doi:10.25143/prom-rsu_2023-10_dt

Rīga Stradiņš University

Sniedze Mūrniece

Near-infrared Spectroscopy-Based Clinical Algorithm Applicability During Spinal Neurosurgery and Postoperative Cognitive Decline

Doctoral Thesis for obtaining the scientific degree
"Doctor of Science (*PhD*)"

Sector Group – Medical and Health Sciences
Sector – Clinical Medicine
Sub-Sector – Anaesthesiology and Resuscitation

Riga, 2023

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Abstract

In patients undergoing spinal surgery in prone position, physiological changes can occur in multiple organ systems. Pressure on pelvis, abdomen and thorax reduces systemic venous return, thereby decreasing cardiac output and increasing pressure in vertebral blood vessels, thus promoting intraoperative bleeding. Concomitantly, lung compliance decreases. The latter noxious factors hamper blood flow and oxygen delivery to the brain. The brain is highly dependent on adequate oxygen delivery, thus, tissue injury, and even cell death may occur already 5 minutes after cerebral ischemia. Postoperative cognitive decline is a potential complication, which may lead to long-term consequences. The exact aetiology and pathophysiology of postoperative cognitive disturbances is not known. Despite intraoperative cerebral ischemia could be a contributing factor to consider, the brain remains one of the least monitored organs intraoperatively.

The aim of the present study was to evaluate the effect of the intraoperative use of a near-infrared spectroscopy-based clinical algorithm on outcome, especially on postoperative cognitive decline.

We included 64 adult patients, scheduled for elective spinal neurosurgery in the prone position. All the patients underwent general anaesthesia and regional cerebral oxygen saturation (rScO2) was monitored intraoperatively by means of an INVOS 4100 cerebral oximeter. Patients were randomised into a study group and a control group. In patients of the study group, a near-infrared spectroscopy-based clinical algorithm was used to restore adequate cerebral oxygen saturation when noticing a drop of 20 % from preoperative baseline of cerebral oxygen saturation, or a fall in regional cerebral oxygen saturation below an absolute value of 50 %. In the control group, intraoperative cerebral oxygen saturation was monitored blindly without using the near-infrared spectroscopy-based clinical algorithm. In both groups, before and after the surgery, cognitive function was evaluated using Montreal Cognitive Assessment Scale (MOCA). Preoperative haemoglobin (Hb) and haematocrit (Hct) concentrations also were noticed, as well as intraoperative mean arterial pressure (MAP), expiratory end-tidal carbon dioxide (EtCO2) levels, peripheral oxygen saturation (SpO2), intraoperative blood loss and length of operation.

In our study, in three patients – two in the study group and one in the control group, intraoperative cerebral desaturation was observed. Two study group patients were 54 and 57 years old. In one study group patient, cerebral saturation fell for 29 % from baseline values and also under an absolute value of 50 %; in the other study group patient, we noticed a cerebral oxygen saturation drop of 27 % below preoperative baseline. The NIRS-based clinical algorithm was initiated. No changes in rScO2 were observed after the first step, which

according to the algorithm, was an assurance of correct head positioning. The next step was a raise in mean arterial pressure in both patients, as assessed by ephedrine administration. After the second step rScO2 values raised above the threshold, and no further intervention was necessary. Mean arterial pressure in the patients at the time of cerebral desaturation was 95 mmHg and 62 mmHg, respectively vs. 124 mmHg and 104 mmHg preoperatively. None of the patients showed postoperative cognitive decline – MOCA score remained unchanged pre- and postoperatively.

In one control group patient, in whom intraoperative cerebral desaturation occurred, but the NIRS-based clinical algorithm was not applied, we detected a rScO2 drop of 21 % from the preoperative baseline values. The patient was 24 years old and showed a postoperative MOCA score decline of 4 points (from 29 points preoperatively to 25 points postoperatively).

In the present study, we found a correlation between lower intraoperative rScO2 values and higher patient age, larger intraoperative blood loss, higher preoperative mean arterial pressure and lower preoperative MOCA score.

In our study, 45.5 % patients from the control group, where cerebral oximetry was monitored blindly, no NIRS algorithm was applied, showed postoperative cognitive decline, compared to the study group where postoperative cognitive decline was observed in 21.4 % of patients.

No correlation was found between intraoperative cerebral oxygenation and postoperative cognitive function. However, patients, who had a rScO2 decrease of > 10 % in any stage of surgery experienced a lower median MOCA score after the surgery.

Near-infrared spectroscopy together with NIRS-based clinical algorithm is useful to manage intraoperative cerebral oxygen desaturation and to avoid postoperative cognitive disturbances.

Keywords*:* cerebral oxygen saturation, intraoperative cerebral desaturation, near-infrared spectroscopy, NIRS-based clinical algorithm, spinal surgery, prone position, postoperative cognitive decline

Anotācija

Uz infrasarkano staru spektroskopijas balstīta klīniskā algoritma izmantošana mugurkaula operācijās un pēcoperācijas kognitīvie traucējumi

Pacientiem, kuriem tiek veikta mugurkaula operācija pozīcijā uz vēdera, ir novērojamas dažādas fizioloģiskas izmaiņas vairākās orgānu sistēmās. Spiediens uz mazo iegurni, paaugstināts intraabdominālais un intratorakālais spiediens samazina venozo asiņu atgriešanos sistēmiskajā cirkulācijā, sirds izsviedi un paaugstina spiedienu mugurkaula asinsvados, radot paaugstinātas asiņošanas draudus operācijas laikā. Papildus tiek ietekmēta arī plaušu izplešamība. Visi iepriekšminētie faktori ietekmē galvas smadzeņu asins plūsmu, kā arī skābekļa piegādi galvas smadzeņu audiem. Galvas smadzenes ir ļoti atkarīgas no adekvātas skābekļa piegādes, tā kā smadzeņu audu bojājums un pat šūnu nāve tiek novērota jau pēc 5 išēmijas minūtēm. Kā iespējama komplikācija ir pēcoperācijas kognitīvi traucējumi, kas var novest pie ilgtermiņa sekām. Precīza pēcoperācijas kognitīvo traucējumu etioloģija joprojām nav skaidra. Lai arī intraoperatīva smadzeņu audu išēmija ir viens no iespējamiem faktoriem, kas var novest pie pēcoperācijas kognitīvas disfunkcijas, galvas smadzenes ir joprojām vismazāk monitorētais orgāns operācijas laikā.

Pētījuma mērķis bija izvērtēt uz infrasarkano staru spektroskopijas principa balstīta smadzeņu desaturācijas algoritma izmantošanu mugurkaula operāciju laikā un iespējamo saistību ar pēcoperācijas kognitīvo funkciju.

Pētījumā tika iekļauti 64 pacienti vecumā virs 18 gadiem, kuriem tika veikta plānveida mugurkaula operācija pozīcijā uz vēdera. Visiem pacientiem tika nodrošināta standarta vispārējā anestēzija. Visiem pacientiem operācijas laikā tika monitorēta reģionālā galvas smadzeņu skābekļa saturācija (rScO2), izmantojot *INVOS 4100* cerebrālo oksimetru. Pacienti tika randomizēti divās grupās – pētījuma un kontroles grupā. Pētījuma grupas pacientiem, operācijas laikā novērojot smadzeņu desaturāciju (cerebrālās saturācijas krišanos par 20 % no pacienta pirmsoperācijas izejas vērtībām vai saturācijas krišanos zem absolūtās cerebrālās saturācijas vērtības 50 %), tika izmantots uz infrasarkano staru spektroskopijas principa balstīts smadzeņu desaturācijas algoritms (*NIRS* algoritms), lai atjaunotu adekvātu smadzeņu saturāciju. Kontroles grupā cerebrālā saturācija tika monitorēta aizklāti, uz infrasarkano staru spektroskopijas principa balstīts smadzeņu desaturācijas algoritms netika izmantots. Abās grupās pirms un pēc operācijas tika izvērtēta pacientu kognitīvā funkcija, izmantojot Monreālas kognitīvā izvērtējuma skalu (*Montreal Cognitive Assessment Score (MOCA)*). Tika fiksēts arī pirmsoperācijas hemoglobīna (Hb), hematoktrīta (Hct) līmenis, kā arī vidējais arteriālais asinsspiediens (*MAP*) operācijas laikā, oglekļa dioksīds izelpā (EtCO2), perifērā skābekļa saturācija (SpO2), asins zudums operācijas laikā un kopējais operācijas laiks.

Mūsu pētījumā intraoperatīva smadzeņu desaturācija tika novērota 3 pacientiem – 2 pētījuma grupas un 1 kontroles grupas pacientam. Pētījuma grupas pacienti bija 54 un 57 gadus veci. Vienam pacientam novēroja intraoperatīvu smadzeņu desaturāciju par 29 % no izejas rScO2 vērtībām un vienlaicīgi arī absolūtās vērtības krišanos zem 50 %; otram pacientam novēroja intraoperatīvu smadzeņu skābekļa vērtību krišanos par 27 % no pacienta izejas pamatvērtībām. Abos gadījumos tika izmantots *NIRS* algoritms. Pēc pirmā algoritma soļa – neitrālas galvas pozīcijas nodrošināšanas – nekādas izmaiņas rScO2 vērtībās netika novērotas. Kā nākamais solis, pamatojoties uz algoritmu, tika paaugstināts vidējais asinsspiediens, izmantojot efedrīna bolusa devas. Pēc otrā soļa rScO2 vērtības atgriezās normas robežās un tālāka iejaukšanās nebija nepieciešama. Vidējais asinsspiediens cerebrālās desaturācijas laikā abiem pacientiem bija attiecīgi 95 mmHg (izejas *MAP* 124 mmHg) un 62 mmHg (izejas *MAP* 104 mmHg). Neviens no pacientiem neuzrādīja pēcoperācijas kognitīvus traucējumus – *MOCA* punktu skaits palika nemainīgs pirms un pēc operācijas.

Kontroles grupas pacients, kuram konstatēja intraoperatīvu smadzeņu desaturāciju, bet *NIRS* algoritms netika izmantots, novēroja rScO2 vērtību krišanos par 21 % no izejas vērtībām. Pacients bija 24 gadus vecs un uzrādīja pēcoperācijas *MOCA* rezultāta krišanos par 4 punktiem (no 29 *MOCA* punktiem pirms operācijas uz 25 *MOCA* punktiem pēc operācijas).

Kopumā mūsu pētījumā tika novērota korelācija starp zemākām intraoperatīvām rScO2 vērtībām un lielāku pacienta vecumu, lielāku asins zudumu operācijas laikā, augstāku pirmsoperācijas vidējo asinsspiedienu un zemākiem pirmsoperācijas *MOCA* punktiem.

Mūsu pētījumā 45,5 % kontroles grupas pacientu, kur cerebrālā oksigenācija tika monitorēta aizklāti un NIRS algoritms netika izmantots, uzrādīja pēcoperācijas kognitīvus traucējumus, salīdzinot ar pētījuma grupu, kur pēcoperācijas kognitīvus traucējumus konstatēja 21.4 % pacientu.

Korelācija starp intraoperatīviem rScO2 mērījumiem un pēcoperācijas kognitīvo funkciju netika atrasta, taču pētījums parādīja, ka pacientiem, kuriem operācijas laikā novēroja rScO2 krišanos par > 10 %, bija zemāks vidējais pēcoperācijas *MOCA* punktu skaits.

Galvas smadzeņu skābekļa intraoperatīva monitorēšana kombinācijā ar *NIRS* algoritmu ir svarīga, lai novērstu smadzeņu desaturāciju operācijas laikā un lai izvairītos no pēcoperācijas kognitīviem traucējumiem.

Atslēgvārdi: galvas smadzeņu skābekļa saturācija, intraoperatīva cerebrālā desaturācija, infrasarkano staru spektroskopija, uz infrasarkano staru spektroskopijas principa balstīts smadzeņu desaturācijas algoritms, mugurkaula ķirurģija, vēdera pozīcija, pēcoperācijas kognitīva disfunkcija

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Abbreviations used in the Thesis

APOE	apolipoprotein E
ARDS	acute respiratory distress syndrome
ASA	American Society of Anaesthesiologists
Avg	average
CA	cerebral autoregulation
CaO2	arterial oxygen content
CBF	cerebral blood flow
CEA	carotid endarterectomy
CHS	cerebral hyperperfusion syndrome
CMRO2	cerebral metabolic rate for oxygen consumption
CNS	central nervous system
CO	cardiac output
CPP	cerebral perfusion pressure
CPR	cardiopulmonary resuscitation
CV	cardioversion
CvO2	oxygen in mixed venous blood
DVT	deep venous thromboses
DO2	oxygen delivery
Dx	dextra
EtCO2	end-tidal carbon dioxide
FiO2	fraction of inspired oxygen
Hb	haemoglobin
Hct	haematocrit
ICP	intracranial pressure
INVOS	*in vivo* optical spectroscopy
LE	laminectomy
MAC	minimal alveolar concentration
MAP	mean systemic arterial pressure
Max	maximum
MDE	microdiscectomy
Min	minimum
MISS	minimally invasive spine surgery
mmHg	millimetre of mercury
MoCA	Montreal Cognitive Assessment Score
NIBP	non-invasive blood pressure

NIRS	near-infrared spectroscopy
O2	oxygen molecule
PaCO	partial pressure of carbon dioxide in arterial blood
PaO2	partial pressure of oxygen in arterial blood
PE	pulmonary embolism
PEEP	positive end expiratory pressure
pH	potential of hydrogen
PND	perioperative neurocognitive disorder
POCD	postoperative cognitive dysfunction
POVL	postoperative visual loss
PvO2	mixed venous oxygen tension
ROC	receiver operating characteristic
ROSC	return of spontaneous circulation
rScO2	regional cerebral oxygen saturation
SAH	subarachnoid haemorrhage
SaO2	arterial oxygen saturation of haemoglobin
SD	standard deviation
Sin	sinistra
SjVO2	jugular bulb oximetry
Spin Tu	spinal tumour
SpO2	peripheral oxygen saturation
SPSS	Statistical Package for the Social Sciences
SvO2	mixed venous oxygen saturation
TLIF	transforaminal lumbar interbody fusion
TNFα	tumour necrosis factor-alpha
TPF	transpedicular fixation
V/Q	ventilation – perfusion relationship
VO2	oxygen consumption
WHO	World Health Organisation

Introduction

Spinal surgery covers a wide range of operations on the spinal column and the underlying tissues and vary from uncomplicated microdiscectomy to surgery of life-threatening spinal fusions and spinal tumour evacuation, occasionally with long operation time and large blood loss. It also has been shown over the years that the number of spine surgeries has grown remarkably (Grotle, 2019). At the same time, operating techniques have progressed notably. Minimally invasive procedures with small incisions and a minimum of blood loss are performed, allowing patients to return to their daily activities sooner (Momin, 2020). The operating technique is not the only factor that determines postoperative outcome of the patients, anaesthesia-related factors also should be considered.

Spinal surgery patients are at risk of multiple postoperative complications that may be of neurological origin, such as radicular pain, motor weakness, or surgery-related infections, wound rupture, haematoma, or others (Willhuber, 2019). Several postoperative complications can also be associated with prone positioning, which is used for the majority of spinal surgeries. Prone positioning provides the best surgical conditions regarding visualization of the field. At the same time, prone positioning may promote different physiological changes, such as increased intra-abdominal and thoracic pressures potentially causing multiple organ failure and respiratory changes, postoperative visual loss (Kwee, 2015), motor weakness due to anterior spinal artery hypoperfusion (Bebawy, 2015). Respiratory changes and reduced venous return in systemic circulation, causing reduced cardiac output, and not less importantly, intraoperative rotation of the head to the left or right, and/or flexion or extension of the neck, can promote cerebral hypoperfusion and deteriorate delivery of oxygen and substrates to the brain. There are studies showing that elderly patients undergoing spine surgery in the prone position experience cerebral desaturation more than twice as likely as patients in the supine position (Deiner, 2014).

As the organ most in need of a constant oxygen supply, because of a high metabolic activity, the brain consumes approximately 20 % of the oxygen delivered to the body (Rink, 2011). Due to its dependence on autoregulated blood flow with continuous oxygen delivery, hypoxic brain damage can be initiated after only 5 minutes of ischemia (Bebawy, 2015) leading to severe consequences.

Postoperative cognitive dysfunction or decline (POCD) following non-cardiac surgery, affects a number of patients of all ages (Monk, 2008). New-onset cognitive disturbances following a surgical intervention, may not only alter postoperative patient recovery (Denault, 2014), but may also result in long-term consequences (Steinmetz, 2009). The exact aetiology of POCD remains unclear. Its pathogenesis is multifactorial, including age, pre-existing comorbidities (cardiac, cerebrovascular), alcohol abuse, and intra- and postoperative complications. While several studies claim that POCD is transient (Abildstrom, 2000), others show significant cognitive impairment even 6 and 8 years after surgery (Selnes, 2008; Steinmetz, 2009) and even death (McDonagh, 2010).

Despite advances in technology and improved patient safety, the brain remains one of the least monitored organs during surgery. Several methods are available to assess various products of brain metabolism or physiological functions. Jugular bulb cannulation and jugular venous oximetry provide insight into cerebral blood flow and the oxygenation status of brain tissue. A Clark electrode, inserted directly into the brain parenchyma, shows the oxygenation status of brain tissue. A cerebral microdialysis catheter, inserted at the site of injury can measure various biochemical markers, such as glucose, lactate, pyruvate, glutamate, aspartate and potassium (Mahajan, 2013). Unfortunately, all of these methods are highly invasive, which is restricting their use in clinical practice.

Near-infrared spectroscopy (NIRS) has been a well-known technology in medicine since 1977. Jobsis then introduced NIRS for tissue oxygen monitoring (Jobsis, 1977). Cerebral oximeters are non-invasive devices that can be used from the beginning of cardiac surgery or for monitoring traumatic brain injury (Davies, 2015), as well as during abdominal, orthopaedic, urological, gynaecological or thoracic surgical procedures (Nielsen, 2014). Nowadays, NIRS devices, such as cerebral oximeters, are widely used to monitor continuous cerebral oxygen saturation in real time and are widely used to predict brain outcome after cardiac arrest, and even to monitor the brain during reanimation (Cournoyer, 2016).

A NIRS-based algorithm is available (Denault, 2014) to help clinicians guide the intraoperative management of patients in cases when cerebral oxygen saturation decreases and active management is required to restore adequate levels and avoid cerebral hypoxia.

Aim of the Thesis

The goal of this Thesis was to evaluate cerebral oxygen saturation in patients undergoing spinal neurosurgery in the prone position using Near-infrared spectroscopy in conjunction with a NIRS-based clinical algorithm, with a further aim of assessing a possible relationship between cerebral oxygenation and a postoperative cognitive decline.

Objectives of the Thesis

1. To determine whether patients undergoing spinal neurosurgery in the prone position experience cerebral desaturation.
2. To evaluate cognitive function pre- and postoperatively in patients, who were subjected to monitoring of regional cerebral oxygen saturation with cerebral oximetry device while undergoing spinal neurosurgery in the prone position.
3. To identify the value of NIRS-based clinical algorithm in patients where cerebral desaturation was seen in terms of restorage of rScO2 adequate values and postoperative cognitive function.
4. To evaluate the correlation and association of patient age, haemoglobin, haematocrit, length of surgery, intraoperative blood loss, preoperative and intraoperative systemic MAP, intraoperative end-tidal carbon dioxide, peripheral oxygen saturation, preoperative cognitive function with intraoperative rScO2 values.
5. To identify, whether intraoperative rScO2 values correlate with postoperative cognitive function.
6. To evaluate the usefulness of cerebral oxygen monitoring and a NIRS-based clinical algorithm during spinal surgery with the aim of preventing postoperative cognitive decline.

Hypothesis of the Thesis

Providing adequate cerebral oxygen saturation during spinal neurosurgery in the prone position is essential for avoiding postoperative cognitive decline.

Novelty

A significant number of patients suffer from postoperative cognitive disturbances that impair recovery and return to their daily activities. Apparently, postoperative cognitive decline remains unrecognised unless cognitive monitoring function tools are applied.

Patient safety is one of the most important goals in clinical practice. However, the brain remains one of the least monitored organs intraoperatively.

We have attempted to implement two factors that may improve intraoperative patient safety and avoid postoperative cognitive complications. The first factor is the use of intraoperative cerebral oximetry to monitor cerebral oxygen saturation, which is a non-invasive and easy-to-use method. The second is a tool to assess the patient’s cognitive status using the Montreal Cognitive Assessment Score (MOCA). Our study is one of the few to use cerebral oximetry intraoperatively in spinal surgery patients, and the first to use the MOCA to assess cognitive function in spinal surgery patients.

Organisation

The study was performed in the Anaesthesiology Clinic of Riga East Clinical University Hospital. Selection of patients, who gave their informed consent to participate, as well as pre- and postoperative evaluation of the participants was carried out in the Neurology and Neurosurgery Clinic of Riga East Clinical University Hospital.

Personal Contribution

The author took part in all stages of the study such as patient selection, preoperative and postoperative patient evaluation, intraoperative patient management, and collection and analysis of data. The author also reviewed the literature, performed statistical analyses, and interpreted the results.

Ethical Concerns

The study protocol and patient informed consent form were approved by the Research Ethics Committee and Ethics Committee of the Rīga Stradiņš University (Approval No. 6-2/11/59; 85/29.12.2016). All patients gave their informed consent for participation in the study.

1 Literature Review

1.1 Oxygen and its transport in the human body

A continuous supply of oxygen (O2) is of vital importance for cell metabolism of the human body. Oxygen is also one of the most administered medicines in the daily practice of anaesthesia and intensive care medicine (Dunn, 2016). Not only lack of oxygen, as in hypoxic conditions, but also excessive oxygen, as in hyperoxia, may lead to grave consequences.

The oxygen transport in human body can be provided in two ways – by convection and by diffusion; convection is an active process requiring energy, but diffusion is a passive process in which oxygen moves down a partial pressure gradient (Dunn, 2016).

In blood, oxygen is bound to the allosteric protein – haemoglobin (Hb) by forming oxyhaemoglobin. As soon as the oxygen molecule diffuses through the alveolar membrane to the pulmonary capillary, it is bound to haemoglobin. One haemoglobin molecule is capable of binding four molecules of oxygen. In the human body, with a haemoglobin concentration of 15 g/dl, Hb has a maximum oxygen carrying capacity of 20.85 ml O2/100 ml, or approximately 1.39 ml O2 g/Hb (Hüfner's constant).

The oxygen amount in arterial blood consists of oxygen, which is bound to haemoglobin, and oxygen which is dissolved in plasma. The individual amount of oxygen in each 100 ml of arterial blood can be expressed with the equation:

$$\text{Arterial oxygen content} = \text{bound oxygen} + \text{dissolved oxygen}$$

$$CaO2 = (1.31 \text{ X } Hb \text{ X } SaO2 \text{ X } 0.01) + (0.0225 \text{ X } PaO2) \tag{1}$$

1.31 – Hüfner's constant

Hb – the amount of haemoglobin (g/dl)

SaO2 – the arterial Hb saturation in per cent

0.0225 – the solubility coefficient of oxygen at the body temperature

PaO2 – the partial pressure of oxygen in the arterial blood (kPa)

The global oxygen delivery traditionally has been described with the equation:

$$\text{Oxygen delivery (DO2)} = \text{cardiac output (CO) X arterial oxygen content}$$

$$DO2 = CO \text{ X } \{(1.31 \text{ X } Hb \text{ X } SaO2 \text{ x } 0.01) + (0.0225 \text{ X } PaO2)\} \tag{2}$$

This equation describes oxygen delivery in general, not taking in account the metabolic activity and the oxygen demand of the different body tissues. From the equation it is also possible to see the major factors affecting oxygen delivery, namely: cardiac output and its alterations, the arterial blood oxygen saturation and the haemoglobin concentration.

Tissue oxygen consumption (VO2) can be measured by using Fick's equation and measuring oxygen in mixed venous blood (CvO2):

$$CvO2 = (1.31 \text{ x } Hb \text{ X } SvO2 \text{ X } 0.01) + (0.0225 \text{ X } PvO2) \quad (3)$$

SvO2 – mixed venous oxygen saturation

PvO2 – mixed venous oxygen tension

Oxygen delivery and oxygen consumption, according to the above equation, is measured in global values without taking in account regional differences.

Oxygen consumption (VO2) may be increased during exposure to factors such as exercise, shivering, trauma, sepsis and pain. Moreover, it decreases during sedation, analgesia, neuromuscular blockade, hypovolemia, mechanical ventilation and hypothermia. However, a decrease in VO2 also can be manipulated, for example, by inducing therapeutic hypothermia, thereby reducing metabolism (Dunn, 2016).

1.2 Neurophysiology (Cerebral blood flow, cerebral autoregulation, oxygen consumption in the brain)

Weighting only 2 % of the total body mass, the brain is one of the most metabolically active organs of the human body (Rink, 2011). Cerebral blood flow, being responsible for adequate delivery of oxygen and energy substrates and removal of waste products, is critically important for normal brain function (Fantini, 2016). Cerebral blood flow (CBF) is the blood volume that flows through the brain tissue in unit mass per unit time (Rink, 2011). The normal values of CBF are approximately 45–60 ml/100 g/min (Fantini, 2016), which is nearly 15 % of cardiac output (Rink, 2011). CBF depends on cerebral metabolic rate for oxygen consumption (CMRO2) (1), cerebral perfusion pressure (CPP) and autoregulation (2), PaCO2 (3), PaO2 (4) and anaesthetic drugs (5) (Miller, 2011).

Hypothermia and the majority of anaesthetic drugs reduce CMRO2, whereas seizures increase the activity significantly. CMRO2 increases and decreases in direct proportion to CBF. As a rule of thumb, CBF decreases by 7 % for every 1 °C decrease in body core temperature below 37 °C (Miller, 2011).

Cerebral perfusion pressure (CPP) is defined as the difference between systemic mean arterial pressure (MAP, normal range 70–100 mmHg) and intracranial pressure (ICP, normal range 5–15 mmHg) (Fantini, 2016). Cerebral autoregulation (CA) is a homeostatic mechanism, which helps keeping constant brain tissue perfusion during changes in MAP. The mechanism behind CA is not fully understood, but evidently myogenic, metabolic and neurogenic processes are involved (Fantini, 2016). In general, CA means that CBF remains constant when MAP ranges between 50 mmHg and 150 mmHg, and it is more efficient above baseline MAP rather than below baseline MAP (Figure 1.1). However, it should be borne in mind that various factors may influence these limits, as for instance, arterial hypertension, intracranial tumours or inhaled anaesthetics (van den Brule, 2018; Miller, 2011).

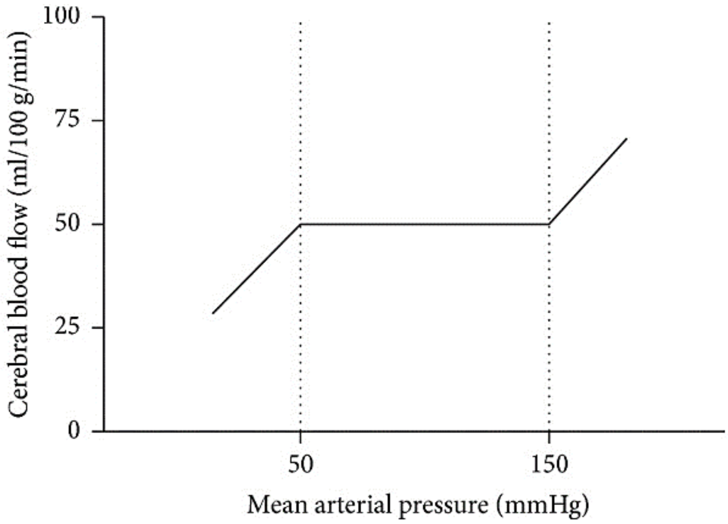

Figure 1.1 **Cerebral autoregulation (van den Brule, 2018)**

Changes in PaCO2 cause corresponding changes in CBF, thus a 1 mmHg increase or decrease in PaCO2 from 40 mmHg may change CBF by 1ml/100g/min. This mechanism is based on the carbon dioxide-mediated alteration in pH, which causes a corresponding cerebral vasoconstriction or vasodilation (Miller, 2011).

A change in oxygen partial pressure of arterial blood (PaO2) has a lower impact on CBF (Barash, 2015). When PaO2 decreases below a threshold value of 50 mmHg, an increase in CBF may be noticed (Miller, 2011).

The different anaesthetics cause different effects on CMRO2 and CBF. For instance, intravenously administered anaesthetics, like, propofol, etomidate, thiopental, as well as benzodiazepines and opioids reduce CMRO2 and consequently, also CBF. Volatile anaesthetics, such as sevoflurane, desflurane, and isoflurane, cause cerebral vasodilation and therefore increase CBF (Miller, 2011).

1.3 Oxygen metabolism of brain tissue

Adult human brain utilizes about 20 % of total oxygen used by the body or approximately 49 ml O2 per minute at rest, although oxygen consumption varies in different brain regions. Grey matter consumes twice as much oxygen as white matter (Rink, 2011). The brain is dependent on constant blood flow and oxygen delivery. After 5 minutes of global ischemia hypoxic brain damage occurs (Barash, 2015). Hypoxia triggers different pathological reactions in central nervous system cells, causing tissue dysfunction, damage and cell death (Chen, 2020).

Brain is a metabolically active organ, and energy consumption in the central nervous system (CNS) is dynamic. Although the precise mechanism of oxygen metabolism in brain cells is poorly understood and numerous mechanisms and pathways are involved, it is well known that oxygen delivery is critically important for brain cellular function. The brain consumes approximately 20 % of the total oxygen supplied and roughly 75–80 % is consumed in the neurons. This energy is used in the neuronal synapses for neuronal membrane restoration after depolarization, vesicle recycling, synthesis of neurotransmitters and axoplasmic transport. Neuronal activity differs among different brain regions. Therefore, energy requirement also varies. Disruption of oxidative metabolism, results in cellular hypoxia, stroke, traumatic brain injury, tumours and early neurodegeneration (Watts, 2018; Fan, 2020).

