allows us to estimate the heart function (i.e. systolic and diastolic function, preload assessment, cardiac output, valve function, perfusion of tissue/organs) indicating the flow and sometimes uncovering the definitive problem (e.g. endocarditis with severe valve dysfunction, mitral valve prolapse due to papillary muscle rupture) . We can easily determine the lactate clearance and the urine output, but they are relatively slow physiological variables. In the following text, we would like to describe the advantages and drawbacks of skeletal muscle near-infrared spectroscopy (NIRS) to estimate global adequacy of flow (i.e. SvO2, SvcO2).

BASIC PRINCIPLES OF NEAR-INFRARED SPECTROSCOPY

The concept of NIRS has already been available during the second half of the 20th century (15-17). In the near infrared (NIR) spectrum (700—1100 nm) photons are capable of deeper tissue penetration (several centimeters or more), even through bone. Metalloproteinase (hemoglobin, 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: light passing through a solution of a colored compound (chromophore) is absorbed by the compound resulting in a reduction in the intensity of the emerging light (18).

The basis for the use of NIRS to monitor changes in de-oxy hemoglobin (Hb) and oxyhemoglobin (HbO2) 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 (19, 20). Consequently, the majority of the NIRS signal reflects the venous or post-extraction compartment of any particular tissue. This phenomenon provides valuable information on the tissue oxygen consumption or extraction in much the same way as mixed venous hemoglobin oximetry is used from the pulmonary artery catheter. The NIRS value of hemoglobin oxygen saturation from the tissue (StO2) 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 StO2 determination (21).

CLINICAL AND TECHNICAL CONSIDERATIONS IN NIRS MEASUREMENTS

Microcirculatory perfusion and tissue oxygen utilization are affected by sepsis and shock (22, 23). Decreased StO2 reflects the presence of hypoperfusion and has been used clinically to guide resuscitation during hypovolemic shock (24). 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, simple, NIRS equipment is becoming light and easy to handle - all characteristics that make this method fit for emergency and critical care use (25, 26).

The thenar eminence has anatomical advantages and 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 the edema formation.

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.

The distance between the source of NIRS 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, the penentration 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 ischemic 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 or 50mmHg over systolic arterial pressure) 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 (Figure 3). Only NIRS devices allowing high sampling and refreshing rate are suitable for VOT.

NIRS FOR EVALUATION OF SKELETAL MUSCLE TISSUE OXYGENATION IN HYPOVOLEMIC SHOCK

During hypovolemic 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 hemoglobin content (14, 29).

Throughout resuscitation, skeletal muscle StO2 appeared to be quite responsive to changes in systemic DO2. SvO2 derived from the 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 ($r = 0.55$) (24).

Furthermore, those trauma patients who develop multiorgan dysfunction or die have lower StO2 within 1 hour of admission, and StO2 is stronger predictor of multiorgan dysfunction or death than other diagnostic modalities (30, 31). Low StO2 within 1 hour of admission identifies trauma patients who will require blood transfusion within the next 24 hours (32).

An area of central interest in anesthesia is the ability of NIRS measurements in thenar muscle to detect blood loss, however, data are conflicting. A 500-ml blood loss at blood donation in awake volunteers did not lead to changes in StO2 (33). A possible explanation could be that tissue hemoglobin and oxygenation at the thenar eminence are not affected by blood loss within the capacity of the compensatory mechanisms of hypovolemia. However, StO2 during the perioperative period in cardiac surgery is lower in patients who develop certain postoperative complications (34).

The resting skeletal muscle StO2 in patients with chronic anemia is lower than StO2 in controls and the storage time of red blood cells influences the change of StO2 after transfusion (35).

