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# Baseline regional cerebral oxygen saturation values in a cohort of elderly surgical patients

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# BASELINE REGIONAL CEREBRAL OXYGEN SATURATION VALUES IN A COHORT OF ELDERLY SURGICAL PATIENTS

Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

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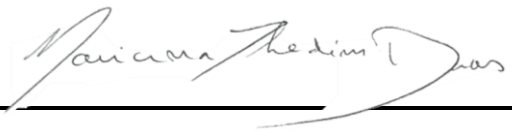

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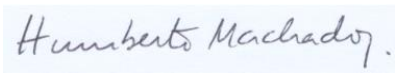

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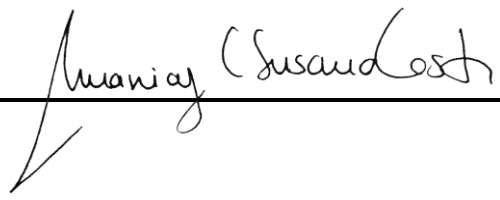

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“There is only one corner of the universe you can be certain of improving, and that's your own self”

Aldous Huxley

# Contents

# Abbreviations List

**ASA** – American Society of Anesthesiologists;
**BMI** – Body Mass Index;
**CCI** – Charlson Comorbidity Index;
**CI** – Confidence Interval;
**COPD** – Chronic Obstructive Pulmonary Disease;
**HLOS** – Hospital Length of Stay;
**INVOS** – In-Vivo Optical Spectroscopy;
**IQR** – Interquartile Range;
**MI** – Myocardial Infarction;
**NIRS** – Near Infrared Spectroscopy;
**N** – Number;
**$rSO_2$** – Regional Cerebral Oxygen Saturation;
**SPSS** – Statistical Package for the Social Sciences;

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# Resumo

O intervalo normal de valores basais de saturação regional de oxigénio cerebral ($rSO_2$) e as variáveis que o podem afetar ainda são um assunto controverso. Frequentemente, os dados existentes encontram-se relacionados com um tipo específico de cirurgia. O objetivo deste estudo consistiu na avaliação dos valores basais de $rSO_2$ em doentes com mais de 65 anos de idade de várias áreas cirúrgicas e na identificação de variáveis relacionadas com esses mesmos valores.

Foi realizada uma análise secundária de um estudo prospetivo realizado entre os dias 23 de julho de 2017 e 2 de maio de 2019. Doentes com ≥ 65 anos com cirurgia eletiva programada foram abordados previamente à cirurgia. O *outcome* primário foi o valor basal de $rSO_2$ medido usando o monitor INVOS$^{TM}$ 5100C. Variáveis pré-operatórias que pudessem influenciar o valor de $rSO_2$ foram consideradas para a análise univariada e multivariada.

Duzentos e cinquenta e quatro doentes foram incluídos na análise. O $rSO_2$ basal foi de 64 [11] (mediana [IQR]), variando entre 29% e 84% num coorte de doentes com 73 [10] anos de idade. Cento e quarenta e dois doentes (56%) foram classificados como estado físico de acordo com a *American Society of Anesthesiologists* (ASA) 2 e a concentração de hemoglobina foi de 13 [3] g/dL. Na análise multivariada, valores mais baixos de $rSO_2$ foram associados a concentração de hemoglobina mais baixa (OR = 0.966, IC 95% (0.956 a 0.976), P <0.001) e a uma classificação do estado físico ASA mais alta (OR = 0.967, IC 95% (0.935 a 0.999), P = 0.047).

Os nossos resultados são compatíveis com os dados existentes, podendo contribuir para a definição de um intervalo normal de valores basais de $rSO_2$ no futuro. A concentração de hemoglobina e o estado físico ASA foram identificados como variáveis independentes associadas ao valor basal de $rSO_2$.



**Palavras-chave:** Saturação regional de oxigénio cerebral, Espetroscopia de infravermelho próximo, Idade avançada;

# Abstract

A normal range for baseline regional cerebral oxygen saturation ($rSO_2$) values and the variables that may affect it are still subject to controversy and often related to a specific type of surgery. The aim of this study was to evaluate the baseline $rSO_2$ in a cohort of elderly patients across multiple surgical areas and to identify variables associated with these values.

A secondary analysis of a prospective study that was conducted between July 23, 2017 to May 2, 2019 was performed. Patients with $\geq$ 65 years scheduled for elective surgery were approached before surgery. Primary outcome was baseline $rSO_2$ collected using INVOS™ 5100C. Preoperative variables that could influence $rSO_2$ were considered. Data was analysed using univariate and multivariate analysis, as appropriate.

Two hundred and fifty-four patients were included in the analysis. Baseline $rSO_2$ was 64 [11] (median [IQR]) ranging between 29% and 84% in a cohort of patients aged 73 [10] years. One hundred and forty-two patients (56%) were American Society of Anesthesiologists (ASA) physical status 2 and haemoglobin concentration was 13 [3] g/dL. On the multivariable analysis, lower baseline $rSO_2$ values were correlated with lower haemoglobin concentration (OR = 0.966, CI 95% (0.956 to 0.976), P < 0.001) and higher ASA physical status (OR = 0.967, CI 95% (0.935 to 0.999), P = 0.047).

Our results were in line with what has been previously found and may contribute to a definition of a normal range of baseline $rSO_2$ values in the future. Haemoglobin concentration and ASA physical status remained as independent variables associated with baseline $rSO_2$.



