

Non-invasive tissue oximetry

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Valorization

Non-invasive tissue oximetry – an integral puzzle piece

Inadequate tissue oxygen delivery is known to result in complications, contributing to morbidity and mortality following or during medical procedures. In order to minimize the risk of adverse outcome, close monitoring of patient's hemodynamic status at all times is indispensable. 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.

To date, numerous studies (of which mostly observational) focused on the use of non-invasive tissue oximetry in surgical patients, proposing its predictive value in relation to clinical outcome. Cerebral oximetry in particular has been the focus in the context of preventing neurological complications following cardiac surgery. These complications, including stroke which appears to be the most detrimental, are complex in nature and elicited by a multitude of preoperative and perioperative factors. Intraoperative cerebral hypoxia resulting from hypoperfusion is generally accepted as a factor contributing to the risk of adverse neurologic outcome.^{1,2} Although the exact etiology is not yet completely understood, continuous assessment of tissue perfusion may aid to a better understanding of the role of tissue hypoxia in the development of postoperative cognitive complications.

While the incidence of neurological complications may seem relatively low, the effects on the patient's physical and psychological health are tremendous with serious implications for the quality of life.³ The reported incidence of stroke following cardiac surgery varies around 4.2%, meaning that every year 33 patients are affected based on 800 procedures annually.⁴ Postoperative stroke entails prolonged hospital stays of on average seven days with an incremental increase of hospital resources.^{5,6} In the United States, for each affected patient the estimated added costs make up to \$18,552, of which \$1,000 are attributable to each additional day of hospitalization.⁷

Another type of neurological complication that may emerge following cardiac surgery is delirium, which is characterized by a state of confusion and inattention. Although often seen as a reversible condition, delirium contributes to persistent functional decline and significant morbidity and mortality risk.⁸ Postoperative delirium is associated with only four extra hospitalization days, but is far more common as compared to stroke, with incidence rates varying around 55%.^{9,10} If non-invasive tissue oximetry could help to prevent part of the neurological complications, such as hypoxia-related stroke or delirium^{2,11}, the odds of an uncomplicated prosperous recovery would increase and a substantial pro-

portion of hospital costs could be saved. The costs of performing the measurement include the purchase of disposable self-adhesive sensors (usually two, for bilateral measurement of tissue oxygenation), which in the United States cost around \$200 per patient¹², and a one-time investment for purchasing the oximeter device. The costs for routine application of clinical oximetry, however, are only marginal compared to the major additional expenses associated with ischemic-related stroke and delirium¹³, let alone the deleterious long-term effects of these complications, i.e. the quality of life.

The pathophysiology of neurologic postoperative complications is complex and multifactorial in nature. Therefore, some neurologic complications are nearly impossible to prevent due to unforeseen events occurring in the perioperative period (e.g. 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 neurologic complication (chapter 3).¹⁴ The cardiopulmonary bypass protocol is, therefore, an important factor in enabling and maintaining adequate tissue perfusion and should be critically evaluated in order 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 since general hemodynamic factors may not adequately represent local tissue oxygenation status.¹⁵

With non-invasive tissue oximetry on the rise and being increasingly applied as a brain monitor, the technique appears to be a viable assessment method for diverting adverse neurologic outcome. On that note, cerebral oximetry showed to adequately reflect real-time changes in tissue oxygenation readings following several iatrogenic events. 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, as mentioned beforehand, which is still not entirely understood. Deoxygenation episodes detected by cerebral oximetry should probably be considered as a contributor, rather than an independent causative factor for clinical neurologic damage and evident changes in neurocognitive function (chapter 2).

In addition to the latter, when performing cerebral oximetry it is important to consider the intrinsic system of cerebral autoregulation. When intact, reactive vasoconstriction and vasodilatation ensures adequate tissue oxygenation, providing cerebral protection. Although often unacknowledged, disturbances in autoregulatory function have shown to result in neurologic complications and thus should be avoided at all times. In this thesis, several modifiable factors requiring strict regulation in order to maintain intact cerebral autoregulation are identified. In turn, a perfusion protocol that includes maintaining these factors within the physiologic range confers to the observed low incidence of neurologic complications by enabling intact autoregulatory function.

Taking these practical considerations into account, one may conclude that tissue oximetry, inherently due to its measurement technique and thus non-invasive nature, cannot independently predict the occurrence of complications with a multifactorial nature such as ischemic stroke or delirium. Similar to most non-invasive monitoring tools and methods, tissue oximetry readings should be interpreted in the context of all clinical information available. The scientific value of this thesis is that non-invasive tissue oximetry derived measurement values should be viewed as an integral piece of information rather than a superior monitoring method.

Besides its original intended use (i.e. brain monitoring), non-invasive tissue oximetry is increasingly applied in somatic tissue monitoring. One example is assessment of distal limb perfusion in patients supported by veno-arterial extracorporeal life support (VA-ECLS). Femoral access techniques often used in VA-ECLS may compromise limb perfusion, therefore predisposing the patient to concomitant tissue damage with potential disastrous effects. 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 (chapter 6).

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 measurement values as compared to the expected physiologic 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. Successively,

avoiding complications contributes to minimizing postoperative morbidity and mitigating health care costs. As is the case in brain monitoring, the costs for performing tissue oximetry are only marginal compared to the costs associated with postoperative 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 hospital costs. 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.¹⁶ In uncomplicated cases, tissue oximetry eliminates the need for prolonged intensive monitoring with savings of \$1,337 (or 6.3%¹⁷) that far outweigh the costs associated with routine use of tissue oximetry.^{17,18}

The relationship between aberrant tissue oximetry readings 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 due to the absence of an intrinsic homeostatic autoregulatory system. In cerebral oximetry, one attempts assessing an entire organ system that is only represented by a regional assessment of tissue oxygenation in the prefrontal cortex. In somatic tissue oximetry on the other hand, the readings appear more representative for clinical outcome.

The versatility of tissue oximetry in the clinical setting may broaden the scope for future studies to focus on new potential applications. One prospective application is assessment of the microcirculatory function. Since 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.

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.

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

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