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### Supplemental Issue

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# **Cerebral Autoregulation Assessment through Near-Infrared Spectroscopy and Arterial Monitoring: Advancements and Clinical Implications**

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Abstract: Cerebral autoregulation, maintaining stable cerebral blood flow across varying arterial pressures, is vital in-patient care during surgery. Traditional views suggest a mean arterial pressure range of 50-150 mm Hg for effective autoregulation. However, patient-specific variations in autoregulatory patterns, particularly in cases of impaired autoregulation, call for personalized hemodynamic and blood pressure management during surgical procedures. In the evaluation of cerebral autoregulation, NIRS serves as a beneficial monitoring tool. The cerebral oximetry index, correlating cerebral oxygen saturation with perfusion pressure, aids in determining autoregulation limits. The literature shows varying impacts of vasoactive drugs on patients with different autoregulatory responses, emphasizing the need for individualized care. In summary, NIRS is crucial for monitoring cerebral autoregulation, and adjusting arterial blood pressure targets based on NIRS data could improve prevention of cerebral hyper/hypoperfusion. This approach, moving away from a generalized strategy, advocates for a more customized, physiologybased patient management. ©2024 NTMS.

**Keywords:** Cerebral Oxymetry; Near Infrared Spectroscopy; Cerebral Autoregulation.

#### 1. Introduction

Monitoring oxygenation at the tissue level has been a prominent research focus in the field of clinical medicine for many years. Significant progress, including the development of the ear oximeter in the 1940s and the pulse oximeter in the 1970s, has been made in this field. These technologies are crucial for advancing cerebral oximetry by enhancing our understanding of how tissues, such as bone, interact with light in the near-infrared region <sup>1</sup>. Using near-infrared spectroscopy (NIRS) technology, it is possible

to continuously and non-invasively monitor the level of oxygen saturation in a specific part of the frontal cortex. The implementation of these technology advancements has dramatically enhanced the quality of patient care in both cardiac and non-cardiac surgical procedures, as well as in critical care environments <sup>2-4</sup>. There is significant discussion about the possibility of cerebral oximetry monitoring being a regular anesthesiology practice in the near future <sup>5</sup>. The objective of this review is to examine the correlation between monitoring

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arterial hemodynamics and cerebral oximetry, with a particular focus on cerebral autoregulation.

#### 1.1. Near-Infrared Spectroscopy

Near Infrared Spectroscopy is a commonly employed non-invasive technique in clinical practice. The method employs near-infrared light measurement within the range of 650-940 nm wavelengths to determine the cerebral oxygen saturation. The emitted light passes through the scalp and the underlying cerebral tissues, allowing for the assessment of regional oxygen saturation based on the difference between oxyhemoglobin and deoxyhemoglobin <sup>6</sup>. The system consists of two optodes, with one optode penetrating into superficial tissue at a depth of 3cm and the other optode penetrating into deep tissue at a depth of 4cm. Unlike the pulse oximeter, which predominantly monitors the arterial blood flow, the regional cerebral oxygen saturation (rScO2) value acquired using NIRS is derived from venous blood, which constitutes 70-75% of the blood flow in brain tissue <sup>7</sup>.

Current challenges in NIRS technology extracerebral signal contamination. NIRS signals can be affected by both intracerebral (non-hemoglobin chromophores, non-metabolized tissue oxygen saturation including capacitance veins) extracerebral components, impacting accuracy. To address this, advanced algorithms are being developed to minimize extracerebral interference and enhance signal specificity. Spatial resolution is one of these. NIRS has limited spatial resolution, hindering precise localization of cerebral activity. Research on higherresolution NIRS technologies or complementary imaging techniques to refine spatial accuracy is ongoing. Advances in the spatial techniques is slow due to restrictions on NIRS depth penetration, affecting monitoring in deeper brain structures. Also, variability in cerebral blood flow among individual patients challenges standardization. Although studies are conducted in volunteers and several critical patients, there is still need for establishing individualized baseline values for more accurate interpretation. Finally, fixed assumptions about the cerebral venoarterial blood ratio affects the accuracy of NIRS techniques 8, 9, 10.

Near-infrared spectroscopy (NIRS) plays a critical role not only in monitoring cerebral perfusion but also in tracking the perfusion of the renal system and spinal cord. Although the fundamental limitation is the distance of subcutaneous tissue to the target structure, its use is highly beneficial in patients where this distance is suitable, especially in the pediatric population or in patients with low adipose tissue.

It is possible that near future may see advancements in multimodal imaging integration, improved signal processing techniques, machine learning applications, quantitative biomarkers, miniaturization and wearable devices.

#### 1.2. Cerebral Autoregulation

Lasen described an auto-regulation plateau range of mean arterial blood pressures (MAP) between 50-150 mm Hg in young patients. 11 8 At this plateau level, cerebral blood flow (CBF) is actively regulated by myogenic regulation of small cerebral arteries and arterioles and remains constant. When blood pressure exceeds these thresholds, the ability of myogenic vaso activity to adjust to these alterations is compromised, resulting in a correlation between CBF and blood pressure.

Although it remains valid due to its basic defining characteristics, it is recognized that CBF regulation involves a multitude of parameters beyond just blood pressure. It has been accepted that autoregulation mechanisms may be affected in certain situations, such as pharmacological medications and alterations in carbon dioxide levels of various diseases, such as prematurity <sup>12-15</sup>. However, in the presence of impaired autoregulation, there can still exist an optimal blood pressure range where the autoregulatory function is at its peak. Determining the optimal range of cerebral perfusion and personalizing blood pressure goals may shift the current clinical paradigm away from 'one size fits all' towards individualized, patient-specific, physiology-based blood pressure management.

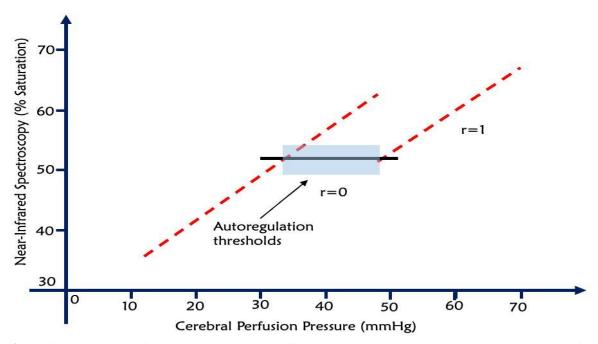
Within the context of traditional knowledge, it is commonly recognized that a perfusion pressure of 50-60 mmHg in the arterial blood is considered acceptable during cardiopulmonary bypass (CPB) for patients undergoing cardiac surgery. However, studies have demonstrated that 35% of patients undergoing cardiac surgery show impaired cerebral autoregulation <sup>15</sup>.

The mean arterial pressure, which constitutes the lower level of autoregulation, exhibits a significant range of variation ranging from 40 to 90 mmHg <sup>16</sup>. Consequently, as determined through the empirical selection of MAP goals, patients may experience different durations of time with MAP levels below the lower threshold of autoregulation during CPB.

## 1.3. NIRS Monitoring in the Evaluation of Cerebral Autoregulation

The cerebral oximetry index is obtained by calculating the Pearson correlation coefficient between cerebral oxygen saturation and perfusion pressure. In an optimal autoregulation curve, it is anticipated that this index will be less than 0.3 at the limits of autoregulation. Outside the limits of autoregulation, this correlation increases <sup>17</sup> (Figure 1).

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**Figure 1:** Calculation of Pearson correlation coefficient between cerebral oxygen saturation and perfusion pressure.

Brady demonstrated in his experimental investigation through a comparison of cerebral oximeter index (COx) and laser doppler (LDx) that spontaneous autoregulatory vasoreactivity can be assessed using the time-domain correlation between arterial blood pressure (ABP) and cerebral oximetry <sup>18</sup>. LDx-COx results were consistent, showing low values above and high values below a cerebral perfusion pressure (CPP) of 35 mmHg. In addition, LDx and COx changes showed a close correlation with every 5 mmHg increase in CPP.

## 1.4. Evaluation of Different Cerebral Autoregulation Patterns with NIRS

It is predictable and interpretable how blood pressure values outside these narrow autoregulation limits affect the cerebral perfusion of a patient with impaired cerebral autoregulation. In the NIRS monitoring algorithmic approach, the initial step in the course of cerebral desaturation is to increase MAP <sup>19</sup>. Demir et al. obtained an individual blood pressure value in a malignant hypertensive renal transplantation patient where cerebral autoregulation could be achieved by increasing the MAP upon developing cerebral desaturation when the patient became normotensive <sup>20</sup>. Nevertheless, individuals with normal cerebral autoregulation may exhibit paradoxical reactions in various hemodynamic situations <sup>21</sup>.

Moerman et al. studied the COx using NIRS in 34 cardiac surgery patients, following the administration of phenylephrine and sodium nitroprusside <sup>15</sup>. COx was higher than 0.3 in 35% of the patients and remained similar after the administration of vasoactive drugs. Patients with impaired cerebral autoregulation were characterized by a pressure-passive cerebral

circulation. In 18% of the patients, COx demonstrated a classic autoregulation pattern, remaining at 0 levels with both baseline and after vasoactive drug administration. However, in 10 patients with intact baseline autoregulation, following the administration of phenylephrine or sodium nitroprusside, cerebral blood flow was reduced, and COx became negative. Futhermore, in 6 patients with intact baseline autoregulation, cerebral blood flow decreased (COx became negative) after the administration of phenylephrine. Conversely, after the administration of sodium nitroprusside, COx increased above 0.3, resulting in an increase in cerebral blood flow. This group was defined by the divergent effects of vasoactive drugs.

#### 2. Conclusions

The conventional definition of cerebral autoregulation is limited in its ability to capture the entire concept fully. The primary objective of cerebral oximetry monitoring extends beyond identifying impaired autoregulation. Studies have shown that patients with normal cerebral autoregulation may have paradoxical responses to commonly used medicines in our routine anesthetic procedures.

Variations in autoregulatory patterns directly affect the determination of blood pressure goals and the management of hemodynamics during surgery. Modifying arterial blood pressure targets through NIRS-based cerebral autoregulation monitoring could be a more efficient approach to preventing cerebral hyper/hypoperfusion than the current standard of treatment.

#### Limitations of the Study

This review acknowledges several limitations that may

impact the generalizability and applicability of its literary findings. Firstly, the reliance on near-infrared spectroscopy (NIRS) for the assessment of cerebral autoregulation, while valuable, presents inherent limitations in terms of sensitivity and specificity. NIRS data can be affected by extraneous factors such as movement artifacts and variations in skin pigmentation, potentially leading to variability in the measurements. Secondly, this review inherently draws heavily from existing literature and theoretical frameworks, which may not fully capture the complexity and individual variability of autoregulatory mechanisms in different patient populations. Additionally, the effects of various vasoactive drugs on cerebral autoregulation have been discussed; however, the adequacy of existing experimental or clinical study data to validate these claims remains debatable. Lastly, the emphasis on personalized hemodynamic management necessitates advanced monitoring equipment and expertise, which may not be readily available in all clinical settings, potentially limiting the widespread applicability of these recommendations. Addressing these limitations in future research could enhance the accuracy and applicability of NIRS-based monitoring in clinical management.

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#### **Author Contributions**

All authors contributed equally to the article.

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None.

#### **Data sharing statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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None.

#### **Informed Statement**

None.

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#### **Bispectral Index Monitoring and Combinations in Anesthesia Safety**

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**Abstract:** Anesthesia should ideally provide adequate hypnosis, analgesia and a suitable environment for surgery. Monitoring the depth of anesthesia is recommended to reduce awareness during anesthesia and improve the administration of anesthetic drugs. Bispectral index (BIS) is a numerical scale based on the analysis of electroencephalogram (EEG) parameters and can reduce the adverse effects associated with over- or under-dosing of anesthetic drugs. BIS monitoring may also provide cost-related advantages, with values between 40 and 60 for BIS indicating adequate depth of anesthesia during the surgical procedure. BIS is the most widely studied and best documented cerebral monitoring method. It can be used in monitoring the depth of sedation in intensive care patients, monitoring EEG suppression in patients with increased intracranial pressure, diagnosis of brain death, and neurologic evaluation after resuscitation. This summary is based on selected literature on BIS monitoring and its combination with other monitoring methods over the last 20 years. ©2024 NTMS.

**Keywords:** Anesthesia General; Bispectral Index; Monitoring; Intraoperative.

#### 1. Introduction

The first official endorsement date for brain function monitoring in anaesthesia safety is October 2005. On this date, the House of Delegates of the American Society of Anesthesiologists approved the "Practice Advisory for Intraoperative Awareness and Brain Function Monitoring" <sup>1</sup>. This document recommends risk assessment for patients and the resulting use of cerebral function monitors on a case-by-case basis. Although cerebral function monitors are not included in standard anaesthetic monitoring, it is recommended that they be used in conjunction with other monitoring methods to improve patient safety. Although there are multiple methods for cerebral function monitoring, Bispectral Index (BIS) monitoring is the most widely researched and used method (Fig. 1).

BIS was developed by Aspect Medical Systems in 1985 to quantitatively evaluate the sedative and hypnotic effects of anaesthetic drugs and includes electroencephalogram (EEG) parameters. It was approved by the Food and Drug Administration in 1996

The BIS monitor is based on four electrodes placed on the forehead to measure the electromyographic activity of the frontalis muscle (Fig. 2). The BIS monitor collects EEG data and uses an algorithm to analyse it. BIS values range from 0 to 100. A value of 0 indicates an isoelectric EEG with complete suppression of brain activity, while a value of 100 indicates that the patient is awake. Values between 40-60 define the level of immobility and hypnosis required for general

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anaesthesia. Below 40 indicates a deep hypnotic state <sup>3</sup>. BIS monitoring can be used for anaesthesia safety in the operating room, sedation assessment in intensive care, neurological status assessment in non-sedated patients and follow-up of patients with possible brain death.



Figure 1: BIS monitör

The reasons why new intraoperative haemodynamic monitoring methods have not been included in anaesthesia standardisation in parallel with technological progress are undoubtedly cost and lack of sufficient evidence level. We aimed to answer the question "where is BIS monitoring in anaesthesia safety from past to present? We conducted this literature review to seek an answer to the question.

#### 2. Discussion

#### 2.1. BIS monitoring and Awareness

Mindfulness can be thought of as the postoperative recall of events that occurred during general anesthesia. However, there is no clear definition. Awareness is reported in different dimensions, while the difference in the form of questioning (structured questions versus direct questions such as "Did you feel any discomfort during the operation?") changes the data results. Therefore, studies on this topic are still controversial. It is not clear whether cerebral monitoring should be included in standard anaesthetic monitoring.

Awareness under anaesthesia is a highly traumatic experience for patients. Studies have shown that patients can have a state of recall even without changes in haemodynamic parameters <sup>4</sup>. Therefore, we may not be able to prevent awareness with standard anesthesia monitoring. In BIS monitoring, values below 60 are indicative of the level of hypnosis as well as the immobility required for surgery. Monitoring the BIS value throughout the operation may be a reliable method to prevent awareness.

Studies on the effects of BIS monitoring on awareness date back about 30 years. In a meta-analysis published in 2004, the frequency of anesthesia awareness was found between 0.1% and 0.2% of all patients

undergoing general anesthesia in many studies <sup>5</sup>. In 2002, Bergman et al. examined 8372 patients receiving general anesthesia and reported 81 cases in which perioperative recall was compatible with awareness. After examination of the cases, they found that 36 patients experienced awareness due to inadequate hypnosis due to inadequate volatile anesthetic concentration, 32 patients experienced awareness due to medication error (pre-induction neuromuscular paralysis), and 13 patients had no apparent reason for awareness <sup>6</sup>. These results suggest that the majority of awareness cases (44%) were due to inadequate depth of anesthesia and thus could be prevented by monitoring of BIS. The limitations of this analysis are the biases introduced during the use of The Anaesthetic Incident Monitoring Study (AIMS). Data interpretations may be subjective due to the non-standardized narrative in the definition of awareness.

Ekman et al. followed 4945 patients receiving general anesthesia with BIS monitoring with a BIS value between 40-60 and used 7826 patients without BIS monitoring as a control group. Compared to the control group, the incidence of recall decreased by 77% in the group using BIS  $^7$ .



Figure 2: BIS sensor.