1.4 Spinal surgery

Spinal surgery is a medical field covering a wide range of operations performed on the vertebral column, the intervertebral discs and surrounding tissues. There are different pathologies of diseases, such as spinal canal stenosis, vertebral disc hernias, spinal tumours or metastasis etc. and spinal trauma (vertebral fractures) requiring urgent or elective surgery.

Spine surgeries are classified as intermediate risk operations. The severity of the surgery depends on various factors, like, type of surgery, underlying patient conditions such as comorbidities, and the surgical technique used. Most spinal surgeries are associated with marked fluid shifts, blood loss, and haemodynamic alterations (Miller, 2011).

Spinal surgery can be divided into anterior or posterior spine surgery. The anterior surgery takes place via the abdomen or the thorax, with the patient in the supine or lateral recumbent position. In posterior spine surgery, the patient is lying in the prone position. Additionally, combined – anteroposterior procedures may be performed (Miller, 2011).

During the last decades, spinal surgery has changed, and correspondingly also the operational methods, and with improved results. For example, minimally invasive spine surgery (MISS) may be performed as an alternative to traditional open techniques. The main goals of MISS are reductions of skin and surrounding tissue damages – factors that reduce postoperative pain and contribute to faster recovery (Byvalsev, 2019). Recently MISS has been used for a large variety of spinal surgeries, such as removal of herniated discs and spinal tumours. However, MISS also have disadvantages that must be taken into account, such as a restricted surgical field and loss of tactile sensation for the surgeon (Sharif, 2018).

Spinal fusion operations are optional for patients with spinal instability, in whom conservative therapy have failed. Often, conventional open transforaminal lumbar interbody fusion (TLIF) operations may be required (Kasliwal, 2018). The latter operations may be challenging regarding intraoperative blood loss, postoperative complications and lengthy hospital stays (Kasliwal, 2018).

1.5 Prone position during surgery, physiological changes and potential complications

Most spinal surgeries are performed with the patient lying in the prone position to ensure the best operating field. Prone positioning requires careful attention to multiple factors, including anatomical variations. Special spinal tables (Jackson table) (Figure 1.2) or frames (Wilson frame) (Figure 1.3) are available.

Figure 1.2 **Jackson table for spinal surgeries**

(Digital image. Mizuho OSI https://www.mizuhosi.com/product/proaxis/. Accessed 11.11.2022)

Figure 1.3 **Wilson frame used for spinal surgeries**

(Digital image. Mizuho OSI. https://www.mizuhosi.com/product/trios/. Accessed 11.11.2022)

A non-physiological position may cause physiological changes in the body that also carries certain risks. Pressure on pelvis and abdomen may lead to increased intra-abdominal pressure causing venous pooling in vena cava inferior and reduced venous return of blood to the systemic circulation (Kwee, 2015). Intra-abdominal pressure that raises above 12 mmHg can cause abdominal compartment syndrome, which may cause multi-organ failure, compromised respiration including decreased lung compliance and derangement of oxygen uptake (Kwee, 2015; Lee, 2015). Pressure on the thoracic cavity leads to direct pressure on the left ventricle that may result in reduced end-diastolic filling and a fall in stroke volume and cardiac index (Kwee, 2015). Even more important, increased abdominal and thoracic pressures lead to increased pressure in vertebral vessels that may result in excessive bleeding during the surgery, obscure the surgical field and prolong the operation time (Kwee, 2015).

Other important complications following surgery in the prone position are postoperative visual loss (POVL) due to central retinal artery occlusion and ischemic optic neuropathy (Bebawy, 2015). The major risk factors for POVL are – anaemia, blood loss over 1000 ml, hypotension, duration of surgery (over 6 hours) and increased intraocular pressure (Barash, 2015).

Another complication of spinal surgery is anterior spinal artery syndrome with artery hypoperfusion (Bebawy, 2015), that may lead to postoperative motor weakness (Barash, 2015).

If patient’s head is not lying in the neutral position, but is rotated to the left or right, or it is in a flexed or extended position, oropharyngeal swelling due to blood congestion, or carotid and vertebrobasilar artery dissection with intimal dissection and thrombosis may be seen (Kwee, 2015). Positioning the patient in a non-physiological position requires that special attention be paid not only to a neutral head position, but also to proper hand positioning to avoid overextensions and brachial plexus injury. Deep venous thromboses (DVT) and pulmonary emboli (PE) also may be observed in spinal surgery patients secondary to hypotension, hypovolemia and hypothermia (Barash, 2015).

It is well known that prone position also may be used to improve oxygenation in patients with respiratory failure, such as in patients with acute respiratory distress syndrome (ARDS) or severe pneumonia. The main benefit of prone positioning is that the ventilation – perfusion relationship (V/Q) in the lungs may be more favourable in the prone position due to the prevailing pathophysiological changes (Broccard, 2003), thereby reducing the fraction of blood perfusing non-ventilated alveoli (Pelosi, 2002). It has been shown that in certain pathological conditions, alveolar inflation as well as transpulmonary pressure is more homogenous in the prone position than in supine position (Pelosi, 2002). On the other hand, the distribution of blood perfusion is gravity independent. The majority of perfusion goes through dorsal lung regions – in both supine and prone position (Broccard, 2003). As a result, reduction of physiological shunt, which is the combination of reduced ventilation – perfusion relationship and true shunt, is achieved (Pelosi, 2002).

1.6 Near-infrared spectroscopy device – cerebral oximetry

In 1977 Jobsis (Jobsis, 1977) introduced the near-infrared spectroscopy principle for monitoring oxygen content of brain tissue. Near-infrared spectroscopy now has been applied in cerebral oximeters, that are non-invasive devices used to estimate cerebral oxygenation.

Cerebral oximetry devices consist of two adhesive electrodes (Figure 1.4), that are attached to patient's forehead – one over the left and one over the right cerebral hemisphere, and a monitor (Figure 1.5). Both electrodes contain a NIR light source and a light detector, usually two, that are placed just a few centimetres away from each other (Figure 1.6) (Scheeren, 2012; Tosch, 2016).

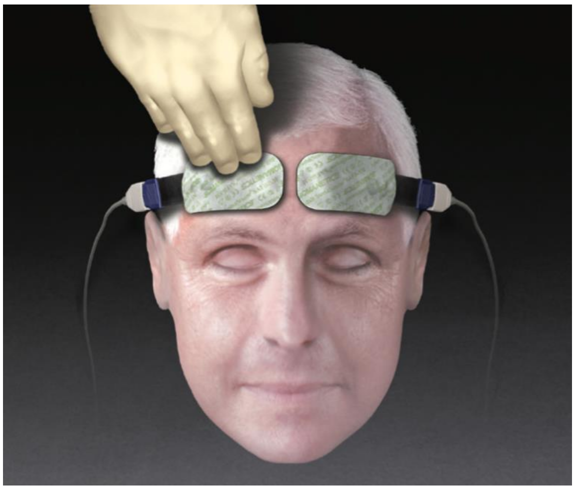

Figure 1.4 **INVOS (*in vivo* optical spectroscopy) sensor placement on the patient's forehead**

(Picture taken from the INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010.)

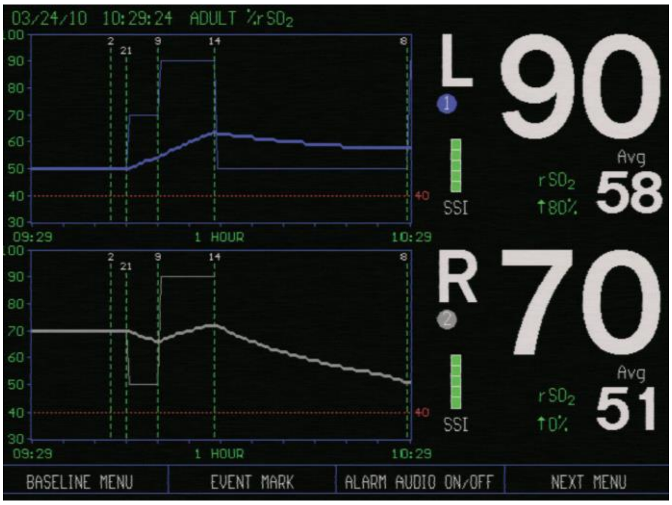

Figure 1.5 **Screen of the INVOS cerebral oximeter showing regional cerebral oxygen saturation (rScO2) values above the left cerebral hemisphere (L) and right cerebral hemisphere (R)**

(Picture taken from The INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010.)

Figure 1.6 **INVOS sensor**

(Picture taken from the INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010.)

The emitted beam from the light source of the cerebral oximeter electrode penetrates underlying tissue – the skull and brain (Figure 1.7). Photons in NIR spectrum, ranging from 700–1100 nm, are capable of penetrating tissues of several centimetres thickness, including bone. In contrast, visible light is absorbed by different tissue components on its way, thus, penetrating only short distances (Scheeren, 2012).

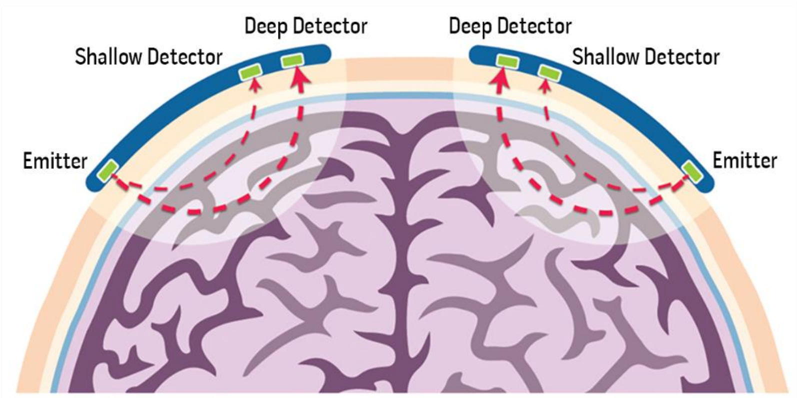

Figure 1.7 **NIR light penetrating brain tissue from the INVOS sensor light emitter**

(Polderman, 2019)

Molecules in tissues that absorb light, are metal complex chromophores such as haemoglobin, bilirubin and cytochromes (Tosch, 2016). Haemoglobin exists in two forms, as oxygenated and deoxygenated haemoglobin and the wavelength for its absorption is different. Oxygenated haemoglobin is absorbed by a wavelength of 700–1150 nm whereas deoxygenated haemoglobin is absorbed by a wavelength of 650–1000 nm. Based on these differences, the total tissue haemoglobin concentration can be calculated in a point, where the absorption spectra for both haemoglobin forms are the same (Tosch, 2016). Emitted light going through the skull and the brain tissues take a boomerang-shaped path and is either absorbed or reflected (Scheeren, 2012). Reflected light travels back to the surface where it hits the cerebral oximeter detectors. The proximal detector senses photons that are reflected from the superficial tissues and the distal detector identifies those coming from deeper brain tissue (Figure 1.7) (Green, 2017).

To calculate cerebral oxygenation, which is displayed as a number on the monitor, cerebral oximeters incorporate the Beer-Lambert law (Tosch, 2016). In general, the Beer-Lambert law states, that light attenuation depends on the substance and the material it goes through, and combines two physics laws. Beer's law assumes that the concentration of the substance through which light travels decreases, and the intensity of light decreases exponentially (Tosch, 2016). Lambert's law states that if the distance that light travels through a substance increases, the intensity of the light decreases exponentially (Tosch, 2016).

Cerebral oximetry electrodes are placed bilaterally on the forehead of the patient, one over the right cerebral haemisphere and one over the left, respectively, 1.5–2 cm above the eyebrows (Green, 2017). With this placement of electrodes, rScO2 will be detected in the frontal cortex, a part of the brain most sensitive to hypoxia and supplied with blood from the anterior and middle cerebral arteries (Green, 2017). Cerebral oximeters are independent of pulsatile blood flow, unlike pulse oximeters (Tosch, 2016), and monitor oxygenation status for the greater part of venous blood. In the cerebral cortex, it is estimated that 70 % of blood is of venous origin, 25 % is arterial, and 5 % is capillary (Biedrzycka, 2016). Cerebral oxygen saturation reflects the balance between oxygen supply and utilization in the monitored area (Scheeren, 2012). What is considered to be normal rScO2 values, differ amongst authors, but values ranging between 60 % and 80 % are considered acceptable (Tosch, 2016).

1.6.1 Cerebral oximeters in clinical practice

Cerebral oximeters are non-invasive, easy-to-use monitoring devices. They provide information about changes in regional cerebral oxygen saturation by measuring oxyhaemoglobin and deoxyhaemoglobin continuously in real time (Fabregas, 2001) allowing for early detection of harmful cerebral desaturation episodes and trends and taking action to prevent them.

Initially, cerebral oximeters were mostly used in adult and pediatric cardiac surgery. Currently, cerebral oximetry has gained popularity in many other surgical fields, such as orthopedic surgery, cardiovascular surgery, neurosurgery, and laparoscopic and gynaecological surgery, as well as in patients with traumatic brain injury in intensive care units and in patients during and after cardiac arrest.

Cerebral oximeters are widely used to monitor oxygen saturation during cardiac surgery, particularly during extracorporeal circulation. During cardiac surgery, many factors may contribute to deterioration of brain oxygen saturation, such as venous cannula malfunction during extracorporeal circulation, embolic events, decreased arterial pressure, reduced oxygenation of arterial blood, hypocapnia, haemodilution, and increased oxygen consumption during rewarming before weaning off extracorporeal circulation (Biedrzycka, 2016). The advantage of NIRS devices during extracorporeal circulation is that they do not require pulsatile blood flow for measurements.

In carotid endarterectomy (CEA), cerebral oximeters have been used to detect critical brain ischemia during internal carotid artery cross-clamping or embolism during shunt insertion (Moerman, 2015). Studies have shown that cerebral oxygen saturation monitoring using near-infrared spectroscopy has advantages over transcranial Doppler ultrasound not only intraoperatively but also in the early postoperative period for detecting cerebral hyperperfusion syndrome (CHS), which is a potentially life-threatening complication after CEA (Pennekamp, 2013).

Orthopedic surgeries, such as shoulder surgeries, are performed in the sitting or “beach chair” position and carry a risk of changes in systemic blood pressure that may fall below the lower limit, which ensures brain autoregulation causing cerebral hypoperfusion and desaturation (Moerman, 2015). Complications, such as stroke, ischemic brain injury, and vegetative states may occur (Miller, 2011). A falling cerebral blood flow can be explained by a decrease in the arterial blood pressure gradient between the heart and the brain. Arterial blood pressure decreases by 0.77 mmHg for every centimeter of head elevation above the heart level. Therefore, the blood pressure measured at the level of the heart does not match the perfusion pressure in the brain. Arterial blood pressure in the "beach chair" position should be measured at the level of the external auditory meatus, which represents the approximate level of the circle of Willis in the brain, although, the brain tissue is also above this level (Miller, 2011). In other orthopedic surgeries, such as knee and hip replacement surgeries, rScO2 decrease may be seen due to regional (spinal, epidural) anaesthesia inducing sympathetic blockade causing vasodilation. However, independent of anaesthesia, in 38 % of patients an rScO2 decrease of < 50 % or 75 % of the baseline can be observed during hip fracture surgery (Nielsen, 2014).

During thoracic surgery with one-lung ventilation, open thoracoscopy, or thoracotomy, patients may experience decreased global oxygen delivery. Studies have shown that during one-lung ventilation a significant number of patients (up to 75 %) suffer from an rScO2 decrease that is more than 20 % below baseline (Nielsen, 2014).

Lower rScO2 values can also be seen following haemodilution during urologic surgeries, or under exposure to Trendelenburg's position during gynaecological laparoscopic operations (Nielsen, 2014).

Near-infrared spectroscopy devices have also been applied in the intensive care settings to monitor rScO2 during traumatic brain injury and during and after cardiac arrest (Hayashida, 2014; Meex, 2013). Trials have been performed to employ rScO2 monitoring devices for patients with head injuries in intensive care units (ICU). In patients with head-injuries, NIRS devices have been used to detect haematoma formation, although there are more limitations than advances. These devices provide information about the frontal cerebral area, as the electrodes are mostly placed on the forehead. However, rScO2 values have failed to show a close correlation with other monitoring methods, such as jugular bulb oximetry (SjVO2), intracranial pressure (ICP) or cerebral perfusion pressure (CPP) (Adelson, 2007). In patients with subarachnoid haemorrhages (SAH), NIRS devices are useful for detecting a reduction in rScO2, which may indicate vasospasm as a potential cause of morbidity (Naidech, 2008).

Schewe et al. (Schewe, 2014) investigated the possible role of non-invasive NIRS devices in monitoring rScO2 during out-of-hospital cardiac arrest. They found that return of spontaneous circulation (ROSC) was associated with higher initial regional cerebral oxygenation, as well as the fact that rScO2 values had a tendency to rise during cardiopulmonary resuscitation (CPR) if a mechanical heart compression device was used (Schewe, 2014). A limitation of this study was its small sample size.

A study by Wutzler et al. showed that in patients with atrial fibrillation, rScO2 increased after successful cardioversion (CV), compared to patients in whom CV did not result in a return of sinus rhythm (Wutzler, 2013). The rise of rScO2 after CV was statistically significant, but no correlations were found between MAP, heart rate, and peripheral oxygen saturation (Wutzler, 2013).

1.6.2 Cerebral oximetry or near-infrared spectroscopy-based algorithm

Cerebral oximeters are easy to use and provide continuous information regarding cerebral oxygen saturation. One of the most important applications of NIRS is the development of a near-infrared spectroscopy-based algorithm to correct cerebral oxygen desaturation as soon as it occurs during surgery with the aim of avoiding hypoxic brain injury. The NIRS algorithm was developed in 2007 by Denault and collegues for cardiac surgery (Denault, 2014). The algorithm was designed to restore imbalance between oxygen delivery and demand by optimizing the factors involved, such as MAP, systemic oxygen saturation, end-tidal carbon dioxide, partial pressure of carbon dioxide, haemoglobin, cardiac function, and cardiac output. Moreover, the underlying reasons for increased brain oxygen consumption, such as convulsions, hyperthermia, and cerebral edema, should be considered. First, the algorithm checks the patient for correct head positioning and inspects central, aortic- or superior vena cava catheters (Figure 1.8) (Denault, 2007).

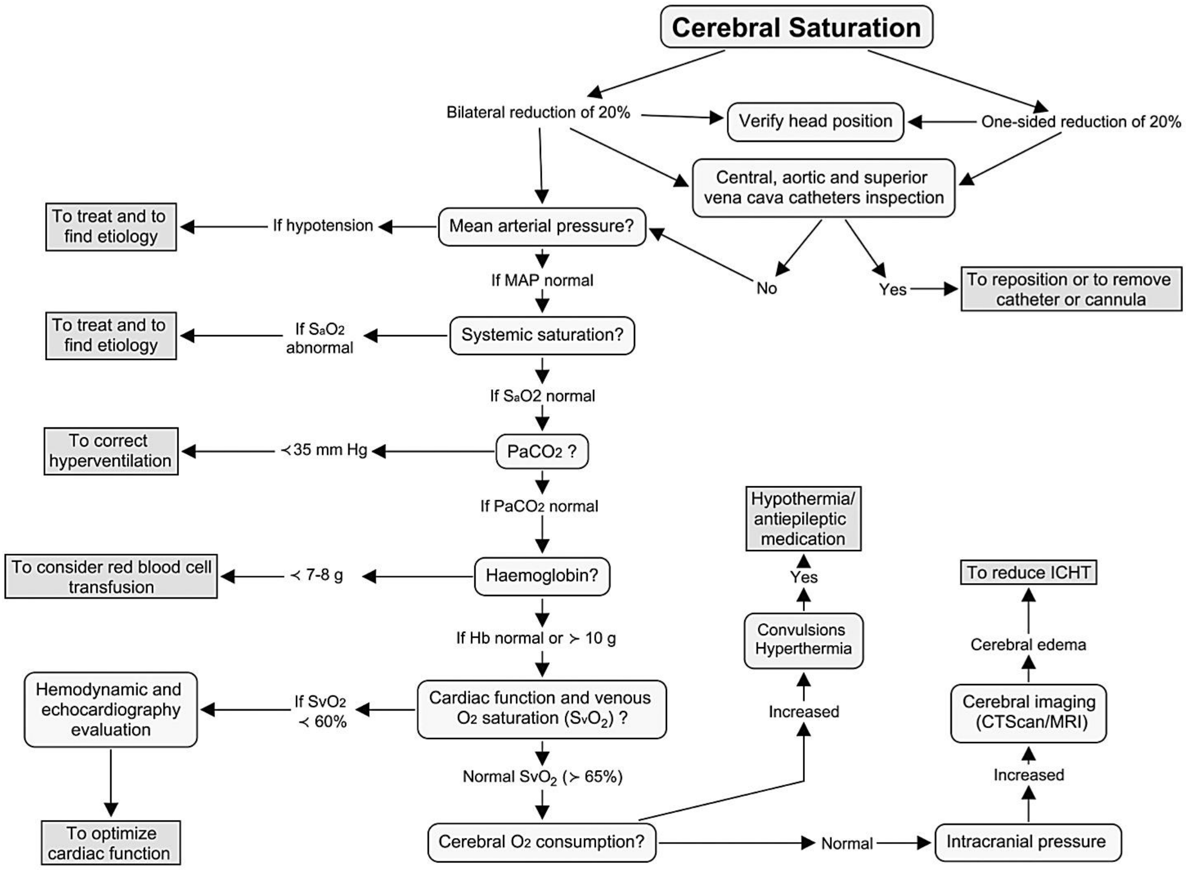

Figure 1.8 **Proposed algorithm in the use of brain oximetry**

MAP – mean arterial pressure, SaO2 – arterial oxygen saturation of haemoglobin, PaCO2 – partial pressure of carbon dioxide in arterial blood, Hb – haemoglobin, SvO2 – mixed venous oxygen saturation, ICHT – intracranial hypertension, CT – computed tomography, MRI – magnetic resonance imaging) (Denault, 2007)

The modified NIRS algorithm, that has been adapted to non-cardiac surgery (Trafidlo, 2015) (Figure 1.9).

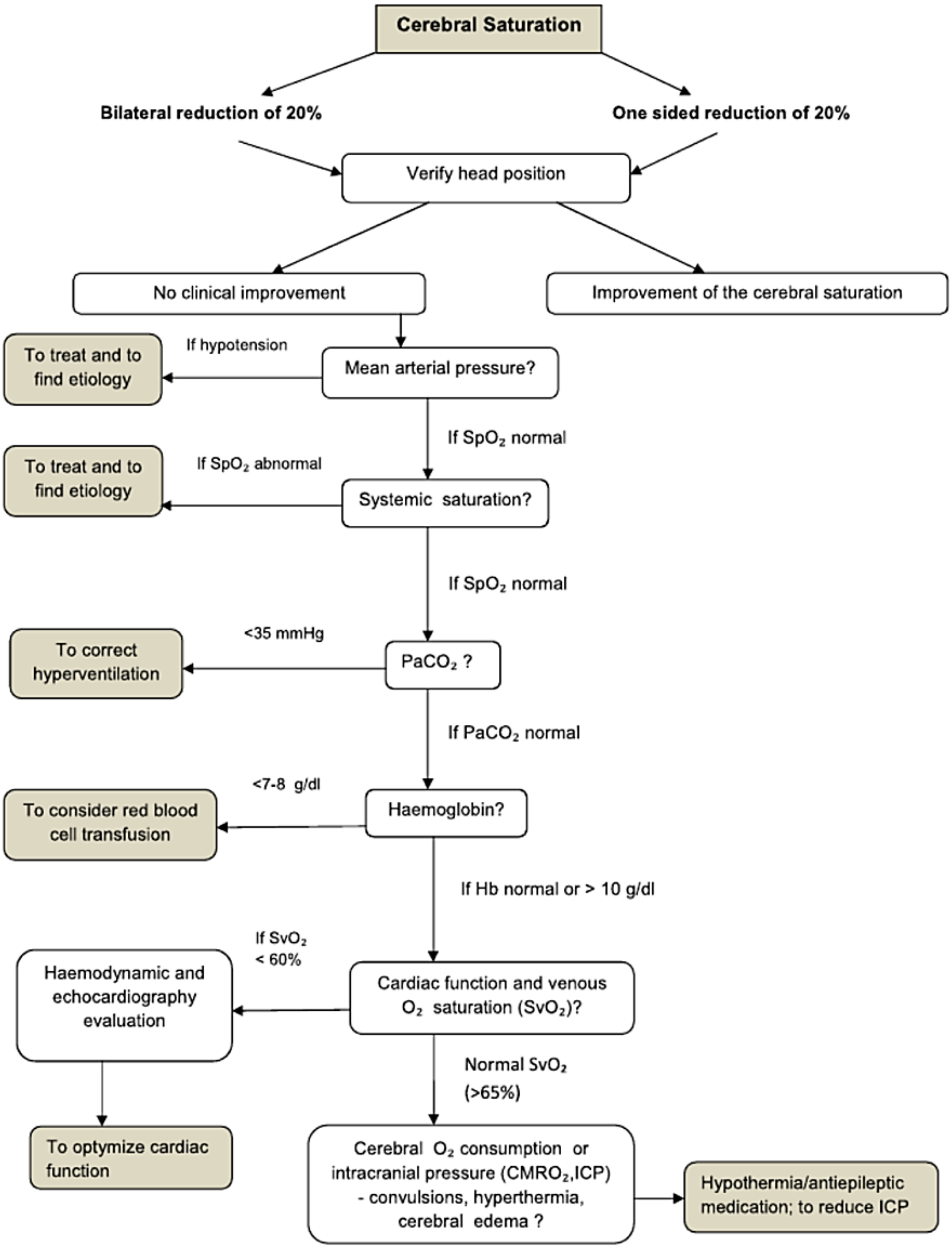

Figure 1.9 **Trafidlo et al. proposed algorithm of procedures applied in case of declining values of NIRS cerebral oximetry**

SpO2 – peripheral oxygen saturation, PaCO2 – partial pressure of carbon dioxide in arterial blood, Hb – haemoglobin, SvO2 – mixed venous oxygen saturation, CMRO2 – cerebral metaboloc rate of oxygen, ICP – intracranial pressure (Trafidlo, 2015).

One of the basic requirements for use of cerebral oximeters is to establish the individual baseline rScO2 values of the patients. Normal rScO2 values are considered to be from 60–80 % (Tosch, 2016), but not all patients present baseline values in this range. What is considered to be abnormal rScO2 values, whereupon the NIRS-based algorithm should be initiated, differs between authors, although the majority define cerebral desaturation as 20 % unilateral or bilateral reduction from the individual baseline values of the patients, or a decrease below an absolute value of $rScO_2$ of 50 % (Denault, 2014). Cerebral oxygenation values, that are observed during the surgery, should be interpreted individually in every patient (Tosch, 2016), taking in account all the patient-related, surgery-related and anaesthesia-related information. Absolute thresholds for cerebral desaturation should also be evaluated individually and interpreted with caution (Vegh, 2016).

As with every other monitoring device, cerebral oximetry has limitations. Before initiating the NIRS algorithm, electrode positioning should be ruled out, emphasizing adequate placement with no light leakage. Since the electrodes are placed on the forehead of the patient, desaturation in the posterior brain circulation may be missed (Denault, 2007).

The near-infrared spectroscopy algorithm was initially developed for use in cardiac surgery; however, with time, NIRS technology for monitoring cerebral oxygenation has been implemented in other surgical fields. Therefore, the algorithm has also been used in adition to cardiac procedures. Monitoring cerebral oxygen saturation without associated interventional algorithms for responding appropriately to desaturation values diminishes the value of this technology (Tosch, 2016).

1.7 Intraoperative cerebral oxygen desaturation

Many studies have shown a positive correlation between intraoperative cerebral desaturation registered with non-invasive near-infrared spectroscopy devices and various postoperative complications. Better outcomes were observed in patients monitored using NIRS devices. NIRS-based algorithms were used intraoperatively to avoid the $rScO_2$ dropping below the threshold. The most studied complications include stroke, postoperative cognitive dysfunction or decline and delirium.

Goldman et al. (Goldman, 2004) studied 1000 patients undergoing coronary bypass surgery or valve surgery. They found that patients in whom cerebral oxygen saturation monitoring had been used and steps had been taken against cerebral desaturation displayed a significantly lower stroke rate than patients in whom cerebral oxygen saturation had not been monitored (0.97 % versus 2.5 %; $p < 0.044$).

Murkin et al. (Murkin, 2007) studied the intraoperative monitoring of cerebral desaturation events during coronary bypass surgery and included 200 patients who were randomised into two groups. An intervention group ($n = 100$) underwent $rScO_2$ monitoring whereas the control group ($n = 100$) $rScO_2$ was monitored blindly, where $rScO_2$ was monitored, but the results were not visible to the anaesthesiologist in charge. The investigators noticed that patients in the control group had longer periods of cerebral desaturation ($p = 0.014$)

and spent more days in the intensive care unit ($p = 0.029$) than the patients in the intervention group. Patients in the control group also had a higher incidence of major postoperative complications, such as stroke, myocardial infarction, and even death ($p = 0.048$). Another study performed on cardiac surgery patients (Slater, 2009) showed that, in patients monitored blindly, the investigators found a positive correlation between cerebral desaturation and postoperative cognitive decline ($p = 0.024$) and prolonged hospital stay (> 6 days) ($p = 0.007$).

1.8 Postoperative cognitive dysfunction, decline

The exact aetiology leading to postoperative cognitive disturbances (POCD) is still unclear and most likely not caused by a single factor. Risk factors that have been associated with POCD are patient-related, such as older age; pre-existing cerebral, cerebrovascular, or cardiac disease; alcohol abuse; and low educational level. In addition, surgery and anaesthesia *per se* may pose their own risk factors. In particular, long surgical procedures, intraoperative, postoperative, or anaesthesia-related complications may occur, as well as long-acting drugs used during anaesthesia (Rundshagen, 2014).

