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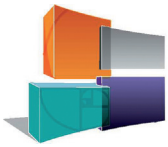

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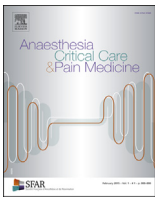

Original Article

Baseline cerebral oximetry values depend on non-modifiable patient characteristics

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ABSTRACT

Objective: The aim of the present study was to evaluate baseline regional cerebral oxygen saturation (rSO_2) values and identify factors influencing preoperative rSO_2 in elective minor surgery.
Study design: Observational analysis *post-hoc*.
Patients and methods: Observational *post-hoc* analysis of data for the patient sample ($n = 50$) of a previously conducted clinical trial in patients undergoing tumourectomy for breast cancer or inguinal hernia repair. Exclusion criteria included pre-existing cerebrovascular diseases, anaemia, baseline pulse oximetry < 97% and low quality rSO_2 sensor signals. Demographic data, comorbidities, and ASA physical status as well as height and weight were collected prospectively from all patients. Baseline rSO_2 values were recorded while the patient breathed room air, using the INVOS 5100C monitor™ (Covidien, Dublin, Ireland).
Results: Thirty-seven women (72%) and 13 men (28%) 48 ± 13 years of age were enrolled in this study. Baseline rSO_2 was 62.01 ± 10.38%. Baseline rSO_2 was significantly different between men (67.6 ± 11.2%) and women (60 ± 9.4%), ($P = 0.023$). There were also differences between baseline rSO_2 and ASA physical status (ASA I: 67.6 ± 10.7%, ASA II: 61.6 ± 8.4%, ASA III: 55.8 ± 13.9%, $P = 0.045$). Baseline rSO_2 had a positive correlation with body weight ($r = 0.347$, $P = 0.014$) and height ($r = 0.345$, $P = 0.014$). We also found significant differences in baseline rSO_2 among patients with and without chronic renal failure ($P = 0.005$). No differences were found in any other studied variables.
Conclusions: Non-modifiable patient characteristics (ASA physical status, sex, chronic renal failure, body weight and height) influence baseline rSO_2.

1. Introduction

Regional cerebral oxygen saturation (rSO_2) is used to monitor cerebral oxygenation based on the principles of near-infrared spectroscopy. Its main advantage is that it evaluates brain oxygenation non-invasively in the frontal region of the cerebral cortex [1]. It is capable of evaluating the relationship between oxygen delivery and demand since it measures haemoglobin saturation in the entire tissue bed, including venous and arterial blood. In this way, cerebral oximetry monitoring can provide an early warning for changes in the relationship between oxygen delivery and consumption. Its use has demonstrated a reduction in postoperative cognitive deficits and hospital stay in situations of cerebral hypoperfusion (cardiac [2], thoracic [3,4] and abdominal surgeries in elderly patients [5,6]).

The main disadvantage of rSO_2 is the absence of a simple, uniform and universal value defining pathological desaturation. This is due to the wide variability of rSO_2 baseline values among patients [7]. Various studies have evaluated different factors influencing baseline rSO_2 without clear results. Determining baseline rSO_2 is important because the definition of cerebral desaturation threshold depends on the baseline value. We designed the present *post-hoc* analysis to establish factors that affect baseline cerebral rSO_2 values.

2. Materials and methods

This *post-hoc* analysis was carried out with data from a previously published clinical trial conducted in a tertiary hospital

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between September 2009 and February 2010 [8]. The study was approved by the Ethics Committee of the Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain (registration number 09/021). After written informed consent, 54 patients aged between 18 and 65 years, who had undergone elective minor surgery (tumourectomy for breast cancer or inguinal hernia repair), were included in the study. Non-inclusion criteria were pre-existing cerebrovascular diseases, anaemia according to WHO criteria (haemoglobin in females < 12 g/dL and in males < 13 g/dL), baseline pulse oximetry $< 97\%$ and low quality rSO_2 sensor signals.