Myles et al. examined 2463 patients in a multicenter study. 1225 adult patients were randomized to general anesthesia with BIS guidance and 1238 patients were randomized to general anesthesia with routine practice. Patients were evaluated 2 to 6 hours, 24 to 36 hours and 30 days after surgery using a blinded observer. There were 2 reports of awareness in the BIS-guided group and 11 in the routine group. The risk of anesthesia awareness was reduced by 82% with BIS guidance 8. In both studies, haemodynamic parameters were used to guide the use of anaesthetic drugs in the non-BIS group. Avidan et al. randomly divided 2000 patients into two groups to reduce anaesthesia awareness in high-risk patients. Patients receiving BIS and anaesthetic agent concentration (ETAC) guided anaesthesia were compared. Postoperative patients were evaluated at intervals (0 to 24 hours, 24 to 72 hours and 30 days after extubation) for anaesthesia awareness. In the BIS and

ETAC groups, 967 and 974 patients were evaluated, respectively. Two definite cases of anaesthetic awareness occurred in each group 9. This study does not support routine BIS monitoring as part of standard practice, unlike other studies which have shown that anaesthetic awareness is reduced with BIS monitoring. In 2011, Avidan et al. increased the number of patients and centres to overcome the limitations of their previous study and again included patients at high risk for awareness. They performed a randomised controlled trial on 6041 patients without using awareness minor risk factors. By configuring the ETAC protocol, they compared the two methods by monitoring 2852 patients with standard monitoring of ETAC (ETAC<0.7 or) and 2861 patients with BIS monitoring (BIS kept between 40-60), and reported 7 cases of definite intraoperative awareness in the BIS group and 2 cases in the ETAC group <sup>10</sup>. In this study, the superiority of the BIS protocol could not be demonstrated. Contrary to expectations, fewer realisation cases occurred in the ETAC group. In both studies, the ETAC protocol was not associated with an increase in postoperative mortality or the amount of anaesthetic agent administered.

Sudhakaran et al. divided 70 patients undergoing thoracolumbar spine surgery into 2 groups and studied the depth of anaesthesia and recovery characteristics. In this study, in which they compared BIS and ETAC monitoring, there were significant reductions in awake time, extubation time and name recall time in both groups.

BIS-guided anesthesia was also associated with reduced time to discharge from the PACU. After 24 hours, none of the patients assessed for awareness complained of awareness, but the study did not specify criteria for assessment of awareness <sup>11</sup>. Considering how low the incidence of awareness is, we do not think it is meaningful to evaluate it in such a small group.

In conclusion, the lack of a clear definition of awareness in the studies on awareness and the use of different methods in its determination, the use of general patient population in some studies and selected high-risk patients in others, the use of hemodynamic parameters as a control group in some studies and ETAC in others may have led to different results. Intraoperative awareness is rare and difficult to detect. Although there is evidence that the use of BIS has positive effects on awareness and early recovery, the level of certainty is low.

## 2.2. Effect of BIS Monitoring on Anesthetic Consumption

The use and control of the appropriate dose of anesthetic agents during the operation is under the control of the anesthesiologist. Improving the use of anesthetic agents is important both in terms of anesthesia safety and cost. Its effect on anesthetic agent consumption makes BIS monitoring valuable in terms of the potential harm of the agents used.

Wong et al., randomly divided 68 patients over 60 years of age who would undergo orthopedic surgery under general anesthesia into 2 groups and examined the effects of BIS monitoring on the recovery profile. In the group not monitored with BIS, they titrated the isoflurane concentration according to clinical practice, and in the BIS group, they titrated it to keep the BIS value between 50-60. Although there was no difference in postoperative cognitive dysfunction between the two groups, total isoflurane use was 30% lower and recovery was significantly faster in the BIS group <sup>12</sup>. In a large meta-analysis of randomized, controlled trials, examined 1380 outpatients from 11 different studies who were monitored with BIS versus standard practice. BIS monitoring significantly reduced anesthetic use by 19% <sup>13</sup>.

In the B-Aware, B-Unaware and BAG-RECALL studies, there was no significant difference between volatile anesthetic concentrations in patients followed with BIS monitoring and control group patients <sup>8, 10, 14</sup>. In studies with propofol, there are studies showing that BIS monitoring can significantly reduce propofol administration <sup>8, 15</sup>.

In a randomised controlled trial by Chan et al. in 921 non-cardiac surgery patients, BIS-guided anaesthesia reduced propofol use by 21% and volatile anaesthetic use by 30% <sup>16</sup>.

In a meta-analysis, BIS-guided anesthesia reduced both the need for propofol and the need for volatile anesthetics (desflurane, sevoflurane, isoflurane) <sup>17</sup>.

There is evidence that the use of BIS monitoring in

There is evidence that the use of BIS monitoring in addition to standard anaesthetic monitoring may prevent both overly deep anaesthesia and inadequate anaesthesia by keeping the depth of anaesthesia constant throughout the operation, but studies are conflicting as to whether it would be beneficial in terms of anaesthetic consumption.

#### 2.3. Effects on Postoperative Outcomes

The quality of recovery and incidence of nausea and vomiting in the period after awakening from general anaesthesia show a strong dose-dependent relationship with the degree of exposure to inhalation anaesthesia<sup>18</sup>. In a metanalysis, BIS-guided anesthesia reduced postoperative nausea and vomiting compared with routine protocols. Regardless of the anesthetics used, it decreased eye opening time, response to verbal command, extubation time and orientation time, and length of stay in the postanesthesia care unit (PACU) <sup>17</sup>.

However, Pavlin et al. showed in a large, randomized clinical trial that although BIS monitoring was associated with a slight reduction in sevoflurane administration, it had no effect on faster recovery and PACU length of stay <sup>19</sup>.

Similarly, analyses from the BAG-RECALL and B-Unaware study populations and the Michigan Awareness Control Study showed no difference in anesthesia administration, time to discharge from the postoperative recovery area, or incidence of

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postoperative nausea and vomiting when BIS guidance was used compared with controls <sup>10, 14, 20</sup>. In a study of 402 patients, it was reported that when BIS monitoring and ETAC monitoring were compared, there was no difference between extubation and recovery times in the two groups of patients <sup>21</sup>.

Since it is not clear that BIS-guided anesthesia provides dose titration, its effect on early recovery findings is also controversial.

#### 2.4. Combinations of BIS Monitoring

BIS monitoring can be applied in combination with many monitoring methods used for patient safety. In studies conducted with different combinations, it is thought that the monitoring method selected according to the operation may increase safety when used in combination with BIS.

Vakil et al. conducted a study evaluating the safety and efficacy of monitored anaesthetic care in pleuroscopy to assess whether end-tidal capnography and bispectral index (BIS) monitoring during propofol sedation reduces the risk of complications <sup>22</sup>. The primary outcome of this study was the incidence of anaesthetic complications in patients undergoing pleuroscopy. Hypoxia was defined as oxygen saturation below 90% for 2 minutes and hypotension was defined as requiring In terms of anaesthesia-related vasopressors. complications, there was no significant difference between those with and without BIS monitoring. This study demonstrated the safety and efficacy of capnographic monitoring with or without BIS monitoring.

Total intravenous anesthesia (TIVA) is currently used as an alternative to inhalation anesthesia. The fact that many diagnostic and interventional procedures in children are performed outside the operating room requires sedation and/or analgesia in these settings. Although TIVA is a good choice, it is very difficult to administer an effective dose that does not cause respiratory depression. More reliable titration can be achieved by performing respiratory monitoring with oximetry and capnograph and by showing the level of sedation with BIS control  $^{23}.$  In obese patients, it has been shown that the performance of the Target Controled Infusion (TCI) system can be improved by administering propofol (Cp 6  $\mu g$  ml-1) and remifentanil (Ce 2 ng ml-1) under BIS guidance  $^{24}.$ 

Today, advanced infusion pumps such as TCI have facilitated TIVA applications. Absolom and Kenny took TCI applications further and developed a closed-loop anesthesia system that automatically delivers the target blood propofol concentration by BIS control. The automated closed-loop control system plays a similar role to anesthesiologist control. It can speed up the drug infusion when the need increases and slow it down when the need decreases. In standard BIS-guided studies, however, it lacks the ability to anticipate changing stimulus intensity and rapidly deliver the required dose. Closed loop systems provide better quality drug delivery. The patient's BIS value controls

the system. The target value is initially selected by the user, then the drug effect is controlled by the device and maintained close to the target value. It has been reported that the quality of recovery in the group receiving closed-loop BIS-controlled propofol infusion was more excellent than in the manually controlled group <sup>25</sup>. In a recent meta-analysis including many studies comparing closed-loop open-loop infusion systems, it has been reported that closed-loop systems reduce propofol requirements during induction, maintain the target depth of anesthesia better and shorten the recovery time <sup>26</sup>.

In a 2016 review, the combined use of cerebral oximetry and BIS monitoring during awake craniotomy was recommended due to significant pharmacokinetic/pharmacodynamic differences between individuals <sup>27</sup>.

In a study involving adult patients undergoing cardiopulmonary bypass surgery, Thudium et al. performed monitoring consisting of assessment of middle cerebral artery flow velocity using Near Infrared Spectroscopy, BIS and transcranial Doppler sonography <sup>28</sup>. Due to the inherent technical limitations of each monitoring component, a multimodal neuromonitoring combining several qualities has been proposed.

#### 3. Conclusion

In conclusion, the use of advanced technologies is emerging as methods that reduce the burden of the anesthesiologist and provide standardization in the operating room environment. BIS monitoring can be combined with standard anesthesia monitoring as well as other advanced monitoring techniques. Each monitoring technique used increases the safety but also increases the cost. Therefore, more comprehensive studies are needed.

#### Limitations of the Study

Differences in the way of questioning when awareness is investigated may affect the results in the studies. Therefore, our comments on this subject may be insufficient

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Conception and Design of the study, Collection and/or Processing and Literature review, Writing Original Manuscript, Analysis and/or interpretation and final version and is responsible for final approval of the submitted manuscript; ETY.

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#### **How Surgical Positions Affect Cerebral Oxygenation**

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**Abstract:** This study investigates the use of cerebral oximetry in various surgical positions and its impact on cerebral oxygenation. We conducted a literature review through Medline, and Ebscohost, focusing on articles published until October 30, 2023. Our findings indicate that: Cerebral oxygenation is affected by all surgical positions, with the most significant clinical impact observed in the seated position. Maintaining cerebral autoregulation is crucial for preventing cerebral hypoxia or desaturation. Upholding a mean arterial pressure above 60 mmHg is essential for this purpose. Anesthesia can negatively impact cerebral oxygenation by potentially impairing cerebral autoregulation. Inhalation anesthetics may have a more beneficial effect on cerebral oxygenation compared to intravenous anesthetics. The risk of cerebral desaturation increases in elderly patients and those with comorbidities. Standardization of cerebral desaturation definitions is needed to better assess its relationship with postoperative complications. The position of the blood pressure transducer can affect the accuracy of intraoperative monitoring. In the seated position, placing it at the level of the acoustic meatus provides a more precise assessment. Our study highlights the importance of considering the effects of different surgical positions on cerebral oxygenation. This knowledge can assist anesthesiologists in monitoring patients intraoperatively and potentially preventing postoperative neurological complications. © 2024 NTMS.

**Keywords:** Cerebral oximetry; Beach chair; cerebral oxygenation; Prone; Near-infrared spectroscopy.

#### 1. Introduction

Surgery is usually performed with the patient supine, but the efficiency of the operation can be improved by offering patients different positions during surgical procedures. The preferred surgical positions include supine, prone, lateral decubitus, sitting, reverse trendelenburg, and trendelenburg, each of which carries some risk. The body's position can impact respiratory, cardiopulmonary physiology, and tissue oxygenation, including that of the brain <sup>1,2</sup>. The anesthesiologist needs to comprehend the effects of the surgical position on intraoperative physiology.

The assessment of brain oxygenation can be accomplished through the utilization of jugular vein oxygen saturation and microdialysis techniques. The utilization of both methodologies is constrained because of their invasive and the inclusion of numerous additional risks. Near-infrared spectroscopy (NIRS) was first used by Frans Jobsis in 1977 for brain tissue. It is a non-invasive method that utilizes infrared light, akin to pulse oximetry, for assessing regional tissue oxygenation (rSO2) through the measurement of the absorption of infrared light by the tissue <sup>3-5</sup>. The frontal

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cortex's regional cerebral oxygen saturation (rScO2) can be determined by comparing the specific

absorbance patterns of oxygenated and non-oxygenated haemoglobin to NIRS. NIRS technology makes it possible to recognize and treat cerebral desaturation events (CDEs) without the need for conventional intraoperative monitoring.

Our study attempted to determine whether cerebral oximetry is useful for different surgery positions and effects on cerebral oximetry.

#### 2. Method

The literature search consisted of retrieving articles from Medline, and Ebscohost from inception until October 30, 2023.

The utilization of both keywords and subject headings was employed in this instance. The search strategy incorporated the following keywords: beach chair, sitting position, cerebral oxygenation, cerebral oximetry, Trendelenburg, Lateral decubitus, prone, and near-infrared spectroscopy. In Medline the advanced search engine was used with the following MeSH (medical subject headings) terms and keywords: (beach chair or sitting or upright), (trendelenburg), (prone), decubitus), (NIRS or near-infrared spectroscopy, oximetry), (cerebral oxygenation or cerebral oximetry). The inclusion criteria encompassed the utilization of intraoperative cerebral saturation monitoring with NIRS in adult patients who were undergoing operating in different surgery positions under general anesthesia or regional anesthesia, as documented in the English-language literature.

#### Sitting/Seated positions

Surgeons utilize the sitting position and the deck chair position in certain neurosurgery and shoulder surgery procedures. The beach chair position (BCP) is preferred over the lateral decubitus technique for several reasons in orthopedic surgery. Firstly, the traditional BCP places less tension on the brachial plexus, which may help to minimize potential complications. Secondly, the BCP is less likely to cause direct neurovascular trauma associated with the position. In addition, traditional BCP provides better visualisation within the joint, allowing for better intervention during the procedure. Finally, if open surgical intervention is necessary, traditional BCP offers easier access 7-9. While the sitting position is associated with fewer complications, it is important to note that serious neurological complications can still occur. The utilization of cerebral oximetry has garnered heightened attention following the documentation of four instances of ischemic brain injury in patients undergoing orthopaedic surgery while positioned in a sitting position 10.

The cerebral oxygen saturation drops more significantly when the patient is in the BCP in comparison to the more markedly compared to baseline values (supine position) <sup>11–14</sup>. The changes in body posture, specifically transitioning from a supine to a

sitting position, result in decreases in cardiac output, mean arterial pressure (MAP), cerebral blood flow (CBF) and cerebral perfusion pressure (CPP), leading to a reduction in cerebral oxygen supply <sup>15,16</sup>. The primary cause for this alteration is the accumulation of blood in the lower limbs as a result of gravitational force and the reduction in the volume of blood flowing back to the heart <sup>17</sup>. Normally, the autoregulation mechanism ensures the maintenance of cerebral perfusion pressure, hence restricting the reduction in cerebral oxygen saturation caused by the change in position <sup>18</sup>. However, a reduction in the mean blood pressure beyond the limit of autoregulation results in a decrease in cerebral perfusion pressure, leading to impaired cerebral oxygenation <sup>19,20</sup>.

#### Prone positions

Patients who undergo spine surgery in the prone position, especially elderly ones, are more than twice as likely to have cerebral desaturation compared with patients in the supine position<sup>21,22</sup>. Although the prone position is known to increase arterial oxygen saturation, especially in patients with ARDS <sup>23,24</sup>, no change in Spo2 was observed in patients who underwent spinal surgery in the prone position, whereas the decrease in bilateral regional cerebral oxygen saturation was accompanied by decreases in heart rate and mean arterial pressure <sup>21,22</sup>. Impaired venous drainage and reduced cerebral perfusion both play a role in the cause of cerebral desaturation in the prone position, which in turn leads to inadequate cerebral oxygenation <sup>25</sup>.

Cerebral oxygenation can be impacted by these interventions when the head is raised off the head support or rotated to the left or right in the prone position. The median value of the measured rScO2 considerably increased by 3 to 5 units when the head was raised from the head support. The lifting of the head may have relieved the pressure on the tissue sensors, which is why this may happen. In addition to this, when the head was moved to the left or right, it dropped on the opposite side. The decrease in brain oxygenation to the contralateral side when the head is shifted to the left or right may be attributed to a decrease in blood flow in the contralateral vertebral artery<sup>26</sup>.

#### Lateral Decubitus

Although the lateral decubitus position is preferred in thoracic surgeries where one-lung ventilation is applied, it is also preferred in shoulder surgeries. When the effect of two different positions on cerebral oxygenation was examined in patients operated on under general anaesthesia in the beach chair position (BCP) and the lateral decubitus position (LDP), the percentage of patients with cerebral desaturation events was significantly higher in the BCP group <sup>12,27</sup>. These studies collectively indicate that the lateral decubitus position may have a more favourable effect on cerebral oxygenation compared to the beach chair position.

Positions and NIRS

On the other hand, the situation is a little bit different in thoracic surgery, where one-lung ventilation is performed. A decline in cerebral oxygenation occurs in thoracic surgery after positioning, although it may not be clinically significant, and it increases when one-lung ventilation (OLV) is switched. During OLV, the collapsed lung receives a hypoxic gas mixture, resulting in atelectasis and ventilation-perfusion mismatch. This decreased oxygen delivery can lead to

hypoxemia, which can subsequently impair cerebral oxygenation. Also, It leads to increased airway pressures and decreased lung compliance. This can decrease venous return, potentially compromising cardiac output and cerebral blood flow. These changes in cerebral oxygenation may be caused by intrapulmonary shunts, hypoxia, and hypercarbia that develop during one-lung ventilation <sup>28-30</sup>.

