Review Article

Non-Invasive Tissue Oximetry—An Integral Puzzle Piece

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Abstract: Non-invasive tissue oximetry is a monitoring method for continuous assessment of tissue oxygenation, which may aid in detection of hemodynamic instability and otherwise unnoticed hypoxia. Numerous studies focused on using non-invasive tissue oximetry intraoperatively, proposing its predictive value in relation to clinical outcome. Tissue oximetry may be part of standard monitoring practice for brain monitoring during cardiac surgery in many clinical centers; however, the monitoring method can be deployed in numerous clinical settings. This succinct overview aims to determine the role of non-invasive tissue oximetry in current clinical practice.

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Comprehensive development of diagnostic and monitoring technologies in modern medicine has helped to better understand the complex pathophysiology of acute circulatory failure in critical cases such as surgical patients or patients admitted to the intensive care unit. In critical care settings, it is vital to assess the patient’s hemodynamic status for optimization of end-organ tissue oxygenation to prevent or minimize morbidity and mortality (1). It is, however, challenging to monitor the state of tissue oxygenation accurately. The use of standard hemodynamic parameters such as blood pressure and pulse oximetry for assessing tissue blood flow is less than accurate (2,3). Despite apparently normal macroperfusion (capillary refill, cardiac output, and blood pressure), tissue hypoperfusion can persist as a result of microcirculatory perfusion defects (4). Various approaches have been introduced to avoid such hypoperfusion—mostly with disappointing or controversial results. A randomized trial of protocol-based care for early septic shock showed that the early goal-directed therapy strategy for septic shock not only proves no survival benefits but also might increase the risk of fluid overload (5). Thus, measuring heart rate, cardiac output, arterial blood pressure, and mixed venous oxygen saturation solely provides information regarding the patient’s central hemodynamic status, reflecting macroperfusion, and normalization of these hemodynamic variables does not ensure sufficient oxygenation at the peripheral tissue level (6,7). The introduction of near-infrared spectroscopy for assessing the adequacy of regional tissue perfusion was an important landmark in the history of tissue monitoring (8). Since then, monitoring regional tissue oxygenation has gained wide interest, and studies began to address the importance of monitoring tissues susceptible to hypoperfusion. Non-invasive tissue oximetry uses near-infrared light for continuous assessment of tissue oxygenation, which may aid in timely detection of hemodynamic instability and otherwise unnoticed hypoxia. To date, numerous studies (of which mostly observational) focused on the use of non-invasive tissue oximetry in surgical patients, elucidating on its predictive value in relation to clinical outcome (9,10,11). Tissue oximetry may be part of standard monitoring practice for brain monitoring during cardiac surgery in many clinical centers; however, the monitoring method can be deployed in various clinical settings.

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Given the diversity of technologies currently available to assess tissue oxygenation status, it is important to consider various applications of non-invasive tissue oximetry. This succinct overview aimed to determine the role of these applications in current clinical practice.

CEREBRAL OXIMETRY AS A TOOL TO PREVENT NEUROLOGICAL COMPLICATIONS

Cerebral oximetry, in particular, is a commonly used application of tissue oximetry with its focus on prevention of neurological complications following cardiac surgery. These complications, including stroke, are highly complex in nature and elicited by a multitude of preoperative and perioperative factors. Hypoperfusion resulting in intraoperative cerebral hypoxia is generally accepted as a factor contributing to the risk of adverse neurologic outcomes (12,13). Although the exact etiology is not yet completely understood, continuous assessment of tissue perfusion may aid in a better understanding of the role of tissue hypoxia in the development of postoperative cognitive complications. Although the incidence of neurological complications may appear relatively low, the effects on the patient’s physical and psychological health are tremendous with serious implications for the quality of life (14). The reported incidence of stroke following cardiac surgery varies around 1.6–2.3% (15,16). Postoperative stroke entails prolonged hospital stays of, on average, 7 days with an incremental increase of hospital resources (17,18). In the United States, for each affected patient, the estimated added costs make up to $18,552, of which $1,000 is attributable to each additional day of hospitalization (19). Another type of neurological complication that may emerge following cardiac surgery is delirium, which is characterized by a state of reversible confusion and inattention. Although often seen as a result of perioperative period (e.g., aortic cross-clamping and embolism originated from the cardiopulmonary bypass circuit) and the role of certain patient characteristics is not subject to change (pre-existing co-morbidities and positive family history of adverse neurovascular events). Another substantial proportion with less of a complex etiology is caused by modifiable factors, and therefore theoretically concerns preventable cases. For example, hemodynamic instability is known to affect the risk of hypoxia. Moreover, hypercapnia and excessive hemodilution are thought to alter the risk of neurological complications (27,28). The cardiopulmonary bypass protocol is, therefore, an important factor in enabling and maintaining adequate tissue perfusion and should be critically evaluated to minimize the risk of neurologic complications. Strict monitoring routines concern another factor of importance in preserving hemodynamic integrity, specifically monitoring at the tissue level because general hemodynamic factors may not adequately represent local tissue oxygenation status (6).