Older age is accepted as one of the leading preconditions for the development of POCD since older brains appear to be more vulnerable. Monk et al. showed that a high percentage of patients, even of younger age, undergoing non-cardiac surgery present POCD at discharge from the hospital. Thus, in their study, 36.6 % of the patients were at the age 18–39 years, 30.4 % were patients 40–59 years of age and 41.4 % were aged 60 years and more (Monk, 2008).

However, the pathogenesis of POCD remains unclear. In a study on mice, Terrando et al. (Terrando, 2011) supported the neuroinflammatory theory. They showed that surgery disrupts the blood – brain barrier as tumour necrosis factor – alpha (TNFα) is released. TNFα facilitates macrophage migration to the hippocampus, which is believed to cause cognitive disturbances after surgery (Terrando, 2011). Another study by Tsai et al. (Tsai, 2010) linked the changes to the apolipoprotein E E4 allele (APOE E4). APOE participates in cholesterol dispensation, which ensures nervous tissue repair and growth after injury (Tsai, 2010). Studies of patients subjected to cardiac surgery or carotid endarterectomy have shown a positive correlation between APOE E4 and POCD (Hayer, 2005; Tardiff, 1997). In contrast, McDonagh et al., who studied 394 patients undergoing non-cardiac surgery, found no association between APOE E4 and postoperative cognitive decline (McDonagh, 2010).

Postoperative cognitive dysfunction (POCD) or decline recently has become a topic of interest. POCD is not a diagnosis based on the International Classification of Diseases (Tsai, 2010) but is defined as a new cognitive impairment that emerges after surgery (Rundshagen, 2014). Simply stated, investigators pinpoint memory problems and difficulties in thinking and performing intellectual tasks as the most prominent signs and symptoms (Tsai, 2010; Rundshagen, 2014).

POCD should be separated from postoperative delirium. The latter is defined as acute, fluctuating disturbances in the mental state, attention, and reduced awareness of the environment (Tsai, 2010; Aldecoa, 2017). These patients are usually disoriented, often with hallucinations, inappropriate behaviour, and varying symptoms during the day (Tsai, 2010). Regarding POCD, patients usually stay oriented, but with a decline in one or more neurophysiological areas after the surgical procedure, as compared to their individual baseline conditions preoperatively (Tsai, 2010).

POCD is divided into acute POCD (recognised during the first week after surgery), intermediate POCD (within 3 months after surgery) and late or long-term POCD (within 1–2 years after the surgical procedure) (Tsai, 2010).

Several discussions have been conducted regarding the timing of POCD examination. In many studies, it has been recommended to start evaluation seven days postoperatively. During the first few days, many factors could interfere with test performance, such as acute pain (Hayer, 2000), mobility disturbances, and drugs used (Ersek, 2004). On the other hand, there are studies showing negative outcomes if POCD is detected only at hospital discharge, on the seventh day or later after the surgery. Monk et al. showed that the risk of death within the first 3 months following surgery was associated with POCD detected at hospital discharge, with mean values less than seven days on average, in patients undergoing non-cardiac surgery (Monk, 2008; Tsai, 2010). Wang et al. reported that 88 % of patients who presented with POCD had been discharged from hospital during the first postoperative week (Wang, 2007; Tsai, 2010). Therefore, investigating patients only at or after the seventh day of surgery may miss patients with POCD (Tsai, 2010).

2 Materials and Methods

This study was designed as a prospective randomised controlled trial of patients undergoing spinal surgery. Patients were collected between September 2018 and July 2020 in the Clinic of Neurology and Neurosurgery of Riga East Clinical University Hospital “Gaiļezers”. Inclusion criteria were patients aged over 18 years, patients scheduled for spinal surgery performed in the prone position. Exclusion criteria were emergency spinal surgery, patients with known cerebrovascular or psychiatric disease, previous history of stroke, inability to undergo preoperative or postoperative cognitive evaluation (severe pre- or postoperative pain, intake of strong opioid pain medication, intake of sedative medication).

The Research Ethics Committee and Ethics Committee of Rīga Stradiņš University approved the study protocol and the informed consent form (Approval No. 6-2/11/59; No. 85/29.12.2016) (see Annex 1).

The preoperative physical status of the patients was evaluated, blood tests were taken from all patients to obtain haemoglobin (Hb) and haematocrit (Hct) concentrations.

Patients were randomised into a study group and a control group by using a computerised randomization program.

2.1 Anaesthesia and intraoperative patient monitoring

All the patients received general anaesthesia. We induced anaesthesia with fentanyl 0.1–0.2 mg, propofol 1–2 mg/kg and cisatracurium 0.2 mg/kg or atracurium 0.3–0.6 mg/kg for endotracheal intubation. Anaesthesia was maintained with a continuous infusion of fentanyl 0.03–0.06 μg/kg/min, and/or fentanyl boluses 0.05–0.1 mg if heart rate or non-invasive blood pressure raised above 20 % from preoperative values. Cisatracurium continuous infusion 0.06–0.1 mg/kg/h or boluses 0.03–0.2 mg/kg or atracurium continuous infusion 0.3–0.6 mg/kg/h or boluses 0.1–0.2 mg/kg were used when the patient displayed signs of spontaneous breathing. Sevoflurane was kept at minimum alveolar concentration (MAC) 0.6–0.8. Initial tidal volume for mechanical ventilation was set to 7–8 ml/kg. Positive end expiratory pressure (PEEP) of 4-6 cmH2O was used and the fraction of inspired oxygen (FiO2) was 0.5. Ventilation was adjusted to keep end-tidal carbon dioxide (EtCO2) in the range of 35 to 45 mmHg.

Intraoperative variables such as non-invasive mean arterial pressure (MAP) was determined every 5 min. The first MAP values (2 to 3 measurements) measured before induction of anaesthesia, were fixed as preoperative values in the study protocol. Peripheral oxygen saturation (SpO2) and end-tidal carbon dioxide (EtCO2) were documented in the study protocol every 5 min. At the end of the surgery, we recorded the duration of operation and intraoperative blood loss. All the patients were extubated in the operating room.

2.2 Intraoperative cerebral oxygen saturation measurements

In all patients, regional cerebral oxygen saturation was continuously monitored using a near-infrared spectroscopy device (NIRS) INVOS (*in vivo* optical spectroscopy) 4100 (Covidien, Minneapolis, USA).

After arriving in the operating room before induction of anaesthesia, breathing room air without additional oxygen, two adhesive INVOS rScO2 sensors were placed on the patients' forehead, one above the right (Dx) and one above the left (Sin) eyebrow. Sensors were connected to the INVOS cerebral oximeter monitor. The preoperative rScO2 values were observed 3–5 minutes with patient breathing room air, at the time point where they did not change anymore and stayed stable, they were fixed in the study protocol and set as baseline rScO2 values. By establishing baseline rScO2 values, INVOS further tracked the changes in rScO2 values for the left (Sin) and the right side (Dx), respectively, showing the raise or drop from baseline rScO2 values in percentage. Then, regional cerebral oxygen saturation values were registered in the study protocol every 5 minutes as single point measurements.

All the measurements noted in the study protocol, were described as follows: PreOp (Preoperative) values – fixed after the patient had arrived in the operating room, before induction of anaesthesia; Sup (Supine) values – fixed at the time and after the induction of anaesthesia when the patient was still lying supine; Prone values – fixed when the patient was lying in the prone position; Sup2 (Supine 2) values – fixed at the end of the surgery when the patient was turned back to the supine position.

2.3 NIRS-based interventional algorithm

In the study group intraoperative rScO2 values were kept within a range of 20 % from baseline, or above an absolute rScO2 value of 50 %. As soon as the rScO2 values dropped bilaterally or unilaterally below 20 % from baseline, or below an absolute value of 50 %, the NIRS algorithm was started (Denault, 2014). Based on this algorithm, steps are taken in the following order: 1) the position of the head is verified (rotation of the head to the left or right, and/or flexion or extension of the neck are excluded), to rule out mechanical obstruction that could alter cerebral blood and oxygen supply; 2) MAP is increased to maintain cerebral perfusion pressure; 3) systemic oxygenation status is improved if arterial oxygen saturation (SaO2) is low; 4) partial pressure of carbon dioxide (PaCO2) is normalised if hypocapnia or hypercapnia is identified; 5) haemoglobin is optimised (according to the algorithm, Hb less than 7–8 g/dl requires red blood cell transfusion); 6) cardiac function is evaluated if the previous steps failed; as a last step, 7) cerebral oxygen consumption should be estimated (convulsions, hyperthermia) (Denault, 2014). Since the algorithm was created for cardiac surgery patients, it also included a step in which central aortic and superior vena cava catheters were inspected. Our algorithm was adapted for use in spinal surgery patients. If rScO2 values did not raise above the threshold values after the two first steps, an arterial blood gas sample would be taken to evaluate SaO2, PaCO2 or Hb level.

Control group patients received standard intraoperative anaesthetic management, rScO2 was monitored blindly, and the investigator was kept unaware about the NIRS results. If MAP dropped below 65 mmHg (Van Diepen, 2017), excessive bleeding was excluded and when indicated, ephedrine boluses were administered. If SpO2 dropped under 94 %, inspired oxygen concentration was raised above 50 % (Kane, 2013). If haemorrhage of more than 500 ml occurred, arterial blood gas analyses was performed to detect Hb levels and to evaluate the necessity for a blood transfusion. A haemoglobin concentration below 7 to 8 g/dl during haemorrhage was considered a trigger for transfusion (Kozek-Langenecker, 2017).

In the control group, if the rScO2 value dropped by more than 30 % from the individual baseline values, the INVOS system was set to give an alarm, and after all the necessary actions had been taken to restore cerebral oxygenation, the patient was excluded from the study.

2.4 Cognitive evaluation

To evaluate patient cognitive status, we used Montreal Cognitive Assessment (MoCA) test. The test was used in both groups. The first test was performed in the ward during the preoperative visit, 1 to 2 days before surgery. The second test was performed two days after the surgery to avoid any interaction of the intraoperative anaesthetic or acute postoperative pain with the performance of the test. The MoCA test evaluates the following parameters: attention, concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculation and orientation (MoCA Montreal Cognitive Assessment) (see Annex 2). The MoCA test has been validated in several languages, including Latvian and Russian since these tests have to be performed in the patient's native language. The test takes approximately 10–15 min to complete. The MoCA test scores range from 0 to 30 points. Postoperative cognitive decline was defined as a reduction in postoperative MoCA test scores compared to preoperative MoCA scores. The MoCA test was performed by one person, the author of the study, to ensure that the test was performed in the same manner.

3 Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) V.23. Data distribution was tested using the Kolmogorov-Smirnov test. Since most variables did not fit a normal distribution, non-parametric tests were chosen for the analysis. Groups were compared using the t-test for parametric data and Mann-Whitney test for non-parametric data. Values were presented as the mean ± standard deviation (SD).

Statistical significance was assumed at $p < 0.05$. The Kruskal-Wallis test was performed to determine the p value between three or four patient groups.

Repeated measurements during different phases of a surgery were analysed using repeated measures ANOVA (and Huynh-Feldt correction if the sphericity assumption was violated) in JASP Version 0.11.1.

Spearman's rank correlation coefficient and significance was used to describe correlations between variables. A positive correlation means that as one variable increases, the other variable also increases. A negative correlation coefficient means that, as the value of one variable increases, the value for the other decreases. The Spearman's rho correlation coefficient $\rho = 1$ shows the perfect correlation; $\rho = 0.02$ – a very low correlation; $\rho = 0.2$–0.4 – a low correlation that may warrant further investigation; $\rho = 0.4$–0.6 – a reasonable correlation; $\rho = 0.6$–0.8 – a high correlation; and $\rho = 0.8$–1.0 – a very high correlation.

4 Results

In the present study, a total of 64 adult neurosurgical patients were included – 37 (57.8 %) women and 27 (42.2 %) men aged 55 ± 15 (mean ± SD) years. Forty-two patients belonged to the study group (21 (50 %) women and 21 (50 %) men; mean age 56 ± 13 years), and 22 patients belonged to the control group patients (16 (72.7 %) women and 6 (27.3 %) men; mean age 53 ± 17 years), p = 0.7 (Table 4.1).

Table 4.1

Percentage distribution of patients by age groups – study group, control group and all study patients together

Age	Study group		Control group		Total	
	n	%	n	%	n	%
18–30	0	0	4	18	4	6
31–40	4	10	2	9	6	9
41–50	10	24	3	14	13	20
51–60	15	36	2	9	17	27
61–70	6	14	9	41	15	23
71–80	5	12	2	9	7	11
81–90	2	5	0	0	2	3
91–100	0	0	0	0	0	0

* n – number of patients.

One patient of the control group was excluded from the study because the regional cerebral oxygen saturation values dropped by more than 30 % from the patient's individual baseline values and the INVOS device alarm was activated, which initiated the necessary actions to restore cerebral oxygenation.

4.1 Type of surgery

Patients underwent the following spinal surgeries in the prone position: 6 patients (9.4 %) had laminectomy (LE), 28 patients (43.8 %) had minimal invasive microdiscectomy (MDE), 12 patients (18.8 %) had spinal tumour evacuation (Spin Tu) and 18 patients (28.1 %) underwent transpedicular spinal fixation (TPF).

The distribution between study and control group is shown in Figure 4.1.

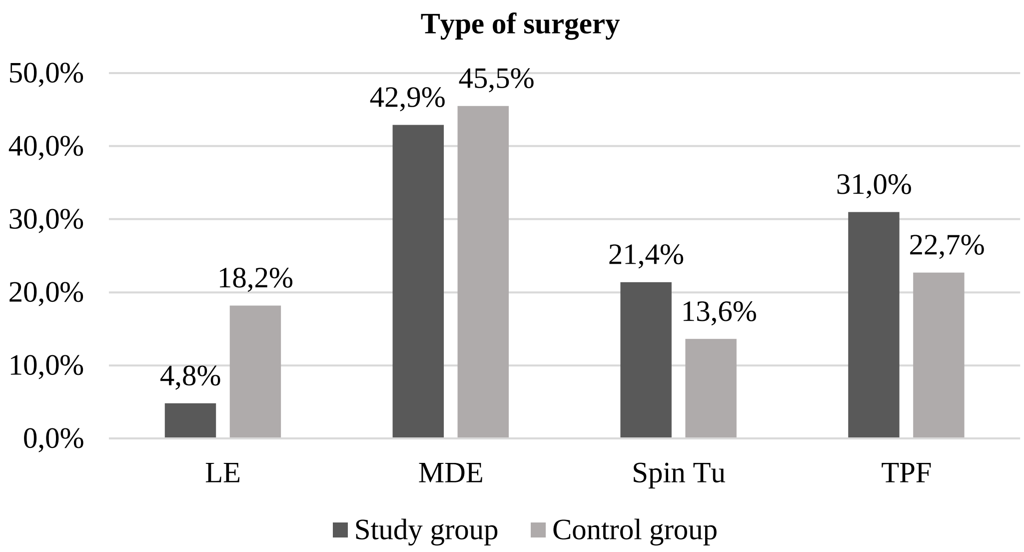

Figure 4.1 **Type of surgery performed in the study and control groups**

LE – laminectomy, MDE – microdiscectomy, Spin Tu – spinal tumour evacuation, TPF – transpedicular fixation.

4.2 Preoperative laboratory tests

Before the operation standard preoperative laboratory tests were made to determine preoperative haemoglobin und haematocrit level. In the study group, the mean Hb was 14 ± 2 mg/dl, while in the control group it was 13 ± 1 mg/dl (p = 0.06). Similarly, no significant difference was found in the mean Hct value between the study and the control group (Table 4.2).

Table 4.2

Mean Hb (mg/dl) and Hct (%) level in study group, control group patients and in all study patients together (mean ± SD)

Indicator	Study group		Control group		p value	Total	
	Mean	SD	Mean	SD		Mean	SD
Hb (mg/dl)	14	2	13	1	0.06	14	2
Hct (%)	42	4	40	4	0.1	41	4

4.3 Duration of the operation

The mean duration of the operation was 116 ± 16 min for all the patients. In the study group, the mean operation time was 128 ± 42 min compared to 104 ± 49 min in the control group. The operation time in the study group was significantly longer than the operation time in the control group with a p value of 0.028.

4.4 Intraoperative blood loss

At the end of surgery, the mean blood loss was 236 ± 103 ml in total in all study patients. The mean intraoperative blood loss did not show any significant differences between the groups and was 245 ± 97 ml in the study group and 220 ± 115 ml in the control group.

4.5 Preoperative and intraoperative non-invasive measurements

4.5.1 Mean systemic non-invasive arterial blood pressure (MAP)

The preoperative MAP of 103 ± 10 mmHg in the study group was significantly higher than that of 93 ± 9 mmHg in the control group ($p = 0.001$). The following intraoperatively measured MAP values, presented after intubation as average, minimum, and maximum values when the patient was lying supine, during the surgery with the patient lying in the prone position, and at the end of the surgery when the patient was again in the supine position, did not show any statistical differences between the groups, as displayed in Table 4.3.

Table 4.3

The average (Avg), minimum (Min) and maximum (Max) mean systemic arterial pressure in millimetre of mercury (mmHg) in the study group, control group patients and in total (mean ± SD)*

Indicator	Study group		Control group		p value	Total	
	Mean	SD	Mean	SD		Mean	SD
Avg MAP PreOp (mmHg)	103	10	93	9	**0.001**	100	11
Avg MAP Sup (mmHg)	88	15	85	16	0.287	87	16
Min MAP Sup (mmHg)	77	19	78	17	0.477	77	18
Max MAP Sup (mmHg)	101	25	90	18	0.092	97	23
Avg MAP Prone (mmHg)	82	9	80	7	0.466	81	9
Min MAP Prone (mmHg)	65	13	69	8	0.436	66	12
Max MAP Prone (mmHg)	102	17	96	10	0.204	100	15
Avg MAP Sup2 (mmHg)	90	14	87	12	0.440	89	13
Min MAP Sup2 (mmHg)	81	19	82	14	0.851	82	17
Max MAP Sup2 (mmHg)	97	18	92	13	0.286	95	16

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2).

In the study group, the MAP analysis using repeated measures ANOVA with Huynh-Feldt correction shows that there is a significant difference between at least two phases ($p < 0.001$).

The post-hoc analysis shows that the difference is among Prone, Supine, Supine 2 and the Preoperative values; and between Prone and Supine 2 ($p = 0.005$) (Table 4.4).

Table 4.4

The repeated measures ANOVA and post-hoc analysis for MAP in the study group

Operation stage	Operation stage	Mean difference	SE	p value
PreOp	Prone	20.27	1.619	< 0.001
PreOp	Sup	15.216	2.581	< 0.001
PreOp	Sup2	13.324	2.674	< 0.001
Prone	Sup 2	−6.946	2.057	0.005

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2), standard error (SE).

In the control group, the MAP analysis using repeated measures ANOVA with Huynh-Feldt correction shows that there is a significant difference between at least two phases ($p = 0.009$).

The post-hoc analysis shows that the difference is among Prone, Supine and the Preoperative values; and between Prone and Supine 2 ($p = 0.04$) (Table 4.5).

Table 4.5

The repeated measures ANOVA and post-hoc analysis for MAP in the control group

Operation stage	Operation stage	Mean difference	SE	p value
PreOp	Prone	13.65	2.269	< 0.001
PreOp	Sup	9	3.039	0.04
Prone	Sup 2	−7.25	2.489	0.04

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2), standard error (SE).

4.5.2 Cerebral oximetry measurements

Regional cerebral oximetry (rScO2) was determined pre- and intraoperatively in all patients of the study. Distribution of data between the study group and the control group and the levels of statistical significance are shown in Table 4.6. The rScO2 values are also presented separately for values measured above the right (Dx) and the left (Sin) cerebral hemisphere, respectively.

Table 4.6

Preoperative (Preop) and average (Avg), minimum (Min), maximum (Max) rScO_2 values in percentage above right (Dx) and left cerebral hemisphere (Sin) in the study group, the control group and in the total patient population (mean ± SD) *

Indicator	Study group		Control group		p value	Total	
	Mean	SD	Mean	SD		Mean	SD
Preop rScO2 Dx (%)	71	9	75	9	**0.047**	73	9
Preop rScO2 Sin (%)	72	10	76	9	0.141	73	10
Avg Sup rScO2 Dx (%)	78	11	80	12	0.412	79	11
Min Sup rScO2 Dx (%)	77	11	78	12	0.578	77	11
Max Sup rScO2 Dx (%)	80	11	82	12	0.571	81	11
Avg Sup rScO2 Sin (%)	79	11	79	11	0.806	79	11
Min Sup rScO2 Sin (%)	76	11	77	10	0.702	76	11
Max Sup rScO2 Sin (%)	81	11	81	12	0.898	81	11
Avg Prone rScO2 Dx (%)	77	8	82	9	**0.010**	79	8
Min Prone rScO2 Dx (%)	71	9	78	10	**0.004**	74	10
Max Prone rScO2 Dx (%)	83	7	86	8	0.143	84	8
Avg Prone rScO2 Sin (%)	77	8	82	7	**0.017**	79	8
Min Prone rScO2 Sin (%)	73	9	79	8	**0.012**	75	9
Max Prone rScO2 Sin (%)	82	8	86	7	0.105	84	8
Avg Sup2 rScO2 Dx (%)	77	9	81	10	0.051	78	10
Min Sup2 rScO2 Dx (%)	75	10	80	10	0.051	77	10
Max Sup2 rScO2 Dx (%)	78	9	83	10	0.067	80	9
Avg Sup2 rScO2 Sin (%)	77	10	81	9	0.054	78	10
Min Sup2 rScO2 Sin (%)	75	11	80	9	0.078	76	11
Max Sup2 rScO2 Sin (%)	78	9	83	10	0.058	80	9

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned supine (Sup2) again.

We found a significantly lower preoperative mean rScO2 Dx in the study group as compared to the control group. We also observed that the average and minimal rScO2 values above the right and the left cerebral hemisphere with the patient lying in the prone position were statistically higher in the control group (Table 4.6).

Study group

Regional cerebral oxygenation above the right cerebral hemisphere (rScO2 Dx) analysis using repeated measures ANOVA with Huynh-Feldt correction shows that there is a significant difference between at least two phases ($p < 0.001$).

The post-hoc analysis shows that the difference is among Prone, Supine, Supine 2 and the Preoperative values (Table 4.7).

Table 4.7

The repeated measures ANOVA and post-hoc analysis for rScO2 Dx in the study group

Operation stage	Operation stage	Mean difference	SE	p value
PreOp	Prone	−5.919	1.254	< 0.001
PreOp	Sup	−7.865	1.235	< 0.001
PreOp	Sup2	−5.459	1.167	< 0.001

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2), standard error (SE).

Regional cerebral oxygenation above the left cerebral hemisphere (rScO2 Sin) analysis using repeated measures ANOVA with Huynh-Feldt correction showed that there was a significant difference between at least two phases ($p < 0.001$).

The post-hoc analysis showed that the difference was among Prone, Supine, Supine 2 and the Preoperative values (Table 4.8).

Table 4.8

The repeated measures ANOVA and post-hoc analysis for rScO2 Sin in the study group

Operation stage	Operation stage	Mean difference	SE	p value
PreOp	Prone	−6.056	1.186	< 0.001
PreOp	Sup	−7.611	1.172	< 0.001
PreOp	Sup2	−4.694	1.162	0.001

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2), standard error (SE).

Control group

Regional cerebral oxygenation above the right and left cerebral hemispheres (rScO2 Dx and rScO2 Sin) analysis using repeated measures ANOVA with Huynh-Feldt correction showed that there was a significant difference between at least two phases (both $p < 0.001$).

The post-hoc analysis showed that the difference was among Prone, Supine, Supine 2, and the Preoperative values (Tables 4.9 and 4.10).

Table 4.9

The repeated measures ANOVA and post-hoc analysis for rScO2 Dx in the control group

Operation stage	Operation stage	Mean difference	SE	p value
PreOp	Prone	−6.706	1.439	0.002
PreOp	Sup	−6.353	1.447	0.002
PreOp	Sup2	−6.059	1.598	0.006

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2), standard error (SE).

Table 4.10

The repeated measures ANOVA and post-hoc analysis for rScO2 Sin in the control group

Operation stage	Operation stage	Mean difference	SE	p value
PreOp	Prone	−6.824	1.493	0.002
PreOp	Sup	−5.412	1.401	0.007
PreOp	Sup2	−5.588	1.683	0.017

* Preoperative (PreOp), after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2), standard error (SE).

4.5.3 Peripheral oxygen saturation (SpO2)

Table 4.11 shows the peripheral oxygen saturation measured by pulse oximetry (SpO2) at the same time-points as the variables presented above, i.e. sampled preoperatively in the operating room, with the patients breathing room air before induction of anaesthesia and lying supine, and in the prone position, and at the end of the surgery when the patients were turned back into the supine position.

Table 4.11

Average (Avg), minimum (Min), maximum (Max) SpO2 values presented as percentages in the study group, the control group and in total patient population, respectively (mean ± SD)*

Indicator	Study group		Control group		p value	Total	
	Mean	SD	Mean	SD		Mean	SD
Avg PreOp SpO2 (%)	99.07	1.47	97.73	2.41	**0.026**	98.61	1.94
Avg SpO2 Sup (%)	99.77	0.58	99.15	1.42	0.059	99.56	0.99
Min SpO2 Sup (%)	99.49	1.23	99.10	1.45	0.183	99.36	1.31
Max SpO2 Sup (%)	99.92	0.27	99.25	1.41	**0.017**	99.69	0.90
Avg SpO2 Prone (%)	99.93	0.46	99.82	0.50	0.089	99.89	0.48
Min SpO2 Prone (%)	99.76	1.25	99.59	0.96	0.078	99.70	1.15
Max SpO2 Prone (%)	100.00	0	99.91	0.29	**0.049**	99.97	0.18
Avg SpO2 Sup 2 (%)	99.88	0.44	99.20	1.41	**0.008**	99.65	0.95
Min SpO2 Sup 2 (%)	99.69	1.14	99.05	1.65	**0.016**	99.47	1.36
Max SpO2 Sup 2 (%)	100	0	99.41	1.33	**0.001**	99.80	0.82

* preoperatively (Preop), after the intubation with the patients lying supine (Sup), in the prone position (Prone), at the end of the surgery when the patients were turned supine again (Sup2).

4.5.4 End-tidal expired carbon dioxide (EtCO2)

End-tidal expired carbon dioxide measurements after intubation in the supine position, in the prone position and at the end of the surgery in supine position before extubation are shown in Table 4.12.

Table 4.12

Average (Avg), minimum (Min) and maximum (Max) EtCO2 values in millimetre of mercury in the study group, in the control group and in the patients in total (mean ± SD)*

Indicator	Study group		Control group		p value	Total	
	Mean	SD	Mean	SD		Mean	SD
Avg EtCO2 Sup (mmHg)	34	4	35	2	0.657	34	4
Min EtCO2 Sup (mmHg)	33	4	35	2	0.467	34	4
Max EtCO2 Sup (mmHg)	35	4	35	3	0.830	35	4
Avg EtCO2 Prone (mmHg)	35	2	34	2	0.236	35	2
Min EtCO2 Prone (mmHg)	33	3	33	2	0.744	33	3
Max EtCO2 Prone (mmHg)	37	2	36	2	**0.027**	37	2
Avg EtCO2 Sup 2 (mmHg)	35	3	35	3	0.600	35	3
Min EtCO2 Sup 2 (mmHg)	35	3	35	3	0.682	35	3
Max EtCO2 Sup 2 (mmHg)	35	3	35	3	0.564	35	3

* After the intubation with patients lying supine (Sup) and in the prone position (Prone), at the end of the surgery when the patients were turned supine (Sup2) again.

4.6 Patient demographic parameters and intraoperative measurements based on the type of surgery performed

Statistically significant differences among patients based on the type of surgery (LE, MDE, Spinal Tu evacuation, TPF) were observed in the following parameters and measurements:

- age,
- intraoperative blood loss,
- duration of the operation,
- minimal value of the rScO2 above the right cerebral hemisphere in the supine position, and average rScO2 value above the left cerebral hemisphere in the supine position after the intubation.

Patients in the LE group were the oldest (73 ± 7 years), and those in the MDE group were the youngest (48 ± 13 years) ($p = 0.001$).

Intraoperative blood loss was statistically the highest during TPF operations, and it was 311 ± 98 ml with the p value < 0.000.

In terms of operation time, the longest operation time was observed in the Spinal Tumour evacuation group, which was 163 ± 54 min compared to LE – 103 ± 39 min, MDE – 100 ± 31 min, and TPF – 126 ± 42 min ($p = 0.004$).

When analysing patient rScO2 measurements based on the type of surgery, the only statistically significant differences observed were as follows – the minimal value of rScO2 above the right cerebral hemisphere with the patient lying supine at the start of surgery was the highest in the MDE group (rScO2 82 ± 10 %, $p = 0.043$) and the average rScO2 value over the left cerebral hemisphere with the patient lying supine at the start of surgery was also the highest in the MDE group (rScO2 83 ± 9 %, p = 0.44) (Table 4.13).