Table 1: Identification cerebral desaturation events.

Author	Year	Definition of CDE	Definition of Baseline
Aguirre et al (14)	2016	rScO2 value decrease of ≥20% from baseline	Postoxygenation/preinduction
Aguirre et al (47)	2018	rScO2 value decrease of ≥20% from baseline	Postoxygenation/preinduction
Cox et al (51)	2017	Decrease in rSO2 of 20% or greater from baseline or an absolute rSO2 <55%	Preoxygenation/upright
Hayashi et al (45)	2022	rSO2 values decreased 20% of the baseline value or when the absolute rSO2 values were <50%	Pre OLV
Murphy et al (27)	2014	2-min time interval with a ≥20% decrease in SctO2 from baseline values	Preinductions;no details of oxygenation
Woo et al (50)	2018	Decrease in rSO2 of 20% or greater from baseline for 15s or more in either hemisphere of the brain	Postinduction/presitting
Koh et al (11)	2013	SctO2 decreased ≥20% from baseline awake values or SctO2 ≤55%	Preinduction
Doe et al (44)	2016	SctO2 decreased ≥30%	Before surgery
Hayashi et al (49)	2017	Decrease of ≥20% from the baseline rSO2 value or an absolute rSO2 value of <50%	Postinduction/presitting
Picton et al (43)	2015	Absolute rSo2 value $< 55\%$ or a decrease from baseline of $\ge 20\%$ sustained for $\ge 3$ min	Preoperative holding room (Room air)
Jeong et al (50)	2012	Decline in SctO2 more than 20% from baseline for more than 15 s	Preinduction

#### Trendelenburg

The Trendelenburg position is widely used in laparoscopic and robotic surgeries and involves placing the patient in a head-down tilt to facilitate visualisation of the surgical field. The potential effects of this position on cerebral oxygenation have been a subject of interest in recent years. The Trendelenburg position leads to increased intracranial pressure with elevated mean arterial pressure (MAP) and central venous pressure, resulting in a downward trend in cerebral perfusion pressure 31. Another reason is that the position increases the pressure in the abdomen, which can compress the inferior vena cava (IVC). IVC compression decreases venous return to the heart, which can lead to decreased cerebral blood flow and decreased cerebral oxygenation. The elevation of the angle of the Trendelenburg position results in an exacerbated occurrence of this effect, resulting in a reduction in cerebral saturation <sup>32,33</sup>.

The combined effect of the Trendelenburg position and carbon dioxide (CO2) pneumoperitoneum has been shown to impact cardiovascular, cerebrovascular, and respiratory homeostasis during robotic prostatectomy. Furthermore, the creation of a pneumoperitoneum and placement in a Trendelenburg position may lead to a significant increase in intracranial pressure (ICP), potentially affecting patients with cerebral ischemia or cerebrovascular disorders 31.34–37.

The effects of Trendelenburg position on cerebral oxygenation may vary depending on several factors, such as the angle of the position, and the patient's underlying medical conditions.

#### Reverse Trendelenburg

The reverse trendelenburg position is generally preferred in endoscopic sinus surgery because it reduces bleeding and venous congestion, thus providing a better view of the surgical field <sup>38</sup>. In a

manner akin to the seated posture, this position elicits a gravitational impact whereby the blood tends to accumulate in the peripheral regions of the body. As a result, there is a reduction in cardiac output, leading to a subsequent decline in the perfusion of the cerebral region. There appears to be a reduction in cerebral oxygenation, although it is not deemed clinically significant, as the angle of the position increases <sup>39</sup>.

The impact of various surgical positions on cerebral oxygenation when considered collectively;

- 1) Cerebral oxygenation is altered in all surgical positions, whether clinically significant or not, and the most crucial clinical effect is seen in the seated position 10,12–14
- 2) The maintenance of cerebral autoregulation is important for the prevention of cerebral hypoxia or cerebral desaturation. To achieve the desired outcome, it is imperative to uphold the mean arterial pressure above 60 mmHg <sup>4,17,19,21</sup>.
- 3) The oxygenation of the brain decreases in anaesthetised patients. It is kept in mind that the administration of general anesthesia can potentially elicit unfavourable consequences on cerebral autoregulation  $^{40-42}$ .
- 4) Inhalation anesthetics have a more positive effect on cerebral oxygenation than i.v anesthetics. Propofol has both cerebrovascular and cardiovascular effects, which result in an enhanced negative impact on cerebral autoregulation <sup>22,24,43</sup>
- 5) The frequency of cerebral desaturation increases in patients with elderly and comorbidities <sup>5,22,28,30</sup>.
- 6) Different definitions of cerebral desaturation in studies may not be sufficient to demonstrate the relationship between cerebral oxygenation and postoperative complications <sup>11,14,43–46</sup>. Thresholds, baseline measurements and time below threshold may have different effects or relationships on postoperative complications.
- 7) The position of the transducer for blood pressure measurement may cause inaccurate measurements and assessments during intra-operative patient monitoring using conventional hemodynamic monitoring methods. Particularly when in the seated position, placing the transducer at the level of the acoustic meatus yields a more precise evaluation of blood pressure, specifically in terms of reflecting the mean blood pressure at the cranial level <sup>14,47,48</sup>. In the seated position, it is necessary to make an arithmetic correction to the mean arterial pressure (MAP) measured at different locations to determine the blood pressure at the level of the brain. This correction involves adding 1 millimetre of mercury (mmHg) for every 1.35 centimetres of distance

#### 3. Conclusion

The cerebral oximetry is subject to alteration based on the positioning of the patient. Cerebral autoregulation plays a role as a crucial factor in the regulation of cerebral oxygenation. Knowledge of the effects of different surgical positions on cerebral oximetry may assist the anaesthetist in intraoperative patient follow-up. In addition, early recognition of cerebral desaturation and hypoxia may prevent adverse effects of postoperative neurological complications.

#### Limitations of the Study

The limitation of the study is small sample size.

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#### **Conflict of Interests**

The authors have no conflicts of interest to declare.

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#### **Author Contributions**

Concept, study design, conduct the study, data collection, analyze the data, literature rewiev, write the manuscript.

#### **Ethical Approval**

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#### **Data sharing statement**

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# The Role of Cerebral Oximetry in Predicting and Preventing Postoperative Cognitive Dysfunction

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**Abstract:** Postoperative Cognitive Dysfunction (POCD) is a serious problem that is frequently seen in elderly patients and can cause permanent cognitive decline, prolonged hospital stay, loss of independence, decreased quality of life and even mortality. Identifying individuals at risk of developing POCD can prevent this condition by enabling the development of early interventions. Cerebral perfusion disorder is considered to be one of POCD's mechanisms. There are studies on the predictability and preventability of cognitive disorders that may develop after surgery with the use of cerebral oxygenation monitoring. However, the effect of intraoperative cerebral oximetry use on POCD, especially in elderly patients, is controversial. This may be due to multifactoriality in the POCD mechanism. In this article, we aimed to present the study results and inferences regarding the relationships between the areas of monitoring cerebral oxygenation and the pathogenesis of POCD. © 2024 NTMS.

**Keywords:** Postoperative Neurocognitive Disoders; Spectroscopy; Near-infrared; Regional Cerebral Oxygen Saturation (rScO2); NIRS-based Clinical Algorithm.

#### 1. Introduction

#### Monitoring Cerebral Oxygenation

Efforts have been devoted to monitoring tissue oxygenation for more than a century. The ear oximeter was developed in the 1940s and the pulse oximeter in the 1970s. Near Infrared Spectroscopy (NIRS) was first introduced by Franz Jöbsis in 1977. Near-infrared Spectroscopy (NIRS) is a noninvasive and relatively low-cost device that measures tissue oxygen saturation and changes in hemoglobin volüme <sup>1</sup>. NIRS uses near infrared (NIR) light lengths of 700-1000 nm, similar to pulse oximetry <sup>2</sup>. NIR rays are not absorbed by water or protein, but penetrate into deeper tissues and are

absorbed by substances called chromophores. Chromophores are molecules such as oxyhemoglobin  $(O_2Hb)$ , deoxyhemoglobin (HHb), myoglobin, bilirubin, cytochrome oxidase, urobilin, and they can absorb light of 200-800 nm wavelength. NIRS measures the light absorbed by chromophores  $^3$ . The value of NIRS is expressed as 'Regional Oxygen Saturation (rScO<sub>2</sub>)' and NIRS provides continuous, noninvasive monitoring of rScO<sub>2</sub>  $^{2,3}$ .

NIRS electrodes are placed in the frontotemporal region. While pulse oximetry is dependent on pulsatile blood flow (plethysmographic) and measures only the

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oxyhemoglobin of arterial blood, NIRS measures the difference between O2Hb and HHb which reflects oxygen uptake in the tissue bed and is not flow dependent<sup>2</sup>. Therefore, it can be used during cardiopulmonary bypass <sup>4</sup>.

The value of NIRS estimates the average of arterial, venous and capillary oxygenation at the tissue level. Since 70-80% of the blood in the brain is in the venous compartment, NIRS mainly reflects venous blood oxygenation, but the rScO2 value represents the weighted average of tissue oxygenation. In other words, it shows the balance between oxygen need and oxygen delivery rather than oxygen delivery <sup>2,5</sup>.

There are other devices developed to evaluate tissue oxygenation that use different techniques. While the measurement value in the INVOS device is expressed as 'regional oxygen saturation - Rsco2', in the NIRO device it is expressed as 'tissue oxygenation index - TOI' and in the FORE SIGHT device it is expressed as 'cerebral tissue oxygen saturation - SctO2'<sup>6</sup>.

#### Where is Cerebral Oxygenation Monitoring Used?

Although there is insufficient evidence to recommend the use of NIRS as a routine monitoring method in general anesthesia, its use is common especially in cardiac and carotid endarterectomy surgeries. The frequent occurrence of neurological dysfunctions after cardiac surgery has supported the clinical use of cerebral oximetry <sup>2</sup>. Reducing the risk of postoperative neurological complications is an important goal <sup>4</sup>.

There are also studies on its use in non-cardiac surgeries such as surgery which using a sitting or head-up position where cerebral desaturation may occur (for example, the sunbed position in shoulder surgery and single lung ventilation)<sup>4</sup>. NIRS probes can be used to monitor regional tissue oxygenation in pediatric patients by placing them in different parts of the body such as the forehead (cerebral), abdomen (mesentery), and waist (renal) <sup>2</sup>.

#### What is Cerebral Oxygen Desaturation Value?

There is wide interindividual variability for regional cerebral tissue oxygen saturation value. The normal range is between 60% and 75%, with a coefficient of variation of approximately 10% for absolute baseline values <sup>6</sup>. Physiological values have been reported as 55-60% in some cardiac patients <sup>7</sup>. Since the normal value of the cerebral oximeter can vary greatly between individuals, it is more appropriate to use it as a trend monitör <sup>6</sup>. In the clinic, the trend in values is more important than absolute values 7. Ideally, baseline NIRS, inspiratory CO2 concentration (FiCO2), carbon dioxide partial pressure (PaCO2), oxygen saturation (SaO2) and vital values should be noted before induction of anesthesia. Although there is no consensus on what amount of decrease in cerebral oxygen saturation from baseline will pose a clinically significant threat to brain oxygenation, the 'paradigm' used to define abnormal is a decrease of more than 20% from baseline, a difference of more than nine units between the right and left, and values below 50%. The values below 40% are considered a sign of cerebral ischemia <sup>3,4</sup>.

#### Intraoperative Neuromonitoring

Postoperative neurological complications may result from neuronal/vascular damage, embolism and inflammation. The heterogeneity of pathological processes causes different clinical phenotypes of neurocognitive disorders (such as postoperative delirium-POD, postoperative cognitive dysfunction-POCD, and stroke). Multifactorial etiology provides the basis for the use of different neurological monitoring methods, especially during cardiac surgery 8

Currently, there is no single neuromonitoring method that can be considered adequate and ideal. The concept of 'Multimodel Neuromonitoring' refers to the combination of hemodynamic parameters and special invasive-noninvasive neuromonitoring methods <sup>9</sup>. Transcranial Doppler (TCD), Jugular venous bulb saturation (JVBS), electroencephalogram (EEG) and NIRS are among these monitoring methods <sup>8</sup>. The relationship between the NIRS and postoperative neurocognitive functions has been the subject of studies.

#### Postoperative Cognitive Dysfunction

Postoperative Cognitive Dysfunction (POCD) is defined as a significant decrease in cognitive functions that occurs after anesthesia and surgery compared to the preoperative period. Decline is observed in multiple main neurocognitive areas such as executive function, verbal memory, visuospatial abstraction, attention and psychomotor speed <sup>10-12</sup>.

The mechanism that causes POCD is not yet fully understood <sup>10,13</sup>. It is thought to have a multifactorial etiology <sup>14</sup>. Age is the major identified risk factor for POCD, other risk factors include cardiac surgery, prolonged cardiopulmonary bypass (CPB) duration, preoperative mild cognitive impairment (MCI), pre-existing cerebral, vascular or cardiac disease, history of alcohol abuse, low education level, extensive surgeries performed under general anesthesia, development of intra/postoperative complications, secondary surgeries, ischemia, homeostasis disorder, use of long-acting anesthetics and the presence of genetic predisposing factors (carrying the APOE4 genotype, etc.) <sup>10, 15-17</sup>. Possibly, microembolism, perfusion problems, and inflammatory response contribute to the pathogenesis of cognitive decline in cardiac surgery patients and lead to cerebral tissue hypoxia <sup>13,18</sup>. There are studies showing that the incidence of cerebral oxygen

inflammatory response contribute to the pathogenesis of cognitive decline in cardiac surgery patients and lead to cerebral tissue hypoxia <sup>13,18</sup>. There are studies showing that the incidence of cerebral oxygen desaturation is significant in non-cardiac surgeries such as brain surgery, carotid surgery, general surgery, and thoracic surgery <sup>19</sup>. There are studies in the literature investigating the relationship between regional cerebral oxygen desaturation and neurological complications.

Can Cerebral Oxygenation Monitoring Be Used to Predict and Prevent the Development of POCD?

The proper functioning of the central nervous system is extremely dependent on providing adequate nutrient and oxygen supply, effective removal of waste products, and maintaining an appropriate neurochemical environment. A condition such as hypoxia, hypoglycemia or any medication that affects the metabolic state of the brain and general homeostasis may cause postoperative functional impairment of the brain.

Cerebral hypoperfusion due to hypotension may lead to cognitive deficits, but strong enough evidence has not been obtained in studies on this<sup>13</sup>. The effect of NIRS-guided intervention on neurocognitive disorders after cardiac and non-cardiac surgeries is still a controversial issue <sup>18</sup>.

Tian et al. examined 12 randomized controlled trials (RCTs) involving cardiac surgery patients and showed that intraoperative cerebral desaturation was associated with the incidence of POD) and that rScO2-guided intraoperative intervention was associated with a lower risk of POD/POCD and shorter intensive care stay. The definition of cerebral desaturation in the reviewed studies was accepted as a decrease below 70-90% of the initial rScO2 or a decrease below 50-60% of the absolute rScO2 value <sup>18</sup>.

Holmgaard et al. examined the relationship between intraoperative decrease in cerebral oxygen saturation and POCD in patients undergoing pump-assisted heart surgery. The rScO2 value was calculated as the average of the left and right sensor values, based on the cumulative periods during which the rScO2 was ≥10% below the preoperative value for each patient. No significant difference was found between patients with and without POCD at discharge in terms of cumulative times with preoperative rScO2 values ≥10% below. Additionally, no significant difference was found when preoperative rScO2. mean rScO2 during cardiopulmonary bypass (CPB) or intraoperative rScO2 and minimum rScO2 values of patients with and without POCD at discharge were analyzed. They could not find any relationship between intraoperative rScO2 variables and the occurrence of POCD after cardiac surgery <sup>20</sup>.

Tang et al. followed 76 patients who underwent thoracic surgery with single lung ventilation with FORESIGHT cerebral oximetry and evaluated them with a mini mental state exam. They found that there was a relationship between the intraoperative decrease in SctO2 and early cognitive impairment <sup>19</sup>.

In the study of Chen et al., 7 RCTs- including non-cardiac surgeries (2 studies on abdominal surgery patients and 4 studies on orthopedic surgery patients) were analyzed. In the subgroup analysis of abdominal surgery and orthopedic surgery in elderly patients, the mean intraoperative cerebral oxygen saturation of patients with POCD was found to be significantly lower than the group without POCD <sup>21</sup>.

Murniece et al. examined the effect of an intraoperative NIRS-based clinical algorithm on postoperative cognitive functions in patients who underwent spinal surgery in the prone position. The study group (23 patients) received intervention if rScO2 values decreased bilaterally or unilaterally by more than 20% from baseline values or fell below the absolute value of 50%. In the control group (11 patients), standard intraoperative anesthesia monitoring was applied, rScO2 was monitored blindly, and intervention was made according to hemodynamic parameters and the amount of bleeding. Montreal-Cognitive Assessment (MoCA) test was applied to both groups preoperatively and on postoperative day two. rScO2 fell below the threshold in three patients in the study group and one patient in the control group. While none of the three patients had POCD, one patient in the control group developed POCD. It has been suggested that a significant rScO2 decrease may occur while other intraoperative measurements remain stable and that the use of a NIRS-based clinical algorithm may help prevent POCD in patients after spine surgery <sup>22</sup>.

