DEPARTMENT OF ANESTHESIOLOGY

JOURNAL CLUB

Wednesday May 21, 2014
1800 HOURS

LOCATION:
Olivea
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PRESENTING ARTICLES:
Dr. Michael Kahn & Dr. Serena Shum

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SUGGESTED GUIDELINES FOR CRITICAL APPRAISAL OF PAPERS
ANESTHESIOLOGY JOURNAL CLUB
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Two presenters will be assigned to choose and present summaries of their papers. Ideally the two papers will represent similar topics but contrasting research methodologies. The focus remains on critical appraisal of the research and manuscript, more than on the actual contents of the article. Each presenter will then lead an open discussion about the article, based around the guidelines below. The object is to open up the appraisal to wide discussion involving all participants, who will be expected to contribute pending suspension of bar privileges.

GENERAL

1. Title of paper: Does it seem like an important problem? Does it reflect the purpose/results?
2. Authors, institution and country of origin

INTRODUCTION

1. What is the problem being addressed?
2. What is the current state of knowledge of the problem studied?
3. What is the hypothesis being tested?
4. How does testing the hypothesis help solve the stated problem?

METHODOLOGY

1. Study design:
   a) Clinical trial vs. systematic review/meta-analysis
   b) Prospective vs. retrospective
   c) Observational vs. Experimental
   d) Randomized or not
   e) Blinded or not

2. Population studied:
   a) Human, animal, other
   b) Justification
   c) Control groups: experimental vs. historical
   d) Is the sample size/power calculated, and how?
   e) Is the population similar to your own practice?
   f) Single vs. multi-centre

3. Is the study ethically sound?
   a) Clinical equipoise
   b) Does treatment meet standard of care (esp controls)?
   c) Appropriate consent and institutional ethics approval

4. Exclusions: what groups are excluded and why?

5. Experimental protocol
   a) Is it designed to test the hypothesis?

b) Is it detailed enough to be reproducible?
c) Is the methodology validated?
d) Are the drugs/equipment used detailed?
e) How does the randomization take place?

6. What are the primary endpoints?
7. Is power sufficient to justify secondary endpoints?
8. Is the protocol clinically relevant?
9. Data collection and analysis
10. Statistical analysis: Is it appropriate? Are results

RESULTS

1. Are the groups comparable?
2. Were any subjects/data eliminated?
3. Analyzed by intent to treat?
4. Are adequate details of results provided? - data, graphs, tables

DISCUSSION

1. What is the main conclusion of the study?
2. Do the results support this conclusion?
3. Do the results address the stated purpose/hypothesis of the study?
4. How do the authors explain the results obtained?
5. Are there any alternative interpretations to the data?
6. Are the results clinically as well statistically relevant?
7. How do the results compare with those of previous studies?
8. What do the results add to the existing literature?
9. What are the limitations of the methods or analysis used?
10. What are the unanswered questions for future work?

APPLICABILITY OF THE PAPER

1. Have you learned something important from reading this paper?
2. Will the results of this study alter your clinical practice?
3. Was the food and wine up to the high standards expected by self-respecting anesthesiologists?

Cerebral Oximetry and Cognitive Dysfunction in Elderly Patients Undergoing Surgery for Hip Fractures: A Prospective Observational Study

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Abstract: *Aim:* This study was conducted to examine perioperative cerebral oximetry changes in elderly patients undergoing hip fracture repair and evaluate the correlation between regional oxygen saturation (rSO_2) values, postoperative cognitive dysfunction (POCD) and hospital stay.

Materials and Methods: This prospective observational study included 69 patients. Data recorded included demographic information, rSO_2 values from baseline until the second postoperative hour and Mini Mental State Examination (MMSE) scores preoperatively and on postoperative day 7. MMSE score ≤23 was considered evidence of cognitive dysfunction. Postoperative confusion or agitation, medications administered for postoperative agitation, and hospital length of stay were also recorded. Data were analyzed with Student's t-test, Pearson's correlation or multiple regression analysis as appropriate.

Results: Patient age was 74±13 years. Baseline left sided rSO_2 values were 60±10 and increased significantly after intubation. Baseline rSO_2 L<50 and <45 was observed in 11.6% and 10.1% of patients respectively. Perioperative cerebral desaturation occurred in 40% of patients. MMSE score was 26.23 ± 2.77 before surgery and 25.94 ± 2.52 on postoperative day 7 (p=0.326). MMSE scores ≤ 23 were observed preoperatively in 6 and postoperatively in 9 patients. Patients with cognitive dysfunction had lower preoperative hematocrit, hemoglobin, SpO_2 and rSO_2 values at all times, compared to patients who did not. There was no correlation between rSO_2 or POCD and hospital stay. Patients with baseline rSO_2 <55 required more medications for postoperative agitation.