NIRS FOR EVALUATION OF SKELETAL MUSCLE TISSUE OXYGENATION IN CARDIOGENIC SHOCK

We studied skeletal muscle StO2 in patients with severe left heart failure due to primary heart disease (left ventricular systolic ejection fraction < 40%, pulmonary artery occlusion pressure > 18 mmHg) with or without additional severe sepsis, and compared it with SvO2 (36). 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 ($58 \pm 13\%$ and $84 \pm 4\%$, respectively; $p < 0.001$). There was a good correlation between StO2-SvO2 and between SvO2 -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%) (36). Overestimation may be due to the NIRS method, which does not discriminate between vascular compartments of underlined tissue.
Our data is supported by previous work of Boekstegers et al. who measured the oxygen partial pressure distribution in the biceps muscle (37). 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 StO2 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 = StO2/24.0 (38).

NIRS FOR EVALUATION OF SKELETAL MUSCLE TISSUE OXYGENATION IN SEPTIC SHOCK

In sepsis StO2 values can be at the higher end of the normal spectrum (36, 39, 40) or markedly low (41, 42). In the early stage of septic shock low StO2 values (i.e., StO2 < 75%) when measured on the thenar eminence) specifically predict extremely low ScvO2 values and higher mortality (43, 42).
The thenar muscle tissue deoxygenation during stagnant ischemia at admission and after hemodynamic stabilization is significantly slower in septic shock patients compared to severe sepsis, localized infection and healthy controls (40, 44). The rate of StO2 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 (40). These results are in accordance with those reported in a baboon septic shock model (45). 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 (46).
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 (42) or second - a low oxygen extraction due to mitochondrial dysfunction and/or alteration of oxygen diffusion (interstitial edema) (42, 44, 23). 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. (47)
The previous chapter described a study in patients with severe left heart failure with or without additional severe sepsis/septic shock (36), we hypothesized disagreement between StO2 and SvO2 in the group of patients with sepsis, because in patients with a 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. StO2 correlated neither with SvO2 nor with serum lactate.
The high StO2 / low SvO2 seen in severe sepsis and septic shock, suggest blood flow redistribution. StO2 probably correlates with ScvO2, which is measured in the mixture of blood from the head and both arms (48). In healthy resting individuals, ScvO2 is slightly lower than SvO2 (49). This relationship changes in periods of cardiovascular instability. Scheinman and co-workers performed the earliest comparison of ScvO2 and SvO2 in both hemodynamically stable and shocked patients (50). In stable patients, ScvO2 was similar to SvO2. In patients with a failing heart ScvO2 was slightly higher than SvO2 and in shock patients the difference between SvO2 to ScvO2 was even more expressed ($47.5\% \pm 15.11\%$ vs. $58.0\% \pm 13.05\%$, respectively, $p<0.001$). Lee and co-workers described similar findings (51). Other more detailed studies in mixed groups of critically-ill patients designed to test if the ScvO2 measurements could substitute the SvO2 showed problematically large confidence limits (52) and poor correlation between the two values (53).
The hypothesis that slower skeletal muscle StO2 deoxygenation rate (more disturbed tissue oxygen extraction) is proportional to the ScvO2-SvO2 difference in patients with severe heart failure with additional sepsis/septic shock was confirmed (54). We showed that these patients had a clinically considerable ScvO2-SvO2 discrepancy. Monitoring ScvO2 is a simpler and cheaper assessment of global DO2 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 level of ScvO2 in patients in the latter stages of septic shock was found in the non-survivors (55). 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 favorable impression of an adequate body perfusion. Future studies that implement NIRS into treatment algorithms are ongoing. Our proposed algorithm for use of skeletal muscle StO2 in critically ill patients is presented in Figure 4.

SUMMARY

The present review provides a foundation to understand the potential value and limitations of skeletal muscle NIRS as a tool in the assessment of patients in different types of shock. Despite continuous controversies, skeletal muscle NIRS clearly takes monitoring from global to local level, from invasive to non-invasive, and closer to the entrance in the hospital.
In low cardiac output states with preserved oxygen extraction ratio (cardiogenic, hypovolemic types of shock) StO2 measurements correlate well with invasive global indexes of oxygen delivery and consumption. In hypovolemic shock and in 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 measurements of oxygen delivery it could provide an integrated approach to hemodynamic resuscitation in different types and phases of shock.