In the study of Ding et al., they investigated the role of rScO2 monitoring in preventing POCD in elderly patients. Six RCTs including 377 patients were examined, and the incidence of POCD ranged from 17% to 89%, and the overall prevalence was found to be 47% in the pooled analysis. The use of rScO2 monitoring has been found to be associated with a lower risk of POCD and a shorter length of hospital stay in older patients undergoing noncardiac surgery. It has been suggested that rScO2 monitoring in high-risk populations may have the potential to prevent POCD <sup>23</sup>. In the past, evidence on whether interventions for cerebral oxygen desaturations reduce the risk of neurological outcomes has been limited to case reports and observational studies. Randomized, controlled algorithm-based interventional trials for cerebral desaturations in patients undergoing cardiac surgery are now available<sup>24,25</sup>. According to meta-analyses, there is insufficient evidence to support or refuse whether interventions for cerebral desaturations during surgery improve neurological outcomes<sup>4</sup>. Differences in results between studies may be due to different rScO2 monitoring principles and the heterogeneity of the patient groups monitored.

NIRS reflects mixed arterial and venous saturation in localized areas of the frontal lobes, not the entire brain. If cerebral ischemia develops in brain regions other than the frontal lobe, intraoperative rSO2 values may remain normal. In case of cortical atrophy in elderly patients, inaccurate measurements may occur due to the increased distance between the skin and brain tissue. POCD has a multifactorial etiology and there are multiple neurocognitive tests to evaluate. Different neurocognitive tests were used in the studies, and this may cause the difference in the results obtained. The mechanism of delayed cognitive recovery is unknown and perhaps cannot be prevented simply by avoiding compromised cerebral oxygenation during surgery.

Hogue et al. found that hypotension was also common in the postoperative intensive care unit and was associated with brain injury biomarker release<sup>4</sup>. Therefore, a strategy to ensure cerebral perfusion both in the operating room and in the intensive care unit may be necessary.

#### 2. Conclusion

In conclusion, NIRS is an easy-to-use, non-invasive cerebral oxygenation monitoring method that may help prevent cerebral desaturation and hypoxic brain injury intraoperatively. However, all available information regarding the patient, surgery, and anesthesia should be carefully evaluated, and it is recommended to plan intervention on a patient-by-patient basis after excluding false positive measurements due to placement of NIRS device probes.

#### **Limitations of the Study**

This review paper has several important limitations. First, our study only includes articles published in Turkish and English. This might have excluded potentially significant studies in other languages and poses a risk of language bias. Second, most of the studies included in the review come from specific geographical regions, which limits the generalizability of the findings on a global scale. Additionally, there is considerable methodological diversity and variability in the quality of the included studies. Different data collection and analysis methods make it difficult to compare results, which may affect the overall validity of the review. Some studies carry a high risk of bias due to methodological shortcomings and inadequate reporting. Finally, as this review focuses on a specific topic, other relevant subjects or subtopics have been excluded. This narrows the scope of our research question and limits the broader interpretation of our findings. Therefore, it is important for readers to consider these limitations when evaluating our results.

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#### **Conflict of Interests**

T The authors declare no competing interests.

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#### **Author Contributions**

TSA and AS designed the study. TSA and AS read the draft and approved the final scenario.

#### **Ethical Approval**

None.

Data sharing statement

None.

Consent to participate

None.

**Informed Statement** 

None.

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#### **Use of Somatic Oximetry in Traumatic Organ Injuries**

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**Abstract:** Somatic oximetry, despite its frequent application in the clinical assessment of trauma patients, suffers from a notable dearth of randomized controlled trials, leading to an absence of systematic reviews or a defined level of evidence pertaining to its clinical utility. Somatic oximetry can provide information not only in direct monitoring of traumatized tissue but also in monitoring standardized areas such as the thenar region, shedding light on compensatory mechanisms of the body. The employment of the vascular occlusion test in somatic oximetry affords dynamic measurements, presenting a valuable tool for assessing the efficacy of diverse therapeutic interventions. Recent research findings establish that somatic oximetry plays a pivotal role in gauging the need for resuscitation during the initial evaluation of trauma patients. Furthermore, its application extends to monitoring oxygenation levels in damaged extremities and superficially located internal organs, particularly in the pediatric population. Despite the demonstrated benefits, a significant impediment to the widespread adoption of standardized somatic oximetry, specifically utilizing StO2, arises from the prevalent practice of amalgamating data from trauma and cardiac arrest patients. This practice hinders the establishment of a standardized evaluation protocol before the completion of resuscitation efforts. Consequently, the potential of somatic oximetry in mitigating secondary damage remains inadequately explored and warrants further rigorous scientific investigation. © 2024 NTMS.

Physiologic/instrumentation; **Keywords:** Monitoring, Near-Infrared; Oximetry; Trauma; Injuries.

#### 1. Introduction

Near-infrared spectroscopy (NIRS) technology has revolutionized the ability to continuously monitor the oxygenation of superficial tissues, providing valuable insights into tissue perfusion and oxygen supply. This non-invasive technique employs the principles of light absorption and scattering to measure changes in the concentration of oxygenated and deoxygenated

hemoglobin in tissues. Thus, the key advantage of NIRS is its ability to provide real-time information about tissue oxygen levels. It offers a non-stop window into the oxygen status of the tissue, which is particularly critical in scenarios such as trauma care, surgery, and intensive care units.

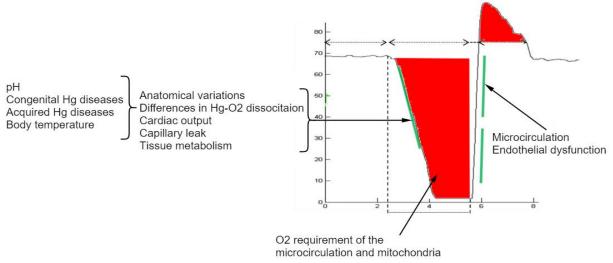
Critics have raised concerns about the specificity of

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NIRS values, as they include contributions from both arterial and venous circulation <sup>1</sup>. While this critique is valid, it's crucial to understand that NIRS is capable to provide a holistic view of tissue oxygenation. Rather than pinpointing the source of oxygenation, NIRS serves as an indicator of overall tissue health and oxygen supply. Recent research has explored ways to enhance the specificity of NIRS data through advanced signal synthesis and processing techniques, which may improve its clinical utility.

The vascular occlusion test is a notable application of

NIRS. This test involves temporarily blocking blood flow to a specific region, allowing for the assessment of tissue oxygen requirements. It's a rapid and practical way to understand how well tissues can adapt to changes in oxygen supply, providing insights into vascular function and potential issues with tissue perfusion <sup>2</sup>. The vascular occlusion test can capture a range of physiological parameters, including patient-specific anatomical variations, hemoglobin concentration, hemoglobin structure, cardiac output, pH, and body temperature (Figure 1).



**Figure 1:** The descriptive nature of the vascular occlusion test is given. The descent on the left side gives the rate of desaturation of tissue oxygen saturation, which is related to the fitness of the patient. The ascend on the right side gives the rate of resaturation of tissue oxygen saturation, which is related to the state of the microcirculation, which is mainly determined by the endothelial function. The area under the curve inbetween the two green lines is positively correlated to the oxygen requirement of the tissue, and if they are active, the mitochondria. Finally, the small red area above the baseline may indicate the antioxidant capacity of the tissue.

Despite all of this convenience and benefits, the literature on the use of somatic oximetry (stO2) in trauma patients predominantly consists of case reports and observational studies. While these studies have provided valuable insights into the potential utility of stO2 in clinical settings, there is a growing need for more robust evidence in the form of randomized controlled trials (RCTs) to establish its efficacy. Additionally, the majority of observational studies conducted in the field of Emergency Medicine are not specific to trauma patients, rather the data for trauma patients and cardiac arrest patients are often presented in a combined manner.

StO2 holds the promise of being a crucial tool for assessing the intensive care needs of trauma patients and optimizing treatment. Trauma patients present a unique set of challenges, including varying degrees of tissue damage, hemorrhage, and fluctuations in oxygen demands. The real-time, non-invasive monitoring provided by stO2 can offer valuable insights into the dynamic nature of tissue oxygenation in these complex cases.

This review aims to examine the current status of somatic oximetry's clinical use in trauma patients by thoroughly analyzing relevant studies and data. The goal is to provide a comprehensive understanding of the potential advantages and limitations of stO2 in this patient group, including its role in early detection of tissue hypoxia, guiding resuscitation efforts, and improving patient outcomes.

## 1.1. Does somatic oximetry fit into the initial assessment of traumatic organ injury?

The earliest reports of stO2 use in trauma patients are from intensive care units. The prototype NIRS devices were compared with arterial base deficit, lactate, gastric mucosal pH and mixed venous hemoglobin oxygen saturation <sup>3</sup>. It was concluded that the skeletal muscle stO2 is capable to reflect whole body oxygenation status. Following studies showed that stO2 non-invasively derived from the thenar region is able to quantify the severity of hemorrhagic shock <sup>4</sup>. A multicentre study including 383 patients showed that stO2 was noninferior to base deficit when used to predict multiple organ dysfunction or death <sup>5</sup>.

Following the validation of thenar muscle-derived stO2, shown to be comparably accurate to the earlier invasive monitors, investigations delved into its

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standalone efficacy. A notable single-center study focused on somatic oximetry in adult trauma patients, showcasing several strengths including a robust patient cohort, a concise data collection period of 9 months, and inclusion of diverse trauma types (head, chest, abdomen, and extremity). The study's key finding emphasized that the initial rate of deoxygenation, in conjunction with age and Glasgow Coma Scale score, successfully predicted the necessity for life-saving interventions. However, the study lacked insights into the correlation between organ injury and specific outcomes, such as blood product transfusions or mechanical ventilation. Notably, reported outcomes like a Glasgow Coma Scale Score <15 were deemed insufficiently informative. A nuanced exploration of these associations is crucial for a comprehensive understanding of somatic oximetry's predictive value in trauma management <sup>6</sup>.

A study including 325 patients found the stO2 value of 65% as the cutoff for marked increase in consumption of packed red bood cell  $^7$ .

A study including 184 pediatric trauma patients reported that stO2 value<70% and a heart rate increased above 2 standard deviations predicts need for life saving interventions during the pediatric intensive care unit stay 8. The study exhibits several limitations, such as the absence of a defined protocol for determining which cases should be monitored with NIRS and which should not. However the study reported the results of monitored and not monitored groups. The main limitation is that prehospital rate of life saving interventions was similar between groups with lower and higher stO2 values (64,6% vs 52,2%), which suggests that the outcome measured the response to prehospital interventions, which were standardized nor explained. Also the number of patients in each group were not balanced.

A recent prospective cohort study conducted over an 18-month period reported a two-fold increase in the rate of life-saving interventions in cases where the stO2

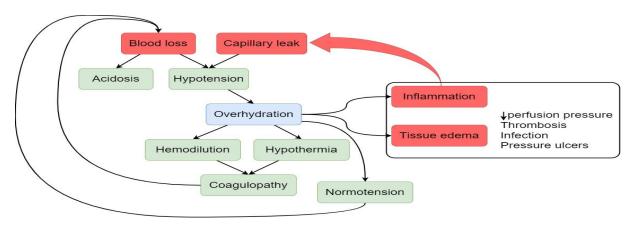
value was below 70% <sup>9</sup>. The strengths of this study include the inclusion of both blunt (67.6%) and penetrating (28.4%) traumas, a more homogeneous age group, and a balanced number of patients in each group. Reports from military medicine include valuable data related to the question. A case report series including data from 40 military personnel obtained within 3 months reports that initial stO2 value < 70% indicates clinical shock, and somatic oximetry is able to show improvement associated with resuscitation maneuvers <sup>10</sup>. The literature in military medicine reports that an stO2 value below 75% indicates the severity of injury and the effectiveness of resuscitative efforts <sup>11</sup>.

Finally, thenar oximetry is capable to differentiate between mild, moderate and severe shock states <sup>12</sup>.

## 1.2. Does somatic oximetry fit into the initial treatment of traumatic organ injury?

A major milestone in trauma literature investigated whether there is a difference between immediate or delayed fluid resuscitation in hypotensive trauma patients. The study found that there was a difference, but not in terms of reversing hypotension efficiently. Rather, it was interesting to learn that giving more fluids may harm the patient. In that study, patients who received around 2.5 liters of crystalloids instead of 375 ml died more frequently (38% vs 30%) <sup>13</sup>. A later study investigated the same question in rats and reported that immediate resuscitation lead to less mortality. However, stratifing the groups in terms of received fluids revealed once more that mortality had a positive correlation with the amount of fluids given <sup>14</sup>. These and many other studies formed the basis of low volume fluid resuscitation which is a component of damage control resuscitation.

It turns out that damage control resuscitation necessitates permissive hypotension during the initial assessment and organ repair to prevent unnecessary hemodilution and edema (Figure 2).



**Figure 2:** The physiologic mechanisms associated with overhydration, one of the aggressive resuscitation strategies, is given. The initial acidosis may, mprove tissue oxygenation with a right shift of the oxygen-hemoglobin dissociation curve, and hypotension may decrease the blood loss. On the contrary, overhydration may cause hemodilution and other side effects, all of which may promote further blood loss and inflammation. Please note that monitoring tissue oxygen saturation can both prevent and diagnose the harmful conditions given on the right rectangle. Thus tissue oxygen saturation is a goal-directed dynamic monitor.

The vascular occlusion test is the workhorse of near-infrared spectroscopy <sup>15</sup>. Although it is criticized for mixing arterial, venous, and tissue oximetry values, the different phases allow for a thorough evaluation of all these sites (Figure 1). It has been reported that the desaturation phase can identify hemorrhagic shock, whereas the resaturation phase can identify septic shock <sup>16–19</sup>. Thus, it is capable of identifying the causes shown on the right side of Figure 2.

1.3. Is there a potential for somatic oximetry to guide or individualize the therapeutic interventions?

Although somatic oximetry may not be an omnipotent marker capable to guide the therapy, it may be a very good complement to any form of disease with hypoperfusion. Acute compartment syndrome following limb injury is an established disease, which benefits most form somatic oximetry. An injured limb may be lost due to arterial dissection or compartment syndrome. Both civilian and military literature suggest that somatic oximetry is capable to detect an underperfused limb and quantitatively monitor the oxygenation of the limb, and monitor the benefit and harm of any therapeutic maneuver. (20-22. The key points to remember when using somatic oxymetry to monitor an injured limb are that 1) the most effective way is to also monitor the opposite limb, if possible and 2) a hyperemic state is expected in a sufficiently perfused limb during the first 72 hours of trauma <sup>23,24</sup>. As far as this literature review, there is no other established disease which may benefit from somatic oximetry, yet. The following parapgraphs will explain some of the controversy in the literature.

There is substantial amount of literature comparing cerebral oximetry with intracranial pressure monitors, cerebral microdialysis and jugular venous blood gas analysis in traumatic brain injury <sup>25,26</sup>. Intracranial pressure is an important parameter since its increase is related with decreased cerebral perfusion and neuronal death. Devices capable to continuously measure intracranial pressure via an intracranial catheter and adjust it via a peristaltic pump are invasive devices, with their own set of complications <sup>27</sup>. They ease the management of a patient with a tumor, hematoma or edema <sup>28,29</sup>. Subtle changes in intracranial pressure are overcome by the cerebral autoregulation. Due to that, the attending clinican should include all factors related to cerebral autoregulation (arterial blood pressure, partial pressure of arterial carbondoxide, body temperature and sedative drugs, just to name a few). Please note that NIRS (but not stO2) is mainly used to monitor cerebral autoregulation <sup>30</sup>.

All the aforementioned monitoring approaches share a common limitation. This is exemplified in a patient scenario featuring head and thorax injuries coupled with cerebral edema and adult respiratory deficiency syndrome. The dilemma arises when implementing a lung-protective ventilation strategy. On one hand, this strategy may lead to normoxemia and gradual

triggering hypercapnia, subsequently increased cerebral blood flow and exacerbating cerebral edema. The implications for neurological outcomes remain challenging to ascertain, with somatic oximetry and jugular venous blood gas analysis potentially yielding more favorable results, while intracranial pressure monitoring and cerebral microdialysis, contingent on their placement, may indicate less favorable outcomes. In light of these complex physiological dynamics, it should not be surprising that near-infrared spectroscopy has not proven efficacious in detecting intracranial hematomas. The intricate interplay of these monitoring modalities underscores the need for a nuanced understanding of their limitations and advantages in diverse clinical scenarios 31,32. This review did not find any evidence indicating a potential for somatic oximetry to alleviate secondary injury or improve outcomes. Nor was it possible to identify any randomized controlled clinical study in English literature with an active arm using somatic oximetry as an intervention.