Table 4.13

Age, preoperative and intraoperative values measured in the laminectomy (LE), microdiscectomy (MDE), spinal tumour (Spin Tu) and transpedicular fixation (TPF) group (mean ± SD)*

Indicator	LE		MDE		Spin Tu		TPF		p value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	73	7	48	13	58	11	56	16	**0.001**
Intraoperative blood loss (ml)	192	107	184	82	271	81	311	98	**0.000**
Hb (mg/dl)	13	1	14	2	14	1	13	2	0.072
Hct (%)	39	4	42	3	40	3	40	5	0.173
Duration of the operation (min)	103	39	100	31	163	54	126	42	**0.004**
PreOp rScO2 Dx (%)	73	5	75	9	74	10	69	11	0.356
Avg Sup rScO2 Dx (%)	77	7	84	9	76	14	75	11	0.063
Min Sup rScO2 Dx (%)	76	7	82	10	73	14	73	11	**0.043**
Max Sup rScO2 Dx (%)	78	7	86	9	78	14	77	12	**0.050**
PreOp rScO2 Sin (%)	72	9	75	9	75	11	70	10	0.270
Avg Sup rScO2 Sin (%)	72	9	83	9	77	13	76	11	**0.044**
Min Sup rScO2 Sin (%)	71	9	81	10	73	12	74	10	0.080
Max Sup rScO2 Sin (%)	73	8	85	9	79	14	78	12	**0.050**
Avg Prone rScO2 Dx (%)	78	7	81	8	77	11	77	8	0.425
Min Prone rScO2 Dx (%)	73	8	77	9	71	13	71	8	0.268
Max Prone rScO2 Dx (%)	82	7	86	6	83	9	81	8	0.159
Avg Prone rScO2 Sin (%)	75	6	81	7	77	10	78	8	0.287
Min Prone rScO2 Sin (%)	71	9	78	8	74	13	73	9	0.246
Max Prone rScO2 Sin (%)	79	5	86	7	83	9	83	9	0.244
Avg Sup2 rScO2 Dx (%)	78	7	81	7	76	13	75	11	0.192
Min Sup2 rScO2 Dx (%)	77	6	80	8	74	14	74	11	0.355
Max Sup2 rScO2 Dx (%)	78	7	84	7	78	12	76	10	0.080
Avg Sup2 rScO2 Sin (%)	73	7	81	7	77	14	76	11	0.174
Min Sup2 rScO2 Sin (%)	72	8	79	8	75	15	75	12	0.326
Max Sup2 rScO2 Sin (%)	74	7	83	7	79	12	78	10	0.093
MAP PreOp (mmHg)	94	4	99	12	103	12	100	10	0.434
Avg MAP Sup (mmHg)	80	19	87	16	87	13	88	17	0.861
Min MAP Sup (mmHg)	71	19	81	15	68	25	80	17	0.421
Max MAP Sup (mmHg)	88	22	94	23	105	23	100	23	0.345
Avg MAP Prone (mmHg)	75	9	81	8	85	8	81	9	0.217
Min MAP Prone (mmHg)	62	11	68	8	69	7	63	18	0.461
Max MAP Prone (mmHg)	94	7	98	15	107	16	102	16	0.348
Avg MAP Sup 2 (mmHg)	80	12	90	13	94	10	86	16	0.187
Min MAP Sup 2 (mmHg)	77	13	84	12	82	29	79	16	0.392
Max MAP Sup 2 (mmHg)	83	12	96	16	101	6	95	21	0.061
Avg CO2 Sup (mmHg)	34	4	35	3	33	5	34	3	0.977
Min CO2 Sup (mmHg)	34	5	35	3	32	6	34	3	0.731
Max CO2 Sup (mmHg)	35	3	35	4	34	4	36	4	0.958
Avg EtCO2 Prone (mmHg)	34	2	35	2	35	3	35	2	0.334
Min EtCO2 Prone (mmHg)	32	2	34	2	32	4	33	3	0.482
Max EtCO2 Prone (mmHg)	35	3	37	2	37	2	37	2	0.178

Table 4.13 continued

Indicator	LE		MDE		Spin Tu		TPF		p value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
SpO2 PreOp (%)	99	2	99	2	99	2	99	2	0.817
Avg SpO2 Sup (%)	100	1	100	1	99	1	100	1	0.873
Min SpO2 Sup (%)	100	1	99	1	99	2	99	1	0.909
Max SpO2 Sup (%)	100	1	100	1	100	0	100	1	0.960
Avg SpO2 Prone (%)	100	0	100	0	100	1	100	0	0.903
Min SpO2 Prone (%)	100	0	100	1	99	2	100	0	0.782
Max SpO2 Prone (%)	100	0	100	0	100	0	100	0	0.817
Avg SpO2 Sup2 (%)	98	2	100	1	100	0	100	1	0.403
Min SpO2 Sup2 (%)	98	2	99	1	100	1	100	1	0.486
Max SpO2 Sup2 (%)	98	2	100	0	100	0	100	0	0.070

* Age (years), intraoperative blood loss (ml), Hb (mg/dl), Hct (%), duration of the operation (min), preoperative values and values after the intubation with patient lying supine (Sup), in the prone position (Prone), at the end of the surgery when patient was turned again supine (Sup2) of the rScO2 in percentage above right (Dx) and left (Sin) cerebral hemisphere, MAP, EtCO2, SpO2; Avg – average, Min – minimum, Max – maximum.

4.7 MOCA Test

When analysing our MOCA cognitive test results, we found statistically significant differences in MOCA preoperative evaluation points between the study and control groups: MOCA preoperative points in the study group were 25 ± 2 and 26 ± 2 in the control group (p = 0.034) (Table 4.14).

Table 4.14

Montreal Cognitive Assessment Score in the study group, control group patients and in total (mean ± SD)*

Indicator	Study group		Control group		p value	Total	
	Mean	SD	Mean	SD		Mean	SD
MOCA PreOp	25	2	26	2	**0.034**	26	2
MOCA PostOp	26	2	26	2	0.919	26	2

* Preoperative (PreOp) and postoperative (PostOp) points.

No relevant differences in MOCA points, neither preoperatively, nor postoperatively, were observed when comparing patients based on the type of operation performed (Table 4.15).

Table 4.15

Montreal Cognitive Assessment Score in the laminectomy (LE), microdiscectomy (MDE), spinal tumour (Spin Tu) and transpedicular fixation (TPF) group (mean ± SD)*

Indicator	LE		MDE		Spin Tu		TPF		p value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
MOCA PreOp	25	1	26	3	26	2	26	2	0.766
MOCA PostOp	25	1	26	2	25	2	26	2	0.124

* Preoperative (PreOp) and postoperative (PostOp) points.

4.8 Intraoperative cerebral oxygen desaturation

In our study, intraoperative cerebral desaturation occurred in three patients, two in the study group and one in the control group. Desaturation time for all the patients were between 5 to 8 minutes.

Study group

In the study group, cerebral oxygen saturation in two patients dropped by 20 % from their individual baseline values, and a drop under the absolute value of rScO2 of 50 % was registered. The NIRS-based interventional algorithm was used.

Patient 1 was a 54 years old woman, undergoing spinal tumour evacuation. The preoperatively determined baseline values were rScO2 of 68 % above the right cerebral hemisphere and 69 % above the left one. An intraoperative rScO2 drop for 29 % from baseline values and under the absolute value of 50 % (bilaterally) was observed with the minimal rScO2 value of 48 % while lying in the prone position. According to the NIRS-based interventional algorithm, neutral head positioning was provided as a first step; however, no changes in rScO2 were observed. As a next step, the patient received a dose of ephedrine 10 mg intravenously to raise the mean arterial blood pressure. During the cerebral desaturation period, the MAP was over 95 mmHg, which was 24 % lower than the preoperatively measured baseline value. After the second step, the rScO2 values increased above 50 %, then above the baseline, and no further intervention was necessary.

The patient's operation time was higher than the average in the study group and was 270 min compared to 128 ± 42 min in the other study group patients ($p = 0.0001$). The operation time was also longer than the mean operation time measured in the spinal tumour patient group, which was 153.2 ± 44.3 min ($p < 0.001$).

Patient's preoperative systemic MAP – 124 mmHg – was higher than that measured in the other study group patients (MAP 103 ± 10 mmHg, $p = 0.03$). It was also higher than the preoperative MAP in the other spinal tumour patients with the mean preoperative systemic MAP of 100.9 ± 9.8 mmHg ($p < 0.001$).

The *second study group patient* was a man, 57 years old, undergoing microdiscectomy (at the single level of L4–5) operation. The baseline rScO2 values were as follows: rScO2 Dx 85 % and rScO2 Sin 87 %. During the operation with the patient lying in the prone position, rScO2 values dropped to minimal rScO2 value of 63 % (bilaterally) (by 27 % from patient's individual baseline values measured preoperatively before intubation). In addition, the second patient did not show any changes in rScO2 values after correct head positioning was achieved. At the time of cerebral desaturation, the MAP decreased to 62 mmHg (baseline MAP value – 104 mmHg), as the next step intravenous ephedrine 10 mg was given. A further decrease in MAP was observed, with the lowest MAP of 56 mmHg. Another 10 mg of ephedrine was administered. Together with MAP, rScO2 values increased above the threshold values, and no further intervention was necessary.

The cognitive function based on the MOCA test points in both study group patients, where NIRS-based interventional algorithm was used, stayed consistent – preoperatively and postoperatively. In *patient 1*, MOCA score preoperatively was 26 points and also postoperatively – 26 points. In *patient 2*, MOCA score preoperatively and postoperatively was 23 points.

Control group

In the control group, cerebral oxygen desaturation was found in one patient. The patient was a 24 years old woman, who underwent a two level transpedicular lumbar spinal fixation after trauma. The preoperative baseline rScO2 values were rScO2 Sin 92 % and rScO2 Dx 87 %. We observed an intraoperative drop of rScO2 by 21 % from baseline value (to rScO2 of 73 % Dx with patient lying in the prone position).

By analysing and comparing this patient's demographic data and intraoperative measurements, we did not observe any statistically significant differences from the other patients in the control group. Analysing the patient's measurements retrospectively, we saw a MAP decrease at the time when rScO2 decrease was also observed, from baseline 91 mmHg to MAP 71 mmHg (MAP value decreased by 22 %).

MOCA score in the patient described above decreased by 4 points postoperatively – from MOCA 29 points preoperatively to MOCA 25 points postoperatively, which is defined as postoperative cognitive dysfunction.

4.9 Postoperative cognitive decline and MOCA score

Out of a total of 64 patients included in the study, postoperative cognitive decline was observed in 19 patients (29.6 %), respectively, 9 out of 42 patients (21.4 %) in the study group and 10 out of 22 patients (45.5 %) in the control group.

The following postoperative MOCA score reductions were observed:

- 1 point was seen in 8 patients (5 in the study group and 3 in the control group);
- for 2 points – in 7 patients (3 – study group, 4 – control group);
- for 3 points – in 1 patient (1 – control group);
- for 4 points – in 3 patients (1 – study group, 2 – control group).

The statistically significant difference in comparison with other patients who did not have postoperative MOCA decrease was observed in the following measurements: average rScO2 value in the prone position over the left cerebral hemisphere and maximum EtCO2 value in the supine position (Table 4.16).

Table 4.16

Average (Avg) rScO2 in percentage in prone position above left cerebral hemisphere (Sin) and maximum (Max) EtCO2 in millimetre of mercury after the intubation in patient lying supine in the patients where postoperative MOCA score decrease was observed and in the other patients in the study

Indicator	Patients with postoperative MOCA score decrease		Other patients in the study		p value
	Mean	SD	Mean	SD	
Avg prone rScO2 Sin (%)	82	7	78	8	0.048
Max EtCO2 Sup (mmHg)	37	3	34	4	0.041

We also analysed separately those patients, who had a postoperative decrease in MOCA score of 4 points. No statistically significant differences were observed when compared to all other patients in the study.

Table 4.17 shows the percentage of patients with a postoperative MOCA score decrease in each MOCA domain.

Table 4.17

The number of patients in percentage (%) that showed postoperative MOCA point decrease analysed within separate MOCA domains in study group, control group and in total

MOCA Domain	Study group N (%)	Control group N (%)	p value	Total N (%)
Visuospatial / Executive	13.0	16.7	0.771	14.3
Naming	0	0	–	0
Memory	No points			
Attention	21.7	25.0	0.827	22.9

Table 4.17 continued

MOCA Domain	Study group N (%)	Control group N (%)	p value	Total N (%)
Language	8.7	41.7	**0.021**	20.0
Abstraction	0	8.3	0.160	2.9
Delayed recall	26.1	33.3	0.652	28.6
Orientation	13.0	0	0.191	8.6

4.10 Spearman's rho correlation analysis

Using Spearman's rho rank correlation to analyse all patients included in the study, we found a negative correlation between intraoperative rScO2 values and patient age, intraoperative blood loss and preoperative MAP value, and a positive correlation with preoperative MOCA values (Table 4.18, Figures 4.2–4.5).

Table 4.18

Spearman's rho correlation coefficients ρ between age, intraoperative blood loss, MAP Preoperative, MOCA preoperative score and intraoperative rScO2 values in all study patients

Indicator	Spearman's rho correlation coefficient and p value	Intraoperative rScO2 values
Age	Spearman's rho correlation coefficient (ρ)	−0.352
	p value	0.004
Intraoperative blood loss	Spearman's rho correlation coefficient (ρ)	−0.248
	p value	0.049
MAP Preoperative	Spearman's rho correlation coefficient (ρ)	−0.306
	p value	0.014
MOCA Preoperative	Spearman's rho correlation coefficient (ρ)	0.326
	p value	0.009

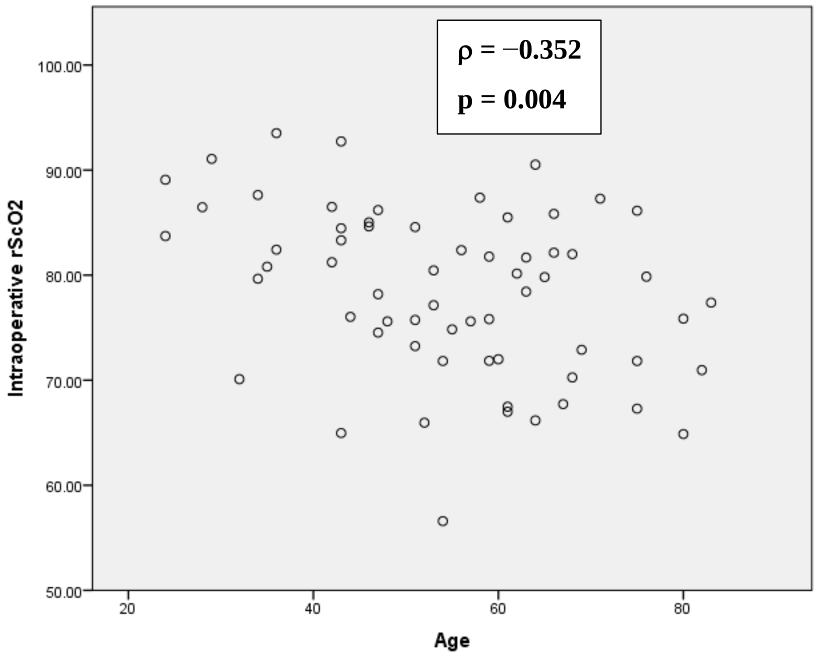

Figure 4.2 **Spearman's rho correlation between age and intraoperative rScO2 values in all study patients**

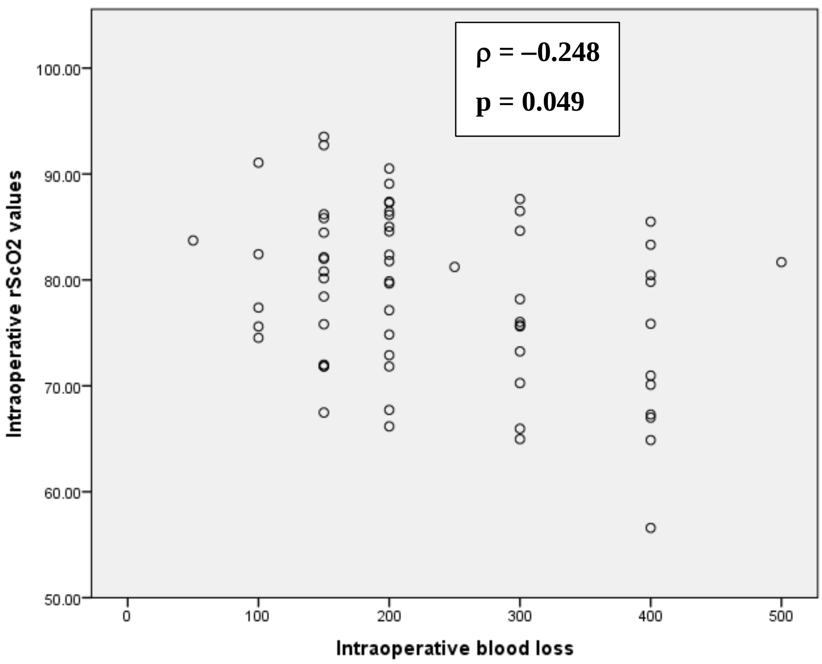

Figure 4.3 **Spearman's rho correlation between intraoperative blood loss and intraoperative rScO2 values in all study patients**

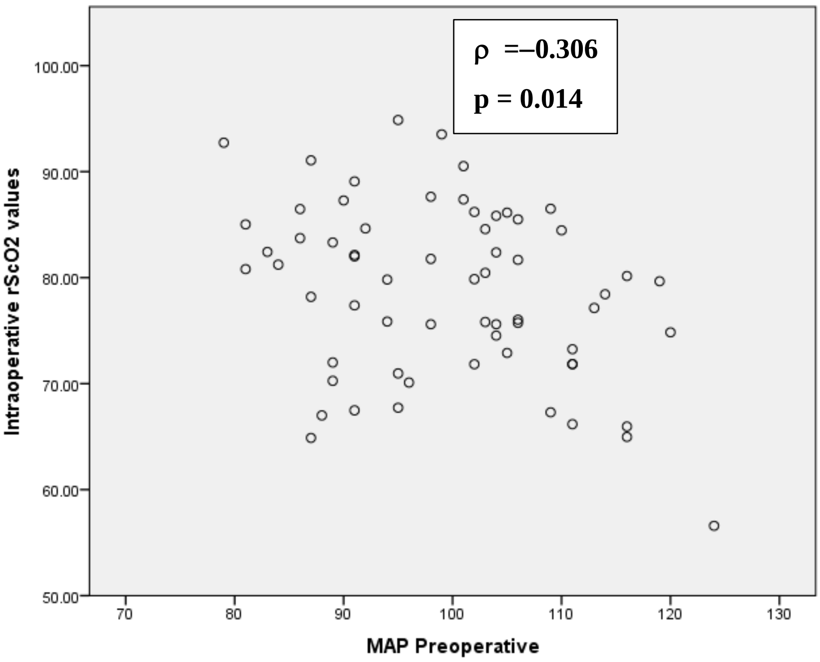

Figure 4.4 **Spearman's rho correlation between MAP Preoperative values and intraoperative rScO2 values in all study patients**

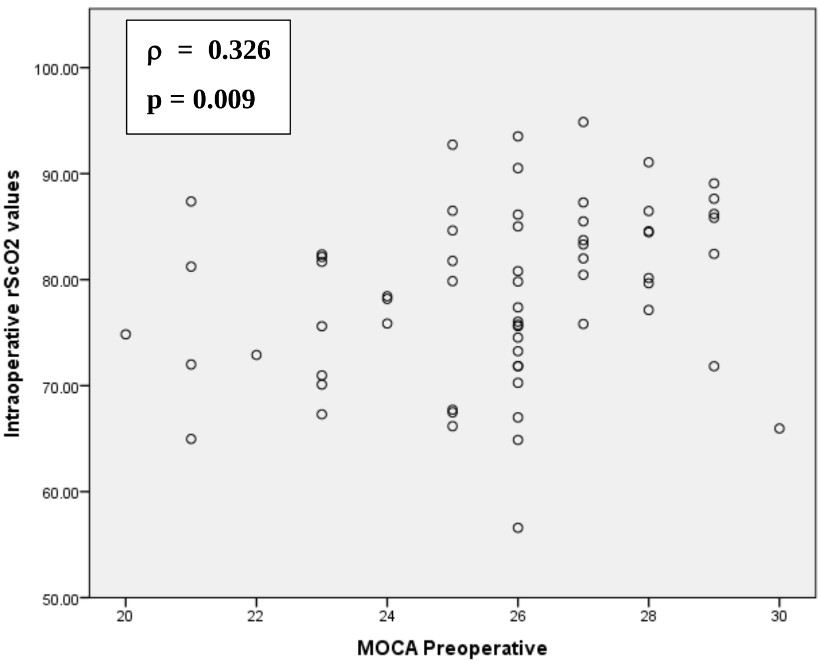

Figure 4.5 **Spearman's rho correlation between MOCA preoperative score and intraoperative rScO2 values in all study patients**

Linear regression showed that factors explaining 28.5 % of the variance in the intraoperative rScO2 values were age (B = −0.134, 95 % CI [−0.266, −0.001], p = 0.048) and preoperative systemic MAP (B = −0.204, 95 % CI [−0.384, −0.024], p = 0.027), controlling for other factors (intraoperative blood loss, Hb, Hct, duration of surgery, intraoperative systemic MAP, EtCO2, SpO2, MOCA score).

We also investigated whether intraoperative rScO2 values correlated with other measured variables, separately for the study group and the control group. For the study group, we found a negative correlation between intraoperative rScO2 measurements and preoperative MAP ($\rho = -0.354$, $p = 0.021$) (Figure 4.6). In the control group, we found a negative correlation between intraoperative rScO2 and patient age ($\rho = -0.655$, $p = 0.001$) (Figure 4.7).

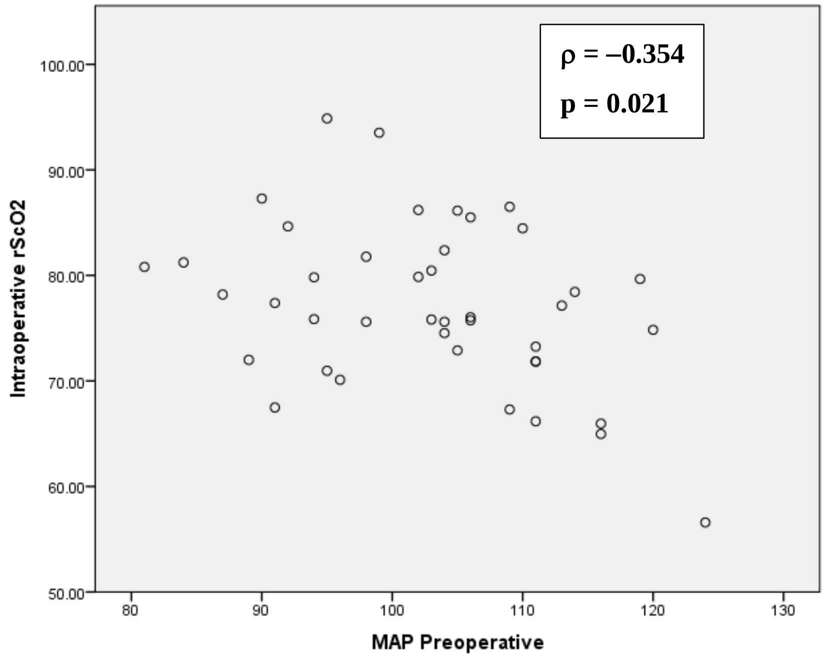

Figure 4.6 **Spearman's rho correlation between MAP preoperative values and intraoperative rScO2 values in study group patients**

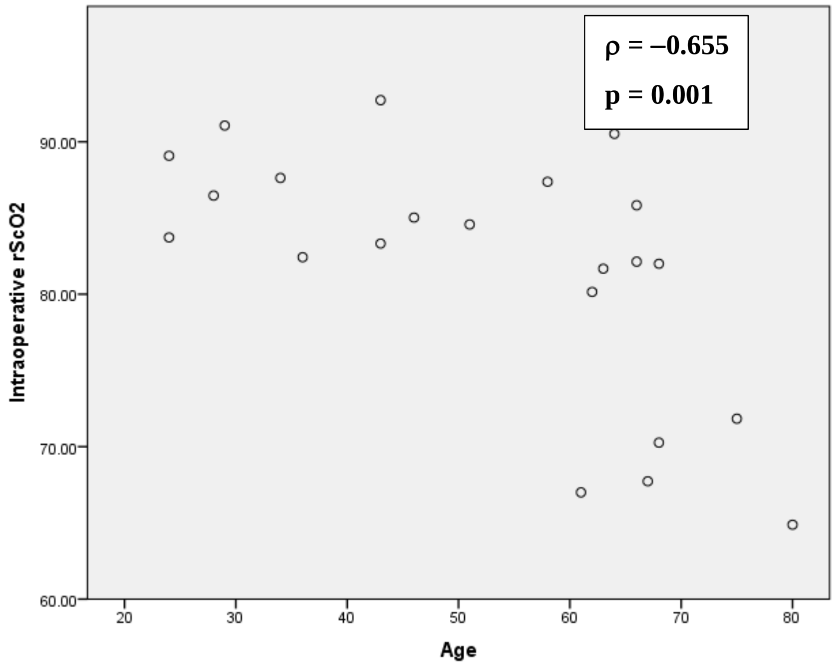

Figure 4.7 **Spearman's rho correlation between age and intraoperative rScO2 values in control group patients**

Postoperative MOCA score did not correlate with intraoperative rScO2 values. However, patients who had a decrease in rScO2 of > 10 % at any stage of surgery had a lower median postoperative MOCA score. Patients who had a decrease in rScO2 > 10 % had a median postoperative MOCA score of 26.0 (IQR 1.5). Patients who had no decrease or a decrease of < 10 % had a median postoperative MOCA score of 25.5 (IQR 3). This difference was statistically significant ($p = 0.02$) (Figure 4.8).

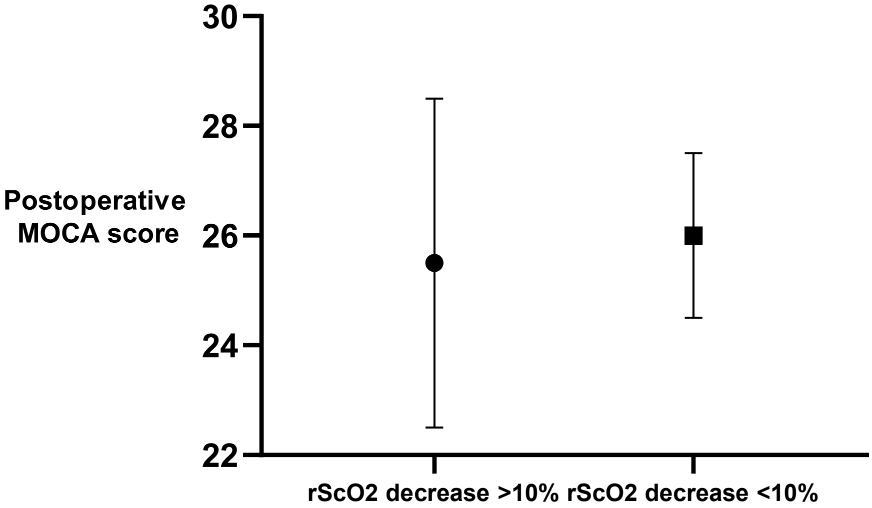

Figure 4.8 **Median postoperative MOCA score in patients with intraoperative rScO2 decrease > 10 % and in patients with no decrease or rScO2 decrease < 10 %**

5 Discussion

Spinal surgery is a medical field covering a wide range of different operations performed on the spinal column and surrounding tissues. The type of operation, the surgical technique, the operation time, the intraoperative blood loss, the professional skills of the medical staff and other relevant factors determine the intraoperative management and the postoperative outcome. Spinal surgery is a complex area of medicine that is challenging for both clinicians and researchers. We aimed to find out whether cerebral desaturation can occur during spinal surgery in the prone position and the potential usefulness of a near-infrared spectroscopy-based clinical algorithm. We also speculated whether cerebral desaturation was associated with a postoperative cognitive decline. In particular, we sought to identify which factors influence cerebral oxygenation in patients undergoing spinal surgery, such as patient age, preoperative haemoglobin and haematocrit levels, end-tidal carbon dioxide concentration, peripheral arterial oxygen saturation, intraoperative blood loss and the duration of the surgery. Our working hypothesis was that providing adequate cerebral oxygen saturation during spinal neurosurgery in the prone position is essential to prevent POCD.

Several recent studies have elucidated the monitoring of cerebral oxygen saturation by using NIRS devices – cerebral oximeters. As non-invasive devices, they have gained popularity in many different fields of surgery as well as in various conditions requiring treatment in the ICU, including both adult and paediatric patient populations. A limited number of studies have focused specifically on monitoring cerebral oxygenation using NIRS devices intraoperatively during spinal surgery and only a few studies have evaluated cognitive function as part of the postoperative outcome (Trafidlo, 2015).

5.1 Age

Age plays a significant role in terms of intraoperative cerebral desaturation. Elderly patients suffer from intraoperative cerebral desaturation, often due to reduced physiological reserves (Casati, 2005). Recent studies have shown that higher age is associated with a reduction of intraoperative rScO2 (Tobias, 2008; Burkhart, 2011). Almost 20–40 % of elderly patients experience cerebral desaturation during non-cardiac surgery (Casati, 2005; Papadopoulos, 2012; Deiner, 2014) and elderly people make up more than 30 % of all patients requiring anaesthesia for surgeries (Casati, 2005). The age at which patients are included in the elderly patient population varies from study to study. Sixty-five years and older is the most commonly used definition. In our study, we included adult patients aged 18 years and above, with a mean age of 55 ± 15 years (mean ± SD). Patients aged 61 years and older accounted for

64 % of the study population. In our study, intraoperative cerebral desaturation of more than 20 % from baseline or an absolute drop in rScO2 to below 50 % was observed in three patients. Two of them were 54 and 57 years old and the third patient was only 24 years old, showing that even young patients can experience a significant drop in rScO2 during surgery.

As mentioned above (Casati, 2005; Deiner, 2014; Papadopoulos, 2012), patients at the age of 65 years and older show lower intraoperative rScO2 values. In contrast, we observed significantly higher average and minimum intraoperative rScO2 values over both cerebral hemispheres in the prone position in the control group, in which the majority of the patients were aged 61–70 years. At the same time, most of the patients in the study group (36 %) were in the age group of 51–60 years, but presented with lower rScO2 values in the prone position.

Generally, our study predicts a negative correlation between patient age and intraoperative rScO2 values ($\rho = -0.352$, $p = 0.004$), which is consistent with the studies mentioned above (Casati, 2005; Deiner, 2014; Papadopoulos, 2012). This raises the question of what is the cut-off age, at which increased attention should be paid to the possibility of intraoperative cerebral desaturation. In addition, the fact that three patients in our study with significant intraoperative cerebral desaturation were notably younger than 65 years, made us analyse and look for other factors that could potentially cause cerebral desaturation.