Conclusion: Cognitive dysfunction occurs preoperatively and postoperatively in elderly patients with hip fractures, and is associated with low cerebral rSO_2 values.

Keywords: Anemia*,* anesthesia*,* cerebral oximetry, cognitive dysfunction, elderly, hip fracture, monitoring.

INTRODUCTION

Postoperative cognitive dysfunction (POCD) is an issue that has received significant attention in recent years. The incidence of POCD varies by patient population, but seems higher in cardiac surgery and vascular surgery patients and in the elderly [1]. Patient age, low educational level and previous cerebro-vascular accident [2] are known risk factors for developing POCD, whereas the type of anesthesia does not seem significant [3]. Proposed mechanisms leading to POCD include brain tissue hypo-perfusion, hypoxia or embolism, and the effects of anesthetic agents on the brain.

Trans-cranial cerebral tissue oximetry is a useful tool for monitoring patients undergoing cardiac or vascular surgery and for elderly patients. Normative range for cerebral regional oxygen saturation (rSO_2) is defined as values from 55 to 78 [4]. Cerebral oximetry values are influenced by age, arterial hemoglobin oxygen saturation (sPO_2), carbon dioxide partial pressure, hemoglobin concentration and cardiac index [5-7]. Low cerebral rSO_2 values and episodes of cerebral desaturation are associated with POCD and prolonged hospital stay [8].

However, more data are needed to better evaluate the role of cerebral rSO_2 monitoring in different patient populations [9]. Elderly patients with hip fractures are challenging because they have co-morbidities that could influence rSO_2 values [10, 11]. Furthermore, massive or limited fat embolism can result in reduced cerebral rSO_2 values in patients with hip fractures [12].

This study was conducted to evaluate changes of cerebral rSO_2 values and investigate whether cerebral rSO_2 changes are associated with postoperative cognitive decline in elderly patients undergoing hip fracture surgery.

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MATERIALS AND METHODOLOGY

This prospective observational study was conducted at the University Hospital of Ioannina over a twenty month period in 2008 and 2009. The study was approved by the Institution Ethics Committee and written informed consent was obtained from all patients. In total, 69 patients (27 men, 42 women) scheduled to undergo surgery for isolated sub-trochanteric or inter-trochanteric hip fractures enrolled.

Inclusion criteria were age > 60, operation (scheduled or urgent) for isolated hip fracture, American Society of Anesthesiologists (ASA) physical status 1-3 and patient consent.

Exclusion criteria were age > 90, ASA physical status > 3, renal failure requiring hemodialysis, liver cirrhosis with ongoing liver dysfunction (elevated baseline bilirubin or prolonged INR), known dementia, stroke or other central nervous system disease, history of serious psychiatric illness, alcohol or drug abuse, multiple trauma and the presence of head injury.

Demographic information (age, sex, height, and weight), co-morbidities, ASA physical status, hemoglobin, hematocrit (Hct) and type of anesthesia (general or subarachnoid) were recorded preoperatively on all patients. Cognitive function was assessed preoperatively and on the 7th postoperative day, using the MMSE test.

On arrival to the operating room a venous catheter, electrocardiography (Lead II), cuff for non-invasive blood pressure measurement, pulse oximetry and sensors for cerebral oximetry were placed. Supplemental oxygen administration (40% by Venturi mask) started after baseline rSO2 values were recorded.

The INVOS 5100C (Somanetics Inc., Troy, MI, 48083-4208 USA) monitor was used to measure cerebral rSO_2 values, with sensors placed on the patients' forehead, in accordance with manufacturer's instructions. Baseline rSO_2 value was defined as the average value over a 1-min period beginning approximately 3 min after application of the sensors, but before administration of oxygen and induction of anesthesia. Cerebral rSO_2 data were recorded every 10-seconds.