#### 2. Conclusion

A recent study investigating the role of somatic oximetry in trauma patients found that alterations in somatic oximetry values are associated with occult shock 33. Considering the relationship between occult shock and infection rate and mortality in major trauma patients, somatic oximetry may be expected to become part of a multimodal monitoring approach 34. An additional advantage lies in the applicability of somatic oximetry in damage control resuscitation and low-volume fluid resuscitation. Furthermore, compelling evidence supports the capability of somatic oximetry to tailor treatment approaches for hemorrhagic shock and extremity injuries, thereby underscoring its potential for personalized and targeted interventions in critical care scenarios.

#### Limitations of the Study

This review has several limitations. Firstly, much of the literature on somatic oximetry consists of case reports and observational studies rather than randomized controlled trials, limiting the robustness of the conclusions. Additionally, many studies combine data from trauma and cardiac arrest patients, complicating the interpretation specific to trauma care. The variability in study designs, patient populations, and intervention protocols further complicates the synthesis of findings. Finally, the lack of standardized evaluation protocols and the potential publication bias towards positive outcomes should be considered when interpreting the results. Further rigorous research is needed to establish standardized guidelines and confirm the clinical utility of somatic oximetry in trauma patients.

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#### **Conflict of Interests**

The authors declare no competing interests.

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#### **Author Contributions**

All authors contributed equally to the article.

#### **Ethical Approval**

None.

#### **Data sharing statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

#### Consent to participate

None.

#### **Informed Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## **Investigating the Relationship Between Cerebral Oximetry and Arterial Blood Gas Parameters**

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Abstract: Cerebral oximetry, employing near-infrared spectroscopy (NIRS) through a transcutaneous membrane, is a non-invasive monitoring method designed to assess average regional tissue oxygenation in the frontal cortex. The literature consistently underscores its invaluable role in gauging cerebral tissue oxygen levels throughout the perioperative period. Notably, guidelines routinely recommend the use of NIRS in adult cardiac surgery. In contrast, arterial blood gas analysis remains a standard practice in cardiac surgery to measure general systemic oxygenation. While arterial blood gas analysis provides insights into overall systemic oxygenation, NIRS focuses specifically on regional oxygenation within the brain tissue. This paper delves into the intricate relationship between NIRS and arterial blood gas parameters, shedding light on their correlation and significance in the context of assessing oxygenation levels. © 2024 NTMS.

**Keywords:** Cerebral Oximetry; Arterial Blood Gas; Cardiac Surgery.

#### 1. Introduction

Cerebral oximetry and arterial blood gas (ABG) analysis represent distinct methodologies in the assessment of oxygen levels within the human body. Despite their shared objective of evaluating oxygenation, these methods diverge in terms of their application and measurement locations. ABG analysis entails the measurement of oxygen, carbon dioxide, pH, and other components using a sample extracted from the arterial system. This diagnostic test is commonly employed to appraise blood oxygen and carbon dioxide content, as well as to assess acid-base equilibrium and

electrolyte levels. In contrast, cerebral oximetry and ABG analysis target different facets of oxygenation. Cerebral oximetry specifically gauges oxygenation in the brain tissue on a regional scale, whereas ABG analysis provides insights into overall systemic oxygenation <sup>1</sup>.

Cerebral oximetry monitors employ non-invasive continuous monitoring through near-infrared spectroscopy (NIRS) technology to assess cerebral oxygenation. Numerous studies have demonstrated their effectiveness in evaluating cerebral tissue oxygen levels during cardiac surgeries, hypotensive surgeries,

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and prolonged monitoring of patients in the trendelenburg position <sup>2</sup>. Beyond surgical settings, these monitors are now being employed in scenarios where cerebral blood flow (CBF) ceases, such as cardiac arrests, with the aim of sustaining cerebral blood flow through cardiopulmonary resuscitation. The operational principle is grounded in The measurement of near-infrared light with a specific wavelength of 750 - 100nm. The ability of near-infrared light to penetrate tissues and be absorbed by certain chromophores forms the basis of regional cerebral oxygen saturation measurement. In contrast to pulse oximeters, which primarily measure arterial blood flow, values for cerebral regional oxygen saturation (rSO<sub>2</sub>) obtained from NIRS are predominantly reflective of venous blood, as venous blood constitutes ~75% of the blood flow in brain tissue. Consequently, oxygen saturation derived from NIRS serves as a representation of venous oxygen saturation for the respective organ <sup>3</sup>. Studies have indicated a positive linear correlation between cerebral oximetry and jugular venous saturations 4. NIRS, a non-invasive technique, enables exploration of cerebral hemodynamics and oxygenation. Integrated with CBF measurements, it has the potential to unveil insights into oxygen distribution, metabolism and function. However, interpreting experimental results can be complex due to the influence of various factors on measured NIRS signals, encompassing both scalp and cerebral hemodynamics.

The interaction between Arterial Blood Pressure (ABP) and CBF has been thoroughly examined, playing a comprehending fundamental role in cerebral autoregulation. Previous studies have explored the influence of alterations in ABG levels on both ABP and CBF. Yet, the comprehensive characterization of the relationship between ABP, alterations in ABG, and NIRS signals remains an area that warrants further exploration <sup>5</sup>. The regulation of CBF is generally known to be directed by changes in the pH of cerebrospinal fluid, often influenced by pCO<sub>2</sub>. Both high and low pH values exert a direct effect on the relaxation and contraction of smooth muscles. However, some findings suggest that PaCO2 may act independently or in conjunction with pH. This effect is thought to extend beyond the regulation of smooth muscles, potentially affecting endothelial cells, nerves, and astrocytes. The results also indicate that arterial pCO<sub>2</sub> may have an impact on regulating smooth muscle contractility through the endothelium. Cerebral autoregulation is strongly linked to carbon dioxide partial pressure but is much less affected by changes in arterial oxygen saturation <sup>6</sup>.

In a study of pediatric patients with repaired congenital heart disease, the relationship between cerebral and somatic regional oxygen saturation renal, splanchnic, and muscle regions was compared to blood gas lactate levels. Cerebral rSO<sub>2</sub> showed the strongest inverse correlation with lactate levels, followed by renal, splanchnic, and muscle rSO<sub>2</sub>. The average cerebral and renal rSO<sub>2</sub> predicted a lactate level of 3.0 mmol/litre

with 95% sensitivity and 83% specificity. Based on the findings, it is broadly inferred that an average cerebral and renal  $\rm rSO_2$  measured using NIRS, predicting values below 65%, may serve as an early indicator of increased lactate levels in acyanotic children following congenital heart surgery. This implies its potential utility in identifying global hypoperfusion associated with low cardiac output syndrome within this specific population  $^7$ .

In a meta-analysis conducted on children with congenital heart disease, the aim was to determine the correlation between venous oxygen saturations corresponding to NIRS oximetry. The findings demonstrate a robust correlation between cerebral NIRS oximetry and oxygen saturation levels in the superior vena cava or jugular vein. Additionally, renal NIRS oximetry exhibits a significant correlation with oxygen saturations in the inferior vena cava. Conversely, a weaker correlation was observed between cerebral NIRS oximetry and oxygen saturations in the inferior vena cava <sup>8</sup>. De Waal et al. demonstrated an increase in end-tidal CO2, cerebral blood volume, and rSO<sub>2</sub>, along with significant cerebral vasodilation, elevated PaCO2 and increased CBF after insufflation in children undergoing laparoscopic fundoplication. In contrast, post-pneumoperitoneum rSO<sub>2</sub> values were similar to preoperative values. However, De Waal et al. established the initial rSO<sub>2</sub> values before insufflation after inducing moderate hypocapnia, detecting approximately a 25% increase in PaCO<sub>2</sub> during pneumoperitoneum <sup>9</sup>. In a study by Kaya et.al., evaluating whether lower pneumoperitoneum pressure than standard pressure during laparoscopic nephrectomy would allow higher cerebral oxygen saturation, a moderate positive correlation between cerebral rSO<sub>2</sub> and PaCO<sub>2</sub> was found <sup>10</sup>.

Given this context, we conducted a comparative analysis of the correlation between intraoperative NIRS values and blood gas parameters in patients who underwent open-heart surgery at the Ondokuz Mayıs University Hospital Cardiovascular Surgery Operating Room between January 2021 and August 2023. The retrospective evaluation included intraoperative NIRS values and blood gas parameters of 170 patients. This study was approved by the Ondokuz Mayis University Clinical Research Ethics Committee (approval number; 2023/291). The statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) program, version 25 (IBM, Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was employed for normality tests. Descriptive statistics were presented as mean (± standard deviation) for quantitative data with normal distribution, and as median (interquartile range) for data without normal distribution, while frequencies (and percentages) were used for categorical data. The correlation between the lowest/highest blood gas parameters (pH, PaCO2, PaO2, lactate, hemoglobin) and cerebral rSO2 values was examined. The correlation between rSO2 and pH, pCO2, pO2, Hb, and lactate was assessed using the Turunc E. et al.

Pearson correlation test. The correlation coefficient (r) values were interpreted as indicating a 'weak' relationship if r=0.00–0.24, 'moderate' if r=0.25–0.49, 'strong' if r=0.50–0.74, and 'very strong' if r=0.75-1.00. p value <0.05 was considered statistically significant.

Patient and procedural characteristics are summarized in Table 1. Upon evaluating the results of our study, a positive correlation was observed between the decrease in rSO<sub>2</sub> and pH, PaO2, and hemoglobin values, while a negative correlation was noted with paCO<sub>2</sub> and lactate values (Fig.1). The increase in lactate levels, affecting cardiac output and potentially impairing oxygen delivery, was considered to contribute to the reduction in cerebral oxygenation. When considering the time effect on ABG, a correlation with cerebral rSO<sub>2</sub> is evident (Table 2).

**Table 1:** Patient demographic and surgical characteristics and clinical outcomes.

	$\mathbf{n} = 170$
Age, years	$60.3 \pm 12.3$
Sex, female/male n (%)	63 (37.1)/107 (62.9)
BMI (kg/m²)	$27.1 \pm 5.1$
Comorbidities, n (%)	
Cardiovascular system <sup>a</sup>	38 (22.4)
Endocrine system <sup>b</sup>	29 (17.1)
Respiratory system <sup>c</sup>	5 (2.9)
> 1 more system	55 (32.4)
Surgery type, n (%)	
CABG	89 (52.4)
AVR/MVR	42 (24.7)
CABG + AVR	31 (18.2)
ASD	4 (2.4)
Bypass time (min)	$146.2 \pm 57$
Cross-clamp time (min)	92.8 ± 44.1

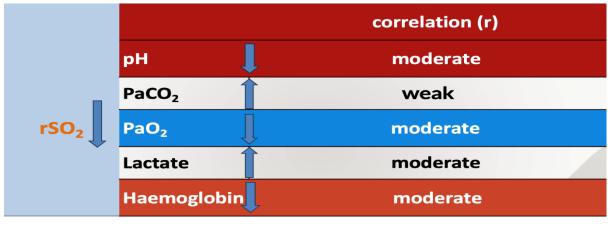
Continuous variables are presented as mean ± standard deviation and categorical variables are presented as counts (percentages). Statistically significant difference is highlighted in bold. *Abbreviations:*, *ASD* atrial septal defect, *AVR* aortic valve replacement, *BMI* body mass index, *CABG* coronary artery bypass grafting, *MVR* mitral valve replacement. <sup>a</sup>Hypertension, <sup>b</sup> Type 2 diabetes, <sup>c</sup> Asthma.

**Table 2:** Assessment of Correlation Coefficient (r) Values Between NIRS, Arterial Blood Gas, and Haemoglobin.

	pН		$PaO_2$		PaCO <sub>2</sub>		Hb		Lactate	
	r	p	r	p	r	p	r	p	r	p
rSO <sub>2</sub> (right)	0.332	0.069	0,255	0.002	-0,190	0.872	0,305	0.000	-0,347	0.038
rSO <sub>2</sub> (left)	0.325	0.001	0.308	0.022	-0.191	0.185	0.405	0.049	-0.349	0.077

Significant difference is highlighted in bold. Abbrevations: NIRS: Near-Infrared Spectroscopy, rSO<sub>2</sub>: Regional cerebral oxygen saturation; r: Correlation coefficient; PaO<sub>2</sub>: Partial pressure of arterial oxygen; PaCO<sub>2</sub>: Partial pressure of arterial carbon dioxide; Hb: Haemoglobin concentration.

Figure 1: The correlation between rSO2 and arterial blood gas parameters.



#### 2. Conclusion

In summary, the role of cerebral oximetry as a pivotal protective monitor in safeguarding cerebral functions is underscored by its potential to provide valuable insights during various medical procedures. A thorough examination of existing literature yields no conclusive evidence supporting a direct correlation with ABG analysis. Nevertheless, the significance of cerebral oximetry should not be diminished; instead, it should be acknowledged as a complementary monitor, amplifying the capacity to improve patient outcomes across diverse surgical scenarios, encompassing both cardiac and non-cardiac procedures.

This perspective is fortified by a wealth of accumulating evidence and the widening spectrum of applications observed in clinical practice. Rather than positioning cerebral oximetry as a substitute for ABG analysis, it should be recognized as an invaluable ally, contributing to a more comprehensive understanding of oxygen dynamics and aiding in the nuanced management of patients undergoing surgery. Limitations of the Study

Our study has several limitations. Firstly, the presence of clinical, physiological, and metabolic variations among patients can significantly impact both cerebral oximetry and blood gas analysis results, potentially weakening the correlation between the two methods. Secondly, technical constraints related to cerebral oximetry devices may hinder accurate measurements, particularly in conditions of low perfusion. Thirdly, the reliance on small sample sizes and the absence of long-term data limits our comprehensive understanding of the clinical benefits of cerebral oximetry and blood gas analysis. Lastly, the retrospective research design introduces inherent biases.

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## **Conflict of Interests**

The authors declare that they have no conflict of interest.

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## **Author Contributions**

BD: Conceived and designed the study, collected data, and wrote the manuscript. ET, EO: Contributed to data collection. ET, OK: Analyzed and interpreted results, participated in data collection. BD, ET, OK, EO: Involved in data collection. BD, ET: Contributed to study design, supervised the work, performed analysis, and provided data and analysis tools. All authors have read and approved the final version of the manuscript.

## **Ethical Approval**

The study was commenced after receiving approval from the local ethics committee (Ondokuz Mayis University Clinical Research Ethics Committee (approval number; 2023/291)).

## Data sharing statement

None.

## **Consent to participate**

Informed consent was not applicable.

#### **Informed Statement**

The study complies with the principles of the Declaration of Helsinki. The consent of all the patients was obtained before commencing the study.

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# An Innovative Approach in Emergency Medicine: Monitoring Brain Oxygenation with Cerebral Oximetry

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Abstract: The monitoring of cerebral oxygenation is a method that is not commonly integrated into the majority of existing emergency departments (ED), but it has attracted increasing attention, particularly in recent years. As the severity of ischemia escalates during cardiopulmonary resuscitation (CPR), the probability of both survival and favorable neurological outcomes diminishes. Therefore, the imperative development of methods to quantify the magnitude of ischemia, particularly cerebral ischemia, during resuscitation is critical for enhancing overall outcomes. Cerebral oximetry (CO), using near-infrared spectroscopy, represents a noninvasive method for measuring brain oxygenation. The objective of this manuscript is to present an overview of the application of cerebral oximetry in the ED. ©2024 NTMS.

**Keywords:** Oximetry; Spectroscopy; Near- infrared; Emergencies.

#### 1. Introduction

Cerebral oximetry is a medical technique that measures the oxygen saturation of the blood in the brain. This monitoring method provides real-time information about the levels of oxygen in the brain tissue, helping healthcare professionals assess and manage the oxygen supply to the brain. By monitoring cerebral oxygenation levels, healthcare providers can make informed decisions to optimize oxygen delivery and prevent potential complications related to inadequate brain oxygenation <sup>1</sup>.

#### 1.1 Historical Background

Cerebral oximeters, like pulse oximeters, are non-invasive devices capable of continuous monitoring, operating on similar pyhsical principles. This technology was first described by Jobsis in 1977 <sup>2</sup>. According to his study, the relatively high levels of brain tissue transparency in the near-infrared range (650-1000 nm) facilitated real time, non-invasive

detection of hemoglobin oxygenation using transillumination spectroscopy. Two decades later, the first commercial devices were developed and are now utilized in various medical settings, including cardiovascular surgery, neurosurgery, anesthesia management, and intensive care units (Figure 1).