**Keywords:** Regional cerebral oxygen saturation; Near-infrared spectroscopy; Elderly

# Introduction

The brain is a vital organ essential for the survival of the human being. Although it is the target of hypnotic drugs during anaesthesia, it remains one of the least monitored organs.[1,2] The brain needs a tight management[3] and this is related to the high metabolism rate and oxygen demand for its well-functioning.[1,4]

**The aging population**

Individuals older than 65 represent the fastest growing segment of the population in many parts of the developed world. Aging increases the probability of a person to undergo surgery and, therefore, the number of people who will require anaesthesia for therapeutic and/or diagnostic procedures is expected to increase.[5,6] Anaesthetic drugs are linked to potential neurotoxicity and have an impact in the brain's metabolism, namely oxygenation.[1] It has been shown that the elderly have an increased sensitivity to anaesthetic drugs and are more prone to their haemodynamic depressing side effects, therefore even more special focus is needed regarding cerebral monitoring in this segment of the population.[7]

**The NIRS technology**

The Near Infrared Spectroscopy (NIRS) is a technology widely used in several areas and has been gaining popularity in anaesthesiology to measure cerebral oximetry.[4,8]

NIRS monitoring allows the recognition of desaturation events[9] and may play a part in the identification of cerebral ischemia. It can be used as part of a portable device which allows real-time, non-invasive monitoring of tissue oxygen saturation, not only in the operative room, but also as a bedside monitor.[10]

Several systems use NIRS technology, one of which is INVOS™ 5100C (Medtronic, Ireland) that allows recording of regional cerebral oxygen saturation ($rSO_2$) by placing small sensors in the patient's forehead.[11] In each sensor there are two photodetectors separated by 3 cm and 4 cm from the emitting diodes of near-infrared light.[12] These diodes emit near-infrared light at 730 and 810nm which provides two advantages: this wavelength can be absorbed by haemoglobin and biological tissues are relatively transparent to it.[13,14,15,16]

INVOS system is based on the balance between the tissue's supply and demand for oxygen.[17] The system measures the oxygen content of the tissues and targets the venous and arterial haemoglobin oxygenation fraction, rather than the arterial compartment only.[2,11,18]

The INVOS system integrates a modified Beer-Lambert law technology and spatially resolved spectroscopy.[19]

The Beer Lambert law, that was actually discovered in Portugal by a French mathematician while looking at red wine[20], may be modified in order to calculate the concentration of a substance with only a few parameters: the extinction coefficient of the substance, the amount of light attenuation and the pathlength that light travels.[8,21] Oxygenated and deoxygenated haemoglobin have different absorption properties in the near-infrared light spectrum which allows for the estimation of their relative concentration[22], the oxyhaemoglobin/total haemoglobin ratio, that is presented as a percentage in the monitor.[15]

In order to avoid contamination from structures other than the brain itself, a principle of spatially resolved spectroscopy is used which states that the distance between the light emitter and detector is proportional to the depth of the investigated tissue.[17] After penetrating the brain, the light is partially scattered and creates an arch between the emitting diodes and the two photodetectors (**Figure 1**). The amount of near-infrared light that is scattered across more superficial tissues (brain, muscle, skull and skin) is measured by the proximal photodetector and the amount which is scattered deeper in the brain is captured by the distal photodetector.[23] Cerebral oxygen saturation value is then calculated through a subtraction algorithm.[24]

**NIRS in clinical practice**

The NIRS technology is most commonly used in anaesthesia during neurosurgery and cardiac surgery.[4] Nonetheless, research is ongoing to investigate its utility in other surgical areas as well for specific patient positionings, such as the beach-chair position.[25]

Before induction of general anaesthesia, the baseline value for each patient should be determined while the patient is still awake so it can be considered as a reference value.[26,27]

NIRS monitoring provides continuous measurements of $rSO_2$ during surgery and anaesthesia. A decrease of 20% or more in baseline $rSO_2$ during the intraoperative period has been considered a marker of brain hypoperfusion.[26,28,29] Cerebral perfusion optimization guided by $rSO_2$ was found to be associated with better outcomes in specific scenarios.[9,30,2]

Lower baseline $rSO_2$ values and intraoperative desaturations were related with worse postoperative outcomes such as cognitive dysfunction[31,32], postoperative delirium[33], higher mortality rate[34,35] and longer hospital length of stay (HLOS).[36]

There is still no consensus regarding the normal range of baseline $rSO_2$ values. This may be due, among others, to the variability of patients' characteristics in each study, type of monitor used and other variables that may influence $rSO_2$.[37] Baseline $rSO_2$ values have

been proposed, however, the available data are sparse and most of the times related to one specific surgical setting.[26,38–40]

Outliers of baseline $rSO_2$ values may be considered as a warning sign during the intraoperative period. Lower values can demonstrate the lack of the brain's ability to increase oxygen extraction during a decline in oxygen distribution.[2] Also, higher baseline $rSO_2$ may also alert for a pathological situation of non-metabolizing tissue with no consumption of oxygen.[41]

Taking this into account, it is fundamental to study baseline $rSO_2$ in different populations in order to establish normative range values. Additionally, more data are needed regarding variables that influence baseline $rSO_2$ to allow for a better perioperative management across multiple surgical areas.

The aim of this study was to evaluate the baseline $rSO_2$ in a cohort of elderly surgical patients and to identify preoperative variables associated with lower baseline $rSO_2$ values.

# Methods

This study is a secondary analysis of a prospective observational cohort study approved by the Centro Hospitalar Universitário do Porto Institutional Review Board (REF[a] 2016.253 (216-DEFI/205-CES and ClinicalTrials.gov Identifier NCT03171766). It was conducted in Centro Hospitalar Universitário do Porto, a tertiary hospital in Portugal from July 23, 2017 to May 2, 2019.