Demographic data, comorbidities, haemoglobin and ASA physical status were prospectively collected from all patients. Noted comorbidities were arterial hypertension, chronic kidney disease, ischemic heart disease, Diabetes Mellitus and chronic obstructive pulmonary disease. Chronic kidney disease was defined as glomerular filtration rate < 60 mL/min/1.73m^2.

Baseline rSO_2 values were measured while the patient breathed room air, using the INVOS 5100C^{TM} monitor (Covidien, Dublin, Ireland). Sensors were placed on the patients' foreheads, in accordance with the manufacturer's instructions. Before recording the data, we checked for a good signal, free of artifacts, using the Signal Strength Indicator (SSI). No premedication was administered. Also, bispectral index data (BIS VISTA, Aspect Medical Systems TM, Massachusetts, USA), mean arterial pressure, heart rate and pulse oximetry (Cicero EM PM8060^{TM}, Dräger, Lübeck, Germany) were simultaneously recorded.

In the original conducted trial, patients were randomly assigned propofol or sevoflurane anaesthesia. Anaesthesia was maintained with propofol (4–8 mg/kg/h) or sevoflurane (1–2% end-tidal concentration) according to group. Both groups used remifentanil with doses of between 0.05–0.3 μg/kg/min at the anaesthesiologist's discretion. Neuromuscular block was achieved with a cisatracurium bolus, maintaining one or two responses in a train-of-four stimulation.

This *post-hoc* analysis used data for a patient sample ($n = 50$) from a previously conducted clinical trial. The mean differences were analysed using Student *t*-tests and ANOVA for quantitative variables. Distributions were evaluated by Kolmogorov-Smirnoff Z tests. Differences between proportions were tested via contingency analysis using Chi^2 tests and by Fisher exact tests when needed. Correlations among variables with continuous data were assessed with Pearson's *r*. Linear regression was used to identify variables associated with baseline rSO_2 and to analyse the contribution of these variables to the observed baseline rSO_2 variability. Statistical analysis was performed using the SPSS-PC statistical software program (version 15.0; SPSS, Inc., Chicago, IL, 134 USA).

3. Results

Fifty-four patients ranging from 18 to 65 years of age who had been scheduled for breast cancer tumourectomy (22 patients) or inguinal hernia repair (32 patients) were considered for the study. Four patients did not meet inclusion criteria (one because of pre-existing cerebrovascular disease, another due to anaemia, and two more because of poor signal quality of rSO_2 sensors). Fifty patients, 37 women (72%) and 13 men (28%), 48 ± 13 years in age completed the study. Eleven out of 50 patients (22%) were classified as ASA physical status I, 31 (62%) as ASA II and 8 as ASA III (16%). Demographic data, baseline rSO_2 values from the left and the right cerebral hemispheres, baseline pulse oximetry, preoperative haemoglobin and haemodynamic data are shown in Table 1.

Baseline rSO_2 was $62.01 \pm 10.38\%$. The average asymmetry between rSO_2 baseline between the right and left hemispheres was $2 \pm 0.2\%$. Baseline rSO_2 on the right ($61.7 \pm 10.5\%$) and left sides ($62.4 \pm 10.4\%$) were statistically similar ($P = 0.179$). The correlation between both values was positive and highly significant ($r = 0.941$, $P < 0.001$, Fig. 1). Baseline rSO_2 was similar in both types of surgery ($60.7 \pm 9.7\%$ in breast cancer tumourectomy and $63.9 \pm 11.3\%$ in inguinal hernia repair) with no significant differences ($P = 0.291$). Neither were there differences as to the type of anaesthesia (sevoflurane $61.1 \pm 10\%$ and propofol $64.5 \pm 11.4\%$, $P = 0.327$).

Table 1
Demographic data, baseline rSO_2 values, baseline pulse oximetry, preoperative haemoglobin and baseline haemodynamic data. Data are summarized as means ± standard deviations (SD).