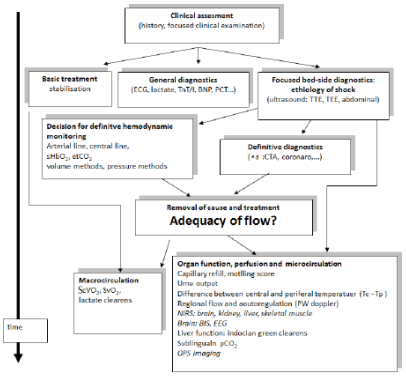

Fig 1. Diagnostic and therapeutic approach

ECG- electrocardiogram, TnT/I – cardiac troponin, BNP- brain natriuretic peptide, PCT- procalcitonin, TTE- transthoracic echocardiography, TEE- trans-esophageal echocardiography, sHbO2- arterial hemoglobin saturation, etCO2- end tidal CO2, CTA-computer tomography, SvO2-mixed venous oxygen extraction, ScvO2-central venous oxygen saturation, NIRS- near infrared spectroscopy, BIS-bispectral index, EEG –electroencephalography, pCO2-CO2 partial pressure, OPS- orthogonal polarization spectral imaging

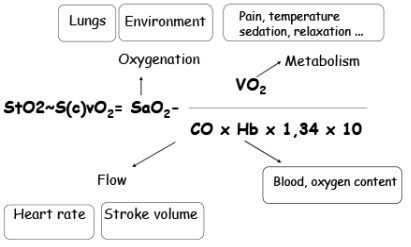

Fig 2. Diagnostic and therapeutic approach to assessment of adequacy of flow based on oxygen consumption/delivery relationship presented as central /mix venous oxygen saturation and its relationship with skeletal muscle tissue oxygenation

StO2-tissue oxygen saturation, SvO2-mixed venous oxygen extraction, ScvO2-central venous oxygen saturation, VO2-oxygen consumption, CO- cardiac output, Hb- arterial hemoglobin concentration, SaO2- arterial hemoglobin saturation

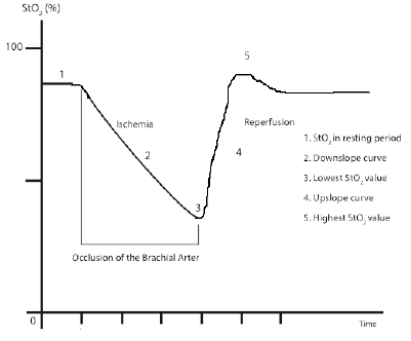

Fig 3. Schematic presentation of thenar skeletal muscle StO2 before, during and after vascular occlusion test

During the vascular occlusion the skeletal muscle StO2 gradually declines from resting StO2 (basal StO2). The rate of deceleration is determined form the StO2 downslope curve (downslope StO2 curve, tissue deoxygenation, %/min) as surrogate of tissue oxygen consumption. After reaching predetermined minimal StO2 value (lowest StO2 value) the vascular occlusion is released and StO2 value begins to rise. The velocity of upslope curve (upslope StO2 curve, %/min) is determined as surrogate marker of microcirculatory reactivity. After the occlusion StO2 increases to higher values compared to basal StO2 due to post-ischemic vasodilatation (highest StO2 value, %). StO2 slowly returns to resting StO2.

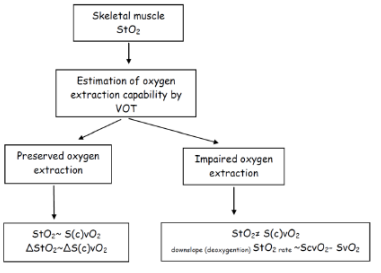

Fig 4. The algorithm for skeletal muscle StO2 use in critically ill patients

VOT-vascular occlusion test, StO2-tissue oxygen saturation, SvO2-mixed venous oxygen extraction, ScvO2-central venous oxygen saturation

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