5.2 Mean arterial blood pressure (MAP), the choice of vasoconstrictors

Mean arterial blood pressure is a crucial factor in the assurance of adequate cerebral perfusion pressure, including appropriate cerebral oxygen delivery. As stated in the intraoperative NIRS algorithm (Denault, 2007; Trafidlo, 2015), the evaluation of MAP is the second step after verifying head position if cerebral desaturation occurs. Based on the cerebral autoregulation, proper brain tissue perfusion remains constant in a range of 50–150 mmHg (van den Brule, 2018). The recommended MAP, which ensures the best organ perfusion, including the brain, is 65 mmHg (Van Diepen, 2017). Intraoperative hypotension is defined as an absolute MAP < 65 mmHg or relative MAP decrease under 20 % or more from baseline (Meng, 2018). In our study MAP at the time of cerebral desaturation in one of our study group patients was lower than 65 mmHg (56–62 mmHg). In the other study group patient, MAP was 24 % lower than baseline at the time of cerebral desaturation. Both patients received ephedrine boluses and rScO2 raised above the threshold, confirming the importance of arterial blood pressure in maintaining adequate cerebral saturation.

The choice of vasoconstrictors that increase MAP and preserve rScO2 has been discussed in several studies. Previous studies have shown that ephedrine, which was used in our patients, increases MAP but does not decrease (or even increase) rScO2, as compared, for example, with phenylephrine where MAP increases at the same level, but rScO2 decreases significantly (Vanpeteghem, 2020; Koch, 2020; Nissen, 2010).

On the other hand, other patients with a MAP < 65 mmHg or MAP values lower than 20 % below baseline did not show cerebral desaturation. The question of interest is – whether a MAP of 65 mmHg can be accepted as a standard value regarding the appropriate cerebral perfusion and therefore oxygen delivery, or whether an individual MAP- threshold should be aimed at? Moreover, which MAP value should be considered as baseline, the one measured at the time of preoperative patient visit, or the one measured in the operating room before induction of anaesthesia? In the preoperative check, MAP is not always measured. On the other hand, blood pressure measured immediately before the operation is strongly influenced by preoperative stress and intake of antihypertensive drugs and other medicines. Zhang and colleagues (Zhang, 2021) showed that cerebral oximetry itself can be used to identify optimal MAP intraoperative range to ensure adequate cerebral autoregulation. Their study showed that optimal MAP targets for elderly patients (≥ 65 years) were between 67.8 ± 8.9 and 116.4 ± 10.5 mmHg, and for middle aged patients (45–64 years) between 71.2 ± 12.5 and 111.3 ± 8.9 mmHg (Zhang, 2021). In our patient population mean intraoperative arterial blood pressure varied from 66 ± 12 to 100 ± 15 mmHg, which was consistent with the findings of Zhang et al., although the values in our study were derived from all age groups.

The importance of preoperative blood pressure management is already well known, as patients with hypertension have increased risk of postoperative complications, such as cardiovascular events, neurologic deficits or even death (Varon, 2008). We detected significantly higher preoperative MAP in our study group patients compared to control group patients. At the same time in the study group patients, we observed lower preoperative rScO2 values and lower rScO2 values in the prone position. A negative correlation was found between preoperative MAP and intraoperative rScO2 values. The same finding was observed in our one study group patient where significant cerebral desaturation occurred. In this one study group patient, preoperative MAP was remarkably higher than the group average and intraoperative cerebral desaturation was observed. Studies evaluating preoperative variables affecting intraoperative rScO2 measurements do not mention MAP as one of them (Thiele, 2020). To our knowledge, no studies have specifically investigated preoperative blood pressure in relation to intraoperative cerebral oxygenation.

Our study showed that blood pressure plays an important role in maintaining adequate cerebral saturation levels intraoperatively. In their study, Jo et al. suggest that the brain could be used as an index organ for overall haemodynamic stability (Jo, 2020). And as in our study, Jo et al. also demonstrate that changes in MAP correlate with rScO2, although the correlation is weak (Jo, 2020). The exact role of MAP in maintaining adequate cerebral oxygenation should be debated. Are there absolute MAP levels that require intervention and how should they be managed?

5.3 Hb, Hct, intraoperative blood loss

Blood is the main carrier of haemoglobin, and Hb is the main molecule involved in O2 transport. It is therefore useful to discuss Hb, Hct and intraoperative blood loss in relation to cerebral oxygen saturation.

Haemoglobin has been shown to be significantly associated with cerebral rScO2 values, and a linear relationship can be seen with lower Hb levels corresponding to lower rScO2 values (Ookawara, 2020). According to the World Health Organization (WHO), anaemia is defined as haemoglobin < 13 mg/dl for men and < 12 mg/dl for non-pregnant women (WHO, 2011). Poor postoperative outcomes have been described in patients with different preoperative haemoglobin levels – 10 mg/dl, 11 mg/dl and 12 mg/dl, although it is still debatable whether they are caused by low haemoglobin levels or other factors (Van Straten, 2009). In our study, we did not find any correlation between preoperative haemoglobin or haematocrit levels and intraoperative rScO2 values. That can be explained by the fact that the mean preoperative haemoglobin and haematocrit levels in the study and control group were in the normal range and the patients were not anaemic based on the WHO definition. To our knowledge, there are no studies where Hb or Hct levels were analysed in regard to intraoperative rScO2 or postoperative outcomes in spinal surgery patients.

The same linear relationship as for Hb and rScO2 can also be seen for blood loss and rScO2. Torella et al. (Torella, 2004) noticed that cerebral oxygen saturation decreases proportionally to blood loss. This is consistent with our finding of a negative correlation between intraoperative blood loss and cerebral oxygenation. However, Torrella and colleagues observed a remarkably higher median blood loss of 650 ml (400–1800 ml) (Torella, 2004) compared to a mean intraoperative blood loss of 236 ± 103 ml (100–500 ml) in our study material as a whole.

5.4 The length of operation

The length of surgery has been described as a factor in postoperative complications. It has been shown that postoperative complications (surgical site infection, wound dehiscence, bleeding, pneumonia, urinary tract infection, renal failure, sepsis, cardiac complications) double with operative time that exceeds two or more hours (Cheng, 2018). Prolonged surgery time has also been considered as a risk factor for postoperative cognitive decline (Rundshagen, 2014; Borozdina, 2018). When we looked separately at the patients that presented with POCD, we found the same trend as in the above studies. The mean duration of surgery for patients with POCD was 130 ± 44 min, compared to 115 ± 46 min in patients without POCD. However, the findings were not significantly different.

5.5 Cerebral oxygenation during spinal surgery in the prone position

Authors also have evaluated whether changes in cerebral oxygenation can be seen only during spinal surgery in the prone position or in the prone position in general. Deiner et al. showed, as in our current study, that patients experience cerebral desaturation when undergoing surgery in the prone position (Deiner, 2014). Their study compared elderly patients (≥ 68 years) who underwent surgery in the prone position with patients who underwent surgery in the supine position. The researchers observed that cerebral desaturation was related to the prone position, as the patients operated in the prone position were twice as likely to experience a cerebral desaturation than those operated in the supine position (Deiner, 2014). In our patients, we observed higher average and minimal cerebral oxygenation values in the prone position over both cerebral hemispheres in the control group compared to the study group. The majority of patients in the control group (41 %) were aged between 61 and 70 years. At the same time, most of the patients in the study group were younger – between 51 and 60 years old.

A few years ago, Andersen and colleagues (Andersen, 2014) demonstrated the importance of neutral head position for maintaining cerebral oxygenation in the prone position, since rotation of the head to the right or left and/or flexion or extension of the neck can cause a decrease in rScO2. In our study, correction of head position was performed as the first measure against cerebral desaturation, as correct head positioning is also the first step in the NIRS-based clinical algorithm (Denault, 2014; Trafidlo, 2015). In our cases, no improvement in rScO2 values was seen after repeated confirmation of correct, neutral head position.

5.6 Postoperative cognitive decline

In the present study, we aimed at investigating whether intraoperative cerebral desaturation leads to postoperative cognitive disturbances by evaluating preoperative and postoperative patient cognitive status using the MOCA test. We observed a decrease in postoperative MOCA scores in 19 patients that accounted for 29,6 % or almost one third of the total patient population. Moreover, postoperative cognitive decline was observed in almost half of the patients in the control group (45.5 %), where rScO2 was monitored blindly compared to

21.4 % patients in the study group. In the same way, more patients in the control group presented a decrease in the MOCA score of 4, 3 and 2 points, whereas in the study group, the majority of patients showed MOCA score decrease by only 1 or 2 points postoperatively. The largest difference between the groups was observed in the MOCA language domain, where 41.7 % of the patients in the control group showed postoperative decline compared to only 8.7 % of the patients in the study group. This finding is difficult to explain because centres responsible for the language are located in different areas of the brain (Broca's, Wernicke's areas). What we did find in the control group was a negative correlation between intraoperative rScO2 values and patient age, showing that the aging brain is more dependent on adequate oxygen delivery.

Trafidlo et al. (Trafidlo, 2015) also investigated spinal surgery patients operated in the prone position and showed that in the group without NIRS monitoring, more patients presented with postoperative cognitive deficiencies. Many studies have shown that patients after cardiac and non-cardiac surgery suffer from postoperative cognitive decline or dysfunction (van Dijk, 2000; Jensen, 2006; Newman, 2007). To our knowledge, Trafidlo et al. (Trafidlo, 2015) is the only study so far that has monitored cerebral oxygen saturation during spinal surgery and analysed it in relation to postoperative cognitive outcome. There are studies describing POCD as a transient postoperative disturbance (Rundshagen, 2014). Other studies show that POCD can significantly impair postoperative recovery and even increase postoperative mortality (Monk, 2008; Steinmetz, 2009). Unlike delirium, POCD may go unrecognised unless preoperative and postoperative neurophysiological tests are used.

Zorrilla-Vaca et al. (Zorilla-Vaca, 2018) performed a meta-analysis and found that the incidence of POCD is reduced when cerebral oximetry-guided intraoperative management is applied. Based on the findings of the latter investigators, the thresholds for interventions were most commonly either rScO2 < 75 % of baseline, or an absolute value of rScO2 < 55–60 % (Zorilla-Vaca, 2018). We used the NIRS-based intraoperative intervention algorithm of Denault et al. (Denault, 2014), which has been adapted to non-cardiac surgery by Trafidlo et al. (Trafidlo, 2015). Based on these algorithms, the threshold for intervention is a drop in rScO2 of 20 % or more from baseline (unilateral or bilateral) or rScO2 < 50 %. Zorilla-Vaca and colleagues also found and described that neurological deficits are more likely to occur with an rScO2 reduction of more than 30 % (Zorilla-Vaca, 2018). This lead us to the question as to whether a drop in rScO2 of 20 % below baseline may represent a clinically significant desaturation. In addition, it is still not strictly defined whether rScO2 baseline values should be determined preoperatively in the patient breathing room air (Dworschak, 2012) or with supplemental oxygen (Heringlake, 2011). In our study, we set the baseline values according to

Dworschak et al. (Dworschak, 2012) with patients breathing room air. We observed that the two patients in our study group, who experienced a drop in rScO2 of 20 % or more below baseline and a drop in rScO2 below 50 %, which were eliminated, had no postoperative cognitive decline, and vice versa – the patient in our control group, who experienced cerebral desaturation but no interventions were applied, was found to have POCD. Furthermore, patients who had an intraoperative decrease in rScO2 of > 10 % had a lower median postoperative MOCA score. Therefore, our study results were in line with the findings of Green et al., who affirmed that both a 20 % decrease in rScO2 from baseline values is significant and that in clinical practice steps should be taken beforehand to limit a smaller decrease, for example, of 10 % (Green, 2017). Lin et al. also suggest in their study that a decrease in cerebral oxygen saturation of more than 11 % could be used as a potential predictor of postoperative neurocognitive impairment (Lin, 2013). In addition, it has been advised to use cerebral oximetry as a trend monitor, tracking changes in saturation, rather than using absolute rScO2 values (Bickler, 2013).

In our patients, the time spent in cerebral desaturation was from 5 to 8 minutes. Based on brain physiology, hypoxic brain damage can occur as early as 5 min of hypoxia (Bebawy, 2015). Therefore, if cerebral desaturation is detected, intervention must not be delayed. Literature data regarding this issue are very contradictory. While one study shows that POCD develops as early as < 5 min of exposure to cerebral oxygenation values of < 65 % (Tang, 2012), other studies claim that the time of the cerebral desaturation should be 2 hours to result in neurological impairment (Kurth, 2009). It should be noted that the latter study was conducted on piglets.

The brain is the primary endpoint for many anaesthetics, and anaesthesia has therefore been recognised as one of the risk factors for postoperative neurological disorders (Casati, 2005). Nevertheless, the brain is one of the least monitored organs intraoperatively. The aim of the intraoperative monitoring of cerebral oxygenation saturation is to detect harmful physiological events that can lead to brain damage (Mahajan, 2013) and to prevent them. Several studies have shown that patients suffer from postoperative cognitive decline or dysfunction following cardiac and non-cardiac surgery (van Dijk, 2000; Jensen, 2006; Newman, 2007). Some studies describe POCD as transient postoperative disturbance (Rundshagen, 2014), whereas other studies show that POCD can significantly impair postoperative recovery and even increase postoperative mortality (Monk, 2008; Steinmetz, 2009).

Cerebral oximeters are non-invasive devices that provide continuous real-time monitoring of cerebral oxygenation. Intraoperative monitoring of cerebral oxygenation should be applied together with NIRS-based intraoperative intervention algorithm, as simple interventions may provide clear benefits.

5.7 Strengths and limitations

In recent studies, researchers have assessed cerebral oxygenation intraoperatively during non-cardiac surgery (Moerman, 2015; Nielsen, 2014). In some of the latter studies, the cerebral oximeters were applied in patients undergoing surgery in the prone position (Andersen, 2014; Deiner, 2014). In addition, an intraoperative NIRS-based clinical algorithm was used (Denault, 2007; Tosch, 2016). It has been demonstrated that patients, experiencing intraoperative cerebral desaturation, suffer from various postoperative complications (Goldman, 2004; Murkin, 2007) including POCD (Zorilla-Vaca, 2018). However, to our knowledge, only one study has included intraoperative monitoring of cerebral oxygenation and evaluated postoperative cognitive outcome after spinal surgery (Trafidlo, 2015). Thus, Trafidlo et al. evaluated POCD by using different neurocognitive tests, such as N–back Test, Trail Making Test A and B, Stroop Colour-Word Interference Test Part 1 and 2 and others (Trafidlo, 2015). Our aim was to show that there is a simple test, such as MOCA, that can evaluate cognitive function in a short period of time during preoperative and postoperative patient evaluation. The MOCA test is easy to use. It is available in several languages and covers a wide range of cognitive domains, such as short-term memory, visuo-spatial abilities, executive functions, attention, concentration, working memory, language, and orientation to time and place (MoCA Montreal Cognitive Assessment). In our opinion, it is important to use easily applicable tests to monitor cognitive function and detect POCD, which take little time and are understandable to patients (in their native language). Recently, Soehle at el. have also suggested that cognitive evaluation tests should take only a couple of minutes, without requiring excessive staff training in order to be implemented in clinical practice (Soehle, 2022). The discussion could arise regarding the fact that the same MOCA test was used to evaluate patient cognitive status preoperatively and postoperatively and could lead to a learning effect. Unfortunately, there was no other option to avoid this, as there is only one version of MOCA test that is validated in Latvian and Russian.

Another limitation of our study was that patients with postoperative cognitive decline were not inspected repeatedly after the surgery. The cognitive function was evaluated only once after surgery, and no other possible postoperative complications were assessed. In addition, no intraoperative PaO_2 or $PaCO_2$ measurements were taken to minimise invasive manipulations, although they would show changes in oxygen and carbon dioxide concentrations more accurately than SpO2 and EtCO2. In the current study, we also did not analyse patient comorbidities as a factor that could influence intraoperative cerebral saturation or postoperative cognitive decline. Another limitation of the study is the number of patients included in the study due to the limited budget available for the study and the high cost of cerebral oximetry electrodes.

Conclusions

1. Patients undergoing various spinal surgeries in the prone position may experience intraoperative cerebral desaturation and rScO2 values below 20 % of individual baseline values or a drop in rScO2 below the absolute value of 50 % can be seen. Otherwise, intraoperative cerebral desaturation will remain unrecognised unless cerebral oximeters are used and cerebral oxygenation is monitored.
2. In the control group, where rScO2 was monitored blindly and no NIRS algorithm was applied, 45.5 % of patients showed postoperative cognitive decline compared to the study group, where postoperative cognitive decline was observed in 21.4 % of patients. More patients in the control group showed a larger postoperative MOCA score decrease (2, 3 and 4 points) compared to the study group, where most of the patients presented with postoperative MOCA score decrease of 1–2 points.
3. No postoperative cognitive decline was observed in patients in whom intraoperative regional cerebral oxygen saturation was monitored and cerebral desaturation was treated according to the NIRS algorithm. In patient in whom intraoperative regional cerebral oxygenation was monitored blindly, cerebral desaturation was detected, but the NIRS algorithm was not applied, postoperative cognitive decline was noticed.
4. A statistically significant negative correlation was found between intraoperative rScO2 values and age, intraoperative blood loss and preoperative mean arterial blood pressure. In addition, a positive correlation was observed between intraoperative rScO2 and preoperative MOCA score.
5. Postoperative MOCA score was not correlated with intraoperative rScO2 values. However, patients with an intraoperative decrease in rScO2 of > 10 % had a lower median postoperative MOCA score.
6. During spinal neurosurgery in the prone position, cerebral oximetry combined with a NIRS-based clinical algorithm gives valuable information about cerebral oxygenation and prevents postoperative cognitive decline. Ensuring adequate cerebral oxygen saturation is essential for patient safety.

Publications

Articles

1. Murniece, S., Soehle, M., Vanags, I., Mamaja, B. Regional cerebral oxygen saturation monitoring during spinal surgery in order to identify patients at risk. Applied Sciences, 2020; 10(6), 2069; https://doi.org/10.3390/app10062069
2. Murniece, S., Soehle, M., Vanags, I., Mamaja, B. Near-infrared spectroscopy based clinical algorithm applicability during spinal neurosurgery and postoperative cognitive disturbances. Medicina, 2019; 55(5), 179; https://doi.org/10.3390/medicina55050179
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Presentations at international conferences

1. Murniece, S. Cerebral oxygen saturation monitoring and near-infrared spectroscopy based clinical algorithm applicability during spinal neurosurgery. 10^{th} Baltanest. 07.–08.10.2021, Virtual Event. (Oral presentation)
2. Murniece, S., Soehle, M., Vanags, I., Mamaja, B. Regional oxygen saturation monitoring during spinal surgery in order to identify patients at risk for cerebral desaturation. Euroanaesthesia 2020. 28.–30.11.2020, Virtual Event (Poster presentation)
3. Murniece, S., Vanags, I., Soehle, M., Mamaja, B. The value of a near-infrared spectroscopy based clinical algorithm in patients undergoing spinal surgery and its relation to postoperative cognitive decline. Euroanaesthesia 2019. 01.–03.06.2019, Vienna, Austria (Poster presentation)
4. Berezovskis, R., Murniece, S., Mamaja, B. Postoperative cognitive dysfunction in patients undergoing spinal neurosurgery. Euroanaesthesia 2019. 01.–03.06.2019, Vienna, Austria (Poster presentation)
5. Murniece, S., Soehle, M., Vanags, I., Mamaja, B. NIRS-based intraoperative patient management during spinal neurosurgery in prone position and postoperative cognitive disturbances. Update on Neuro-Anaesthesia and Neuro-Intensive Care, Interdisciplinary neuroscience. 07.–09.11.2018, Brussels, Belgium (Oral presentation, nominated for best abstract)
6. Murniece, S., Vanags, I., Soehle, M., Mamaja, B. Near-infrared spectroscopy based clinical algorithm applicability during spinal neurosurgery in prone position to avoid postoperative cognitive dysfunction. 9^{th} International Baltic Congress of Anaesthesiology. Intensive Care and Pain Management, 25.–27.10.2018, Vilnius, Lithuania (Poster presentation)
7. Berezovskis, R., Murniece, S., Mamaja, B. Postoperative cognitive dysfunction after spinal neurosurgery in prone position. 9^{th} International Baltic Congress of Anaesthesiology, Intensive Care and Pain Management. 25.–27.10. 2018, Vilnius, Lithuania (Poster presentation)
8. Murniece, S., Vanags, I., Mamaja, B. Intraoperative regional cerebral oxygen saturation monitoring using near-infrared spectroscopy device during spinal neurosurgery in prone position and postoperative cognitive dysfunction. Euroanaesthesia 2018. 02.–04.06.2018, Copenhagen, Denmark. Thesis book: European Journal of Anaesthesiology, 2018; 35(56):162 (Oral presentation)

9. Murniece, S., Stepanovs, J., Vanags, I., Mamaja, B. Prone positions influence on regional cerebral oxygen saturation in patients undergoing spinal neurosurgery. 13th International Conference on Neurology and Neurosurgery. 19.–21.06.2017, Paris, France. Thesis book: Journal of Neurophysiology; 8 (4), 37. DOI: 10.4172/2155-9562-C1-052 (Oral presentation)
10. Murniece, S., Skudre, A., Vjugins, J., Stepanovs, J., Vanags, I., Mamaja, B. Cerebral oxygen saturation monitoring during spinal neurosurgery in prone position using near-infrared spectroscopy (NIRS). Euroanaesthesia 2017. 03.–05.06.2017, Geneve, Switzerland. Thesis book: European Journal of Anaesthesiology; 34 (55), 160. (Poster presentation, Maquet grant winner)
11. Murniece, S., Skudre, A., Vjugins, J., Stepanovs, J., Mamaja, B. Noninvasive cerebral oxygen saturation monitoring during neurosurgical spine surgery in prone position. 8th International Baltic congress of Anesthesiology and Intensive Care. 01.–03.12.2016, Tallinn, Estonia. Thesis book: http://baltanest2016.com/abstracts/ [18.08.2017] (Poster presentation)

Presentations at the local conferences in Latvia

1. Murniece, S, Soehle, M., Vanags, I., Mamaja, B. Cerebral oximetry guided intraoperative algorithm relation to postoperative cognitive function in spinal surgery patients. RSU conference “Knowledge for use in practice”. 01.–05.04.2019, Riga, Latvia. (Poster presentation)
2. Berezovskis, R., Mūrniece, S., Mamaja, B. Development of postoperative cognitive dysfunction after spinal neurosurgery. RSU conference “Knowledge for use in practice”, 01.–05.04.2019. Riga, Latvia. (Poster presentation)
3. Murniece, S., Vanags, I., Mamaja, B. Prone position, intraoperative cerebral oxygenation monitoring and postoperative cognitive dysfunction. RSU Scientific conference 2018. 22.–23.03.2018, Riga, Latvia. Thesis book: p86 (Poster presentation)
4. Murniece, S., Stepanovs, J., Vanags, I., Mamaja, B. Non-invasive Regional Cerebral Oxygen Saturation Intraoperative Monitoring during Spinal Neurosurgery and Postoperative Period Evaluation. RSU Scientific conference 2017. 06.–07.04.2017, Riga, Latvia. Thesis book: p104 (Poster presentation)

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Acknowledgements

I am most grateful to my scientific supervisors Assoc. Prof. Biruta Mamaja and Prof. Indulis Vanags for all their help, support in most difficult moments and for their huge contribution to my scientific work. I am honoured to have Prof. Vanags as one of my supervisors. I am grateful for his scientific expertise and enduring interest in my work. My greatest and deepest gratitude goes to Assoc. Prof. Mamaja for being my biggest motivation to finish my thesis and always keeping faith in me.

My special thanks go to Prof. Martin Soehle for being the most supportive mentor and scientific consultant. I appreciate the time invested despite the busy schedule.

I am obliged to Prof. Lars Bjertnaes for his invaluable expertise and honest opinion.

I sincerely thank my former colleagues from RAKUS Gaiļezers Clinic of Anaesthesiology and Neurosurgery for always supporting me in my research. Especially I want to thank Dr. Anita Skudre for helping to develop the topic of the thesis and Dr. Jevgeņijs Stepanovs for the possibility to dedicate myself to neuroanaesthesiology.

I owe a thank-you to Inese Poļaka and her enormous help in statistics, also in the weekends and late evenings.

I thank all the patients who participated in the study and did not say no.

Finally, I am more than grateful to my fiancé Christian for going through this together and staying by my side no matter what, and my mother Dagmāra for her endless belief in me.

Annexes

Annex 1

The Rīga Stradiņš University

Research Ethics Committee approval

Veidlapa Nr. E-9(3)
APSTIPRINĀTA
ar Rīgas Stradiņa universitātes rektora
2018. gada 26. septembra rīkojumu Nr. 5-1/238/2018

Rīgas Stradiņa universitātes
Pētījumu ētikas komitejas
LĒMUMS
Rīgā

19.12.2019. Nr.6-2/11/ 59

	Komitejas sastāvs	Kvalifikācija	Nodarbošanās
1.	Profesors Olafs Brūvers	Dr.theo.	teologs
2.	Asoc.prof. Santa Purviņa	Dr.med.	farmakologs
3.	Asoc.prof. Voldemārs Arnis	Dr.biol.	rehabilitologs
4.	Profesore Regīna Kleina	Dr.med.	patalogs
5.	Profesors Guntars Pupelis	Dr.med.	ķirurgs
6.	Asoc.prof. Viesturs Liguts	Dr.med.	toksikologs
7.	Docente Iveta Jankovska	Dr.med.	ortodonts
8.	Docents Kristaps Circenis	Dr.med.	docētājs

Pieteikuma iesniedzējs/i: **Sniedze Mūrniece**
Doktorantūras nodaļa

Pētījuma / pētnieciskā darba nosaukums: "Uz smadzeņu skābekļa piesātinājumu balstīta klīniska algoritma izmantošana mugurkaula ķirurģijā un saistība ar pēcoperācijas kognitīvu disfunkciju"

Iesniegšanas datums: 18.12.2019.

Pētījuma protokols:
Izskatot augstāk minētā pētījuma pieteikuma materiālus (protokolu) ir redzams, ka pētījuma mērķis tiek sasniegts veicot klīnisku pētījumu (asins paraugu ņemšanu noteiktos un izdarot atbilstošas analīzes, pārbaudes, mērījumus), operācijas laikā veicot atbilstošu parametru mērījumus smadzeņu skābekļa piesātinājumam, iegūto datu apstrādi un analīzi, kā arī izsakot priekšlikumus. Personu (pacientu, dalībnieku) datu izmantošana, glabāšana, aizsardzība, informēta brīvprātīga piedalīšanās, anonimitāte un konfidencialitāte ir ievērota un nodrošināta. Līdz ar to pieteikums atbilst pētījuma ētikas prasībām.

Komitejas lēmums: **piekrist** pētījumam

Komitejas priekšsēdētājs Olafs Brūvers Tituls: Dr. miss., prof.

Paraksts

RĪGAS STRADIŅA UNIVERSITĀTE
ĒTIKAS KOMITEJA

I.Bēniņa
67061596

The Rīga Stradiņš University

Ethics Committee approval

Veidlapa Nr. E-9 (2)

RSU ĒTIKAS KOMITEJAS LĒMUMS NR. 85 / 29.12.2016.

Rīga, Dzirciema iela 16, LV-1007
Tel. 67061596

	Komitejas sastāvs	Kvalifikācija	Nodarbošanās
1.	Profesors Olafs Brūvers	Dr.theo.	teologs
2.	Profesore Vija Sīle	Dr.phil.	filozofs
3.	Asoc.prof. Santa Purviņa	Dr.med.	farmakologs
4.	Asoc.prof. Voldemārs Arnis	Dr.biol.	rehabilitologs
5.	Profesore Regīna Kleina	Dr.med.	patalogs
6.	Profesors Guntars Pupelis	Dr.med.	ķirurgs
7.	Asoc.prof. Viesturs Liguts	Dr.med.	toksikologs
8.	Docente Iveta Jankovska	Dr.med.	
9.	Docents Kristaps Circenis	Dr.med.	

Pieteikuma iesniedzējs: **Sniedze Mūrniece**
Medicīnas fakultāte, doktorantūra

Pētījuma nosaukums: „ Cerebrālās oksimetrijas monitorēšanas ietekme uz pēcoperācijas perioda norisi un ķirurģisko iznākumu pacientiem mugurkaula ķirurģijas laikā pozīcijā uz vēdera"

Iesniegšanas datums: 29.12.2016.

Pētījuma protokols: Izskatot iesniegtos pētījuma dokumentus (protokolu) ir redzams, ka pētījuma mērķis tiek sasniegts veicot ar pacientiem, bez kāda apdraudējuma veselībai un drošībai, cerebrālās oksimetrijas mērījumus operāciju laikā un iegūstot demogrāfiskos rādītājus ar standarta pirmsoperācijas izmeklējumu datiem, iegūto datu apstrādi un analīzi, kā arī izsakot priekšlikumus. Personu (pacientu, dalībnieku) datu aizsardzība, brīvprātīga informēta piekrišana piedalīties pētījumā un konfidencialitāte tiek nodrošināta. Līdz ar to pieteikums atbilst pētījuma ētikas prasībām.

Izskaidrošanas formulārs: ir

Piekrišana piedalīties pētījumā: ir

Komitejas lēmums: **piekrist** pētījumam

Komitejas priekšsēdētājs Olafs Brūvers Tituls: Dr. miss., prof.

Paraksts

ĒTIKAS KOMITEJA

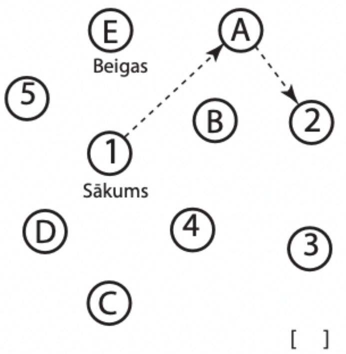
Ētikas komitejas sēdes datums: 29.12.2016.