Inclusion criteria included 65 years or older patients scheduled for elective surgery (neurosurgery, urologic surgery, general surgery, orthopaedics surgery, vascular surgery, otorhinolaryngology surgery and maxillofacial surgery) under general or regional anaesthesia or monitored anaesthesia care; and expected to stay a minimum of two nights as in-hospital patients. Patients were excluded if they were scheduled for ophthalmologic or plastic surgery procedures; planned postoperative care in the Intensive Care Unit; had a history of cerebral tumour, stroke or transient stroke; were unable to understand cognitive assessment tests (aphasia, hearing impairment, untreated motor or speech disorders); had a diagnosis of dementia; were chronically medicated with anti-psychotic or anti-cholinergic drugs; and first language other than Portuguese.

After informed and written consent, the following data were obtained pre-operatively: age; sex; body mass index (BMI); number of years of formal education; chronic medication with benzodiazepines or opioids; co-morbidities such as diabetes mellitus, arterial hypertension, dyslipidaemia, obesity, chronic obstructive pulmonary disease (COPD), heart failure, ischemic heart disease/ previous myocardial infarction (MI), chronic kidney disease, peripheral arterial disease, asthma, atrial fibrillation/ flutter, cancer or depression; Charlson Comorbidity Index (CCI); American Society of Anesthesiologists (ASA) physical status; 5-item FRAIL questionnaire (robust, pre-frail or frail)[42]; functional status (partially dependent/ dependent vs independent for activities of daily life); smoking history (ex-smoker/ no smoker vs active smoker); and alcohol use (absent/ light if less than 1 drink per day vs moderate/ severe if more than 1 drink for women or 2 drinks for men per day). Blood laboratory analysis were collected from hospital records. Primary outcome was baseline $rSO_2$.

The baseline $rSO_2$ value was obtained using an INVOS™ 5100C monitor while the participant was in a resting condition, seated down and breathing room air with no additional oxygen supply. A single sensor was placed in the patient's forehead approximately 1 cm above the supra-orbital margin on the opposite side to the patients' dominant hand. The midline of the forehead was avoided due to proximity to superior sagittal sinus which could affect $rSO_2$ readings.[12] After 60 seconds of continuous recording of $rSO_2$ we considered the value that was displayed on the monitor.

Data were collected using Castor EDC platform[43] where a code was generated for each patient to maintain anonymity.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp). The Shapiro-Wilk test and histograms were used to assess the normality of data and, as all continuous variables showed evidence of non-normal distribution, measures of central tendency were presented as median and interquartile range [IQR].

For univariate analysis we used the Spearman's rank-order correlation test for continuous variables including age, BMI, years of formal education, haemoglobin and creatinine. The Kruskal-Wallis rank sum test was used for categorical variables with more than two categories such as the 5-item FRAIL questionnaire and ASA physical status. The Mann-Whitney U test was used for dichotomous categorical variables including sex, chronic medication with opioids and benzodiazepines, co-morbidities as well as functional status, smoking history or alcohol use.

We used a Generalized Linear Model to perform the multivariate analysis. Age was forced into the model and variables with $P < 0.1$ on the univariate analysis were considered into the adjusted model. Statistical significance was set at 5% of confidence interval ($P < 0.05$).

# Results

Seven hundred and fifty-two patients were identified as potential participants, however, 294 were not approached due to logistic constraints, 13 patients declined to participate, 163 had exclusion criteria, 11 were found ineligible during interviews and 9 had their surgery cancelled. From the remaining 262 patients, 3 were excluded due to lack of $rSO_2$ assessment, 1 due to the presence of jaundice[44] in the moment of the interview and 4 due to current treatment with haemodialysis.[45] Ultimately, the total number of patients included in this analysis was 254 (**Figure 2**).

The median age of the cohort was 73 [10] years, 165 (65%) were males, with a BMI of 26 [5] $Kg.m^2$, median years of formal education of 4 [3] and 58 (23%) were chronically medicated with benzodiazepines. One hundred and eighty-three (72%) were diagnosed with arterial hypertension, 66 (26%) had diabetes mellitus and 123 (48%) dyslipidaemia. Haemoglobin concentration was 13 [3] g/dL and median CCI score was 4 [3]. One hundred and forty-two patients (56%) were ASA 2 and 55 (22%) were considered frail. Thirty-seven (15%) patients were partially dependent/ dependent for activities of daily life, 21 (8%) were active smokers and 71 (28%) had a moderate or severe consumption of alcohol. Most of the participants were schedule either for general surgery (79 (31%)) or urologic surgery (96 (38%)).

The median baseline $rSO_2$ was 64 [11] ranging between 29% and 84%. Ten (4%) had readings < 50%. The distribution of baseline $rSO_2$ values are shown in **Figure 3**.

On univariate analysis (**Table I**), patients with co-morbidities such as COPD (57 [14] vs 64 [11], P = 0.013) had lower values of baseline $rSO_2$ than those who did not, as well as patients with ischemic heart disease or previous MI (63 [10] vs 65 [12], P = 0.022), peripheral arterial disease (61 [9] vs 65 [11], P = 0.031) and depression (60 [14] vs 65 [11], P = 0.002). Haemoglobin concentration showed a positive correlation with baseline $rSO_2$ values as shown in **Figure 4** ($r_s$ = 0.533, P < 0.001). CCI was negatively correlated with baseline $rSO_2$ ($r_s$ = - 0.186, P = 0.003) and higher ASA physical status was associated with lower values of baseline $rSO_2$ (55 [10] vs 62 [13] vs 66 [11] vs 68 [16], P < 0.001) (**Figure 5**).