## 1.2 Physics

Cerebral oximeter typically consists of sensors or probes that are attached to the patient's forehead (Figure 2). These sensors use near-infrared spectroscopy (NIRS) to measure the amount of oxygenated hemoglobin (HbO2) and deoxygenated hemoglobin (HbO) in the blood of the brain. The cerebral oximeter emits near-infrared light into the tissues of the forehead. The near-infrared light penetrates the skin and underlying tissues and is partially absorbed by Hb in the blood. Detectors in the cerebral oximeter measure the amount of near-infrared light that is absorbed by

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HbO2 and deoxygenated Hb. HbO2 and Hb absorb light differently at specific wavelengths (Figure 3) <sup>3</sup>. By comparing the amount of light absorbed at these specific wavelengths, the cerebral oximeter calculates the ratio of HbO2 to total hemoglobin, providing an estimate of the oxygen saturation level in the blood <sup>4</sup>.



Figure 1: General view of the cerebral oximeter device.

The estimation of cerebral hemoglobin oxygen saturation is achieved through the application of the Beer-Lambert law 5. Additionally, the presence of extracranial blood poses a potential challenge to accurate CO measurements. To address this issue, cerebral oximeters utilize multiple probes and employ spatial resolution techniques <sup>6</sup>. Spatial resolution relies on the principle that the depth of tissue examined is determined by the distance between the light emitter and the light detector <sup>7</sup>. The system calculates the ratio of oxyhemoglobin to total hemoglobin within the monitored region as a percentage, presenting it to the user as Regional Oxygen Saturation (rSO2). Typically, cerebral arterial blood oxygen saturation ranges from 98% to 100%, while venous blood tends to have an oxygen saturation of nearly 60%. Consequently, normal rSO2 values are expected to fall between 60% and 80%.

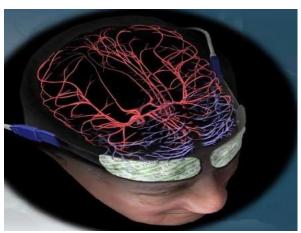


Figure 2: Placement of cerebral oximeter probes.

1.3 Limitations of Cerebral Oximetry Measurements
Currently, several CO devices are available for clinical
use, each exhibiting variability in measurements due to
differences in emitted light wavelengths, variations in
light sources among devices, and the utilization of

diverse mathematical algorithms for determining cerebral oxygenation values 8. Moreover, extracranial contamination, skin pigmentation, and physiological conditions contribute to the variability of rSO2 values <sup>9,10</sup>. Anatomical variations like incomplete Circle of Willis or carotid artery stenosis can further introduce errors in CO values. Therefore, conducting bilateral CO is recommended to minimize potential biases. An overview of various factors that could result in decreased cerebral oxygenation values due to alterations in blood flow or oxygen levels is provided in Table 1. Furthermore, all CO devices exhibit limitations in clinical use, encompassing compromised accuracy in the presence of electrosurgical equipment like diathermy, limited coverage restricted to regional cerebral oxygenation, and the absence of monitoring in significant brain regions <sup>3,11</sup>.

## 1.4 Clinical Applications

As outlined above, continuous monitoring of CO facilitates the early detection of changes in brain oxygenation, enabling timely interventions to enhance oxygen delivery and prevent adverse outcomes <sup>12</sup>. CO is considered as a safeguard and used in various medical procedures characterized by iatrogenic brain ischemia, including carotid endarterectomy in patients with high-grade carotid artery stenosis, temporary clipping during brain aneurysm surgery, hypothermic circulatory arrest for aortic arch procedures, and other pathologies like traumatic brain injury and stroke that inherently lead to brain ischemia <sup>13-15</sup>.

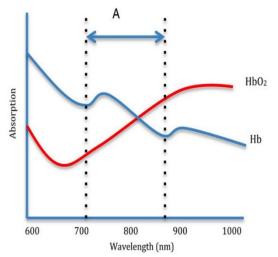
**Table 1:** Factors leading to decreased cerebral oxygenation values.

Oxygen Content	Cerebral Blood Flow
Hemoglobin concentration	Cardiac output
Inspired oxygen concentration	Acid-base status
Pulmonary function	Arterial inflow/venous outflow
Hemoglobin saturation	Major hemorrhage

1.5 Cerebral Oximetry in Emergency Department CO is not widely used in ED, but has attracted attention, especially in last few years. Despite advances in CPR, survival and neurological recovery after cardiac arrest remain very poor due to the impact of severe ischemia and subsequent reperfusion injury <sup>16</sup>. As the severity of ischemia intensifies during CPR, there is a reduction in the probability of survival and the attainment of favorable neurological outcomes <sup>17</sup>. The consequences of hypoxic-ischemic brain injury following the return of spontaneous circulation (ROSC) post-cardiac arrest are profound, leading to significant mortality and morbidity <sup>18</sup>. Consequently, the imperative to enhance overall outcomes necessitates the creation of methodologies for quantifying the extent of cerebral

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ischemia throughout the resuscitation process. Numerous preclinical and clinical studies have demonstrated that rSO2 during CPR is correlated with enhanced survival rates following cardiac arrest and improved neurological outcomes <sup>19,20</sup>.



**Figure 3:** Absorption spectra for oxygenated and deoxygenated hemoglobin. Area A represents light wavelengths used by cerebral oximeters 3. Hb: Deoxygenated hemoglobin, HbO2: Oxygenated Hemoglobin.

#### 2. Discussion

The evaluation of central and cerebral circulation through CO in the prehospital setting has the potential to enhance patient outcomes <sup>21</sup>. In a CPR environment, the ideal rSO2 monitor should be characterized by a compact, lightweight design and a durable battery. Absolute real-time values, accompanied by suitable indicators, ought to be measured without the need for frequent calibration. Additionally, the monitor should exhibit an absence of detection limits, insensitivity to ambient light, and resistance to extracranial contamination. None of the currently available devices, however, encompass all the aforementioned features indicative of an ideal pre-hospital rSO2 monitor. However, in cases of out-of-hospital cardiac arrest (OHCA), CO monitoring can be used both pre-hospital and during transport to measure CPR effectiveness in patients reaching advanced life support <sup>22,23</sup>.

The use of CO monitoring was also examined to determine the potential role of baseline and rSO2 in monitoring CPR effectiveness and predicting ROSC. In a meta-analysis reviewing 13 studies conducted by Liu and colleagues, it was demonstrated that, during CO monitoring, male gender and the location of the arrest may exert an influence on the initial or average rSO2 and ROSC <sup>24</sup>. Studies have also indicated that the outcomes may be influenced by geographical variations attributed to country-spesific legislation. For instance, in Japan, unlike in many other countries, termination of resuscitation at the scene of OHCA cases is not permitted, and application of CO may contribute to delays <sup>21</sup>.

The integration of noninvasive neuromonitoring in the ED and ICU could serve as a valuable adjunct to

clinical diagnosis and radiological imaging, especially in patients without primary brain injury <sup>25</sup>. In one metaanalysis using NIRS monitoring during resuscitation, a strong correlation was observed between ROSC and NIRS saturation <sup>26</sup>. Similarly, NIRS has proven to be valuable in the early detection of changes in cerebrovascular parameters during respiratory distress in patients with acute respiratory distress syndrome and COVID-19 <sup>27</sup>. The presence of systemic inflammation, commonly noted in sepsis patients frequently encountered in the ED, triggers changes in cerebral blood flow, disruption of the brain-blood barrier, and alterations in autoregulation, ultimately contributing to sepsis-related brain dysfunction <sup>28</sup>. In adults, benefits continuous assessment of cerebral autoregulation could also be provided by NIRS <sup>29,30</sup>.

#### 3. Conclusion

Growing evidence emphasizes the pivotal role of non-invasive cerebral oximetry as a crucial monitoring approach in the care of patients undergoing anesthesia or sedation in the intensive care unit, particularly when the primary injury does not affect the brain directly. This significance extends beyond the perioperative context to include applications in the emergency department and the ICU. NIRS offers distinct advantages as a non-invasive, cost-effective, safe, and readily accessible bedside tool, holding substantial potential for diagnosing and treating patients at risk of neurological complications. Larger-scale studies are necessary to facilitate the widespread integration of NIRS into daily routine practice.

## Limitations of the Study

Further research is required to validate cerebral oximetry monitoring in improving patient outcomes in emergency department.

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#### **Conflict of Interests**

The authors have no conflicts of interest to declare.

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## **Author Contributions**

Conception and Design of the study, Collection and/or Processing and Literature review, Writing Original Manuscript, Analysis and/or interpretation and final version and is responsible for final approval of the submitted manuscript; ÖGÇ.

## **Ethical Approval**

None.

## **Data sharing statement**

None.

#### Consent to participate

None.

#### **Informed Statement**

None.

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## **Use of Cerebral Oximetry in Anemic Patient**

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Abstract: Anemia increases the duration of hospital stay, costs, mortality, and morbidity. It is a serious health problem commonly seen in both perioperative and critical care patients. The primary purpose of blood is to transport oxygen to cells for the realization of energy-producing aerobic metabolism. Near-Infrared Spectroscopy (NIRS) technique is a non-invasive monitoring method that assesses average regional tissue oxygenation. The cerebral oximeter was placed bilaterally on the frontal cortex and measured near the transcutaneous membrane. It is believed that NIRS monitoring will be an effective key in resolving the dilemma of anemia and transfusion in patients by detecting tissue oxygenation disorders. Clinical studies are required for this. In this article, the connection between NIRS and anemia will be discussed. ©2024 NTMS.

**Keywords:** Cerebral Oximeter; Anemia; Tissue Oxygenation.

## 1. Introduction

Anemia is a common health problem encountered during the perioperative period. The World Health Organization has defined anemia as hemoglobin levels below 13 gr/dL in men and below 12 gr/dL in women. Anemia is a widespread health issue globally and is associated with mortality and morbidity <sup>1</sup>. According to the results of the World Health Organization's anemia prevalence studies, 48.8% of the world's population is anemic, and in Turkey, this rate is 25% <sup>2</sup>. Clinicians do not give the problem of anemia the same level of attention as other problems that increase mortality and morbidity to the same extent <sup>2</sup>. This is thought to be due to the existence of a simple solution such as blood transfusion. However, due to its complications and cost burden, the notion that blood transfusion is not entirely benign is increasingly being recognized. Knowing that both anemia and blood transfusion are factors that

increase mortality and morbidity, it is believed that determining when to perform blood transfusion in the treatment of anemia during the perioperative period can prevent complications arising from these problems <sup>3</sup>. One of the most important factors ensuring adequate oxygenation of the tissues is the hemoglobin value. In anemia, there is a reduction in blood oxygen content and a disruption in tissue oxygenation. As a result, tissue hypoxia, organ failure, and death are observed <sup>4</sup>. There is a high incidence of anemia in surgical patients, most of which is treatable. Successful treatment of anemia in the preoperative period can prevent many blood transfusions. Anemia treatment should definitely be done before elective surgery. Ideally, anemia should be treated four weeks before elective surgery, as proceeding with surgery without treating anemia can lead to unnecessary blood transfusions.

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This is associated with mortality and morbidity. Therefore, especially in surgeries with a high risk of bleeding, anemia should be treated before proceeding with surgery <sup>1,3</sup>.

Pulse oximetry is the most commonly used method for measuring oxygen levels in anesthesia practice. By attaching it to the distal extremities, the ratio of oxygenated hemoglobin to deoxygenated hemoglobin within the arterial system is measured. However, in individuals undergoing surgical procedures (such as surgery or hypotensive open-heart applications) who experience cardiac arrest, measuring oxygen levels with a pulse oximeter on any extremity can lead to erroneous monitoring of oxygen levels within the cerebral vascular system. To evaluate cerebral tissue oxygenation and perfusion, cerebral oximetry has emerged as a specialized monitoring tool in anesthesia over the last two decades. There are two extensions of pulse oximetry: mixed venous blood oxygen saturation (SvO2) and cerebral oximetry. Evaluating SvO2 is challenging due to its dependence on factors like hemoglobin concentration, cardiac output, arterial oxygen saturation, and whole-body oxygen consumption. Therefore, cerebral oximetry has become more popular for assessing cerebral oxygenation. Cerebral oximetry employs non-invasive NIRS to monitor cerebral oxygenation. Its principle of operation is similar to that of conventional pulse oximetry, evaluating the ratio of oxygenated hemoglobin to deoxygenated hemoglobin. The selfadhesive emitters and sensor pads applied to the skin for cerebral oximetry measure light attenuation noninvasively at a predetermined distance from the NIRS emitter. It operates based on the detection of light emitted by the transmitter diode and detected by receiver diodes 5.

## 2. Discussion

The purpose of blood transfusion is to increase the oxygen-carrying capacity of the blood, correct hemostasis, increase oxygen delivery to tissues, and provide volume expansion to increase cardiac filling. Factors leading to unnecessary blood transfusion in anemia include lack of education, lack of knowledge, being the easiest option, quickly and easily correcting anemia, and lack of monitoring <sup>6</sup>. Parameters like hemoglobin, hematocrit, vital signs, and blood loss are insufficient in monitoring tissue oxygenation. Studies to date have used various parameters in monitoring tissue oxygenation 4. These parameters are divided into global and regional parameters. Global parameters include venous oxygen saturation, central venoarterial carbon dioxide difference, arterial lactate level, lactate pyruvate ratio, and methemoglobin values. Regional parameters are gastric intramucosal pH, gastrointestinal tract tissue oxygenation, sublingual microcirculation, transcutaneous gas measurements, and NIRS <sup>4,7</sup>.

Publications indicate that NIRS is associated with blood loss and can be used to detect early hypovolemia, decrease in total hemoglobin index, and critical hemoglobin value for blood transfusion. A NIRS device consists of a light source emitting light in the near-infrared range (650-1000 nm) at two or more wavelengths and a detector placed at a known distance from the source. NIRS devices contain diodes that generate specific wavelengths and photodiodes made of silicon that can measure the transmission/absorption ratio. NIRS is a technique that measures the amount of absorption undergone by chromophore molecules such as oxyhemoglobin and deoxyhemoglobin, myoglobin, etc., as near-infrared light passes through tissues. The absorption of near-infrared light by chromophores varies depending on whether they are oxygenated or deoxygenated <sup>4,8</sup>.

The incidence of anemia is 20-30% in non-cardiac surgery, 50% in cardiac surgery, and 90% in the postoperative period. Both morbidity and mortality have been found to be associated with anemia even in major non-cardiac surgeries 9,10. Alexander Kulier and colleagues included 5065 patients undergoing coronary artery bypass graft surgery across 70 institutions worldwide and collected 7500 data points per patient. The research examined the effect of preoperative anemia on patients undergoing coronary artery bypass graft surgery. The relationship between preoperative in-hospital cardiac and non-cardiac morbidity and mortality was investigated in 4804 patients who did not receive preoperative blood transfusions. The likelihood of postoperative adverse events is higher in anemic patients undergoing heart surgery. The number of prior comorbidities has a significant impact on tolerance to Therefore, perioperative anemia. individual preoperative hemoglobin levels and the extent of accompanying risk factors should be considered in preoperative risk assessment and subsequent treatment plans such as blood transfusion <sup>11</sup>.

Ülkü Sabuncu and Ayşegül Özgök reported in their letter to the editor titled "The Role of Cerebral Oxygen Saturation Monitoring in Detecting Regional Tissue Hypoxia" that NIRS could be useful in detecting tissue oxygenation. In their article, they considered that even when hemodynamic data of the patient is normal, tissue oxygen delivery could be reduced, and detecting this reduction could be effective in making transfusion decisions. They suggested that NIRS could be used as an additional routine monitoring method for transfusion 12

Aritürk and colleagues investigated whether monitoring cerebral regional oxygen saturation (rSO2) via near-infrared spectroscopy (NIRS) is useful in assessing the effects of severe dilutional anemia on the brain during elective coronary arterial bypass graft (CABG) surgery. In the study, 15 patients had a hemoglobin level below 7 gr/dL and 15 patients had a hemoglobin level above 8 gr/dL. Both groups were monitored with standard monitoring as well as rSO2 monitoring. Initial NIRS values and values recorded during cardiopulmonary bypass were recorded for both groups. It was found that in patients with low hemoglobin values, changes in cerebral rSO2 were

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within acceptable limits and consistent with blood lactate and blood gas analyses. It was thought that monitoring cerebral rSO2 with NIRS could be useful in evaluating the effects of severe dilutional anemia on the brain during CABG surgery <sup>8</sup>.

In a study conducted on premature babies regarding brain tissue oxygen saturation and extraction before and after blood transfusion, it was examined whether pre-transfusion hemoglobin levels were related to rSO2 and fractional tissue oxygen extraction (FTOE), and the changes in these levels after blood transfusion were observed. As a result, it has been shown that cerebral tissue oxygen saturation significantly increased within the first 24 hours in premature babies receiving blood transfusions. However, FTOE was found to be low. It suggests that cerebral oxygenation may be at risk in premature babies when hemoglobin is below 9.7 g/dL <sup>13</sup>. The increase in hemoglobin values after blood transfusion has been shown to improve cerebral tissue oxygenation in other studies related to anemia and cerebral tissue oxygenation in preterm infants <sup>14</sup>. As a result of the conducted studies, it is thought that studies using NIRS in pediatric cases are promising.