Montreal cognitive assessment test (MoCA) in Latvian, Russian and English

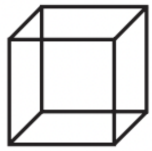
MONTREAL COGNITIVE ASSESSMENT (MOCA)

VĀRDS :
Izglītība : **Dzimšanas dati :**
Dzimums : **Datums :**

VIZUĀLI TELPISKĀS SPĒJAS / VADĪBAS FUNKCIJAS — **PUNKTI**



[ ]

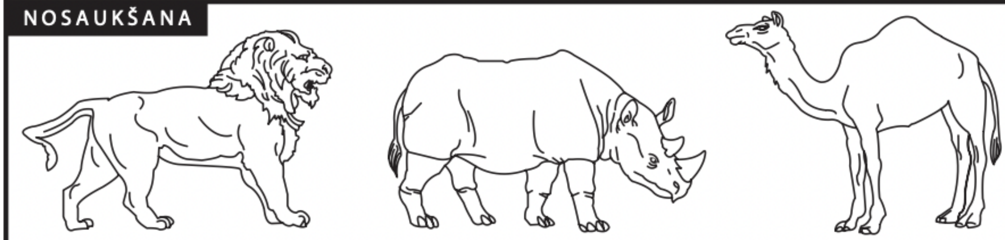


Pārzīmēt kubu [ ]

Uzzīmēt PULKSTENI (desmit minūtes pāri vienpadsmitiem) (3 punkti)

[ ] Kontūra [ ] Ciparnīca [ ] Rādītāji ___/5

NOSAUKŠANA



[ ] [ ] [ ] ___/3

ATMIŅA Izlasiet vārdu sarakstu, lūdziet respondentam tos atkārtot. Veiciet to 2 reizes, pat, ja 1. mēģinājums bijis veiksmīgs. Lūdziet atcerēties šos vārdus vēl pēc 5 minūtēm.

	SUNS	VELVETS	BĒRZS	ROZE	ZILS
1. mēģinājums					
2. mēģinājums					

Nav punkti

UZMANĪBA Nosauciet skaitļu virkni (1 skatilis /sekundē) Respondentam tie jāatkārto tiešā secībā [ ] 2 1 8 5 4
Respondentam tie jāatkārto pretējā secībā [ ] 7 4 2 ___/2

Sauciet burtus. Respondentam jāuzsit ar plaukstu pa galdu pie katra burta A. Punkti netiek doti, ja ir ≥ 2 kļūdas
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B ___/1

Atņemiet pa 7, sākot no 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 vai 5 pareizas darbības: **3 p.**, 2 vai 3 pareizas: **2 p.**, 1 pareiza: **1 p.**, 0 pareizas: **0 p.** ___/3

VALODA Atkārtojiet: Es zinu tikai to, ka Jānis ir vienīgais, kas šodien palīdz. [ ]
Kaķis vienmēr slēpās zem dīvāna, kad suņi bija istabā. [ ] ___/2

Valodas raitums. 1 minūtes laikā nosauciet pēc iespējas vairāk vārdu uz burtu L. [ ] _____ (N ≥ 11 vārdi) ___/1

VISPĀRINĀŠANA Līdzība starp vārdiem, piemēram, banāns – apelsīns = augļi [ ] vilciens - velosipēds [ ] pulkstenis – lineāls ___/2

ATSAUKŠANA ATMIŅĀ

Jāatsauc atmiņā vārdi BEZ NOTEIKTAS SECĪBAS	SUNS [ ]	VELVETS [ ]	BĒRZS [ ]	ROZE [ ]	ZILS [ ]
Izvēles uzdevums: Norāde par kategoriju					
Norāde ar vairākiem atbilžu variantiem					

Punkti tiek piešķirti tikai par pareizām atbildēm BEZ NORĀDES PIEMĒRIEM ___/5

ORIENTĀCIJA [ ] Datums [ ] Mēnesis [ ] Gads [ ] Diena [ ] Vieta [ ] Pilsēta ___/6

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KOPĀ ___/30
Pieskaitīt 1 punktu, ja izglītība ≤ 12 skolas gadiem

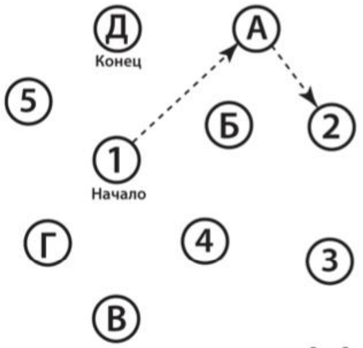
Testu vada ______________________________

Annex 2 continued

Монреальская шкала оценки когнитивных функций

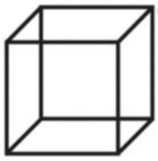
ИМЯ:
Образование: Дата рождения:
Пол: ДАТА:

	БАЛЛЫ
Зрительно-конструктивные/исполнительные навыки	



[ ]

Скопируйте куб



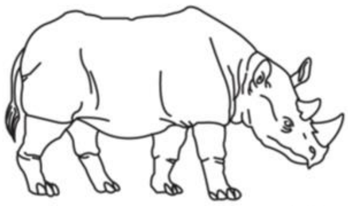
[ ]

Нарисуйте ЧАСЫ (Десять минут двенадцатого) (3 балла)

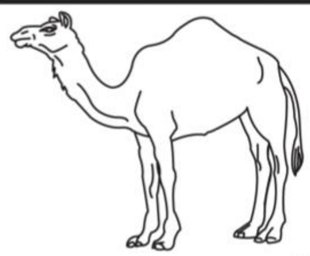
[ ] Контур [ ] Цифры [ ] Стрелки ___/5

НАЗЫВАНИЕ

[ ]



[ ]



[ ] ___/3

ПАМЯТЬ	Прочтите список слов, испытуемый должен повторить их. Делайте 2 попытки. Попросите повторить слова через 5 минут.		ЛИЦО	БАРХАТ	ЦЕРКОВЬ	ФИАЛКА	КРАСНЫЙ	нет баллов
		Попытка 1						
		Попытка 2						

ВНИМАНИЕ Прочтите список цифр (1 цифра/сек). Испытуемый должен повторить их в прямом порядке. [ ] 2 1 8 5 4
Испытуемый должен повторить их в обратном порядке. [ ] 7 4 2 ___/2

Прочтите ряд букв. Испытуемый должен хлопнуть рукой на каждую букву А. Нет баллов при > 2 ошибок. [ ] ФБАВМНАА ЖКЛБАФАКДЕАААЖАМОФААБ ___/1

Серийное вычитание по 7 из 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4-5 правильных отв.: **3 балла**, 2-3 правильных отв.: **2 балла**, 1правильный отв.: **1 балл**, 0 правильных отв.: **0 баллов**. ___/3

РЕЧЬ Повторите: Я знаю только одно, что Иван – это тот, кто может сегодня помочь. [ ]
Кошка всегда пряталась под диваном, когда собаки были в комнате. [ ] ___/2

Беглость речи/ за одну минуту назовите максимальное количество слов, начинающихся на букву Л [ ] _____ (N ≥ 11слов) ___/1

АБСТРАКЦИЯ Что общего между словами, например, банан-яблоко = фрукты [ ] поезд - велосипед [ ] часы - линейка ___/2

ОТСРОЧЕННОЕ ВОСПРОИЗВЕДЕНИЕ	Необходимо назвать слова БЕЗ ПОДСКАЗКИ	ЛИЦО [ ]	БАРХАТ [ ]	ЦЕРКОВЬ [ ]	ФИАЛКА [ ]	КРАСНЫЙ [ ]	Баллы только за слова БЕЗ ПОДСКАЗКИ	___/5
ДОПОЛНИТЕЛЬНО ПО ЖЕЛАНИЮ	Подсказка категории							
	Множественный выбор							

ОРИЕНТАЦИЯ [ ] Дата [ ] Месяц [ ] Год [ ] День недели [ ] Место [ ] Город ___/6

 Version 7.1 www.mocatest.org Норма 26 / 30 КОЛИЧЕСТВО БАЛЛОВ ___/30

Добавить 1 балл, если образование ≤ 12

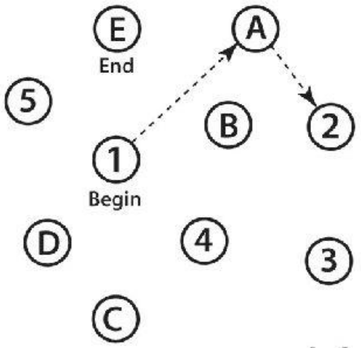
Проведено: ______________________

перевод: Посохина О. В. Смирнова А. Ю.

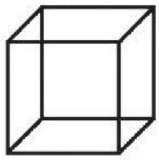
MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

	POINTS
VISUOSPATIAL / EXECUTIVE	



[ ]



Copy cube

[ ]

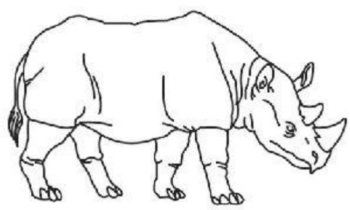
Draw CLOCK (Ten past eleven)
(3 points)

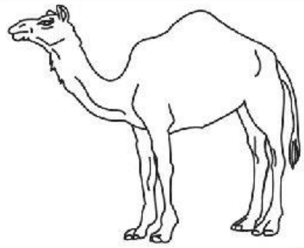
[ ] Contour [ ] Numbers [ ] Hands

___/5

NAMING


[ ]


[ ]


[ ]

___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2
___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B
___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**
___/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]
___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)
___/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler
___/2

DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	___/5
Optional	Category cue							
	Multiple choice cue							

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City
___/6

 www.mocatest.org Normal ≥26 / 30
TOTAL ___/30
Add 1 point if ≤ 12 yr edu

Administered by: ______________________________

First Publication

applied sciences

MDPI

Article

Regional Cerebral Oxygen Saturation Monitoring during Spinal Surgery in Order to Identify Patients at Risk for Cerebral Desaturation

Sniedze Murniece [1,2,*], Martin Soehle [3], Indulis Vanags [2,4] and Biruta Mamaja [1,2]

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Received: 16 February 2020; Accepted: 17 March 2020; Published: 19 March 2020

check for updates

Featured Application: The aim of our study was to evaluate the usefulness of intraoperative cerebral oxygenation monitoring during spinal surgery. Study includes specifically spinal neurosurgical patients, as spinal surgery, being performed in prone position, carries a certain risk for altered cerebral blood perfusion and oxygen supply. As a result, we show a benefit of cerebral oxygen saturation non-invasive intraoperative monitoring using Near infrared spectroscopy devices cerebral oximeters as in couple of patients we saw cerebral oxygen saturation drop below threshold values that would otherwise stay unrecognized as other intraoperative measurements stayed stable during cerebral oxygen desaturation.

Abstract: Background: Near infrared spectroscopy (NIRS) devices are non-invasive and monitor cerebral oxygen saturation ($rScO_2$) continuously. NIRS interventional protocol is available in order to avoid hypoxic brain injury. Methods: We recruited patients scheduled for spinal surgery (n = 44). $rScO_2$ was monitored throughout the surgery using INVOS 4100 cerebral oximeter. If the $rScO_2$ values dropped more than 20% below baseline, or there was an absolute drop to below 50%, NIRS interventional protocol was followed. Results: In two patients $rScO_2$ decreased by more than 20% from baseline values. In one patient $rScO_2$ decreased to below 50%. NIRS protocol was initiated. As the first step, correct head position was verified–in one patient $rScO_2$ increased above the threshold value. In the two remaining patients, mean arterial pressure was raised by injecting Ephedrin boluses as the next step. $rScO_2$ raised above threshold. Patients with desaturation episodes had longer medium time of the operation (114 ± 35 versus 200 ± 98 min, p = 0.01). Pearson's correlation showed a negative correlation between $rScO_2$ and duration of operation (r = −0.9, p = 0.2). Receiver operating characteristic curve analysis showed blood loss to be a strong predictor for possible cerebral desaturation (Area under the curve (AUC): 0.947, 95%CI: 0.836–1.000, p = 0.04). Conclusion: Patients with higher blood loss might experience cerebral desaturation more often than spinal surgery patients without significant blood loss.

Keywords: cerebral oxygen saturation; near infrared spectroscopy; cerebral oximeter; spinal surgery

1. Introduction

Intraoperative patient management is a challenging undertaking. Among a multitude of laboratory tests and technologies available to monitor patients during surgery, clear selection criteria for one or another monitoring technique is necessary.

The human brain is one of the most metabolically active organs consuming in average 20% of all the body oxygen [1]. The dangers of prolonged brain hypoxia, also intraoperatively, are already well documented in numerous studies. A large randomized study including 265 patients undergoing coronary artery bypass surgery showed significant correlation between prolonged intraoperative hypoxia and early cognitive decline and prolonged hospital stay [2]. Intraoperative cerebral desaturation has been proven to predict postoperative cognitive dysfunction and other postoperative complications also in patients undergoing non-cardiac surgery like thoracic, major orthopedic and major abdominal surgery [3].

Still, brain remains one of the least monitored organ during anesthesia and surgery, as the majority of available methods are invasive, like, jugular venous oximetry, requiring cannulation of the jugular bulbus, brain tissue oxygen monitoring using the Clark electrode in the brain parenchyma or cerebral microdialysis [4]. Near infrared spectroscopy (NIRS) has been increasingly implemented in clinical practice. NIRS devices are non-invasive, easy to use and monitor cerebral oxygen saturation ($rScO_2$) continuously.

A NIRS device cerebral oximeter consists of a monitor and two adhesive sensors, which are attached to the patients' forehead: one above the left and one above the right cerebral hemisphere overlying the frontal lobe (Figure 1). In each sensor there is an incorporated light diode-emitting near infrared light and two light detectors proximal and distal collecting the scattered light returning to the surface, permitting to separate data of shallow and deep optical signals [5] (Figure 2).

Figure 1. INVOS (in vivo optical spectroscopy) sensor placement on the patients' forehead (picture taken from the INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010).

Near infrared light, used in the cerebral oximetry, is at wave length 730 and 810 nm, which is capable of penetrating the skull [6]. In the brain tissue, light is either absorbed by hemoglobin (Hb) molecules or scattered back to the brain surface depending on the degree of oxygenation [5].

Cerebral oxygenation values are calculated using the Beer Lambert law. Beer's law claims that the light intensity decreases as the concentration of the substance the light passes through increases [5]. Lambert's law incorporates that the intensity of the light decreases as the distance, which the light is traveling, increases [5]. Based on both laws, oxygen can be measured by how much of the emitted light the substance absorbs and by the amount of light, which is travelling through it. Light absorption will be proportional to the oxygenation status of the tissue [5,7]. Values, at which cerebral oxygen saturation is considered to be normal, differ amongst studies published. Normal baseline cerebral oximetry values range between 60% and 80% [5]. Abnormal $rScO_2$ values are defined as $rScO_2$ drop from ones' individual baseline values for 20% or an absolute drop under a $rScO_2$ of 50% [7], marking those as a trigger values for an intervention [6] (Figure 3).

Figure 2. INVOS sensor with one light diode and two light detectors (picture taken from The INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010).

Figure 3. Cerebral oxygenation values appearance on the INVOS (in vivo optical spectroscopy) monitor (L—left cerebral hemisphere, R—right cerebral hemisphere; picture taken from the INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010).

The NIRS interventional protocol is used to guide patient management in order to mitigate cerebral desaturation and avoid hypoxic brain injury. The most commonly applied protocol has been published by Deschamps and colleagues [8]. The protocol includes steps that should be considered when cerebral desaturation occurs. The protocol also proposes a plan of actions.

Interventions aimed at preserving normal cerebral oxygenation within baseline values, can help to avoid postoperative cognitive disturbances, reduce the days spent in the intensive care unit [9] and avoid complications, like, kidney failure or wound infections [3].

Monitoring of $rScO_2$ using NIRS devices, cerebral oximeters, have been widely used during cardiac surgery, especially during cardiac bypass operations, as cardiac surgery patients often suffer from perioperative neurological complications [5]. Numerous studies regarding NIRS in cardiac surgery show positive correlation between intraoperative cerebral desaturation and postoperative cognitive disturbances, stroke, prolonged hospital stay [6].

Lately, monitoring of cerebral oxygen saturation has gained increasing popularity also in non- cardiac surgeries. During thoracic surgery—thoracotomy or thoracoscopy where at least one measurement lower than 80% from baseline value has been reported [3]. During shoulder surgery in the beach chair position, where cerebral desaturation episodes can be 1 minute up to 1 hour long [3]. In gynecological procedures, where the Trendelenburg position is used, as well as urological operations with hemodilution [3]. Furthermore, vascular surgery, carotid endarterectomy, where $rScO_2$ decreases during clamping of internal carotid artery or with the blood loss during abdominal aortic aneurysm repair [3].

There is a very limited amount of studies available regarding $rScO_2$ intraoperative monitoring during spinal operations, although special attention should be paid due to prone position and possible blood loss. Prone position during spinal surgery might be associated with several physiological challenges, which influences cerebral blood flow and oxygen supply creating conditions for cerebral desaturation. Increased abdominal pressure due to various etiologies might decrease vena cava inferior transvascular pressure and reduce venous return to the heart. Moreover, increased external pressure on the chest, resulting from prone positioning, also reduces cardiac index, in addition to increasing the peak airway pressure, thereby decreasing lung compliance causing a further decrease in cardiac output [10].

The aim of study was to evaluate the usefulness of monitoring intraoperative cerebral oxygenation during spinal surgery in order to discover cerebral desaturation.

2. Materials and Methods

Patients scheduled for spinal surgery were recruited to a prospective study including patients over 18 years of age scheduled for elective spinal surgery. Exclusion criteria were patients undergoing urgent spinal surgery, patients with a history of cerebral disease, like previous stroke, cerebral hematoma or transient ischemic stroke.

In our study INVOS (in vivo optical spectroscopy) 4100 (Covidien, Minneapolis, USA) two channel cerebral oximeter was used. In the operating room two INVOS sensors were attached to the patients' forehead, one above the left (L) and one above the right (R) eyebrow, before induction of anesthesia, while breathing room air. Individual baseline values were obtained. Meanwhile other presurgical measures were assessed, such as percutaneous oxygen saturation (SpO_2) and mean arterial pressure (MAP) by measuring non-invasive blood pressure. Anesthesia was induced using fentanyl 0.1–0.2 mg and propofol 1–2 mg/kg. Tracheal intubation was facilitated with cisatracurium 0.2 mg/kg. Anesthesia was maintained with continuous infusion of fentanyl 0.03–0.06 µg/kg/min, cisatracurium 0.06–0.1 mg/kg/h and sevoflurane at MAC 0.6–0.8. Mechanical lung ventilation was set to 8 mL/kg and fraction of inspired oxygen (FiO_2) to 0.4. Ventilation was set to keep end-tidal carbon dioxide ($EtCO_2$) in the range of 35–45 mmHg and SpO_2 96–100%.

During the surgery, SpO_2, MAP, $EtCO_2$ and $rScO_2$ were documented in the study protocol every 5 min. If the $rScO_2$ values dropped more than 20% from the patients' individual baseline value, or if there was an absolute drop of $rScO_2$ to below 50%, near infrared spectroscopy based interventional protocol was activated to restore $rScO_2$ values above the threshold. In the current study, we followed the NIRS protocol proposed by Deschamps et al. [8]. As the protocol was developed for cardiac surgery patients, we adjusted it to spinal surgery patients. Firstly, the head position is verified, in order to exclude head flexion, extension or rotations to the left or right side. Secondly, MAP is raised by injecting boluses of ephedrine. Thirdly, systemic oxygen saturation is tested and arterial blood oxygen partial pressure (PaO_2) is measured, and if low, FiO_2 is raised above 0.4. Fourthly, if $EtCO_2$ or $PaCO_2$ are low, hyperventilation is corrected. Fifthly, hemoglobin concentration is assessed and red blood cell transfusion is considered. Sixthly, the cardiac function is optimized by using vasopressor infusion. Seventhly, causes of excessive cerebral O_2 consumption, such as convulsions and hyperthermia, are evaluated and treated [8].

In the study protocol, we also noted patients' demographic data (age and sex), comorbidities, daily medication, the type of spinal surgery, preoperative hemoglobin and hematocrit levels, intraoperative blood loss and duration of operation.

Statistical analysis was performed using SPSS V.23. Values were presented as mean ± standard deviation (SD). Statistical significance was assumed if $p < 0.05$. The receiver operating characteristic (ROC) curves, their respective 95% confidence intervals, and significance were compared between patients to identify predicting factors for intraoperative cerebral desaturation.

Study protocol and informed consent form was approved by the Medical Research Ethics Committee of Riga Stradins University (Approval No. 85/29.12.2016).

3. Results

In total, 44 patients scheduled for spinal surgery were included. Demographic characteristics and preoperative laboratory findings, duration of operation, intraoperative blood loss, intraoperative MAP, SpO_2 and $EtCO_2$ are shown in Table 1. We determined $rScO_2$ at the following time points: (1) preoperative baseline; (2) after induction of anesthesia; (3) during prone position and (4) at the end of the surgery in supine position, as shown in Table 2.

Table 1. Demographic characteristics and preoperative laboratory findings, duration of operation, intraoperative blood loss, intraoperative MAP, SpO_2 and $EtCO_2$ in patients undergoing spinal surgery under general anesthesia.

Patients (n), Sex (Male/Female)	44 (20/24)
Age (years)	54 ± 14
Hb level (g/dL)	13 ± 1
Ht (%)	41 ± 4
Duration of operation (min)	121 ± 47
Blood loss (mL)	259 ± 99
Intraoperative MAP (mmHg)	83± 10
Intraoperative SpO_2 (%)	99 ± 0.3
Intraoperative $EtCO_2$ (mmHg)	34 ± 2

Values are shown as mean ± standard deviation. Hb—hemoglobin, Ht—hematocrit, MAP—mean arterial pressure, SpO_2—peripheral oxygen saturation, $EtCO_2$—end-tidal carbon dioxide.

Table 2. Determination of $rScO_2$ before induction of anesthesia, during induction of anesthesia, during anesthesia with prone positioning of the patient and at the end of anesthesia and surgery with the patient in the supine position.

Position	Cerebral Hemisphere	Mean $rScO_2$ (%)
Before induction of anesthesia	Right	72 ± 9
	Left	72 ± 10
During induction of anesthesia	Right	74 ± 9
	Left	73 ± 9
Prone position during anesthesia	Right	73 ± 6
	Left	73 ± 6
Supine at the end of the anesthesia and surgery	Right	73 ± 8
	Left	73 ± 8

Values are shown as mean ± standard deviation. $rScO_2$—regional cerebral oxygen saturation.

In 3 out of 44 patients, we observed intraoperative cerebral desaturation. In two patients $rScO_2$ decreased under 20% from individual baseline. One patient was 57 years old undergoing microdiscectomy, the other one was 24 years old undergoing transpedicular fixation due to trauma. In one patient, 54 years old undergoing extirpation of spinal meningioma, $rScO_2$ decreased to below 50%. In all 3 patients the NIRS interventional protocol was initiated. The first step, the verification of correct head position resulted in no changes in $rScO_2$ in two of the patients while $rScO_2$ increased above the threshold value in one patient. In the remaining two patients, MAP was raised using Ephedrin boluses (5-20 mg) and $rScO_2$ raised above threshold and no further interventions were necessary.

Comparing to other spinal surgery patients who experienced only mild cerebral oxygenation fluctuations intraoperatively, which did not reach desaturation threshold, the patients with desaturation episodes had significantly longer operation medium time—114 ± 35 min in patients without cerebral desaturation compared to medium 200 ± 98 min in patients with intraoperative cerebral desaturation ($p = 0.01$). Pearson's correlation showed a trend towards a negative correlation between $rScO_2$ and duration of operation, although not statistically significant ($r = -0.9$, $p = 0.2$).

Receiver operating characteristic (ROC) curve analysis showed blood loss to be a strong predictor of possible cerebral desaturation (AUC: 0.947, 95% CI: 0.836–1.000, $p = 0.04$; Figure 4).

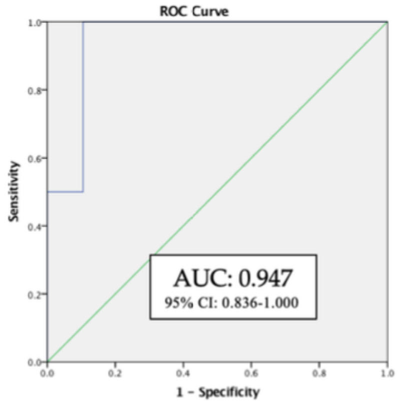

Figure 4. Receiver operating characteristic (ROC) curve for blood loss as a predictor of cerebral desaturation.

4. Discussion

In the present study, NIRS was used for monitoring patients undergoing spinal surgery in the prone position. Three out of 44 (6%) patients showed intraoperative cerebral desaturation, indicating that $rScO_2$ monitoring might not be useful in all spinal surgery patients and careful patient selection could be necessary. On the other hand, no correlation between cerebral oxygen saturation and other intraoperatively monitored parameters, like, MAP, SpO_2 and $EtCO_2$ were seen. Therefore, without $rScO_2$ monitoring, cerebral desaturation episodes would have remained unnoticed.

In patients experiencing intraoperative cerebral desaturation, longer operation time (not statistically significant) and greater blood loss (statistically significant) were recognized as possible predictors of cerebral oxygen desaturation during spinal surgery. Vertzakis et al. [11] showed that NIRS might be a valuable tool for guiding the decision regarding the necessity of blood transfusion during cardiac surgery. In his study significantly fewer patients monitored with INVOS received blood transfusion and significantly fewer red blood cell units were transfused in comparison with the control group with no NIRS monitoring [11].

The patients who experienced intraoperative cerebral desaturation episodes were 24, 54 and 57 years of age. Only one patient had comorbidities. That was adiposities and arterial hypertension, which was treated with one antihypertensive medicine. Therefore, it is not possible to assess whether one or another comorbidity is related to intraoperative cerebral oxygen desaturation. Nevertheless, our study demonstrates that also young people without any known comorbidities can be at risk for cerebral desaturation.

Regarding NIRS interventional protocol, in one patient $rScO_2$ values raised above the threshold after verifying correct head position. The importance of correct head position during prone position also has been emphasized by Andersen et al., where they strongly recommend a neutral head position, as head rotation, flexion or extension can significantly alter cerebral oxygenation [12].

The limitation of our study is the lack of analysis of the postoperative period as one or another monitoring device implementation in clinical practice should also improve postoperative period or organ-related outcome [13]. The majority of studies show clear benefit of $rScO_2$ intraoperative monitoring. Thus, less renal and respiratory failures and a shorter length of stays in intensive care units have been recognized in patients in whom NIRS guided interventions were used during surgery [14]. A lower probability of death and major organ dysfunction also have been reported [15,16]. A number of studies have been performed focusing on cerebral oxygen saturation intraoperative monitoring and postoperative cognitive outcome as postoperative cognitive decline or dysfunction (POCD) impair patient postoperative recovery and can lead to long-term consequences [17]. A randomized study has shown that patients suffering from intraoperative cerebral desaturation also have an increased risk of POCD [2]. What is more important, lower incidence of cognitive deficiencies in patients monitored with NIRS was reported in a study that included spinal surgery patients [18].

Every monitoring device, that can be used intraoperatively, should work in favor of additional patient safety. NIRS devices can help physicians to guide making decisions during the surgery. However, NIRS is believed to be best used as a trend monitor, without following strict thresholds [19]. It seems to be better for recognizing patients at risk than guiding interventions [20].

5. Conclusions

Patients with higher blood loss might experience cerebral desaturation more often than other spinal surgery patients. Therefore, for this category of patients, intraoperative cerebral oxygenation monitoring is very useful.

Author Contributions: Conceptualization, S.M., M.S., B.M., I.V.; methodology, S.M., M.S., B.M., I.V.; formal analysis, S.M.; investigation, S.M.; data curation, S.M.; writing—original draft preparation, S.M.; writing—review and editing, S.M., M.S., B.M., I.V.; visualization, S.M.; supervision, M.S., B.M., I.V. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: The authors would like to thank prof. Lars J Bjertnæs for his suggestions.

Conflicts of Interest: The authors declare no conflict of interest.

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Near Infrared Spectroscopy Based Clinical Algorithm Applicability During Spinal Neurosurgery and Postoperative Cognitive Disturbances

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Received: 1 March 2019; Accepted: 14 May 2019; Published: 21 May 2019

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Abstract: *Background and Objectives:* Postoperative cognitive disturbances (POCD) can significantly alter postoperative recovery. Inadequate intraoperative cerebral oxygen supply is one of the inciting causes of POCD. Near-infrared spectroscopy (NIRS) devices monitor cerebral oxygen saturation continuously and can help to guide intraoperative patient management. The aim of the study was to evaluate the applicability of the NIRS-based clinical algorithm during spinal neurosurgery and to find out whether it can influence postoperative cognitive performance. *Materials and Methods*: Thirty four patients scheduled for spinal neurosurgery were randomized into a study group (n = 23) and a control group (n = 11). We monitored regional cerebral oxygen saturation (rScO2) throughout surgery, using a NIRS device (INVOS 4100). If rScO2 dropped bilaterally or unilaterally by more than 20% from baseline values, or under an absolute value of 50%, the NIRS-based algorithm was initiated in the study group. In the control group, rScO2 was monitored blindly. To evaluate cognitive function, Montreal-Cognitive Assessment (MoCA) scale was used in both groups before and after the surgery. *Results*: In the study group, rScO2 dropped below the threshold in three patients and the NIRS-based algorithm was activated. Firstly, we verified correct positioning of the head; secondly, we increased mean systemic arterial pressure in the three patients by injecting repeated intravenous bolus doses of Ephedrine, ultimately resulting in an rScO2 increase above the approved threshold level. None of the three patients showed POCD. In the control group, one patient showed a drop in rScO2 of 34% from baseline and presented with a POCD. RScO2 drop occurred with other stable intraoperative measurements. *Conclusions*: A significant rScO2 drop may occur during spinal surgery in prone position despite other intraoperative measurements remaining stable, allowing it to stay otherwise unrecognized. Use of the NIRS-based clinical algorithm can help to avoid POCD in patients after spinal surgery.