Frailty (61[12]) was associated with lower baseline $rSO_2$ values compared with pre-frailty (63 [11]) and robustness (69 [12]), (P < 0.001). Patients who were partially dependent or dependent for activities of daily life had lower values of baseline $rSO_2$ than those who were independent for activities of daily life (60 [9] vs 65 [12], P < 0.001).

In the multivariate analysis only haemoglobin concentration (OR = 0.966, CI 95% (0.956 to 0.976), P < 0.001) and ASA physical status (OR = 0.967, CI 95% (0.935 to 0.999), P = 0.047) remained as independent variables associated with lower baseline $rSO_2$.

# Discussion

In this mixed surgical cohort of elderly adults, median baseline $rSO_2$ was 64% [11]. Additionally, we have found that lower haemoglobin concentration and higher ASA physical status were associated with lower baseline $rSO_2$ values. To our knowledge this is the first Portuguese study regarding baseline $rSO_2$ in the elderly.

**Baseline $rSO_2$**

Baseline $rSO_2$ values found in this study were in line with the report of others: Baikoussis et al.[26] found that in older patients submitted to cardiac surgery and carotid surgery, mean baseline $rSO_2$ values were 63.3% and 66.8%, respectively; and Casati et al.[36] report a mean baseline $rSO_2$ values of 63% in a cohort of elderly patients undergoing major abdominal surgery. In a larger sample of patients submitted to cardiac surgery, the median baseline $rSO_2$ was 62% and values below 50% were considered abnormal.[34] On the other hand, our median baseline of $rSO_2$ was higher than the mean 58.6% found by Yao et al[39] in a cohort of 101 patients undergoing cardiac surgery. However, in this study, the authors considered the lowest value of $rSO_2$ for their analysis and cardiac surgical patients may have higher microvascular disease burden which could affect $rSO_2$ values.[38]

In our study baseline $rSO_2$ ranged between 29% and 84%. This range is overall in accordance to what has been presented by Papadopoulos et al[40] in a study of 69 older patients undergoing hip surgery where baseline $rSO_2$ ranged between 34% and 88% but approximately 19% of patients had readings < 50%. In our study, only 4% of the patients had baseline $rSO_2$ readings < 50%. Again, these differences may be explained due to the different patient populations (69 hip fracture patients vs 254 mixed surgical setting patients in our study) and the different methodologies used (they reported values referring to the lowest values of $rSO_2$ in either hemisphere and baseline $rSO_2$ was collected after 3 minutes).

**Variables associated with lower baseline $rSO_2$**

In the logistic regression model, only haemoglobin and ASA physical status were associated with lower baseline $rSO_2$ values, which has been previously described by others.[27,34,46,47]

The $rSO_2$ principle is based on the brain's oxygen demand and supply, and oxygen in the blood is almost carried exclusively by haemoglobin.[48] With lower values of haemoglobin, it is expected that the total amount of oxygen reaching cerebral tissue would also be lower and consequently lower values of $rSO_2$ would be obtained. However, it is still ambiguous if lower values of $rSO_2$ are related to lower values of haemoglobin or if it is due to the algorithm used in NIRS technology that relies in the modified Beer Lambert's law. One of the variables

used in the law, the optical pathlength, is marked as a fixed value in most commercially available monitors[23] and this is inversely related to the concentration of the studied substance, in this case oxyhaemoglobin and deoxyhaemoglobin.[49] With lower haemoglobin concentration, molecules are further apart from each other and the optical pathlength increases resulting in an overestimation of the $rSO_2$.[23,50] Due to this possible overestimation of $rSO_2$, haemoglobin concentration should be considered in the interpretation of $rSO_2$ values.

In this study haemoglobin was strongly associated with baseline $rSO_2$ values. Haemoglobin is reported as a predictor of $rSO_2$[51], however, $rSO_2$ may also be a potential tool to estimate haemoglobin concentration.[52] Since NIRS allows a real time measurement of $rSO_2$, this could be a faster, non-invasive, indirect way to estimate haemoglobin concentration intraoperatively. This association is poorly studied but is promising in the future of anaesthetic management.

ASA physical status classification is commonly used in the perioperative medicine to stratify patients according to their health status, being 1 a normal healthy patient and 6 a declared brain-dead patient.[53] Not surprisingly, we found that higher ASA physical status was associated with lower baseline $rSO_2$ values and this association has been previously reported.[34,38,40] One possible explanation, as stated by Valencia et al.[38], is that patients with higher ASA physical status classifications may have a higher cardiovascular burden. Lower $rSO_2$ values could be a consequence of the cardiovascular effects on micro vascularization of the brain producing a reduced blood flow.[38] An association between other co-morbidities such as diabetes mellitus[26] or dyslipidaemia[26] and $rSO_2$ has been suggested in previous studies. However, we did not find a significant association between $rSO_2$ and those co-morbidities or other cardiovascular risk factors including arterial hypertension, ischemic heart disease, previous MI, peripheral arterial disease or obesity.