The purpose of Liu and colleagues' study was to determine whether the decrease in hemoglobin during surgical operations for the correction of scoliosis in children affects cerebral oxygen saturation. There can be some issues with the surgical correction of scoliosis in childhood. Massive bleeding is one of these. A drop in hemoglobin levels following massive bleeding can disrupt cerebral perfusion, lead to hypoxia in brain tissue, and cause postoperative neurological problems. In this study, in addition to standard monitoring of heart rate, blood pressure, and oxygen saturation, monitoring intraoperative cerebral oxygen saturation provided useful information for ensuring the safety of surgery and anesthesia, and could also serve as a reference for fluid resuscitation and blood transfusion <sup>15</sup>.

## 3. Conclusion

Near-Infrared Spectroscopy (NIRS) has been integrated into anesthesia practices, particularly in cardiovascular surgical cases, alongside standard monitoring (pulse, blood pressure, oxygen saturation, end-tidal carbon dioxide) and blood gas analysis. Research indicates that NIRS is beneficial in assessing tissue oxygenation. It has been noted that tissue oxygenation may be compromised even when hemodynamic parameters of the patient appear adequate, and NIRS can assist in deciding on transfusion in cases of anemia.

Recently, NIRS has been employed as an adjunct monitoring tool in neonatal intensive care units and other surgical settings. Neonatal ICU data includes 24-hour post-transfusion NIRS readings for anemic infants. However, there is insufficient information regarding the long-term outcomes and effects of transfusion monitored by NIRS in anemic patients. Therefore, anesthesiologists and surgeons should identify anemia in the preoperative period and closely

monitor patients with preoperative anemia undergoing planned surgery.

Literature review suggests a lack of sufficient clinical evidence for the use of NIRS in anemic patients, indicating the need for supportive clinical studies to address this gap.

## Limitations of the Study

None.

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## **Conflict of Interests**

The authors have no conflicts of interest to declare.

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## **Author Contributions**

HSK: Study conception, design, data collection and write the manuscript. SA: Data collection, HSK, SA: Analysis and interpretation of results, data collection. HSK, SA: Data collection. HSK: Study design, supervised the work, performed the analysis, contributed data and analysis tools. All authors read and approved the final version of the manuscript.

## **Ethical Approval**

None.

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## **Advancing Patient Care: The Role of Cerebral Oximetry in Intensive Care Units**

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Abstract: One of the most important parameters of patient follow-up in intensive care units is monitoring. The brain is one of our most metabolically active organs and is very sensitive to hypoxia and ischemia. Therefore, monitoring cerebral oxygenation is important. Although there are many methods for monitoring cerebral tissue oxygenation, cerebral oximeters are frequently used due to their bedside use, non-invasiveness and ease of use. These devices work on the basis that near-infrared light is absorbed at different rates by oxygenated hemoglobin and deoxygenated hemoglobin. It can be used in intensive care units to detect cerebral ischemia or hypoxia early and prevent secondary damage in patients with traumatic brain injury (hemorrhage, stroke). ©2024 NTMS.

Keywords: Cerebral; Oximetry; Hypoxia-ischemia.

## 1. Introduction

The human brain is one of the most metabolically active organs in the body. Although the weight of the brain is about 2% of the total body weight, the cerebral blood flow volume constitutes 15-20% of the cardiac output <sup>1</sup>. Adequate delivery of O2 to the brain via precise regulation of cerebral blood flow (CBF) is therefore vital to maintaining optimal function and avoid cellular damage and/or death. Describing the influence of oxygen (O2) availability on CBF and brain metabolism is an essential step toward a better understanding of brain energy homeostasis and associated clinical implications. Impairment of cerebral tissue oxygenation may be due to inadequacies in oxygen delivery to the brain or increases the oxygen that the brain's need. In the last decade, cerebral tissue oxygenation monitoring has become an emerging

monitoring modality mainly because it enables evaluating the coupling of macro-hemodynamic variables with regional or local hemodynamics at the tissue of interest.

There are various methods for cerebral tissue oxygenation monitoring. One of these is the jugular venous oxygen saturation (SjvO2) measurement. SjvO2 is used for indirect assessment of brain tissue oxygen consumption and reflects the dynamic balance between whole brain oxygen supply and consumption. Therefore, it is considered as a useful indicator of the relationship between whole-brain blood flow and brain metabolism <sup>2</sup>. Measurements are obtained from blood taken intermittently from a catheter placed in the jugular bulb and is an invasive method. While it has the advantage of showing the blood oxygen saturation of

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the whole brain, it remains insufficient in the presence of regional hypoxia. There is a risk of hematoma and venous thrombosis in this method, and this risk increases as the follow-up period extended <sup>3</sup>.

Monitoring of brain tissue partial pressure of oxygen (PbtO2) is a new cerebral blood oxygen saturation monitoring technique. PbtO2 provides information about perfusion and circulation, as well as oxygenation of brain tissues at the cellular level <sup>4</sup>. This method is quite invasive because it is performed with microelectrodes implanted in the brain tissue. It reflects partial oxygen pressure in the brain, temperature and pH values <sup>5</sup>. It has a high reliability compared to other methods. However, its clinical use is limited because it is invasive and can cause local brain tissue damage and infection.

Cerebral oximetry evaluates regional tissue oxygenation through the transcutaneous membrane via electrodes placed on the frontal cortex. Near infrared resonance spectroscopy (NIRS) is a monitoring method based on the principle of utilizing the tissue permeability feature of near infrared light <sup>6</sup>. Normal values in healthy people range between 58-82%. NIRS is a non-invasive method and is frequently used intraoperatively and postoperatively in many surgical procedures <sup>7</sup>. Its use is also increasing in intensive care units in patients with traumatic brain injury, stroke and cardiac arrest.



**Figure1:** First day NIRS values of a patient who developed bilateral SAH because of a traffic accident.

## NIRS Working Principle

Its working principle is like a classical pulse oximeter. It works on the basis that the rays coming out of the transmitter diode are detected by the receiver diodes. The spectral absorptions of oxygenated hemoglobin and deoxygenated hemoglobin are different, and NIRS uses this difference <sup>8,9</sup>. The basis of the NIRS operating principle is the Beer-Lambert law. According to this law, light is absorbed according to the properties of the material it passes through. Uptake by tissues is related

to the wavelength of the light. Ultraviolet light, visible light and infrared light are absorbed by DNA, proteins, hemoglobin and water. Therefore, they cannot pass into tissues, and it is not possible to make measurements in the body using this spectrum. Since near infrared light is not absorbed by water or proteins, it can penetrate deeper tissues and is used in cerebral oximeters <sup>10</sup>. Additionally, tissues contain molecules chromophores that can absorb near infrared light. Chromophores have specific absorption depending on the oxygen concentration in the tissue. The amount of light absorbed by tissues depends on the chromophore concentration 8. At least two different wavelengths must be used to compare chromophore concentrations in NIRS measurements. Since the absorption difference between oxygenated hemoglobin and deoxygenated hemoglobin is greatest in light with wavelengths between 700 and 850nm, these two wavelengths are commonly used in measurements <sup>9</sup>. Although two wavelengths were used in devices produced in the past, today multiple wavelengths are used in devices to increase the accuracy of measurements 11. The most advanced devices used today have four electrodes. The oximeters operate as continuous wave (CW), frequency dependent or time dependent, depending on the techniques used.

## NIRS Advantages

NIRS is a low-cost and easy device that can be applied at the bedside. Its biggest advantage is to be non-invasive. Since it does not require pulsatile flow, it can also be used during cardiopulmonary bypass. It cannot distinguish between the arterial and venous systems, so it indicates the balance between oxygen delivery and consumption rather than oxygen delivery <sup>12</sup>. Additionally, it can provide information about cerebral oxygen use and cell metabolism <sup>13,14</sup>.



**Figure 2:** Day 5 NIRS values of the same patient. Delayed cerebral ischemia was detected.

#### NIRS Limitations

The main limitation of cerebral oximeters is that they are affected by signals from extracranial tissue. For this reason, measurements cannot directly reflect brain oxygen saturation. To avoid this limitation, some companies have been able to distinguish the signals coming from the scalp and deep tissue by using two detectors <sup>15,16</sup>. Cerebral oximeters calculate saturation by assuming that arterial and venous blood are in a certain ratio. And the partial pressure of carbon dioxide affects this ratio. This must be considered in these measurements. Measurements may show large differences in cases where the hemoglobin level changes suddenly (hematoma, hemodilution) or in cases where the distance between the light source and the detector increases (tissue edema) 17,18. Head movement can also cause artifacts and inaccurate measurements 19. Another important limitation is that normal values vary widely between individuals. Therefore, there is no cut-off value or gold standard values for diagnosis. Therefore, it can only be used as a trend monitor 19.

#### Clinical Use

The occurrence and progression of brain damage have a great importance on the mortality and morbidity of patients in intensive care unit. Although its mass is small, the brain uses 25% of the glucose and 20% of the oxygen provided for its normal functions. Brain oxygen consumption is 3.5 ml/100gr tissue/1 min. The regulation of blood flow and continued oxygen delivery are very important to maintain its functions. Monitoring cerebral tissue oxygenation is therefore an increasingly common practice in intensive care units.

The most important purpose of monitoring cerebral tissue oxygenation in intensive care units is to prevent secondary brain damage caused by hypoxia or ischemia. Patients with traumatic brain injury, patients with subarachnoid hemorrhage (SAH), patients with stroke, septic encephalopathy and cardiac arrest are monitored by NIRS <sup>20</sup>. Although there is no gold standard in numerical values, an initial NIRS value of less than 40, but more importantly, a change of more than 25% compared to the baseline, is useful in predicting cerebral ischemia <sup>21</sup>.

## Traumatic Brain Injury, Subarachnoid Hemorrhage, and Stroke

Subarachnoid hemorrhage is a serious disease, the complications of which are life threatening and usually require management in intensive care unit. Delayed cerebral ischemia occurs in some of these patients and has negative effects on mortality and morbidity. A study examined whether the use of NIRS in the follow-up of patients with SAH is effective in predicting delayed cerebral ischemia <sup>22</sup>. A patient's NIRS values are shown in Figure 1 and 2. NIRS changes were recorded in cases where patients had newly developed neurological symptoms, lasted longer than an hour, and had a decrease of more than 2 on the Glasgow coma

scale. In these patients with delayed cerebral ischemia, it was observed that there was a decrease of more than 14.7% in NIRS values compared to the baseline level and the sensitivity was calculated as 85.7% <sup>22</sup>. In another study, measurements were made using NIRS in healthy volunteers and patients with stroke, and the correlation with interhemispheric asymmetry and physiological changes was evaluated <sup>23</sup>. In stroke cases, it has been shown that CW-NIRS can detect asymmetry in microvascular hemodynamics between hemispheres physiological cardiac and respiratory during oscillations. It has been shown that, especially in patients where the width of the affected area is unknown, an information can be obtained by making simultaneous measurements in different parts of the head <sup>23</sup>. Similarly, in cases of SAH, intracranial hemorrhage and ischemic stroke, frontal NIRS cerebral oxygenation measurements were correlated compared with regional cerebral blood flow on CT perfusion imaging <sup>24</sup>.

## Sepsis and Its Impact on Cerebral Function

One of the most common clinical conditions in intensive care units is sepsis. Depending on the source of sepsis, sepsis itself can cause brain damage such as brain edema and seizures, and it can affect brain functions due to its systemic effects such as hypotension, hypoxia, and hypercapnia. NIRS may be preferred as it is an uncomplicated, non-invasive method that can be applied at the bedside to evaluate cerebral oxygenation in the follow-up of septic patients <sup>25</sup>. Most of the monitoring performed in septic patients are indicators of macro-circulation, and even these are normal, there may be inadequate microcirculation. The use of NIRS in the thenar region, which is less affected by local factors such as edema and fatty tissue thickness, can provide us indirect information about local microcirculation <sup>26</sup>.

Cardiopulmonary Resuscitation and Cardiac Arrest NIRS is also helpful in monitoring resuscitation effectiveness in arrest cases. In an observational study, it was tried to understand whether tissue oxygenation index (TOI) values obtained by NIRS could be used to evaluate the return of spontaneous circulation (ROSC) in patients undergoing cardiopulmonary resuscitation (CPR) <sup>27</sup>. More than a hundred out-of-hospital cardiac arrest cases were included and it was observed that ROSC was high in those with high initial TOI values and there was a correlation between them. For this reason, it has been suggested that TOI values can be used to predict ROSC, terminate CPR or make ECPR decisions <sup>27</sup>. Many studies on this subject have confirmed the correlation of regional cerebral oxygen saturation (rSO2) values with ROSC <sup>29</sup>. Although there is no exact threshold value in studies, those with an average rSO2 value of 47 (47  $\pm$  11) are associated with a positive outcome, and those with a mean rSO2 value of 38 (38  $\pm$  12) are associated with a poor neurological outcome <sup>28</sup>. As rSO2 values increase, both ROSC rate and neurological outcome increase. NIRS does not require pulsatile flow like pulse oximetry, making it easier to use in CPR applications <sup>29</sup>.

#### 2. Conclusions

As a result, cerebral tissue oxygenation has an important place in clinical follow-up in intensive care units. Among cerebral tissue oxygenation monitors (SjvO2, PbtO2 and rSO2), NIRS has become a monitor with high specificity and sensitivity that is used increasingly more frequently. It is a useful monitoring method in predicting the prognosis in cases of traumatic brain injury (TBI, SAH and Stroke) and in making a rapid treatment plan in case of sudden neurological changes during follow-up. In cases such as sepsis, which are frequently encountered in intensive care, close monitoring of tissue oxygenation is required, and NIRS has a strong place among tissue oxygenation parameters. Higher **NIRS** values cardiopulmonary resuscitation have been associated with better neurological outcomes in adult and pediatric patients. Although it has various limitations, the use of NIRS in monitoring cerebral oxygenation is frequently recommended because it is easy, applicable, low-cost and noninvasive.

## **Limitations of the Study**

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## Capnography in Outpatient Anesthesia

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**Abstract:** The concept of outpatient anesthesia first came up in the 1970s. Performing planned surgery of patients on the same day and then being discharged is called outpatient surgery, and the anesthesia applied in the same session is called outpatient anesthesia. Outpatient surgery is not performed for every patient. There are many factors that determine whether patient population scheduled for outpatient surgery is suitable for outpatient surgery. End-tidal carbon dioxide (ETCO2) is the CO level released at the end of expiration. ETCO2 reflects the adequacy of ventilation and perfusion. ETCO2 measurement can be performed with many techniques. Infrared spectrography is the most common technique. It can be used in intubated and tracheostomized patients who are provided with respiratory support with a mechanical ventilator, as well as in patients who are not intubated and undergo sedoanalgesia, allowing the monitoring of respiration by measuring. The capnogram consists of two main components, inspiration and expiration, and these components point to four separate phases. It is known that drugs used in sedation and analgesia can often have negative effects on respiratory system. Therefore, patients' oxygenation and hemodynamic status should be closely monitored. It can continuously monitor frequency and depth of patients' breathing using a capnograph. An increase in amount of ETCO2 or a decrease in respiratory pattern is interpreted as respiratory depression. In addition to capnography, a parameter showing respiratory status, defined as "Integrated Pulmonary Index" (IPI), consisting of capnography, pulse oximetry, respiratory rate, and mathematical analysis of heart rate, is also used in cases where outpatient sedation is applied. Capnography has been shown to detect hypoxemia and apnea earlier. Use of IPI index and capnography is useful in the respiratory follow-up of patients with comorbid diseases (COPD, OSAS, Obesity.) who underwent moderate and deep sedation. ©2024 NTMS.

**Keywords:** Outpatient Anesthesia; Capnography; Integrated Pulmonary Index.

## 1. Introduction

The outpatient intervention was first applied in Scotland in 1909. The concept of <sup>1</sup> outpatient anesthesia first came to the fore in the 1970s. Along with technological advances, TARD (Turkish

Anesthesiology and Reanimation Society) has published guidelines on the subject in Turkey. Performing the planned surgery of the patient on the same day and then being discharged is called outpatient

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surgery, and the anesthesia applied in the same session is called outpatient anesthesia <sup>2</sup>.

It is derived from the Greek word 'kapnos', which means smoke. Instantaneous measurement of end-tidal carbon dioxide (ETCO2) concentration or partial pressure is called "Capnometry", and the device that makes this measurement is called "Capnometer". The change of end-tidal carbon dioxide concentration or partial pressure in the expiratory volume over time is called "Capnography".

In the literature,  $_{\rm CO2}$  analysis was first discovered in the 20th century and then started to be used in anesthesia in the 1950s  $^3$ .