Keywords: spinal surgery; near-infrared spectroscopy (NIRS); regional cerebral oxygen saturation (rScO2); NIRS-based clinical algorithm; postoperative cognitive disturbances (POCD)

1. Introduction

A significant number of patients of all ages present with postoperative decline in cognitive functions after non-cardiac surgery [1]. Postoperative cognitive disturbances (POCD) tends to improve over a certain period of time in the majority of patients [2], but some patients suffer from permanent cognitive impairment and other major and long-term consequences [3]. Cognitive disturbances following surgery are serious complications [4] that alter postoperative recovery significantly [5]. The exact etiology of the cerebral injury leading to POCD remains unclear, but assumingly includes a combination of patient-related, surgical, and anesthetic factors [6]. Many of these factors cannot be exactly identified. However, some of them can be modified, thereby minimizing the risk of POCD. Inadequate intraoperative cerebral blood flow and oxygen supply is one of the main causes of postoperative delirium and cognitive disturbances [7]. Appropriate oxygen delivery to the brain is one of the main tenets of anesthetic practice [8]. In spite of that, the brain remains one of the least monitored organs during surgery.

In 1977, Jobsis [9] introduced near-infrared spectroscopy (NIRS) as a useful non-invasive tool for regional cerebral oxygen saturation (rScO2) monitoring, which provides continuous, real time information on the balance between cerebral oxygen delivery and consumption [5].

The technology of the NIRS cerebral oximeter depends on the transference and absorption of near-infrared light when it passes through tissue [10]. A cerebral oximeter unit consists of a monitor and two adhesive electrodes that are attached to patients' forehead. The electrode incorporates a light source and light detectors. The light source radiates light in a near-infrared range of 650–940 nm that can penetrate the skull and the underlying brain tissue [11]. In the near-infrared wavelength spectrum, the main chromophores that can absorb light are hemoglobin and cytochrome c oxidase [10]. Based on the oxygenation status of the hemoglobin molecules, light spectrum changes occur [11]. Cerebral oximeter electrodes register the reflected light and quantify rScO2.

One of the intraoperative cerebral oxygen saturation monitoring benefits is the possibility to utilize a NIRS-based clinical algorithm [5] in cases in which rScO2 drops, and it aids in guiding the intraoperative patient management. The level of rScO2 values that should trigger initiation of the algorithm differ among authors, although the majority support either a 20% unilateral or bilateral reduction, or an absolute decline below rScO2 of 50% from the patients' individual baseline value obtained before induction of anesthesia [12].

Neurosurgical spinal operations performed in the prone position carry a specific risk of an altered cerebral blood perfusion, which might impair oxygen supply to the brain. Reduced stroke volume and cardiac index might occur in patients lying in the prone position. Increased intra-abdominal pressure due to direct pressure on the vena cava inferior, and increased intrathoracic pressure with decreased left ventricular compliance and filling, leads to hypotension and reduced end organ perfusion, including the brain [13]. Brain blood supply may also fall in response to iatrogenic hypotension, which is often required during spinal surgery in an attempt to diminish intraoperative bleeding.

Research on postoperative cognitive dysfunction after various types of surgeries has gained increased popularity. Recent studies show that maintenance of adequate intraoperative cerebral oxygen saturation can help to avoid POCD that lead to long term consequences [14,15]. POCD and their risk factors in relation to spinal surgery remain unclear and need further clarification.

The aim of the present study was to investigate whether application of an algorithm based on NIRS during spinal neurosurgery influences postoperative cognitive performance.

2. Materials and Methods

This prospective observational study included 34 patients scheduled for spinal neurosurgery. Inclusion criteria were: Patients over 18 years old, spinal surgery performed in prone position. Exclusion criteria were: Emergency spinal surgery, patients with known cerebrovascular or psychiatric disease, previous stroke, inability to undertake preoperative cognitive evaluation. Medical Research Ethics Committee of Riga Stradins University approved the study protocol and informed consent form (Approval Nr. 85/29.12.2016).

Preoperative blood tests were taken from all patients in the neurosurgical or neurological ward to obtain hemoglobin (Hb) and hematocrit (Ht) levels. Normal Hb values range from 12–16 g/dL for women and 14–18 g/dL for men and Ht from 36–48% for women and 40–54% for men [16]. Prior to surgery, we induced anesthesia with fentanyl 0.1–0.2 mg, propofol 1–2 mg/kg and cisatracurium 0.2 mg/kg for endotracheal intubation and maintained with a continuous infusion of fentanyl 0.03–0.06 μg/kg/min, cisatracurium 0.06–0.1 mg/kg/h and sevoflurane at MAC 0.6–0.8. Initial tidal volume for mechanical ventilation was set to 8 mL/kg and FiO2 to 0.5. Ventilation was set to keep end-tidal carbon dioxide (EtCO2) in the range of 35 to 45 mmHg. Intraoperative values such as non-invasive mean arterial pressure (MAP) was determined every 5 min, while heart rate (HR), peripheral oxygen saturation (SpO2) and end tidal carbon dioxide (EtCO2) were documented in the study protocol as single time point measurements every 5 min. At the end of the surgery, we recorded intraoperative blood loss and the duration of operation.

In all patients rScO2 was continuously monitored throughout the surgery, using NIRS device INVOS (IN Vivo Optical Spectroscopy) 4100 (Covidien, Minneapolis, MN, USA). The INVOS system utilizes near-infrared light at wavelengths that are absorbed by hemoglobin—730 and 810 nm. Two rScO2 sensors were placed on the patients' forehead; one above the right (R) and one above the left (L) cerebral hemisphere after arriving in the operating room. One adhesive INVOS sensor pad was attached above the right eyebrow, the second above the left eyebrow (Figure 1). The distance between the light emitting diode (LED) and two INVOS sensor detectors was 3 and 4 cm (Figure 2). Sensors were connected to the INVOS monitor. The initial values on the screen were set as baseline rScO2 values. The patient is breathing room air before induction of anesthesia. By establishing baseline rScO2 values, INVOS further tracks the changes in rScO2 values for the left side and for the right side (Figure 3).

Figure 1. INVOS (IN Vivo Optical Spectroscopy) sensor placement on the patients' forehead (picture taken from the INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010).

Figure 2. INVOS sensor (picture taken from The INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010).

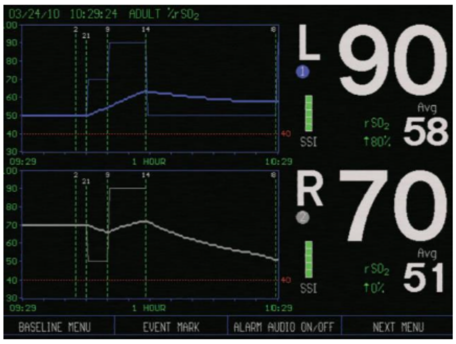

Figure 3. Screen of the INVOS cerebral oximeter showing regional cerebral oxygen saturation (rScO2) values above the left cerebral hemisphere (L) and right cerebral hemisphere (R) (picture taken from The INVOS Cerebral/Somatic Oximeter Operations Manual, Covidien 2010).

Patients were randomized into a study group (n = 23) and a control group (n = 11). In the study group intraoperative rScO2 values were kept in the range of 20% from baseline values or above an absolute rScO2 of 50%. As soon as rScO2 values dropped bilaterally or unilaterally under 20% from baseline values or under an absolute value of 50%, the NIRS-based clinical algorithm was initiated [5]. Based on the algorithm, steps were taken in the following order: The position of the head is verified (head's rotation to the left/right side, and head's flexion and extension is excluded) to rule out mechanical obstruction that could alter cerebral blood and oxygen supply; MAP is increased to maintain cerebral perfusion pressure; systemic oxygenation status is improved if arterial oxygen saturation (SaO2) is low; partial pressure of carbon dioxide (PaCO2) is normalized—hypocapnia or hypercapnia is treated; hemoglobin is optimized (according to the algorithm Hb less than 7–8 g/dL requires red blood cell transfusion); cardiac function is evaluated if the previous steps fail and have been ruled out; as a last step cerebral oxygen consumption should be estimated (convulsions, hyperthermia) [5]. As the algorithm was created for cardiac surgery patients, it also included a step in which central, aortic and superior vena cava catheters were inspected [5].

Control group patients received standard intraoperative anesthetic management, rScO2 was monitored blindly, and the investigator was unaware about the NIRS results. If MAP dropped below 65 mmHg [17], Ephedrin boluses were given, excessive bleeding was excluded. If SpO2 dropped under 94%, inspired oxygen concentration was raised above 50% [18]. If hemorrhage of over 500 ml occurred, arterial blood gas analyses were performed to detect Hb levels and to evaluate the necessity for a blood transfusion (transfusion trigger 7 to 9 g/dL during hemorrhage [19]).

To evaluate cognitive function we used the Montreal-Cognitive Assessment (MoCA) test in both groups before surgery and two days after the surgery to avoid intraoperatively-used anesthetic drug interaction with the test's performance. The MoCA test evaluates the following parameters—attention, concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation [20]. The MoCA test is validated in different languages and is a screening test designed to detect mild cognitive dysfunction. The test takes 10–15 min. MoCA test scores range between 0 and 30 points. Postoperative cognitive decline was defined as reduction in postoperative MoCA test points compared to MoCA points before surgery.

Statistical analysis was performed using SPSS V.23. Groups were compared by *t*-test for parametric data and Mann-Whitney test for non-parametric data. Values were presented as mean ± standard deviation (SD). Statistical significance was assumed if $p < 0.05$. The receiver operating characteristic (ROC) curves, their respective 95% confidence intervals, and significance were compared between patients to identify predicting factors for POCD.

3. Results

Demographic characteristics (age, sex) and preoperative laboratory findings (Ht, Hb), duration of operation, intraoperative blood loss, intraoperative MAP, SpO2 and EtCO2 of the patients are shown in Table 1.

Table 1. Patients' demographic characteristics (age, sex) and preoperative laboratory findings (Hb, Ht), duration of operation, intraoperative blood loss, intraoperative MAP, SpO2, EtCO2 in the study group and the control group.

	Study Group	Control Group	*p*-Value
Patients (n), sex (male/female)	23 (12/11)	11 (6/5)	
Age (years)	55 ± 14	58 ± 14	0.4
Hb level (g/dL)	13 ± 1	13 ± 1	0.1
Ht (%)	40 ± 5	38 ± 6	0.1
Duration of operation (min)	114 ± 45	130 ± 57	0.7
Blood loss (mL)	285 ± 287	345 ± 190	0.2
Intraoperative MAP (mmHg)	87 ± 13	80 ± 6	0.9
Intraoperative SpO2 (%)	99 ± 0.3	99 ± 1	0.7
Intraoperative EtCO2 (mmHg)	35 ± 1	34 ± 1	0.5

Values are shown as mean ± standard deviation. Hb—hemoglobin, Ht—hematocrit, MAP—mean arterial pressure, SpO2—peripheral oxygen saturation, EtCO2—end-tidal carbon dioxide.

In the study and control groups, only mild changes were observed in mean rScO2 values before induction of anesthesia, during induction of anesthesia, in prone position during anesthesia, lying supine at the end of the anesthesia and surgery. The mean rScO2 values are shown in Table 2.

Table 2. RScO2 in the study and control groups before induction of anesthesia, during induction of anesthesia, in prone position during anesthesia and lying supine at the end of the anesthesia and surgery.

Position	Cerebral Hemisphere	Mean rScO2 (%) in the Study Group	Mean rScO2 (%) in the Control Group	*p* Value
Before induction of anesthesia	Right Left	68 ± 7 67 ± 9	68 ± 14 73 ± 11	0.2 0.1
During induction of anesthesia	Right Left	74 ± 9 73 ± 9	70 ± 13 70 ± 10	0.4 0.4
Prone position during anesthesia	Right Left	73 ± 6 73 ± 6	70 ± 6 72 ± 4	0.3 0.7
Supine at the end of the anesthesia and surgery	Right Left	72 ± 8 71 ± 8	70 ± 13 70 ± 6	0.3 0.4

Values are shown as mean ± standard deviation. rScO2—regional cerebral oxygen saturation.

Considering all patients in the study group, an rScO2 drop below 20% from the patients' individual baseline value measured prior to induction of anesthesia occurred in one patient (from rScO2 75% to 59%), and a drop below 50% occurred in 2 patients (from baseline rScO2 65% to 49% intraoperatively, and from baseline rScO2 62% to 47% intraoperatively). NIRS-based clinical algorithm was initiated and all the actions in the algorithm were taken, step by step.

As a first step, based on the NIRS-algorithm, the correct head position was verified—any flexion or rotation of the head was excluded, and a neutral head position was ensured. No increase in rScO2 values was observed. As a second step, MAP was raised. All three patients received boluses of Ephedrin (5–20 mg) resulting in an rScO2 increase above the threshold. No further interventions were necessary. Upon restoring non-critical rScO2, the algorithm was terminated. During the remaining surgery, rScO2 values remained stable and we observed no further decline below threshold. The lowest MAP of all three patients was 75–90 mmHg, recorded during the drop of rScO2. SpO2 and EtCO2 remained stable. No excessive hemorrhage was observed.

None of the three patients showed postoperative cognitive decline.

In the control group, the rScO2 of one of the patients (39 years old) dropped 34% below baseline values (from baseline rScO2 95% to lowest 63% intraoperatively). Other intraoperative readings: MAP 73–83 mmHg, SpO2 100% and EtCO2 35–37 mmHg remained stable during the decrease in rScO2, no excessive hemorrhage (150 mL). The patient showed postoperative cognitive decline (MoCA score decrease of 4 points).

Analyzing all patients included in the study, patients with intraoperative rScO2 drop below the threshold had a statistically significantly longer mean operation time (166 ± 79 min) compared to the patients who did not have significant rScO2 decrease (116 ± 34 min, $p = 0.02$).

In both the study and the control group, mean MoCA score did not change significantly before and after the surgery. In the study group, we noted a MoCA score of 24 ± 2 points before surgery and 25 ± 2 points after the surgery. Correspondingly, in the control group we noticed 26 ± 1 points and 25 ± 1 points before and after the surgery, respectively.

Analyzing all the patients of the study, 3 out of 23 study group patients and 4 out of 11 control group patients showed postoperative cognitive decline of 1–4 points. Regarding those patients we did not observe any statistically significant differences in preoperative laboratory values or intraoperative measurements as compared to the patients without cognitive decline. Medium preoperative and intraoperative rScO2 values did not differ significantly between the patients with postoperative cognitive decline and without.

Receiver operating characteristic (ROC) curve analysis showed rScO2 monitoring to be a weak predictor of POCD (AUC: 0.688, 95% CI: 0.444–0.932, $p = 0.1$) (Figure 4). Neither did the other measurements (patient age, preoperative Hb, Ht level, duration of operation, intraoperative blood loss) appear to be strong predictors for postoperative cognitive decline, as assessed by ROC analysis.

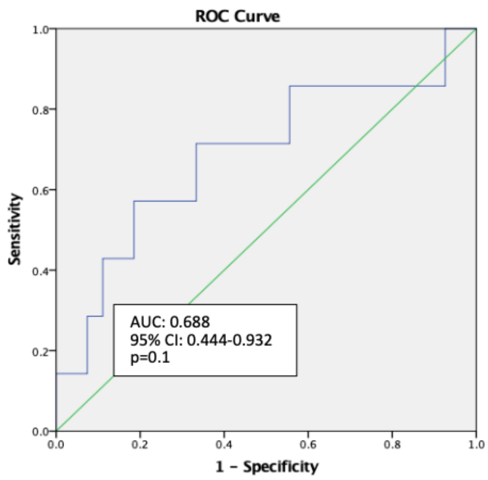

Figure 4. Receiver operating characteristic (ROC) curve for rScO2 monitoring as predictor of postoperative cognitive disturbances (POCD).

4. Discussion

In our prospective study, NIRS-monitoring identified rScO2 drops of more than 20% from baseline and an absolute drop under 50% in 3 out of 23 study group patients and 1 out of 11 control group patients despite no significant changes in MAP, SpO2 and EtCO2. This leads to the assumption that standard minimum intraoperative monitoring used routinely during anesthesia, such as non-invasive blood pressure measurement, pulse oximeter, electrocardiogram, inspired and expired oxygen, and carbon dioxide [21], may not give sufficient information about brain oxygenation. In addition, it may convey a false impression that the concept of cerebral autoregulation and perfusion based on MAP works for every patient, thus adding a future argument in favor of NIRS-monitoring. Furthermore, study group patients, whose rScO2 decreased and the interventions required by the NIRS algorithm were made, did not show POCD, unlike one control group patient where significant rScO2 drop occurred, NIRS algorithm was not used and POCD was observed. Regarding our current study the depth of anesthesia was not monitored, thus representing a major limitation of the study since low BIS values and a prolonged period of deep anesthesia can emerge as risk factors for POCD [22]. Yet some studies are showing no correlation between depth of anesthesia and POCD [23].

A majority of studies show a positive correlation between lower intraoperative rScO2 values and POCD in older patients [24,25]. Our control group patient with intraoperative rScO2 decrease and postoperative cognitive decline was 39 years old, without any other known cardiovascular, neurological or other diseases. Therefore, younger patients with no comorbidities may suffer from POCD.

Shim et al. [4] performed a meta-analysis regarding risk factors for delirium after spinal surgery. After analyzing 33 articles the following risk factors indicated a significant association with postoperative delirium: Age (>65 years), female sex, number of medications used preoperatively, low preoperative hematocrit, albumin, duration of surgery and intraoperative blood loss [4]. In our study ROC curve analysis did not show patient age, preoperative Hb, Ht level, duration of operation or intraoperative blood loss to be strong predictors for postoperative cognitive decline. Nevertheless, more patients should be included in the study in order to estimate precise conclusions about factors that lead to POCD.

Regarding the monitoring of cerebral oxygen saturation during spinal surgery in prone position, only a limited number of studies are available. One of these studies suggests that patients undergoing surgery in prone position suffer from mild cerebral desaturation (rScO2 under 65%) 2.3 times more often ($p = 0.009$) as compared with patients that have been operated upon while lying supine [25], although the study included only elderly patients (≥68 years) [5]. Andersen et al. investigated the position of the head (neutral, head turned to left/right, head lifted from the head support, head down) and its influence on cerebral oxygenation in 48 spinal surgery patients [26]. As a result, they recommend a neutral head position, since a decline in rScO2 of 10 or more units was observed in rotated and lifted position of the head [26]. The verification of the position of the head also appears to be the first step in the NIRS-based clinical algorithm.

Postoperative screening of cognitive disturbances is not performed routinely, unless the patient presents with delirium with clearly visible clinical symptoms. Therefore, postoperative cognitive decline can stay unrecognized even at hospital discharge [14]. One of the tenets in our study was to employ a simple test, such as MoCA. The MoCA assessment requires just 10–15 min to evaluate the patients' cognitive function. An additional benefit includes the relatively easy execution, which can be carried out by anesthesiologists or any other physician. This in turn increases the early detection of patients at risk of experiencing POCD. MoCA has shown a high sensitivity and specificity as a screening test for mild cognitive impairment, as well as for patients that have shown normal results during Mini-Mental State Examination (MMSE) [27–29].

Postoperative cognitive dysfunction or decline is a well-known clinical phenomenon with multifactorial origin [30,31], where intraoperative cerebral hypoxia is supposed to be one of the causes and, unlike other factors, can be modified. Non-invasive cerebral oxygenation monitoring including an easy to use monitor with an NIRS-based clinical algorithm can help to prevent cerebral desaturation intraoperatively and avoid hypoxic brain injury. The NIRS algorithm has been developed as a guideline for cases where cerebral desaturation occurs as it provides step by step interventions in a certain order which are specifically aiming to restore brain oxygenation [5]. Although, it is advisable to act only after careful evaluation of all available information of the patient, surgery and anesthesia, and after ruling out false-positive measurements due to NIRS device adhesive patch displacement [5].

A tailored patient approach, including innovative information and technologies to overcome patient-related health issues, has made the patient management more efficient. Many studies have already shown a clear benefit of intraoperative regional cerebral oxygenation monitoring [15,24–26,32] in different types of surgery. However, the question as to whether NIRS devices should be used routinely in all patients during spinal neurosurgery in prone position, or just for a specific group of patients, remains unclear.

5. Conclusions

A significant rScO2 drop for more than 20% from baseline value or below an absolute value of 50% rScO2 may occur during spinal surgery in prone position with stable intraoperative measurements (MAP, SpO2, HR, EtCO2), which would otherwise remain unnoticed.

The use of an NIRS-based algorithm in patients where the rScO2 drops for more than 20% from baseline values or under an absolute value of 50% can potentially help to avoid postoperative cognitive disturbances after spinal surgery.

Author Contributions: Conceptualization, S.M., M.S., B.M., I.V.; methodology, S.M., M.S., B.M., I.V.; formal analysis, S.M.; investigation, S.M.; data curation, S.M.; writing—original draft preparation, S.M.; writing—review and editing, S.M., M.S., B.M., I.V.; visualization, S.M.; supervision, M.S., B.M., I.V.

Funding: This research received no external funding.

Acknowledgments: The authors would like to thank Lars J Bjertnæs for his suggestions.

Conflicts of Interest: The authors declare no conflict of interest.

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Third Publication

ISSN: 2475-5435

Research Article

International Journal of Psychiatry

Cerebral Oxygenation Changes Observed in Patients Undergoing Spinal Neurosurgery in Prone Position Using Near Infrared Spectroscopy

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Submitted: 07 July 2017; Accepted: 13 July 2017; Published: 16 July 2017

Abstract

Background: *Near infrared spectroscopy (NIRS) devices like cerebral oximeters have lately gained their actuality in different medical fields. Used intraoperative they can early detect harmful event and gives a possibility to avoid from further brain damage. The goal of the study was to determine whether prone position during spinal neurosurgery impacts cerebral oxygen saturation using NIRS.*

Material and methods: *28 patients (mean age 56±12.5y) underwent spinal neurosurgery in prone position (transpedicular fixation (TPF) = 15, micro discectomy (MDE) = 8, spinal tumor removal (spinal Tu) = 5). Cerebral oxygen saturation (rScO2) was continuously monitored using INVOS 4100 cerebral oximeter. We also assessed blood loss, postoperative complications (stroke, organ dysfunction, wound infection, days spent in ICU) and cognitive dysfunction using MoCA Montreal - Cognitive Assessment scale. All patients received standard general anaesthesia. All patients were extubated in the operating room.*

Results: *Significant changes in calculated mean rScO2 values between supine and prone position during the surgery were not observed. Mean rScO2 during the whole surgery was 73% above the right cerebral hemisphere (R), 73% above the left (L). Lying supine during induction R72%, L71%, in prone position R74%, L74%, returning back to spinal position R73%, L73%. 11 out of 28 patients showed a slight to significant decrease in rScO2 values in prone position. One patient showed a rScO2 decrease by 27% from baseline value. Average blood loss was 308ml. Average duration of operation was 110min. No incidence of stroke, organ dysfunction was observed. One patient was admitted to ICU due to blood loss. One patient showed cognitive dysfunction.*

Introduction

Spinal neurosurgery is one of the surgical fields where major medical complications can occur, like - acute myocardial infarction, stroke, pulmonary thromboembolism, pneumonia, sepsis including life threatening complications [1].

One of the factors that complicate perioperative period is prone position during spinal surgery. Prone position causes significant physiological changes in a body and there are many factors that have to be kept in mind while patient is lying prone. Those changes are increased thoracic pressure with a decreased left ventricular compliance and filling, increased intra-abdominal pressure with a direct compression on vena cava inferior-both reducing ventricular volume, stroke volume and resulting in hypotension. Increased risk of abdominal compartment syndrome resulting in decreased perfusion of intra-abdominal organs with the following multi organ failure and others [2]. Arterial hypotension and decreased blood return in systemic circulation directly impacts brain circulation and its oxygen supply. Adequate oxygenation of the brain is one of the main tasks during anaesthesia although brain being one of the most important organs stays one of the least monitored organs during the surgery [3, 4].

Adverse effects of prolonged hypoxia of the brain are already well documented. There are studies showing increased incidence of neurophysiological dysfunction, prolonged hospital length of stay, major organ morbidity and mortality in patients that demonstrate cerebral oxygen desaturation episodes during surgery [5-7].

Jobsis introduced the world with the near infrared spectroscopy use in cerebral oxygen saturation monitoring already in 1977 [8]. This principle has been implemented in cerebral oximetry devices. Cerebral oximeters provide noninvasive, continuous monitoring of cerebral oxygenation giving a possibility of early harmful event detection and early intervention to avoid further damage [4, 9]. Cerebral oximeters work based on near infrared spectroscopy principle which includes wave lengths between 700-1000nm which are capable of penetrating the skull and underlying cerebral tissues

[10]. Two electrodes have been attached to the patient's forehead and incorporate light emitter and light detector. Near infrared light coming from emitter is further absorbed in the cerebral tissue and based on the fact that oxyhemoglobin and deoxyhemoglobin absorbs the near infrared light differently we can estimate the oxygen usage in the brain. First cerebral oximeters have been used already 30 years ago but only lately have gained their popularity in different medical fields.

Materials and methods

28 patients (male 16, female 12, medium age 56±12.5 years) were scheduled for spinal neurosurgery in prone position (transpedicular fixation - 15, micro discectomy - 8, removal of spinal tumours - 5). Regional cerebral oxygen saturation (rScO2) was continuously monitored throughout the whole surgery using INVOS 4100 NIRS cerebral oximetry device. Baseline rScO2 values were determined before the induction of anaesthesia. The accepted normal rScO2 values were between 60-80%. NIBP, HR, EtCO2, SpO2 were also monitored. All patients received standard general anesthesia: induction with fentanyl 0.1-0.2mg, propofol 1-2mg/kg, cisatracurium 0.2mg/kg; maintenance with fentanyl 0.03-0.06µg/kg/min, cisatracurium 0.06-0.1mg/kg/h, and sevoflurane to MAC 0.7-1.0, FiO2 0.5. After the surgery all patients were extubated in the operating room.

We also assessed intraoperative blood loss and postoperative complications (stroke, organ dysfunction, wound infection, days spent in intensive care unit (ICU)) and cognitive dysfunction. Cognitive function was assessed using MoCA Montreal - Cognitive Assessment scale before surgery and 2 days after the surgery. MoCA scores range between 0 and 30. A score 26 or over is considered to be normal.

Statistical analysis was performed using SPSS V.23.

Results

We didn't observe any significant changes in our calculated mean rScO2 values between supine and prone position. Mean rScO2 during induction of anaesthesia was 71% above the left cerebral hemisphere, 72% above the right. When the patient was lying in prone position during surgery, mean rScO2 values were 74% above both cerebral hemispheres. Mean rScO2 at the end of surgery when the patient was lying again supine, was 73% above the left and 73% above the right cerebral hemisphere (**Figure 1**).

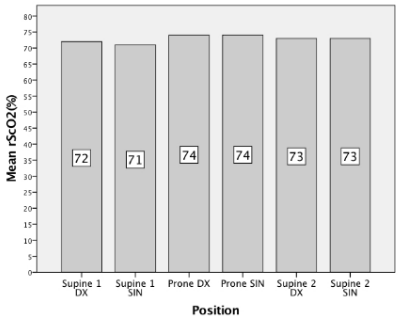

Figure 1: Mean rScO2 (%) values-supine and prone position (Supine1- supine position during induction of anaesthesia; Supine2- supine position at the end of the operation)

Medium rScO2 throughout the whole surgery was 73%± 1.4. The lowest rScO2 values were observed in spinal tumor group: TPF 73% ± 1.25, MDE 76% ± 0.69, Spinal Tu 68% ± 0.90.

Despite our calculated mean rScO2 values, 11 out of 28 patients showed a mild to moderate decrease in rScO2 during prone position with a maximum decrease of 27% in rScO2 from the patient's individual baseline (**Figure 2**).

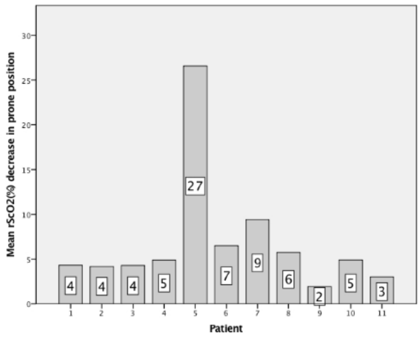

Figure 2: Mean intraoperative rScO2 (%) decrease in prone position from baseline values observed in 11 patients.

The average duration of operation was 110min (TPF=112min; MDE=125min; spinal Tu=126min).

The medium blood loss was 308 ml (TPF=400ml; MDE=175ml; spinal Tu=200ml).

The medium arterial pressure (MAP) was 87 mmHg±7.4. We observed a medium strong correlation between MAP and medium rScO2 values (r=0.31).

We didn't observe any postoperative complications like wound infections, severe organ dysfunction. One patient was admitted to ICU due to intraoperative blood loss management.

We observed a mild cognitive decline for 1-3 points in MoCA scale in 8 patients with a medium rScO2 of 69% in this patient group. One patient showed cognitive dysfunction with the MoCA 27 points before surgery and MoCA 23 points 2 days after the surgery which correlates with patients lower intraoperative rScO2 values of medium rScO2 62% compared to overall average intraoperative rScO2 73% in the whole patient group.

Discussion

Oxygen metabolism in the brain can be detected using different monitoring techniques, like jugular venous oximetry, brain tissue oxygen monitoring (PbO2) - Clark electrode or cerebral micro dialysis, but those are all invasive methods restricting their daily routine use, especially intraoperative [9]. Cerebral oximeters are non-invasive monitors which are easy to use and can provide additional intraoperative patient safety.

Although our first experience showed that there are no significant changes in mean rScO2 values in prone position during spinal neurosurgery, Deiner et al. in his study showed that a mild cerebral desaturation event was 2.30 times more likely for a patient in prone position compared to supine in elderly patient population (>68 years) [11], which is an important mark as the patient population is becoming older.