	Mean ± SD ($n = 50$)
Age (years)	47.7 ± 13.3
Body mass index (kg/m^2)	27.2 ± 5.4
Body weight (kg)	74.1 ± 15.1
Height (cm)	165 ± 9.2
Male/female	14/36
Haemoglobin (g/dL)	13.2 ± 0.9
Baseline rSO_2 (%)	62 ± 10.3
Baseline rSO_2 left (%)	62.4 ± 10.3
Baseline rSO_2 right (%)	61.7 ± 10.5
Mean arterial pressure (mmHg)	92.7 ± 12.2
Baseline pulse oximetry (%)	99.3 ± 1
Heart rate (b/min)	72.1 ± 12.9
BIS	94.7 ± 5

Baseline rSO_2 had a marginally positive significant correlation with measured weight ($r = 0.347$), predicted weight ($r = 0.342$) and height ($r = 0.345$) (Table 2). We also found differences between sexes. Males had a significantly higher rSO_2 ($67.6 \pm 11.2\%$) than females ($60 \pm 9.4\%$; $P = 0.023$). ASA I patients had a baseline rSO_2 value higher than ASA II patients ($67.6 \pm 10.7\%$ and $61.6 \pm 8.4\%$, respectively), which in turn was higher than for ASA III patients ($55.8 \pm 13.9\%$, Fig. 2). These findings were statistically significant ($P = 0.04$). However, a pairwise Bonferroni *t*-test showed that the difference was between ASA I and ASA III ($P = 0.036$). After comparing baseline rSO_2 with patients suffering from chronic kidney disease, we observed statistically significant differences ($P = 0.005$) (Table 3).

Age and body mass index showed no correlation with baseline rSO_2. Mean arterial pressure, preoperative haemoglobin, heart rate, pulse oximetry and BIS did not have any correlation with baseline rSO_2 either.

Hierarchical stepwise linear regression was conducted with baseline rSO_2 as a dependent variable, with measured body weight, predicted weight, height, and ASA physical status as predictors in an attempt to identify variables that could explain the variability of observed rSO_2 values (Models are shown in Table 4). Regression

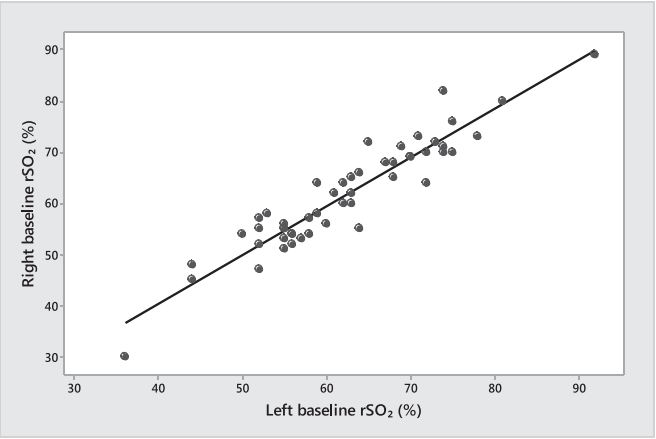

Fig. 1. Correlation between baseline rSO_2 values from the left and the right cerebral hemispheres.

Table 2
Correlation between baseline rSO_2 and demographic and clinical data.

	Pearson correlation *r*	*P* value
Age (years)	−0.198	0.167
Body mass index (kg/m^2)	0.172	0.232
Measured body weight (kg)	0.347	0.014*
Predicted body weight (kg)	0.342	0.015*
Height (cm)	0.345	0.014*
Haemoglobin (g/dL)	0.015	0.915
Mean arterial pressure (mmHg)	−0.064	0.659
Baseline pulse oximetry (%)	0.001	0.996
Heart rate (b/min)	−0.117	0.417
BIS	0.042	0.772

*: *P* value < 0.05 was considered statistically significant.