The choice of anesthesia (general of spinal) was determined by the attending anesthesiologist responsible for each case. General anesthesia was induced with intravenous fentanyl 1.5 μg/kg and propofol 1-2 mg/kg. Rocuronium 0.6 mg/kg was used for muscle relaxation. General anesthesia was maintained with sevoflurane, and depth of anesthesia was adjusted by titrating end-tidal (ET) sevoflurane concentrations between 1 and 2.5% in order to maintain adequate depth of anesthesia, as measured by BIS (BIS Module for the S/5 monitoring system by Datex, Ohmeda, Beaverton, Oregon 97006, USA, BIS Module type E-BIS-00 by GE Healthcare, Helsinki, Finland). Supplemental intravenous fentanyl boluses (2-3 μg/kg) were administered as needed to maintain cardiovascular stability. Initial mechanical ventilation settings were 40% oxygen in air, tidal volume 8 ml/kg; respiratory rate 10-12/min; subsequently, settings were adjusted in order to maintain ET CO_2 between 35 and 37 mmHg. Spinal anesthesia was induced with injection of ropivacaine 7.5 mg/kg (3 mls in total) using a 26G needle at the L2/L3 or L3/L4 interspace, with the midline approach. Mean arterial pressure (MAP) and heart rate remained within 20% of preoperative values in all patients, regardless of the type of anesthesia.

Anesthesia management was aimed at maintaining cerebral rSO_2 above 75% of baseline. Cerebral desaturation (evidence of cerebral hypoxia) was defined as rSO_2 reduction below 75% of baseline or below 50 for more than 15 seconds. When cerebral desaturation occurred, anesthesia providers followed the following treatment algorithm:

- Inspect the ventilator, anesthetic circuit and position of the head.
- Increase blood oxygenation by increasing FiO_2.
- Maintain ET $PaCO_2$ within the upper range of normal. Reduce minute ventilation, to allow ET CO_2 partial pressure to rise if ET CO_2 was < 35 mmHg.
- Restore MAP to baseline if it has dropped by more than 20% below baseline. If INVOS values remain low, then increase MAP by up to 20% above baseline, using intravenous fluids and vasoconstrictors (phenylephrine and/or etilephrine).
- Transfuse packed RBCs in cases where hematocrit is < 27%.
- If the above steps do not restore acceptable rSO_2 values, then give intravenous propofol 0.5 mg/kg bolus to reduce cerebral oxygen consumption.
- In cases of hemodynamic instability, measure cardiac output through a peripheral arterial catheter using the Vigileo system (Edwards LifeSciences, Irvine California 92614-5686, USA) or through trans-esophageal Doppler (CardioQ ODM, Model number 9051-6935, Deltex Medical LTD, PO 19 8TX, UK), and continue hemodynamic stabilization based on hemodynamic data.

Cerebral rSO_2 values were recorded 20 minutes after induction of anesthesia, at the end of surgery and 10 minutes after arrival to the recovery room. In addition, minimum and maximum rSO_2 values were also recorded.

Data collected included hemoglobin and hematocrit values on postoperative day one, hospital length of stay, occurrence of confusion or agitation and the use of medications to treat confusion or agitation. Pharmacologic treatment for confusion or agitation was directed in all cases by the same psychiatrist. In order to maintain consistency, each patient had MMSE preoperatively and one week after surgery by the same examiner. Compared to baseline, reduction of MMSE score by ≥ 2 points was considered evidence of cognitive decline [13].

As this was an observational study, we did not conduct power analysis and there was no randomization or blinding. Data were collected, de-identified and stored in a secure electronic database. All data analysis (except for chi-square) was done with the Statistical Package for the Social Sciences (SPSS) version 17 for Windows (SPSS Inc., Chicago, IL, USA). Chi-square analysis was conducted using the StatCalc component of the Epi Info statistical software package, which is freely available from the website of the Center for

Disease Control and Prevention, at http://wwwn.cdc.gov/epiinfo/. Normality of data was analyzed with the Kolmogorov Smirnov test. Continuous data were analyzed for differences between groups using the two-sided Student's T test, paired T-test or Mann-Whitney U as appropriate. Differences between proportions were analyzed with the chi-square test using Yates correction. Correlations between continuous variables were evaluated with Pearson's r, Spearman's rho, as appropriate. Depending on data distribution, results are presented as mean ± standard deviation (SD) or as median (minimum, maximum).

RESULTS

Of 75 patients who were screened, six patients could not cooperate for MMSE and were excluded. Sixty-nine patients, 27 men (39.1%) and 42 women (60.9%), ages 74±8 years completed the study. 19 of 69 patients (27.5%) were classified as ASA physical status 1, 27 (39.1%) as ASA 2 and 23 (33.3%) as ASA 3. Patient age, preoperative and postoperative hemoglobin and hematocrit, and SpO_2 values are listed in Table **1**.