**Study limitations**

This study has several limitations. First, this is a secondary analysis of a prospective observational study which was not designed or powered to meet our primary outcome. Second, $rSO_2$ was only measured with INVOS™ monitor and the results cannot be generalized for other types of monitors. Third, in this study, $rSO_2$ was measured using only one sensor in one hemisphere and, therefore, potential anatomical variances, such as incomplete circle of Willis or undiagnosed severe carotid stenosis, may have gone unnoticed.[17]

Fourth, this is a single-centre study that included only elderly patients undergoing elective surgery. Generalization to younger patients and other populations should be made with

caution. The population included in this cohort had miscellaneous characteristics which can be a limitation but also a strong point. Fifth, there are other variables associated with $rSO_2$ that were not considered in this study such as partial pressure of carbon dioxide in arterial blood, central venous pressure, cardiac index,[54] temperature[12], skull thickness, and area of cerebrospinal fluid layer.[24] Sixth, we evaluated patients' co-morbidities, but no considerations were made regarding the specific treatment for each pathology which can lead to a potential bias of the status of control of the chronic disease.

# Conclusion

There is evidence that NIRS guided management of cerebral oximetry can be a potential tool to help prevent postoperative adverse outcomes.[9,30] Since it is a trend monitor, a baseline $rSO_2$ determination is fundamental to evaluate desaturations in the intraoperative period. Despite its growing utility in diverse clinical situations, there is still no clear consensus regarding the normal range of baseline $rSO_2$ values.

The median baseline $rSO_2$ value found in this study may contribute to the establishment of normative data since our results were in line with the literature.

In this cohort, only haemoglobin and ASA physical were associated with lower baseline $rSO_2$. Although ASA physical status and haemoglobin concentration were already described as variables that could influence $rSO_2$ values in previous studies, our study supports these findings and highlights that these two variables should be considered when using $rSO_2$ for monitoring. Haemoglobin was strongly associated with $rSO_2$ and $rSO_2$ can potentially estimate haemoglobin concentration. Hence, more studies are needed to understand the effect, direction and magnitude of this relationship.

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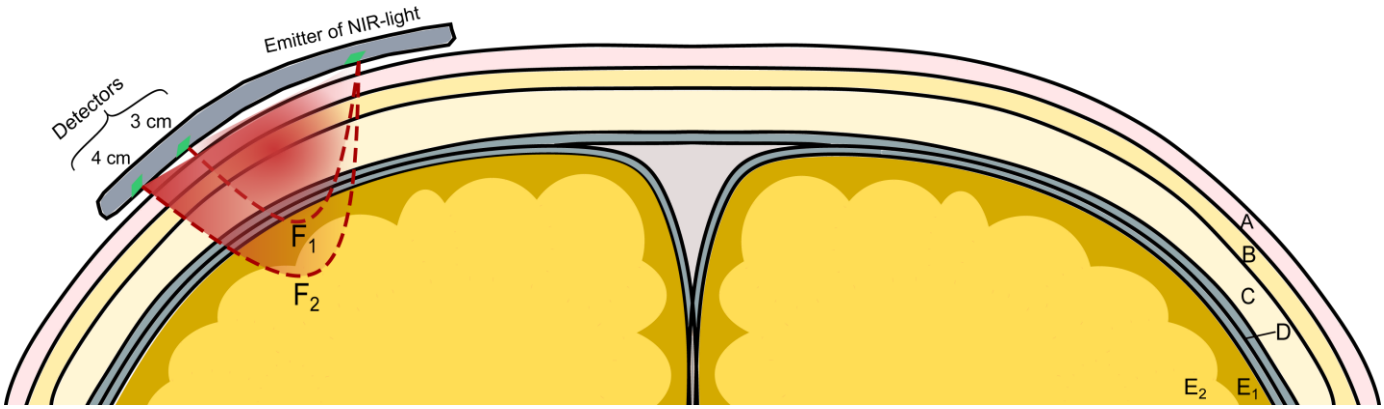


**Figure 1.** Representation of spatially resolved spectroscopy. A-D: extracerebral tissues (A-skin, B-fat layer, C-bone, D-meninges); $E_1$ – grey matter of the brain; $E_2$ – white matter of the brain. $F_1$ represents the arch between the emitter of Near Infrared (NIR) Light and the detector located at 3 cm, where $F_2$ represents the arch between the same emitter and the photodetector placed at 4cm. Regional cerebral oxygen saturation = $F_2 – F_1$.