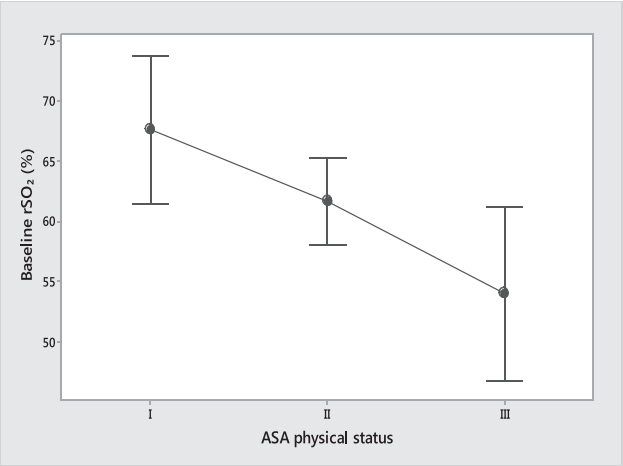

Fig. 2. Baseline rSO_2 according to ASA physical status.

analysis showed that ASA physical status is responsible for 10.6% of the observed baseline rSO_2 variability (adjusted $R^2 = 0.106$; $F_{(1,49)} = 6.792$, $P = 0.012$), whereas ASA physical status and weight combined account for 23.8% of rSO_2 variability (adjusted $R^2 = 0.238$; $F_{(2,49)} = 8.67$; $P = 0.001$). Independent predictors of rSO_2 in the final equation were ASA physical status (β = –0.388; $P = 0.003$) and measured weight (β = 0.383; $P = 0.004$; Table 5).

4. Discussion

Numerous studies have shown that rSO_2 monitoring can improve results in high-risk surgery, optimizing variables that affect the relationship between delivery and consumption of cerebral oxygen. However, the lack of a definite limit due to the variation of baseline values casts a shadow over its promising future as a standard for monitoring. The study of factors influencing rSO_2 allows us to understand and take full advantage of the information it provides.

In our study, we detected potential variables that influence baseline rSO_2 (measured and predicted body weight, height, chronic kidney disease, ASA physical status and sex). Similar to age-related findings in other studies [9–12], we noted that younger patients present a higher basal rSO_2. The variability of the optical characteristics of the cerebral cortex may play an important role. According to Kishi et al. [9], increased myelination of the cerebral cortex with age produces a greater dispersion of the infrared light passing through the brain. This explains why younger patients have higher baseline rSO_2. However, although myelination of the frontal cortex can be extended up to 20–30 years, it is also known that at a later age demyelination occurs [13]. In any case, the variation of optical cerebral characteristics with age could explain the influence of age on baseline rSO_2.

Table 3
Relation between baseline rSO_2 and sex, ASA physical status and comorbidities. Data are summarized as means ± standard deviations (SD).

	Baseline rSO_2	*P* value
Sex		0.023*
Male (13)	67.6 ± 11.2	
Female (37)	60 ± 9.4	
ASA physical status		0.045*[a]
I (11)	67.6 ± 10.7	
II (31)	61.6 ± 8.4	
III (8)	55.8 ± 13.9	
Chronic obstructive pulmonary disease		0.121
No (40)	63.1 ± 10.6	
Yes (10)	57.4 ± 8.1	
Chronic kidney disease		0.005*
No (4)	63.2 ± 9.5	
Yes (46)	48.3 ± 10.2	
Arterial hypertension		0.258
No (33)	63.2 ± 11,2	
Yes (17)	59.6 ± 8.2	
Diabetes Mellitus		0.058
No (43)	63.1 ± 10.2	
Yes (7)	55.14 ± 9.6	
Ischemic heart disease		0.175
No (45)	62.7 ± 10.2	
Yes (5)	56 ± 11.6	

*: *P* value < 0.05 was considered statistically significant.
[a] Bonferroni *t*-test showed that the difference was between ASA I and ASA III ($P = 0.036$).

Table 4
Hierarchical stepwise regression, with baseline rSO_2 as a dependent variable.