Postoperative cognitive dysfunction or decline following surgery is a raising issue [14] and can impair postoperative patient recovery [15]. In our study we observed a mild cognitive decline in 8 patients and cognitive dysfunction in 1 patient which shows a total cognitive impairment in around 1/3 of our patients. Steinmetz et al. in his study has shown that around 1/6 of patients undergoing non-cardiac surgery can present postoperative cognitive dysfunction [12]. In regard to spinal surgery, Trafidlo et al. showed a significant ($p<0.05$) difference in the presence of cognitive deficiencies between the patient groups-one that received intraoperative rScO2 monitoring and one that didn't receive it during spinal neurosurgery in prone position [13].

Evaluating intraoperative changes in rScO2 values is a complex decision making process, since values are affected by many variables, like intraoperative blood loss, patient's hemoglobin level, medications used during operation as well as the patient's comorbidities. Still cerebral oximetry remains a valuable intraoperative monitoring device.

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Fourth Publication

10.1515/chilat-2017-0009

DE GRUYTER OPEN

ACTA CHIRURGICA LATVIENSIS • 2017 (17/1)

ORIGINAL ARTICLE

Regional Cerebral Oxygenation Changes Monitored with Near Infrared Spectroscopy Device During Spinal Neurosurgery in Prone Position and Postoperative Cognitive Dysfunction

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Summary

Introduction. The adverse effects of hypoxia are well known, especially regarding the brain, and can lead to postoperative cognitive disturbances. On the other hand, the brain is still one of the least monitored organs intraoperatively. Near infrared spectroscopy devices are non-invasive continuous cerebral oxygenation monitoring devices that can also be used intraoperatively.

Prone position used during spinal neurosurgery is of particular importance regarding physiological changes that can occur in the human body and can lead to reduced blood and oxygen supply of the brain.

Aim of the Study. The aim of the study was to determine whether prone position used during spinal neurosurgery impacts cerebral oxygenation and patients' cognitive performance after the surgery.

Material and methods. 40 patients were included in the study (32 study group, 8 control group). Patients were scheduled for spinal neurosurgery in prone position. All patients received standard general anaesthesia. In the study group regional cerebral oxygen saturation ($rScO_2$) was continuously monitored using INVOS 4100 near infrared spectroscopy device. During the surgery every 5 minutes in study and control group medium non–invasive blood pressure, heart rate, peripheral oxygen saturation, exhaled CO_2 and cerebral oxygenation measurements were fixed. We also fixed intraoperative blood loss and duration of the operation. Cognitive function was assessed in both groups using Montreal - Cognitive Assessment (MoCA) scale before surgery and two days after the surgery.

Results. We didn't observe any significant changes in our calculated medium $rScO_2$ intraoperative values. During induction of anaesthesia when patients were lying supine $rScO_2$ above the right cerebral hemisphere was $rScO_2$ 72±9.7%, above the left cerebral hemisphere 71± 9.7%. Cerebral oxygen saturation in prone position was $rScO_2$ R 74±10.7% and $rScO_2$ L 74±10.1%. At the end of the surgery when patients were lying supine again $rScO_2$ R was 74±9.3% and $rScO_2$ L was 74±7.9%.

We didn't observe any differences in medium MoCA scores when comparing study and control group. MoCA score before surgery in the study group was 24.1±2.9 points and 24.6±4.1 points in the control group. MoCA performed 2 days after the surgery was 24.6 ±3.2 points in study group and 24.6±2.4 points in control group.

Conclusions. No significant changes were observed in medium MoCA scores between patients who intraoperatively received non-invasive cerebral oxygen saturation monitoring and patients who did not receive it.

Despite medium calculated MoCA scores, individually we observed postoperative cognitive function impairment for MoCA 1-2 points in 5 out of 8 patients in the control group, but in the study group only 1 patient out of 32 showed cognitive dysfunction.

Intraoperative regional cerebral oxygen saturation monitoring can help to obviate cerebral desaturation that can lead to postoperative cognitive decline.

Key words: cerebral oxygenation, prone position, cognitive dysfunction.

INTRODUCTION

Adequate oxygen delivery matching tissue and organ demand and metabolic needs is one of the main tasks during anaesthesia (17,11). The adverse effects of hypoxia are already proven and well known, especially regarding the brain (17). Brain is highly dependent on a continuous oxygen supply and it takes only 5 minutes until hypoxic damage occurs (2). Cognitive disturbances after surgery and anaesthesia may emerge and lately have become widely investigated as postoperative delirium or postoperative cognitive dysfunction may be associated with increased mortality, permanent disability (19) as well as predispose dementia (12). There are studies showing increased incidence and positive correlation between neurophysiological dysfunction, prolonged hospital stay length (14) and major organ morbidity and mortality (5) in patients that experience cerebral oxygen desaturation episodes during surgery. In the century where all range of monitoring devices are widely available, brain is still one of the least monitored organ intraoperatively (17).

Cerebral homeostasis, including its oxygenation status, can be monitored using different devices, like, jugular bulb venous oximetry or microdialysis

catheters (10), but being highly invasive, they can not be used routinely, especially intraoperatively. In 1977 Jobsis already introduced to the world the near infrared light spectroscopy (NIRS) principle that can be used to measure oxygen saturation in the brain (8). NIRS cerebral oximetry devices have been known in clinical practice for about three decades. Previously used mainly in cardiac and vascular surgery and as a monitoring device in neurointensive care units at the beginning, now cerebral oximeters have gained their actuality in different medical fields, like, major abdominal, orthopedic surgery, neurosurgery as well as in patient monitoring during and after cardiac arrest and resuscitation or acute atrial fibrillation episodes. NIRS devices are non-invasive and provide continuous cerebral oxygen saturation ($rScO_2$) measurements. Two adhesive electrodes have been attached to patients' forehead – one above the right and one above the left cerebral hemisphere. Both electrodes include a light emitter that generates near infrared light. 650 – 940 nm length waves are capable to penetrate the skull and underlying cerebral tissue. Based on the fact that oxygenated and deoxygenated hemoglobin in cerebral blood absorbs near infrared light differently, it gives us information about oxygen saturation in the brain (13). The non-absorbed light returns back to the sensor incorporated in cerebral oximeters' electrodes and using special algorithms shows current brain oxygenation status. Normal cerebral oxygen saturation values are estimated to be between 60 – 80%, although it is more important to determine patients' individual baseline and keep numbers within 20% range, as 20% decline from baseline values are considered to be significant (7).
Spinal neurosurgery is a surgical field where one of the main anaesthetic and surgical management challenges is patient lying in prone position. Prone position, being non-physiological, causes multiple significant changes in the human body. Increased intrathoracic pressure decreases left ventricular compliance and filling, increased intraabdominal pressure directly compresses vena cava inferior – both of which reduce ventricular volume, stroke volume resulting in generalized hypotension (9). Arterial hypotension and decreased blood return to systemic circulation directly leads to changes in brain circulation with the following disturbances in its oxygen supply. Brain blood supply is also worsened by artificial hypotension that is often kept during spinal surgery with the purpose to diminish intraoperative bleeding.
The aim of the study was to determine whether prone position used during spinal neurosurgery impacts cerebral oxygenation and patients' cognitive performance after the surgery.

MATERIAL AND METHODS

40 patients were enrolled in our study – 32 patients in the study group, 8 - in the control group. Patients were scheduled for spinal neurosurgery (transpedicular fixation, microdiscectomy, removal of spinal tumours) in prone position. All patients received standard general anaesthesia - induction with fentanyl 0.1–0.2mg, propofol 1-2mg/kg, cisatracurium 0.2mg/kg; maintenance with fentanyl 0.03–0.06μg/kg/min, cisatracurium 0.06–0.1mg/kg/h, sevoflurane to MAC 0.7–1.0, FiO2 0.5. In the study group regional cerebral oxygen saturation ($rScO_2$) was continuously monitored using INVOS 4100 near infrared spectroscopy (NIRS) device. Two self-adhesive electrodes were attached to patients' forehead before induction of anaesthesia – one above the right, one above the left cerebral hemisphere. During the surgery every 5 minutes in study and control group medium non–invasive blood pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2) and exhaled CO2 ($EtCO_2$) measurements were fixed. We also fixed intraoperative blood loss and duration of the operation. Cognitive function was assessed in both groups using Montreal - Cognitive Assessment (MoCA) scale before surgery and two days after the surgery to avoid intraoperatively used drug interaction with the test performance. MoCA scores range between 0 and 30. A score 26 or over is considered to be normal.
Statistical analysis was performed using SPSS V.23.

RESULTS

The medium age in our study group was 56±15.8 years, in the control group 58±9.4 years (Table 1).

Table 1. Patients' characteristics

	Study group	Control group
Patients (n)	32	8
Medium age (years)	56±15.8	58±9.4
ASA * class I (n)	0	0
ASA *class II (n)	17	5
ASA *class III (n)	15	3
ASA *class IV (n)	0	0
Surgery performed:		
Microdiscectomy (n)	9	4
Treanspedicular fixation (n)	18	2
Spinal tumour evacuation (n)	4	2
Others (n)	1	

* ASA class – American association of anesthesiologists developed physical status classification system for assessing the fitness of patients before surgery

The average regional cerebral oxygen saturation $rScO_2$ during the whole surgery in our study group was 71±9.8 % above the right (R) cerebral hemisphere and 70±9.2 % above the left (L) cerebral hemisphere.
During induction of anaesthesia when patients were lying supine $rScO_2$ above the right cerebral hemisphere was $rScO_2$ 72±9.7%, above the left cerebral hemisphere 71±9.7%. At the end of surgery when patients were lying again supine $rScO_2$ R was 74±9.3% and $rScO_2$ L was 74±7.9%.

We didn't observe any significant changes in our calculated medium $rScO_2$ values when patients were lying in prone position. Cerebral oxygen saturation in prone position was $rScO_2$ R 74±10.7% and $rScO_2$ L 74±10.1% (Figure 1).

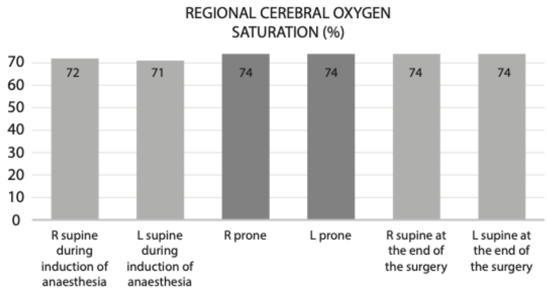

Fig. 1. Medium regional cerebral oxygen saturation $rScO_2$ (%) values above the right (R) cerebral hemisphere and above the left (L) cerebral hemisphere during induction of anaesthesia, in prone position and lying supine at the end of surgery

Despite our calculated mean $rScO_2$ values, 12 out of 32 study group patients individually showed a small to medium drop in $rScO_2$ values in prone position compared to position on spine. The maximum drop we observed in prone position was 34.1% from patients' individual baseline (Figure 2).

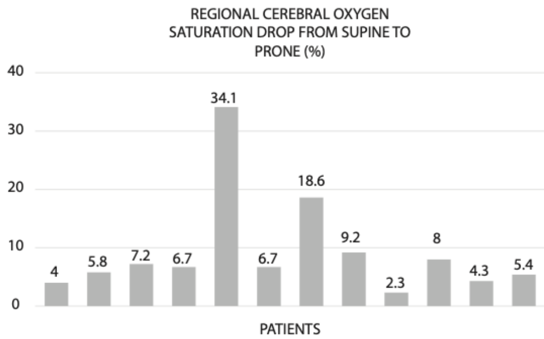

Fig. 2. $rScO_2$ drop in prone position compared to $rScO_2$ values lying supine

The average MAP in the study group was 86±12.7 mmHg which didn't differ much from the average MAP in the control group - 90±12.2 mmHg. In the study group we observed an 11% drop in medium non-invasive blood pressure (MAP) when lying in prone position – from MAP 90 mmHg lying supine to MAP 80 mmHg in prone position. In our control group we observed the same level MAP drop of 10% – from MAP 96mmHg lying supine to MAP 86 mmHg in prone position. We observed medium strong correlation between medium blood pressure and cerebral oxygen saturation values (r=0.31).

The average duration of operation was 110±39.1 min in the study group and 126±48.9 min in the control group. The medium blood loss was 301±335.4 ml – study group, 175±148.8 ml – control group. The average hemoglobin level was 13.56 mg/dl in the study group and 13.57 mg/dl in the control group. We didn't observe any correlation between blood loss, hemoglobin level and $rScO_2$ values (Table 2).

Table 2. Medium duration of operation, medium intraoperative blood loss, medium hemoglobin level in the study group and in the control group

	Study group	Control group
Medium duration of operation (min)	110±39.1	126±48.9
Medium intraoperative blood loss (ml)	301±335.4	175±148.8
Medium hemoglobin level (mg/dl)	13.56	13.57

We didn't observe any differences in medium MoCA scores when comparing the study and the control group. MoCA score before surgery in the study group was 24.1±2.9 points and 24.6±4.1 points in the control group. MoCA performed 2 days after the surgery was 24.6±3.2 points in the study group and 24.6±2.4 points in the control group (Figure 3).

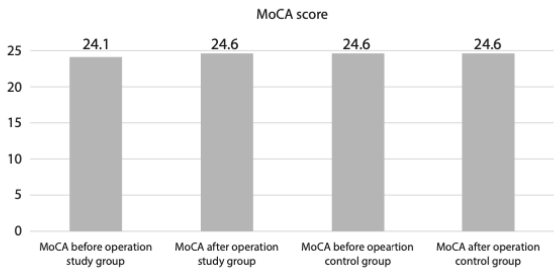

Fig.3. MoCA medium scores in the study group and in the control group before operation and 2 days after operation

In our study group only 1 patient out of 32 showed postoperative cognitive decline. His MoCA score went from MoCA 27 points before surgery to MoCA 23 points after the surgery reveling cognitive dysfunction. We didn't observe any significant changes in other patients' measurements that would differ from average in the study group or would correlate with lower postoperative MoCA score. Patients' intraoperative $rScO_2$ during induction of anaesthesia lying supine was R 75%, L 73%; $rScO_2$ in prone position was R 79%, L 71%; $rScO_2$

lying supine at the end of the surgery was R 73% and L 74%. The average blood loss during the surgery was 150 ml; the duration of operation was 120 min. Patients' hemoglobin level was 15.8 mg/dl.

In our control group 5 out of 8 patients showed a MoCA score decrease of 1 – 2 points after the surgery.

DISCUSSION

There is a limited number of studies published regarding regional cerebral oxygenation monitoring during specifically spinal neurosurgery in prone position. One of them is Deiner et al. (4). In his study he included 211 patients (≥ 68 years) in total. 142 patients underwent surgery lying supine and 63 patients had surgery in prone position. Throughout the whole surgery $rScO_2$ was monitored. They observed that patients undergoing surgery in prone position 2.3 times more often experience mild cerebral desaturation ($rScO_2$ < 65%) than patients having surgery lying supine. In our study patients were significantly younger (medium age 56±15.8 years). We also compared $rScO_2$ values between periods when patients were lying supine at the induction of anaesthesia and at the end of the surgery with the period when patients were lying in prone position. We didn't observe any significant changes in our calculated mean $rScO_2$ values between supine and prone position although in our study it was the same group of patients where measurements were taken.

Our study results are consistent with Fuchs et al. (6) study. He measured how $rScO_2$ changes with different body positions in the same patient group. He included 48 patients (51.3 years) that underwent lumbar discectomy. Besides $rScO_2$ measurements in supine and prone position he also included lateral right, lateral left and sitting positions. In his patient group he didn't observe important changes in $rScO_2$ with different body positions.

Andersen et al. (1) performed a study investigating heads positions influence on $rScO_2$ during spinal neurosurgery in prone position. 48 patients (56.8 years) were included. As a conclusion neutral head position was strongly recommended as the rotation of the head to the left or right showed lower $rScO_2$ measurements. In our study special care was taken while positioning patients in prone position regarding neutral head position, excluding it as a cause for $rScO_2$ intraoperative changes.

Trafidlo group in 2015 (18) published the first study that monitored $rScO_2$ intraoperatively and measured cognitive function in patients undergoing spinal neurosurgery in prone position. In total 43 patients were included - 13 in the study group that received intraoperative $rScO_2$ monitoring using NIRS device and 30 patients in the control group that didn't receive $rScO_2$ intraoperative monitoring. Cognitive function was assesed using a battery of neurocognitive tests preoperatively and after the surgery. They found a significant difference in postoperative cognitive performance where more profound cognitive decline was observed in the control group that didn't receive intraoperative $rScO_2$ monitoring. They met the same study limitation with small patient groups as it is also in our study.

On a daily basis postoperative cognitive dysfunction mostly can not be detected if special neurophysiological tests are not used, although cognitive decline can have serious long term consequences (4) like risk of leaving the labor market prematurely or dependency on social services (16). On the other hand, the significance of NIRS intraoperative utility as a useful additional monitoring device has been described with persuasive results in many other studies, like, Casati et al. (3) who showed that avoiding intraoperative cerebral hypoxia leads to better cognitive performance or Slater et al. (15) which proved that cerebral oxygen desaturation predicts cognitive decline and leads to longer hospital stay.

CONCLUSIONS

No significant changes were observed in medium MoCA scores between patients who intraoperatively received non-invasive cerebral oxygen saturation monitoring and patients who did not receive it.

Despite the calculated medium MoCA scores, individually we observed postoperative cognitive function impairment for MoCA 1-2 points in 5 out of 8 patients in the control group, but in the study group only 1 patient out of 32 showed cognitive dysfunction.

Intraoperative regional cerebral oxygen saturation monitoring can help to obviate cerebral desaturation that can lead to postoperative cognitive decline.

Conflict of interest: None

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Fifth Publication

SURGERY

Changes of Regional Cerebral Oxygen Saturation Using Near Infrared Spectroscopy during Neurosurgical Spine Operations in Prone Position

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Abstract

Near infrared spectroscopy (NIRS) used to maintain cerebral oxygenation during surgery prevents complications such as cognitive dysfunction, organ failure improving postoperative outcome.

The aim of the study was to determine whether prone position during neurosurgical spine surgery using NIRS devices intraoperatively impacts cerebral oxygen saturation.

Fifteen patients undergoing spinal surgery were included in the study. Regional cerebral oxygen saturation ($rScO_2$) was monitored intraoperatively using INVOS 4100. Postoperative complications and days spent in intensive care unit (ICU) were monitored.

Results showed medium $rScO_2$ lying supine left side (L) 72.39 %, right side (R) 72.49 %, in prone position L 74.73 %, R 74.01 %, returning on spine L 74.11 %, R 73.15 %. Seven out of fifteen patients showed a slight up to significant $rScO_2$ decrease when turned from supine to prone position. There was no incidence of postoperative complications, no patients were admitted to ICU.

Patients in prone position intraoperatively experience decrease in cerebral oxygen saturation. Regional cerebral oxygen saturation is a valuable intraoperative measurement in patients undergoing neurosurgical spine operations in prone position to manage perioperative period.

Keywords: regional cerebral oxygenation, prone position, spine surgery.

Introduction

Human brain is a very complex and fragile system. It receives about 15 % of cardiac output, consumes approximately 20 % of all oxygen having the highest metabolic rate of any organ system. Brain is highly vulnerable to desaturation. It consumes oxygen reserves in about 8–10 seconds. Cerebral hypoxia is a leading cause of adverse cerebral outcomes as well as the duration of hypoxia has a direct impact on brain survivability, activity and function. It has been proven that up to 53 % of CABG patients have such complications related to cerebral hypoxia as focal injury, stupor, coma, decrease of intellectual function, seizures, memory deficit, disorientation and death. Cerebral oxygenation cannot be detected by common monitoring devices or can only be detected after damage has already occurred.

Cerebral oximetry is a simple, non-invasive, continuous measurement which gives the ability to monitor regional cerebral oxygen saturation as well as to predict low cardiac output, being an early warning of problems developing in other organ systems. Monitoring standards set by the Association of Anaesthetists of Great Britain and Ireland are: electrocardiography (ECG), pulse oximetry, end tidal carbon dioxide and non-invasive blood pressure; yet, they give little indication of the adequacy of oxygen delivery (DO_2) to the patient during surgery (Bidd, 2013). Systemic arterial and (mixed/central) venous oxygenation can be measured routinely with widely established techniques like pulse oximetry, blood gas analysis, and venous finer oximetry (e.g., in pulmonary artery catheters). However, regional measurement of tissue oxygenation was not possible on a routine clinical basis until recently. Traditionally, tissue oxygenation has been measured by experimental tools that were either invasive (e.g., Clark-type needle electrodes) or dependent on toxic dyes (e.g., palladium phosphorescence), restricting their clinical use (Scheeren, 2012).

Normal values of cerebral oximetry are between 60 % and 80 % or has been kept 20–25 % below the baseline as preoperative readings may differ from patient to patient. Unlike pulse oximetry which is based on light loss due to pulsation of arterial blood, cerebral oximetry bases on light loss due to entire non-pulsative field consisting of approximately 30 % arterial and 70 % venous blood.

The first publications about cerebral oximetry were dated about 30 years ago, but it has gained its importance as an additional monitoring technique in operating rooms and intensive care units only recently. Mostly used in cardiac surgery and for severe head injury monitoring due to high risk for cerebral desaturation because of changes in cerebral blood perfusion and association with such postoperative complications like cognitive dysfunction, stroke, seizures and even death. Lately it has been extensively investigated in association with massive blood loss, surgery in the beach-chair position, surgery in prone position, by head and neck manipulations and one-lung ventilation (Hemmerling, 2008).

Neurosurgical spinal surgery includes one level, to multiple level surgery and patients vary from healthy, stable up to decompensated, hemodynamically unstable and sever trauma patients. Prone position used in spinal surgery leads to physiological changes affecting cerebral blood flow and cerebral oxygenation. The main cause is vena cava inferior and its branches compression causing blood deposition in epidural venous plexus favouring intraoperative blood loss, reducing blood return in the systematic circulation and affecting the cerebral blood flow.

Aim

The aim of the study was to determine whether prone position during neurosurgical spine surgery using NIRS devices intraoperatively impacts cerebral oxygen saturation.

Material and Methods

Fifteen patients scheduled for spinal neurosurgery were included in the study. Inclusion criteria: age > 18 years, spinal surgery performed in prone position (transpedicular fixation (TPF), microdiscectomy (MDE), removal of spinal tumours); exclusion criteria: spinal surgery not performed in prone position. Cerebral oxygen saturation ($rScO_2$) was continuously monitored using INVOS 4100 (COVIDIEN, USA) near infrared spectroscopy oximeter intraoperatively. Non-invasive blood pressure (NIBP), heart rate (HR), end tidal carbon dioxide tension ($EtCO_2$), and peripheral oxygen saturation (SpO_2) were also monitored. All the data was fixed every five minutes. We observed cognitive dysfunction, the rate of postoperative complications – stroke, organ dysfunction, wound infection, days spent in ICU.

All patients received standard anaesthesia. Induction with fentanyl 0.1–0.2 mg, propofol 1–2 mg/kg, miorelaxation with cisatracurium 0.2 mg/kg. For maintenance, there was used fentanyl 0.03–0.06 µg/kg/min, cisatracurium 0.06–0.1 mg/kg/h. During maintenance of anaesthesia sevoflurane was used to achieve MAC 0.7–1.0. Mechanical lung ventilation with inspired oxygen concentration FiO_2 0.5. Two INVOS Cerebral/Somatic Oximetry Adult cerebral oximetry sensors were placed on a patient's forehead before induction of anaesthesia. After operation all the patients were extubated in operating room.

Statistical analysis was performed using the IBM SPSS Statistics.

The study was performed with the approval of Rīga Stradiņš University ethics committee (Nr. 61/28.01.2016).

Results

Fifteen patients (men – 9, woman – 6, mean age – 60 years) were enrolled in the study. Results showed the average regional cerebral oxygen saturation during operation for the left side (L) 79.9 %, the right side (R) 79.52 %. Lying supine before intubation L 72.39 %, R 72.49 %, in prone position L 74.73 %, R 74.01 %, returning back to spinal position L 74.11 %, R 73.15 %. Significant changes in the calculated average $rScO_2$ values between supine and prone position were not observed (Table 1). Despite the calculated average $rScO_2$ values, seven out of fifteen patients showed a slight up to significant decrease in $rScO_2$ when turned from supine to prone position (Table 2). The minimum $rScO_2$ value observed during the whole surgery was 55 % (Table 3). One patient's $rScO_2$ values decreased by 32 % from baseline values when turned to prone position (from 85.5 % supine to 58.5 % in prone position). One patient with stroke in anamnesis showed initial values lying supine 21 % lower than average (57.5 % compared to average $rScO_2$ lying supine 72 %). No cognitive dysfunction, no incidence of stroke or organ dysfunction was observed, no patients were admitted to ICU.

Table 1. Patient details

Patient, No	Age/Sex	Surgery	Blood loss, ml	Mean $rScO_2$, %					
				Supine 1		Prone position		Supine 2	
				Right side	Left side	Right side	Left side	Right side	Left side
1	62/M	TPF	200	72	71	69	65	69	72
2	52/M	TPF	200	85	85	80	80	89	89
3	60/M	TPF	150	57	58	70	71	69	70
4	48/M	TPF	150	72	78	91	94	85	87
5	27/M	MDE	100	86	87	92	92	86	85
6	59/M	TPF	300	61	61	75	78	64	66
7	72/M	MDE	150	69	69	77	80	69	69
8	78/M	MDE	150	69	69	64	64	74	74
9	72/F	MDE	150	74	74	69	68	64	65
10	82/F	TPF	500	70	70	73	73	70	70
11	74/M	TPF	2000	85	86	56	61	71	70
12	49/F	MDE	150	59	55	59	58	60	65
13	54/F	TPF	700	62	62	85	84	74	76
14	37/F	MDE	150	89	89	83	83	83	83
15	84/F	Th1 meningioma	150	75	68	61	63	66	66
Average $rScO_2$ (%)				72	72	74	74	73	74

M – male; F – female; TPF – transpedicular fixation; MDE – microdiscectomy.
Supine 1 – position on spine before prone position at the beginning of surgery.
Supine 2 – position on spine after prone position at the end of surgery.

Table 2. Medium $rScO_2$ (%) in supine and prone position

Patient, No	Medium $rScO_2$, %		$rScO_2$ decrease, %
	Supine position	Prone position	
1	71.75	67.44	4.31
2	85.00	80.83	4.17
3	69.00	64.71	4.29
4	74.00	69.13	4.88
5	85.50	58.93	26.57
6	89.50	83.00	6.50
7	72.00	62.58	9.42

Table 3. Descriptive $rScO_2$ (%) values for each patient during surgery

Patient, No	Mean $rScO_2$ value, %	Std. Deviation	95 % Confidence Interval for mean		Minimum $rScO_2$ value, %	Maximum $rScO_2$ value, %
			Lower bound	Upper bound		
1	69.75	2.72	66.90	72.60	65.00	72.00
2	85.05	3.80	81.07	89.04	80.80	89.33
3	65.98	6.62	59.03	72.94	57.00	71.40
4	84.81	8.28	76.11	93.50	72.00	94.00
5	88.40	3.08	85.17	91.63	85.80	92.38
6	67.32	6.97	60.01	74.64	61.00	78.47
7	72.42	5.03	67.13	77.70	69.00	80.50
8	69.24	4.16	64.87	73.60	64.71	74.00
9	69.43	3.99	65.23	73.62	64.50	74.00
10	71.65	1.45	70.13	73.18	70.67	73.69
11	71.65	12.01	59.04	84.25	56.67	86.00
12	59.37	3.26	55.94	62.79	55.00	65.00
13	74.32	10.11	63.71	84.93	62.50	85.07
14	85.17	3.36	81.64	88.69	83.00	89.50
15	67.03	4.75	62.04	72.01	61.58	75.25
Total	73.44	9.94	71.36	75.52	55.00	94.00

Discussion

Non-invasive cerebral oxygenation monitoring has lately gained its importance and topicality in different medical fields. Being non-invasive, it offers a possibility to use it intraoperatively as an extra monitoring device and enhances patient safety and improves surgical outcome by reducing postoperative complication rate.

According to literature, no significant changes in $rScO_2$ were observed during prone position intraoperatively which also correlates with our first 15 patients' data (Fuchs, 2000). Deiner et al. in their study showed that mild cerebral desaturation episodes were 2.3 times more frequent for elderly patients (> 68 years of age) undergoing surgery in prone position vs. supine (Deiner, 2014). In our study patients' mean age was 60 years and our average values did not show $rScO_2$ decrease when patients were turned from supine to prone position although 7 out of 15 patients $rScO_2$ medium values decreased while being in prone position.

There are studies performed regarding the monitoring of brain saturation and the interventions to restore its proper values to improve treatment outcomes, particularly in regard to the incidence of neurological complications and postoperative cognitive dysfunction as well as the intraoperative reduction of brain saturation which correlates with prolonged treatment in ICUs and increased mortality (Biedrzycka, 2016). In our study we did not observe any postoperative complications such as stroke, organ dysfunction or cognitive dysfunction after surgery which also correlates with the fact that no significant intraoperative $rScO_2$ decrease was observed.

A systematic review was undertaken to determine whether spinal surgery in prone position impacts cerebral oxygenation. Relevant publications were found using PubMed database. Search strategy included MeSH terms: (Spectroscopy) OR (Monitoring/Intraoperative) OR (Spine) OR (Prone position), in total 309 articles were found (published between 2000 and 2014). Only 3 articles met all the criteria ((Spectroscopy) and (Monitoring/Intraoperative) and (Spine) and (Prone position)) showing that cerebral oxygen saturation monitoring during neurosurgical spine surgery in prone position is still an open field for further investigations.

Conclusion

Although our first experience revealed that the average intraoperative cerebral oxygen saturation changes during neurosurgical spine operations in prone position from baseline values is not significant, 7 out of 15 patients showed a mild to moderate decrease in cerebral oxygen saturation.

Regional cerebral oxygen saturation is a valuable intraoperative measurement in patients undergoing neurosurgical spine operations in prone position to manage perioperative period.

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