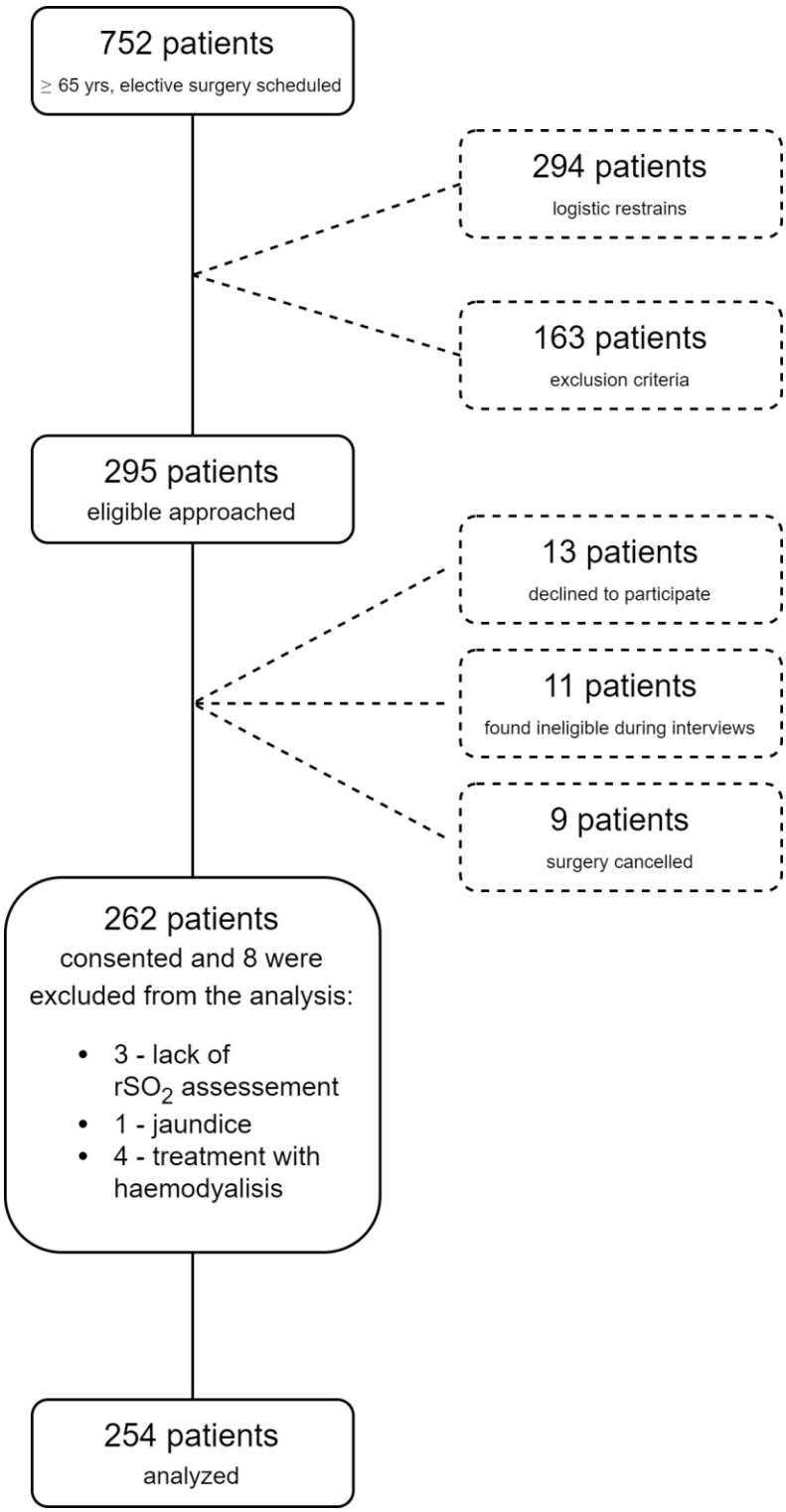


**Figure 2:** Flowchart on recruitment and retention.

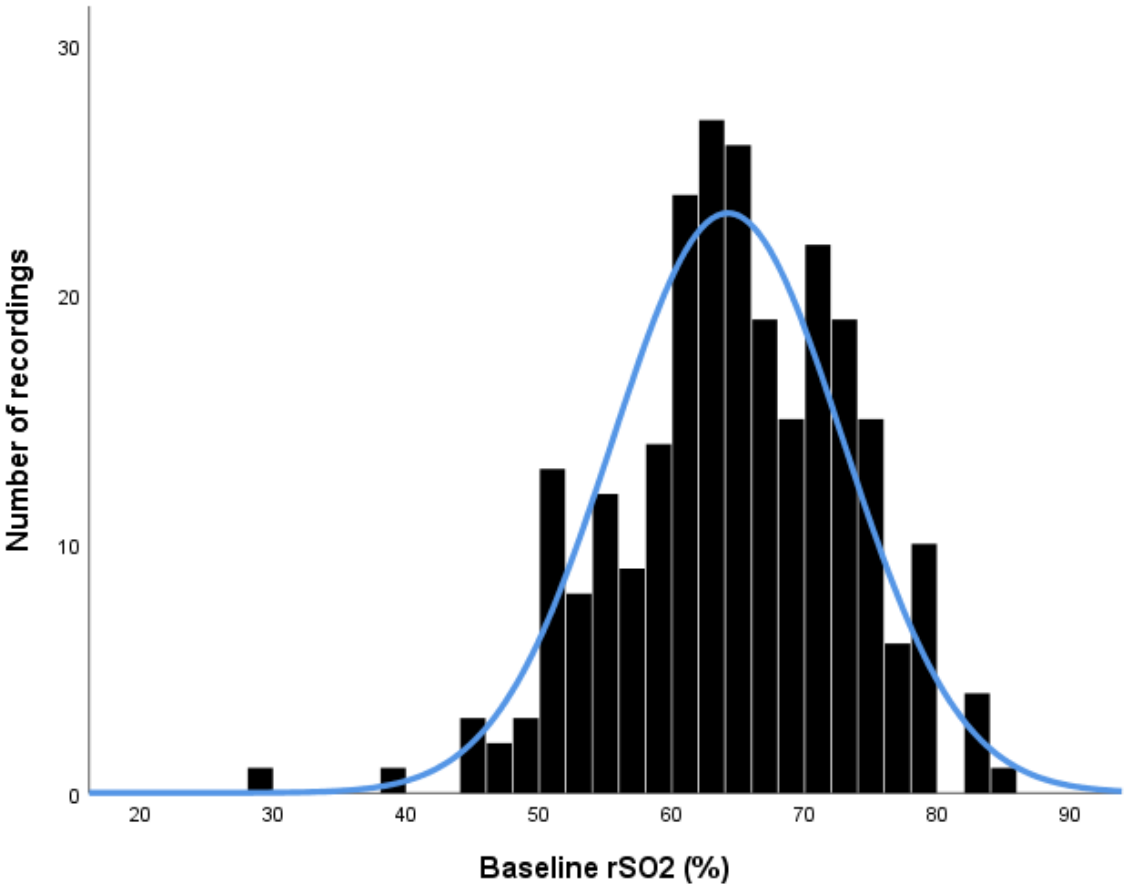


**Figure 3.** Histogram of baseline regional cerebral oxygen saturation ($rSO_2$).

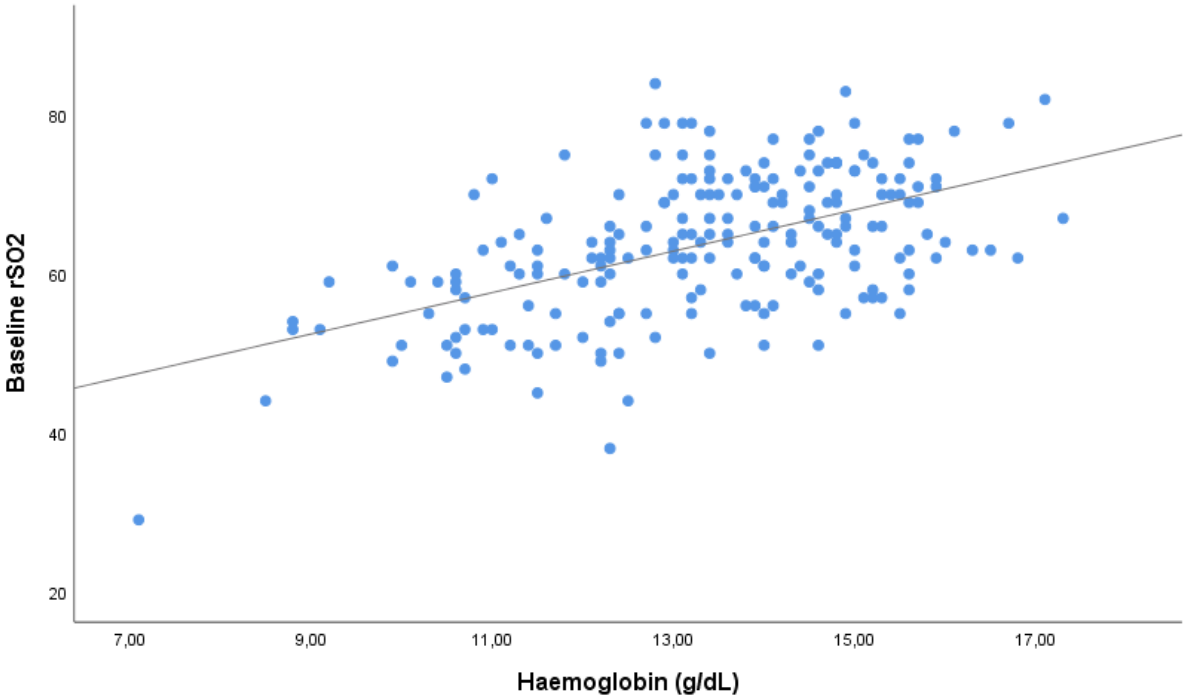