Model	*R*	R^2	Adjusted R^2	Standard error of estimate	R^2 change	*F* change	Significant *F* change
1	0.352[a]	0.124	0.106	9.814	0.124	6.792	0.012
2	0.519[b]	0.27	0.238	9.056	0.146	9.370	0.004

[a] Predictors: (constant), ASA physical status.
[b] Predictors: (constant), ASA physical status, measured body weight.

Table 5
Hierarchical stepwise regression models with baseline rSO_2 as a dependent variable: standardised and non-standardised coefficients.

Model		Non-standardised coefficients		Standardised coefficients	*t*	Significance
		β	Standard error	β		
1	Constant	73.449	4.603		15.956	0.000
	ASA	−5.896	2.262	−0.352	−2.606	0.012
2	Constant	55.348	7.281		7.602	0.000
	ASA	−6.496	2.097	−0.388	−3.098	0.003
	Weight	0.260	0.085	0.383	3.061	0.004

Dependent variable: rSO_2.

Another possible explanation for this finding is the decrease of cerebral blood flow (CBF), and cerebral metabolic rate of oxygen ($CMRO_2$) in elderly patients. rSO_2 evaluates $CBF/CMRO_2$ in the cerebral cortex and in the case of these patients, a decrease in both CBF and $CMRO_2$ was observed. Nevertheless, this reduction is not constant; values of CBF decrease to a greater extent than values of $CMRO_2$. This would justify obtaining lower values of rSO_2 in elderly patients due to the decrease in the $CBF/CMRO_2$ ratio [14].

In our results, we discovered that patients with higher ASA physical status had a lower baseline rSO_2. The reason for this difference has never been studied. However, it could be explained by the fact that subjects with higher ASA physical status have more cardiovascular risk factors. In our research, we found that chronic kidney disease was associated with a lower baseline rSO_2. In other studies, Diabetes Mellitus, chronic renal failure and dyslipidaemia are related to low baseline rSO_2 [15,16]. All these comorbidities produce a decrease of CBF because they affect cerebral microvascularization, which results in low baseline rSO_2. Moreover, it has been observed that patients in haemodialysis have low baseline rSO_2 [17]. This is due to chronic anaemia, but also to lower CBF in these patients during periods between dialysis treatments [18].

In regards to the positive correlation of measured and predicted body weight and height with baseline rSO_2, we did not find any justification. The correlation was weak, although statistically significant. Possibly, this justifies why no correlation was observed between BMI and baseline rSO_2. We could not find an explanation for the differences regarding gender.

It is important to establish the factors that influence baseline rSO_2 because the definition of cerebral desaturation is a 20% decrease of the baseline rSO_2 [19]. For this reason, when relative oximetry such as INVOS™ (Covidien, Dublin, Ireland) is used, baseline rSO_2 should always be measured while the patient is awake, before anaesthetic induction. On the other hand, when FORESIGHT™ (CAS Medical Systems, Branford, CT, USA) is used, there is no need for a pre-induction baseline reading because it is an absolute oximeter [20]. It compensates for light scattering losses, eliminating patient dependent variability.

Nevertheless, we believe that the variability observed in age and comorbidities remains even when an absolute oximeter is used. It could be that this oximeter eliminates the variability among patients due to the optical characteristics of the brain, but not when the variability is because of changes in CBF. Therefore, even when employing FORESIGHT™ (CAS Medical Systems, Branford, CT, USA), it is important to determine baseline values and the factors that influence them.

The first limitation of this *post-hoc* analysis is that the patient cohort was originally recruited from a trial. Another limitation was the exclusion of patients with a pulse oximetry of $< 97\%$ and anaemia. Therefore, it is difficult to study the influence of these factors on rSO_2.

In conclusion, our study reveals that baseline rSO_2 is not only influenced by age and comorbidities, as has been observed in other studies, but also by ASA physical status, sex, height as well as measured and predicted body weight. More studies are needed with larger samples that clarify factors that influence rSO_2. This will help establish cerebral oximetry as a standard monitoring technique for high-risk surgery of cerebral hypoperfusion.

Disclosure of interest

The authors declare that they have no competing interest.

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