## 1.1 Outpatient Anesthesia

One of the most important reasons why outpatient surgery is becoming increasingly common is its many advantages. These advantages can be listed as low risk of nosocomial infection, early discharge, patient/surgeon satisfaction, low cost, higher efficiency <sup>2</sup>, <sup>1</sup>

Outpatient surgery is not performed for every patient. Patient selection criteria in outpatient surgery:

- 1-The surgical intervention to be performed should be completed in an appropriate time. The average duration of a one-day case is 3.5 hours or half a working day. This covers the entire perioperative period. This process should be constant and should be included in the anesthesiologist's work plan.
- 2- The operation should not cause fluid and blood loss.
- 3- There should be minimal risk for postoperative bleeding.
- 4- There should be minimal risk in postoperative airway safety.
- 5- Postoperative pain should be easily controlled by the patient at home.
- 6- There should be nopostoperative nausea and vomiting.
- 7- There should be no intervention that requires the use of a resistor or catheter.
- 8- Patients should be able to provide postoperative care on their own. It should be an intervention that does not restrict patient movement, or it should be with a reliable adult, or a nurse providing postoperative care should be able to be provided.
- 9- Hydration and eating functions should be able to return quickly.

10-The procedure should be schedule to an earlier time in the operation list. In this way, the postoperative care period should be long  $^2$ .

Cases where outpatient surgery can be performed are shown in Table  $1^2$ .

There are many factors that determine whether the patient population scheduled for outpatient surgery is suitable for outpatient surgery. These can be classified as titles depending on surgical procedure, comorbid diseases, social factors <sup>4</sup>.

Procedural factors that may affect perioperative and postoperative outcomes include the invasiveness of the surgical procedure, the duration of surgery, potential blood loss and the need for blood transfusion (intraoperative and postoperative), and the ability to control post-discharge pain with oral analgesics and/or local <sup>5</sup>.

It has been shown that various comorbid conditions affect postoperative outcomes after outpatient treatment and therefore play an important role in patient selection. Independent factors identified in many studies include ASA (American Society of Anesthesiologists) physical status classification, advanced age, obesity (body mass index [BMI]), obstructive sleep apnea (OSA), heart disease, chronic obstructive pulmonary disease (COPD), diabetes (DM), end-stage renal disease (ESRD), transient ischemic attack (TIA)/stroke, chronic opioid use or opioid use disorder, and malignant hyperthermia (MH)

Another factor that plays a role in outpatient selection is social factors. Social factors include the location of post-discharge patient care being close to the hospital, the presence of responsible persons providing patient care, and the availability of facilities to reach the nearest health center in case of any complications.

As a result, patients who will undergo outpatient surgery:

- -General Anesthesia
- -Neuroaxial Anesthesia
- -Peripheral Nerve Blocks
- -Sedo Analgesia is applied.

Each technique has its own advantages and disadvantages. In terms of tissue oxygenation follow-up, patients receiving general anesthesia are included in the standard monitoring (ECG, Pulse Oximeter, Invasive/non-invasive arterial blood pressure, capnography). In addition to standard monitoring, capnography follow-up should be performed for the early detection of apnea in patients receiving neuromuscular monitoring and BIS monitoring and sedation in the follow-up and transfer of patients who have undergone other methods <sup>2</sup>.

## 1.2 Capnography

End-tidal carbon dioxide (ETCO2) is the carbon dioxide level released at the end of expiration. ETCO2 reflects the adequacy of ventilation and perfusion. Non-invasive methods for ETCO2 measurement include capnometry and capnography. Capnometry provides a numerical value for ETCO2. In contrast, capnography offers a more comprehensive measurement, displayed in both graphical and numerical form. Therefore, capnography is currently the most commonly recommended method for monitoring ETCO  $_2$  6.

ETCO<sub>2</sub> measurement can be performed with many techniques. A few of these are Raman spectrography, mass spectrography, molecular correlation spectrography, infrared spectrography. The most commonly used method is infrared spectrography <sup>7</sup>.

Like every wave in the electromagnetic spectrum, infrared light has a wavelength range (0.7  $\mu$ m – 1 mm). Gases absorb infrared light over a range of

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wavelengths. This wavelength range is different for each gas in the exhaled gas mixture. Thanks to photodetectors, capnography measures the CO<sub>2</sub> molecules in the expirium by the mechanism of absorption of infrared rays 8.

Table 1: Interventions Suitable for Outpatient Surgery.

Table 1. Interventions Surable for Outpatient Surgery.				
Dental facial	Fractures, extraction			
Dermatology	Excision of skin lesions			
General Surgery	Biopsy, endoscopy, mass excision, hemorrhoidectomy,			
	hernia repair, laparoscopic interventions, splenectomy,			
	adrenalectomy, varicose vein surgery			
Ophthalmology	Cataract operations, chalazion excision,			
	nasolacrimal canal operation, strabismus repair, tonometry,			
	intraocular injections			
Gynaecology	Biopsy, curettage, hysteroscopy, laparoscopy, uterine			
	polypectomy, vaginal hysterectomy, tubal ligation			
ENT	Adenectomy, tonsillectomy, tympanoplasty,			
	myringotomy, polypectomy, rhinoplasty, mastoidectomy			
Plastic Surgery	Basal cell cancer excision, cleft lip repair, mammoplasty, liposuction, ear correction,			
	debridement, burn dressing, skin graft, etc.			
Urology	Bladder surgery, circumcision, cystoscopy, varicocele,			
	orchiectomy, laparoscopic nephrectomy, prostatectomy			
Orthopedics	Knee arthroscopy, shoulder reconstruction, carpal tunnel			
	an anotical along discretion, tonden name in the			

operation, closed reduction, tendon repair, etc.

Pain Nerve blocks, radiofrequency, epidural injection, chemical sympathectomy

**Physiotherapy** Botox injection

According to the placement localization of the CO<sub>2</sub> sensor, the capnography device is divided into two groups as Mainstream and Sidestream. While the sensor is located on the respiratory tract in devices using mainstream, the sensor is located inside the monitor in devices using sidestream (Figure 1) 9. Normal values of ETCO<sub>2</sub> are 35 mmHg to 45 mmHg.

In cases of hypoventilation, hyperthermia, sepsis, rebreathing, depleted soda lime, very low fresh gas flow, too much depth of anesthesia, IV bicarbonate administration, the CO<sub>2</sub> level in the blood may increase. If the end-tidal carbon dioxide partial pressure value is above 45 mmHg, it is called hypercapnia, and if it is below 35 mmHg, it is called hypocapnia. This condition can be caused by hyperventilation, hypothermia, pain, superficial anesthesia, very high fresh gas flow and a leak in the respiratory system<sup>10</sup>. The reasons for increasing and decreasing ETCO<sub>2</sub> are given in Table 2.

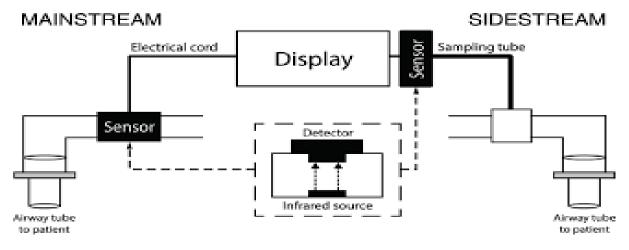


Figure 1: Capnography device types 9.

Table 2: ETCO<sub>2</sub> Changes 8.

## Increased ETCO<sub>2</sub>

## Decreased alveolar ventilation

- Increased respiratory rate
- Increased tidal volume
- Increased equipment dead space

## Increased CO<sub>2</sub> production

- Temperature
- Hypermetabolic state

## Increased inspire Pco<sub>2</sub>

- Re-breathing
- Depletion of CO<sub>2</sub> absorbent
- External CO<sub>2</sub> source

## Decreased ETCO<sub>2</sub>

Increased alveolar ventilation

- Increased respiratory rate
- Increased tidal volume

## Decreased ETCO<sub>2</sub> production

- Hypothermia
- Hypocatabolic state

#### Increased alveolar dead distance

- Increased cardiac output
- Pulmonary embolism
- High end-expiratory pressure during intermittent positive ventilation

## Sampling Error

- Insufficient tidal volume
- Water plugs in the breathing line
- Air intake to the breathing line

In people with normal respiratory functions, a pressure difference of 2-5 mmHg is observed between PaCO<sub>2</sub> and EtCO<sub>2</sub>, reflecting the physiological dead space. In cases of shock, cardiac output and decreased lung perfusion, an increase in pressure difference between PaCO<sub>2</sub> and EtCO<sub>2</sub> may be observed due to ventilation/perfusion (V/P) incompatibility <sup>11</sup>.

Capnography is a non-invasive method that provides monitoring of respiration. It can be used in intubated and tracheostomized patients who are provided with respiratory support with a mechanical ventilator, as well as in patients who are not intubated and undergo sedoanalgesia, allowing the monitoring of respiration by measuring. In this way, it is used in the operating room, intensive care units, emergency services and units where sedoanalgesia is applied. In addition, ETCO<sub>2</sub> usage monitoring can be used as the earliest indicator of spontaneous return to ensure the accuracy of the location of the intubation tube, to quickly detect common respiratory system problems associated with sedation such as respiratory depression, apnea, upper airway obstruction, laryngospasm, bronchospasm, to indicate cardiac output when ventilation is kept constant in the circulatory system, and finally in cardiopulmonary resuscitation <sup>12-14</sup>.

Especially in non-operating room applications, the recommendation of the Turkish Society of Anesthesiology and Reanimation (TARD) in the anesthesia practice guide is as follows: Pulse oximeter or plethysmography, capnograph (must be present even in sedation applications), oxygen analyzer, gas analyzers if old anesthesia devices that are not available are used as respiratory monitors, observation of chest movements, listening to respiratory sounds with a precordial stethoscope, observation or feeling of the movement of the reservoir balloon are required. SpO<sub>2</sub>

monitoring alone is not adequate. Apnea or hypoventilation is noticed later because additional oxygen is administered, in which case capnography is stimulating. It is recommended that EtCO<sub>2</sub> monitoring should be performed not only in moderate and deep sedation, but also in mild sedation. <sup>15</sup> Capnography has previously been shown to detect hypoxemia and apnea earlier in numerous randomized controlled trials <sup>16</sup>. The capnogram consists of two main components, inspiration and expiration, and these components point to four separate phases (Figure 2).

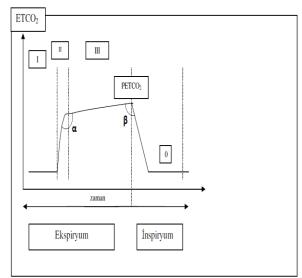


Figure 2: Normal Capnogram Waveform 17.

The first phase (Phase I) starts with the start of expiration and ends as soon as CO<sub>2</sub> is detected. This phase indicates gas elimination in the conductor airways, the 'anatomical dead space'. The anatomical dead space consists of the upper respiratory tract and

the branching of the bronchial tree. In normal adults, 150-180 ml of the 500 ml tidal volume is located in this region. The amount of space is affected by the person's height, body weight, posture, position of the neck and jaw, tracheostomy, or the presence of an endotracheal tube. Anatomical dead space does not play a role in gas exchange. CO<sub>2</sub> cannot be detected in Phase I.

During the phase II period, CO<sub>2</sub> from the alveoli and CO<sub>2</sub> in the anatomical dead space are mixed. In this phase, the CO<sub>2</sub> in the expiratory air rises rapidly. The CO<sub>2</sub> rise rate in Phase II gives information about ventilation-perfusion (V/P). The rise in this phase indicates alveolar dead space. Sudden increase of alveolar dead space indicates V/P disorder.

In the capnogram, the transition between Phase II and Phase III, that is, the point where the alveolar gas is detected, is called the "alpha ( $\alpha$ ) angle". Normally, this angle is around 100- 110° and is an indirect indicator of the V/P of the lung. Airway obstruction, capnograph response time, print speed, and respirator cycle time cause a change in angle.

In Phase III, the air in the anatomical dead space is completely discharged and only air from the alveoli is present. The level of CO<sub>2</sub> in Phase III is usually characterized by a slight increase, or it can also be fixed in the form of a plateau. The alveolar gas at the end of expiration is richer in CO<sub>2</sub> than at the beginning of expiration because CO<sub>2</sub> excretion from the pulmonary capillaries into the alveoli continues at almost constant levels throughout expiration. At the end of expiration, CO<sub>2</sub> is measured more concentrated than the volume. In Phase III, the point where CO<sub>2</sub> is measured as the highest at the end of expiration is called "end tidal CO<sub>2</sub> partial pressure", that is, PETCO <sub>2</sub>. The PaCO<sub>2</sub>-PetCO<sub>2</sub> difference in healthy subjects is usually less than 6 mmHg <sup>17</sup>.

The region where inspiration starts and CO2 decreases rapidly with Phase III is called Phase 0. The angle of about 90° between Phase 0 and Phase III is called the "beta ( $\beta$ ) angle". Beta angle is used to evaluate rebreathing <sup>18</sup>.

Abnormal Wave Patterns:

Hypoxia: (Asthma)



Hypoxia: (Mechanical abstraction, Asthma, bronchial construction)

The shark fin:



Pneumothorax and alveolar leak:



Obese patient with decreased lung compliance:



Sudden drop: Airway vehicle misplacement, Cardiac arrest



Restoration of spontaneous breathing after resuscitation



#### 2. Discussion

It is known that drugs used in sedation and analgesia can often have negative effects on the respiratory system. Therefore, the patient's oxygenation and hemodynamic status should be closely monitored. With the side flow measurement method, CO<sub>2</sub> measurement can be easily performed even when the patient is not intubated with the nasal cannula or face mask to be placed in the patient's airway. It can continuously monitor the frequency and depth of the patient's breathing using a capnograph. An increase in the amount of ETCO<sub>2</sub> or a decrease in the respiratory pattern is interpreted as respiratory depression.

It has been shown that capnography used during endoscopy of morbid patients detects respiratory depression in the early period and instantly detects changes in respiratory pattern <sup>19</sup>.

In a study comparing the monitoring used in sedations given to 154 children in the emergency department, Langhan et al. showed that hypoventilation was less common and timely intervention was performed in cases followed up with capnography. They stated that children in the capnography group were exposed to less hypoventilation and oxygen desaturation <sup>20</sup>.

In addition to capnography, a parameter showing respiratory status, defined as "Integrated Pulmonary Index" (IPI), consisting of capnography, pulse oximetry, respiratory rate, and mathematical analysis of

heart rate, is also used in cases where outpatient sedation is applied. IPI values are 1-2: Red area( Emergency response), 3-4: Yellow area (Requires intervention.), 5-6:Green area (May require attention and intervention), 7: Green area (Close to normal limit but requires attention) 8-10: Normal limits <sup>21</sup>.

Continuous oxygen saturation, as measured by pulse oximetry, provides information about heart rate as well as arterial oxygenation but does not fully reflect ventilation. It has been shown that cutaneous capnography placed on the auricle is useful in the titration of nocturnal non-invasive positive pressure ventilation (NPPV) used in the treatment of hypercapnia as a result of hypoventilation due to OSAS. In conclusion, cutaneous capnography using a digital earlobe sensor can be used to optimize NPPV settings in patients with hypoventilation-induced chronic hypercapnic respiratory failure <sup>22</sup>.

Capnography is an indicator of ventilation. It is indirectly correlated with tissue perfusion and oxygenation. Shock models have shown that the sublingual tissue bed is damaged, and microcirculatory changes in this region may indicate recent changes in other important organs. Measurement of sublingual mucosal pCO2 (Pslco2) by sublingual capnography is technically simple, non-invasive, and yields almost instant results. Sublingual capnography is useful for assessing the severity of shock conditions and adequacy of tissue perfusion <sup>23</sup>.

While there are many studies in the literature on the advantage of the use of capnography in early respiratory depression and respiratory complications in cases undergoing sedation, there are also studies stating that the use of routine capnography is necessary. In a 2016 review, routine measurement of EtCO2 levels during procedure-related sedation was shown to be too costly for five years of preventable catastrophic events <sup>24</sup>

In addition to the mentioned applications, a case-based example of the use of capnography is provided. Initially, moderate sedation with midazolam was administered to a 43-year-old male patient undergoing dental surgery with airway obstruction due to squamous cell polyp. Periodically, the patient experienced desaturation and apnea, and interventions were carried out by stimulating respiration through verbal prompts. During periods of irregular respiratory patterns, there were observed decreases in EtCO2 initially, followed by increases during apneic episodes. The importance of capnography was emphasized in the early detection of hypoxia <sup>25</sup>.

In a 2019 review, the use of colonoscopy using moderate sedation is not routinely recommended in low-risk patients (ASA I/II, BMI <30, young patients with no history of heart or lung disease) <sup>16</sup>.

## 3. Conclusions

Capnography has previously been shown to detect hypoxemia and apnea better in numerous randomized controlled trials. The use of IPI index and capnography is useful in the respiratory follow-up of patients with comorbid diseases (COPD, OSAS, Obesity...) who underwent moderate and deep sedation.

## Limitations of the Study

The studies conducted by different surgical procedures, hospital settings, and surgical teams may make comparability of results difficult. This heterogeneity can make it difficult to draw generally valid conclusions.

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## **Conflict of Interests**

The author declare that they have no conflict of interest.

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#### **Author Contributions**

Conception and Design of the study, Collection and/or Processing and Literature review, Writing Original Manuscript, Analysis and/or interpretation and final version and is responsible for final approval of the submitted manuscript; AÖ.

## **Ethical Approval**

None.

## **Data sharing statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Consent to participate

None.

## **Informed Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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