**Figure 4.** ScatterPlot of baseline regional cerebral oxygen saturation ($rSO_2$) and haemoglobin.

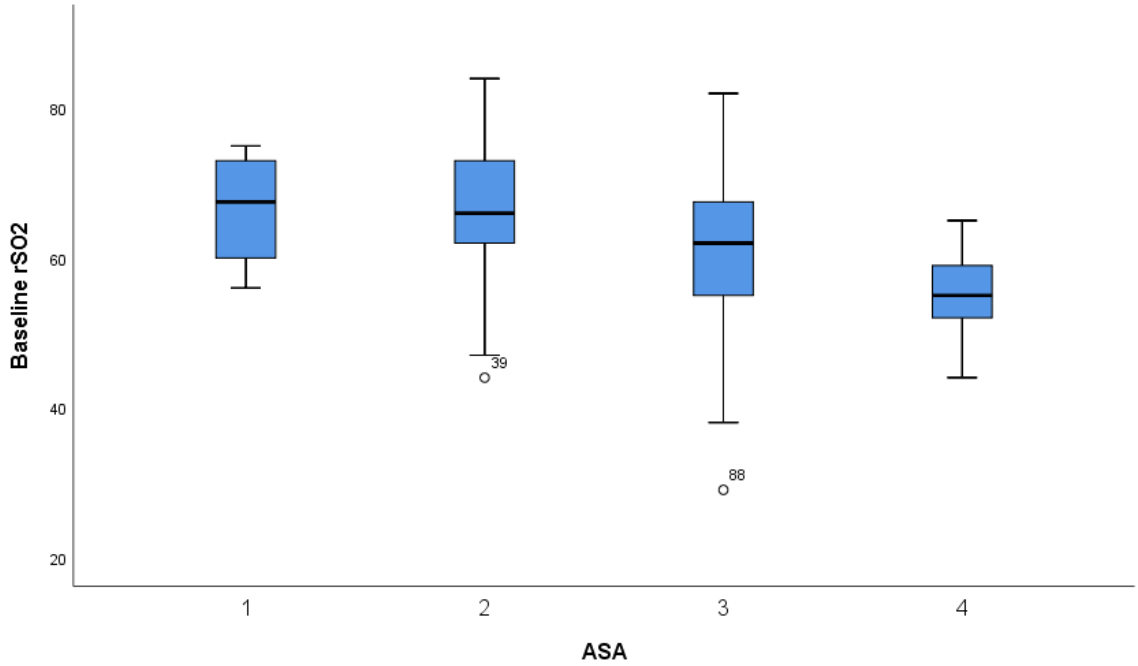


**Figure 5.** BoxPlot of baseline regional cerebral oxygen saturation ($rSO_2$) stratified by American Society of Anesthesiologists (ASA) physical status.