Baseline cerebral rSO_2 was 60.09±10.20 on the left (baseline rSO_2 L) and 58.64±9.92 on the right side (baseline rSO_2 R). Distribution of baseline rSO_2 values was normal bilaterally. Correlation between right and left-side rSO_2 baseline values was strong and highly significant ($r=0.85$, $p<0.001$).

Compared to baseline, cerebral rSO_2 values increased significantly in both hemispheres 20 minutes after anesthesia induction, at the end of surgery and in the recovery room ($p<0.05$). Minimum intra-operative rSO_2 values were 50.36±9.7 (range 27–65) on the right *vs* 51.36±9.47 (range 32-64) on the left side (Table **2**).

Cerebral Desaturations

Preoperatively: Baseline rSO_2 < 50 and < 45 was observed in 11.6 % and 10.1 % of patients on the left side respectively.

Intra-operatively: rSO_2 < 50 or under 75% of baseline was observed in 38% of patients on the left and 45% of patients on the right side. Reduction of rSO_2 by more than 10 points below baseline was recorded in 34.78% of patients on the left and 30.43% of patients on the right side. Cerebral desaturation was not associated with reductions of arterial oxygen saturation. Minimum rSO_2 <50 was observed at some point in 40% and 50% of patients on the left and right hemisphere respectively.

Recovery room: rSO_2 values <50 or reduction under 75% of baseline occurred in 5.8% of patients on the left and 11.6% of patients on the right side. Similarly, rSO_2 values <45 occurred in 2.89% of patients on the left and 4.35% of patients on the right side. Differences between baseline *vs* peri-operative or recovery room rSO_2values were statistically significant ($p<0.001$).

rSO_2 Values and Type of Anesthesia

Fifty-two patients received general anesthesia and 17 patients received spinal anesthesia (Table **3**). Demographic data, baseline rSO_2 values, and preoperative and postoperative hematocrit did not differ significantly between patients receiving general *vs* spinal anesthesia.

With regards to cerebral rSO_2 values, there were no significant differences between general *vs* spinal anesthesia 20 minutes after anesthesia induction, at the end of surgery or in the recovery room. Furthermore, minimum rSO_2 values, duration of minimum rSO_2 values and duration of hospital stay did not differ between patients receiving general *vs* spinal anesthesia.

Mini Mental State Examination

Overall, MMSE score was 26.23 ± 2.77 preoperatively and 25.94 ± 2.52 one week after surgery ($p=0.326$). MMSE scores were similar in patients who received general anesthesia, compared to those who received spinal anesthesia.

MMSE score ≤23 was recorded preoperatively in 6 patients (8.69%) with baseline rSO_2 < 50. MMSE score ≤23 was recorded postoperatively in 3 more patients (a total of 9 patients = 13.04%). Cognitive function decline (reduction of MMSE ≥ 2 points below baseline) was observed in 9 patients (13.04%) in the first week after surgery.

Patients who developed cognitive dysfunction had significantly lower preoperative hematocrit, hemoglobin and SpO_2. and significantly lower cerebral rSO_2 values at all times, compared to patients who did not develop dysfunction. Comparisons between patients who developed cognitive dysfunction *vs* those who did not are presented in Table **4**.

Duration of hospital stay did not differ between patients who did *vs* those who did not develop postoperative cognitive dysfunction ($p = 0.772$).

Table 1. Age, Preoperative and Postoperative Hematocrit, Hemoglobin and SpO2 Values

	Mean ± SD	Minimum	Maximum	Median
Age (year)	74.4 ± 13.3	60	91	75
Preoperative hematocrit (%)	35.9 ± 4.8	25	47	35.9
Preoperative Hb (gm/dl)	11.8 ± 1.8	8.4	16.2	11.9
Postoperative Ht (%)	32.8 ± 3.8	26	42	32.7
Postoperative Hb (gm/dl)	10.7 ± 1.4	8.0	13.0	10.6
Preoperative SpO_2	96.0 ± 2.3	88	99	97
Postoperative SpO_2	97.0 ± 2.1	90	99	97

Table 2. rSO_2 Values at Baseline, 20 Min After Anesthesia Induction, Intraoperative Minimum and Maximum, at End of Surgery and in the Recovery Room

Time	Right Hemisphere	Left Hemisphere	p
Baseline	58.64 ± 9.91 [34-79]	60.09 ± 10.20 [38-88]	0.031
20 minutes after induction	61.99 ± 8.88*[36-78]	62.86 ± 9.00*[44-87]	NS
Intraoperative minimum	50.36 ± 9.70[27-73]	51.36 ± 9.47[32-77]	NS
Intraoperative maximum	72.25 ± 9.02[52-90]	73.39 ± 8.92[55-89]	NS
End of surgery	61.14 ± 9.51*[37-86]	62.03 ± 9.18*[35-86]	NS
In the recovery room	63.42 ± 11.18*[28-86]	64.33 ± 10.60*[34-89]	NS

Data are presented as mean ± SD (minimum, maximum).
* $p < 0.05$ compared to baseline, NS means Not Significant.