With non-invasive tissue oximetry on the rise and being increasingly applied as a brain monitor, the tool appears to be a viable assessment method for diverting adverse neurologic outcome (29). On that note, cerebral oximetry showed to adequately reflect real-time changes in tissue oxygenation readings following several iatrogenic events (10). Despite the abundance of studies implying that oxygen desaturations detected by cerebral oximetry predict neurological outcome, evidence for a causal relationship remains scarce. Part of the explanation can be found in the fact that the development of neurological complications is a complex process, which is still not entirely understood. Deoxygenation episodes detected by cerebral oximetry should be considered as a contributor, rather than an independent causative factor for clinical neurologic damage and evident changes in neurocognitive function (30). In addition, cerebral oximetry solely focuses on regional concentrations of oxygenated and deoxygenated hemoglobin, and therefore, inherently because of its measurement principle, cannot account for cerebrovascular autoregulatory activity. Cerebral autoregulation (CA) ensures a constant cerebral blood flow despite fluctuations in perfusion pressure by continuous control and modification of cerebrovascular resistance. The autonomous cerebral protective system provides protection against hypoxia and
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hyoxia resulting from hypoperfusion and hyper-
perfusion. Although often unacknowledged, disturbances in
autoregulatory function have been shown to result in neu-
rologic complications and thus should be avoided at all
times (31).

Although cerebral oximetry has been shown to con-
tribute to early detection of hypoxia, its measurement
values can potentially be deceptive because disturbances in
CA can remain unnoticed. This is illustrated by the ob-
servation of seemingly normal cerebral oximetry readings
during cerebral hyperperfusion (i.e., “brain luxury perfu-
sion”), while the cerebral autoregulatory activity is im-
peded (32).

Therefore, it is important to consider CA when per-
forming cerebral oximetry. A perfusion protocol that in-
cludes maintaining modifiable factors such as arterial
partial gas pressure to carbon dioxide and intraoperative
hematocrit factors within the physiologic range confers to
the observed low incidence of neurological complications
by enabling intact autoregulatory function (27,28). Rather
than solely focusing on preserving cerebral regional tissue
oxygen saturation (rSO2) within certain predefined limits,
maintaining intact CA should be of primary importance in
minimizing neurologic complications. Similar to most non-
invasive monitoring tools and methods, tissue oximetry
readings should be interpreted in the context of all clinical
information available.

PROSPECTIVE APPLICATIONS OF
TISSUE OXIMETRY

Besides its original intended use (i.e., brain monitoring),
non-invasive tissue oximetry is increasingly applied in so-
matic tissue monitoring. One example is assessment of
distal limb perfusion in patients supported by veno-arterial
extracorporeal life support (VA-ECLS). Femoral access
techniques are often used in VA-ECLS and may com-
promise limb perfusion, therefore predisposing the patient
to concomitant tissue damage with potential disastrous
effects (33,34). Tissue oximetry performed at the calf
muscle proved effective for identification of endangered
limb perfusion by showcasing aberrant tissue oximetry
readings before any other clinical parameters showed any
evident change (34).

Another example of somatic tissue oximetry applies to
monitoring autologous breast reconstructive surgery, in
which abdominal wall tissue is transplanted to the chest
area using microsurgical anastomoses. Graft failure, in the
worst case, could lead to loss of the entire tissue flap with a
major additional risk of physical and psychological burden
for the patient. By immediately depicting deviant mea-
surement values as compared with the expected physi-
ological tissue response, tissue oximetry appears superior to
other applied monitoring techniques, which solely provide
delayed timing of alarm signals. Tissue oximetry could aid
in timely detection of circulatory compromise and thereby
lower the rate of complications resulting from ischemic
tissue damage (35). Successively, avoiding complications
contributes to minimizing postoperative morbidity and
mitigating health-care costs. As is the case in brain mon-
itoring, the costs for performing tissue oximetry are only
marginal compared with the costs associated with post-
operative complications. In case of arterial or venous
thrombosis, surgical re-intervention is necessary to increase
the chance of successful flap salvage. This will add around
$76,000 per hour spent in the operating room to the hos-
pital costs (36). Also, patients experiencing complications
generally consume two extra hospital days, leading to
another $7,000 in added costs per patient operated in the
United States (36). In uncomplicated cases, tissue oximetry
eliminates the need for prolonged intensive monitoring
with savings of $1,337 (or 6.3% (37)) that far outweigh the
costs associated with routine use of tissue oximetry (37,38).
The relationship between aberrant tissue oximetry read-
ings and clinical outcome appears to be more clear in the
somatic applications of tissue oximetry. Complications
arising from peripheral tissue ischemia (e.g., the distal limb
and autologous breast flaps) are elementary in nature
because of the absence of an intrinsic homeostatic autor-
egulatory system. In cerebral oximetry, one attempts
assessing an entire organ system that is only represented by
a regional assessment of tissue oxygenation in the pre-
frontal cortex. In somatic tissue oximetry, on the other
hand, the readings appear more representative of clinical
outcome.