**Table I: Preoperative characteristics of the cohort and univariate analysis.** IQR: interquartile range; N: Number; COPD: Chronic Obstructive Pulmonary Disease; MI: Myocardial Infarction; ASA: American Society of Anesthesiologists; $rSO_2$: regional cerebral oxygen saturation

| | TOTAL=254 | BASELINE $RSO_2$, MEDIAN [IQR] YES VS NO | P-VALUE |
|---|---|---|---|
| **PREOPERATIVE VARIABLES** | | | |
| **AGE, YEARS, MEDIAN [IQR]** | 73 [10] | - | 0.400* |
| **SEX, N (%)** | | | 0.240‡ |
| MALE | 165 (65) | 65 [11] | - |
| FEMALE | 89 (35) | 64 [11] | - |
| **EDUCATION, YEARS, MEDIAN [IQR]** | 4 [3] | | 0.725* |
| **CHRONIC MEDICATION N (%)** | | | |
| BENZODIAZEPINES | 58 (23) | 63 [13] vs 65 [10] | 0.258‡ |
| OPIOIDS | 15 (6) | 62 [5] vs 64 [12] | 0.086‡ |
| **CO-MORBIDITIES, N (%)** | | | |
| DIABETES MELLITUS | 66 (26) | 64 [14] vs 65 [11] | 0.089‡ |
| ARTERIAL HYPERTENSION | 183 (72) | 64 [11] vs 65 [11] | 0.474‡ |
| DYSLIPIDAEMIA | 123 (48) | 64 [14] vs 64 [10] | 0.821‡ |
| OBESITY | 51 (20) | 62 [9] vs 65 [11] | 0.201‡ |
| COPD | 17 (7) | 57 [14] vs 64 [11] | 0.013‡ |
| HEART FAILURE | 21 (8) | 64 [16] vs 64 [11] | 0.194‡ |
| ISCHEMIC HEART DISEASE / PREVIOUS MI | 29 (11) | 63 [10] vs 65 [12] | 0.022‡ |
| CHRONIC KIDNEY DISEASE | 20 (8) | 64 [8] vs 64 [12] | 0.412‡ |
| PERIPHERAL ARTERIAL DISEASE | 18 (7) | 61 [9] vs 65 [11] | 0.031‡ |
| ASTHMA | 7 (3) | 70 [27] vs 64 [11] | 0.665‡ |
| ATRIAL FIBRILLATION/FLUTTER | 22 (9) | 63 [16] vs 64 [10] | 0.133‡ |
| CANCER | 49 (19) | 64 [12] vs 64 [11] | 0.378‡ |
| DEPRESSION | 35 (14) | 60 [14] vs 65 [11] | 0.002‡ |
| **BLOOD LABORATORY ANALYSIS, MEDIAN [IQR]** | | | |
| HAEMOGLOBIN (g/dL) [N=208] | 13 [3] | - | <0.001* |
| CREATININE (mg/dL) [N=201] | 1[0] | - | 0.201* |
| **CHARLSON COMORBIDITY INDEX, MEDIAN [IQR]** | 4[3] | - | 0.003* |
| **ASA, PHYSICAL STATUS, N (%)** | | | <0.001+ |
| 1 | 4 (2) | 68 [16] | - |
| 2 | 142 (56) | 66 [11] | - |
| 3 | 99 (39) | 62 [13] | - |
| 4 | 9 (4) | 55 [10] | - |
| **FRAIL QUESTIONNAIRE, N (%)** | | | <0.001+ |
| ROBUST (SCORE 0) | 87 (34) | 69 [12] | - |
| PRE-FRAIL (SCORE 1 AND 2) | 112 (44) | 63 [11] | - |
| FRAIL (SCORE 3 TO 5) | 55 (22) | 61 [12] | - |
| **FUNCTIONAL STATUS, N (%)** | | | <0.001‡ |
| INDEPENDENT | 217 (85) | 65 [12] | - |
| PARTIALLY DEPENDENT / DEPENDENT | 37 (15) | 60 [9] | - |
| **SMOKING, N (%)** | | | 0.885‡ |
| NO/EX-SMOKER | 233 (92) | 64 [11] | - |
| ACTIVE SMOKER | 21 (8) | 65 [15] | - |
| **ALCOHOL, N (%)** | | | 0.229‡ |
| ABSENT/LIGHT | 183 (72) | 64 [11] | - |
| MODERATE/SEVERE | 71 (28) | 65 [12] | - |
| **SURGICAL AREA, N (%)** | | | |
| GENERAL SURGERY | 79 (31) | 65 [13] | - |
| UROLOGIC SURGERY | 96 (38) | 66 [11] | - |
| VASCULAR SURGERY | 39 (15) | 62 [11] | - |
| NEUROSURGERY | 7 (3) | 60 [11] | - |
| ORTHOPAEDICS SURGERY | 23 (9) | 62 [9] | - |
| OTORHINOLARYNGOLOGY SURGERY | 7 (3) | 58 [17] | - |
| MAXILLOFACIAL SURGERY | 3 (1) | 69 [.] | - |
| **PRIMARY OUTCOME** | | | |
| **BASELINE $RSO_2$, MEDIAN [IQR]** | 64 [11] | - | - |

*Spearman's rank-order correlation test
+ Kruskal-Wallis rank sum test
‡ Mann-Whitney U test