Table 3. rSO_2 Values and Anesthetic Technique

	General (n=52)	Spinal (n=17)	p
Sex (men/women)	20/32	7/10	NS
Age	73.81 ± 14.52	76.12 ± 8.38	NS
Weight	67.06 ± 9.88	71.47 ± 15.65	NS
Preoperative Ht	35.82 ± 4.8	36.18 ± 4.82	NS
Postoperative Ht	33.41 ± 3.86	31.5 ± 1.30	NS
Baseline rSO_2 L	59.73 ± 10	61.18 ± 11.00	NS
Baseline rSO_2 R	58.23 ± 9.85	59.88 ± 10.00	NS
Minimum rSO_2 L	50.83 ± 9.32	53.00 ± 10.00	NS
Minimum rSO_2 R	50.06 ± 9.79	51.29 ± 9.67	NS
Duration of min rSO_2 L	49.9 ± 42.54	51.18 ± 24.60	NS
Maximum rSO_2 R	72.96 ± 9.07	70.06 ± 8.74	NS
rSO_2 L at 20´	62.79 ± 8.56	63.06 ± 10.53	NS
rSO_2 R at 20´	61.83 ± 8.96	62.47 ± 8.86	NS
rSO_2 L in recovery	65.38 ± 10.39	61.12 ± 10.9	NS
rSO_2 R in recovery	64.48 ± 11.48	60.18 ± 9.81	NS
Hospital stay (days)	9.90 ± 4.53	8.94 ± 2.54	NS

Data are presented as mean ± SD, NS means Not Significant.

Low Baseline rSO_2 Values and Outcome

Correlation and regression analysis did not show any association between baseline cerebral rSO_2 values and outcome variables (length of hospital stay, agitation, confusion). However, further analysis using independent samples t-test showed that, compared to patients with baseline rSO_2 L ≥ 55, patients with baseline rSO_2 L < 55 had significantly lower preoperative hematocrit (33.11 ± 3.99 *vs* 37.21 ± 4.57, $p < 0.001$), and also had significantly lower intra-operative, minimum and recovery room rSO_2 values.

Similarly, parametric (t-test) and non-parametric testing (Mann-Whitney test) showed that patients with baseline rSO_2 L < 55 required significantly more medications for treatment of postoperative agitation. However, hospital stay did not differ between these two patient groups.

Table 4. Baseline, Intraoperative and Outcome Data in Patients who Did *vs* Patients who Did Not Develop Cognitive Dysfunction

	Cognitive Dysfunction		p
	Yes (n=18)	No (n=51)	
Age	76.65 ± 8.65	73.63 ± 14.44	NS
Preoperative Ht	33.32 ± 4.44	36.76 ± 4.60	0.009
Preoperative Hb	10.73 ± 1.56	12.20 ± 1.69	0.002
Postoperative Ht	33.67 ± 3.22	32.57 ± 3.51	NS
Postoperative Hb	10.26 ± 1.15	10.82 ± 1.44	NS
Preoperative SpO_2	94.82 ± 2.90	96.63 ± 1.92	0.004
Baseline L	53.71 ± 10.69	62.17 ± 9.21	0.002
Baseline R	53.06 ±12.10	60.46 ± 8.45	0.007
rSO_2 L at 20 min	55.35 ± 9.10	65.31 ± 7.60	<0.001
rSO_2 R at 20 min	55.00 ± 9.20	64.27 ± 7.54	<0.001
Min rSO_2 L	42.35 ± 6.40	54.31 ± 8.41	<0.001
Min rSO_2 R	42.00 ± 7.80	53.10 ± 8.70	<0.001
rSO_2 L end	56.76 ± 9.86	63.75 ± 8.35	0.006
rSO_2 R end	56.29 ± 8.91	62.73 ± 9.24	0.014
rSO_2 L recovery	57.53 ± 12.10	66.56 ± 9.14	0.002
rSO_2 R recovery	56.18 ± 12.63	65.79 ± 9.67	0.002
Days in hospital	9.41 ± 3.18	9.75 ± 4.43	NS
Agitation	0.12 ± 0.33	0.13 ± 0.40	NS

Comparisons using student's t test.
$P<0.05$ was considered significant for all comparisons, NS means Not Significant.