Another application of non-invasive tissue oximetry in
which the regional measurement is applied to assess an
organ system is renal oximetry. Particularly in children and
infants undergoing cardiac surgery, in whom acute kidney
injury is a dreadful complication contributing to increased
morbidity and mortality. Although typical assessment of
renal function is performed using serum creatinine levels
and urine output, changes in these markers may be severely
delayed (39,40). On the other hand, lowered renal oximetry
readings have been shown to correlate with acute kidney
injury (39,40) and other parameters representing renal
dysfunction such as peak creatinine level (39).

The versatility of tissue oximetry in the clinical setting
broadens the scope for future studies to focus on new
potential applications. One prospective application is as-
essment of microcirculatory function (41). Intraoperative
monitoring of peripheral microvascular reactivity enables
eyearly detection of alterations in microcirculatory function
and may contribute to preventing impaired tissue perfusion
and adverse patient outcome. In general, microvascular
alterations associated with microcirculatory dysfunction
are predominant factors in the process of tissue hypoxia,
and if left untreated result in ischemic tissue damage. Combining continuous non-invasive tissue oxygenation monitoring with a reproducible ischemia reperfusion challenge allows dynamic assessment of vascular reactivity and potentially early recognition of altered vascular reactivity and function. Parameters resulting from a so called vascular occlusion test include the occlusion slope, reperfusion slope, and the hyperemic area which provide information regarding the current status of local tissue metabolism (42), the local reperfusion reserve (42), and tissue oxygen consumption (43), respectively. Because microcirculatory dysfunction precedes tissue hypoxia, adopting tissue oximetry as a part of standard microcirculatory monitoring may prove to be the next big frontier in critical care management. The clinical relevance of alterations identified by dynamic measurements of peripheral tissue oxygenation, however, remains to be further explored. The current literature describes a variety of measurement protocols and calculation methods (41,42,44); thus, further studies are warranted to determine the optimal approach in performing tissue oximetry combined with a vascular occlusion test.

CONSIDERATIONS IN TISSUE OXIMETRY: A WORK IN PROGRESS

Despite the need for superior continuous and non-invasive monitoring methods in patient care, tissue oximetry is not yet part of standard routine practice. A multitude of anecdotal reports and recent reviews have tempered the enthusiasm for routine use of rSO2 by questioning whether it leads to improved patient outcomes or not (45). One of the causative factors is the lack of intervention-guided trials linking disturbances in tissue oxygen saturation to adverse clinical outcome. Although multiple studies reported an association between tissue oxygen desaturation and post-surgical complications, it remains unclear whether this is part of a causal relationship or just a reflection of overall morbidity.

Furthermore, cerebral oximetry data has been implemented as part of the Society of Thoracic Surgeons Adult Cardiac Surgery Database effective from January 2008 to provide evidence, potentially improving patient outcome (46).

An important factor precluding routine use of tissue oximetry is the lack of clear application-specific rSO2 thresholds requiring immediate intervention. In previous attempts to determine a clear threshold or change in rSO2 necessitating prompt intervention, published studies were insufficient in taking the limitations of the measurement into account. Clinical oximetry devices are destined for either trend or absolute rSO2 monitoring, using an algorithm that requires the assumption of a fixed ratio of arterial to venous blood in the vascular bed in the area of interest. This algorithm, however, cannot adapt to all possible applications of tissue oximetry. Hence, one must be cautious when interpreting absolute rSO2 values derived from measurements performed in different areas. To date, there are no clear indications when intervention to correct rSO2 is warranted. One may argue that this is partially because of the fact that studies up until now failed to demonstrate a causal relationship between tissue oxygen desaturations identified by tissue oximetry and adverse clinical outcome. In addition, the use of different monitoring devices across studies makes standardized application of cerebral oximetry even more challenging. Oximetry devices from different manufacturers each use different algorithms for estimation of local oxygen content, and use varying numbers and wavelengths of near-infrared light. Furthermore, because every device differs in terms of hardware and software (data acquisition, filtering, and processing), each device should be used in accordance with a device-specific and application-specific set of desaturation thresholds. Not only the specific measurement device but also the different applications in tissue oximetry directly affect the measurement and derived rSO2 values. Development of standardized desaturation thresholds for the different applications will aid in interpretation of rSO2 values and thereby establish routine use of tissue oximetry.

With the limitations of non-invasive assessment of tissue oxygenation being identified, future studies should focus on interpretation of measured data and aim at determining clinically relevant and application-specific threshold values for tissue desaturation-related injury. Furthermore, the types of interventions necessary for correcting tissue oxygenation values and its effects on clinical outcome require further clarification.

CONCLUSION

Overall, non-invasive tissue oximetry is a promising tool for (regional) assessment of tissue oxygenation. The measurement readings should be considered as an integral source of information, a puzzle piece that together with all clinical information aids in decision-making and minimizing the risk of complications.

REFERENCES

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