DISCUSSION

The number of elderly people requiring surgery has increased significantly due to increasing life expectancy [8], and aging is accompanied by reduced physiological reserve and numerous co-morbidities. Compared to subjects younger than 65 years, peri-operative complications and postoperative cognitive decline occur more frequently in elderly patients [14]. In our study mean patient age was 74 years.

The main findings of our study were the wide range of observed rSO_2 values (baseline rSO_2 L=60±10, range 34-88, minimum intra-operative rSO_2 50.36±9.7, range 27-73, maximum intra-operative values 72.25±9.02, range 52-90) and the high percentage of patients with peri-operative rSO_2 < 55. Cognitive dysfunction was evident preoperatively in 6 (8.69%) of patients, compared to 9 (13%) patients postoperatively, despite a protocol to optimize cerebral oxygen supply/demand. MMSE values one week after surgery did not differ significantly compared to baseline ($p = 0.326$). The absence of a significant difference between pre-operative and postoperative MMSE values could be explained by the protocol to promptly treat intra-operative cerebral desaturation. Preoperative cerebral desaturation was documented in several patients, and may have contributed to the preoperative cognitive dysfunction observed in our study. Similarly, the observed improvement of cerebral rSO_2 after induction of anesthesia, and the protocol used to preserve intra-operative cerebral perfusion and oxygenation may have protected the CNS from further insult.

Madsen *et al*. established that the normal range for rSO_2 values in 39 resting subjects without cardio-respiratory disease is 55-78 [4], whereas Kim *et al*. reported that mean baseline rSO_2 value was 71 ± 6 in healthy volunteers aged 20-36 years [6]. Similarly, Casati *et al*. reported baseline values 63 ± 8 in healthy elderly (72 ± 5 years) general surgery patients [8], while Edmonds *et al*. reported baseline values 67 ± 10 in 1000 patients (ages 20-90 years) undergoing cardiac surgery [15].

Our findings (low baseline rSO2 values with wide variability of baseline rSO_2 values), can be explained by patient age, low preoperative hematocrit values and perhaps inadequate preoperative fluid resuscitation. In addition, cerebral fat embolism, although a rare event, may contribute to low preoperative rSO2 values.

Cerebral rSO_2 values increased significantly after blood transfusion in our study. This finding is in agreement with the study by Kishi *et al*., which showed negative correlation between cerebral rSO_2 and age, and positive correlation with hemoglobin concentration [5]. Similarly Liem *et al*. reported positive correlation between rSO_2 and hematocrit in newborn infants [16], whereas Yoshitani *et al*. documented positive correlation of rSO_2 with hemoglobin and MAP [17]. Green also reported positive correlation between rSO_2 and hemoglobin, and negative correlation with blood loss [10]. In our study, patients with rSO_2 < 55 had significantly lower hematocrit compared with those having rSO_2 >55.

A significant correlation between reductions of rSO_2 and SpO_2 in healthy adults was mentioned by Germon *et al.* [18]. However, in agreement with results reported by Pedersen *et al.* [19], our study did not show any association between intraoperative cerebral desaturation measured by INVOS and arterial desaturation measured by pulse oximetry.

Depression of the cardiovascular system by general anesthesia can cause inadequate brain perfusion and perhaps result in postoperative neuropsychological dysfunction in elderly patients [20]. Similarly, a study on 60 geriatric (>60 years old) patients undergoing repair of proximal femur fracture, showed that, although cerebral desaturation was more common in patients having spinal anesthesia, the number of patients with at least one rSO_2 dip below baseline did not differ between groups [21]. However, the use of general *vs* spinal anesthesia did not affect cerebral oxygen saturation (rSO_2) or postoperative outcome in our study.

Cognitive function was assessed in our study using the MMSE test, and we considered values ≤ 23 as evidence of cognitive dysfunction. Advantages of the MMSE test include high validity and reliability, ease of use, brevity and suitability for bedside use [22]. In addition, MMSE is very appropriate for repeated cognitive assessments over time. Because other, more sensitive and specific tests evaluating different components of cognitive function have been proposed [3, 8, 23], use of the MMSE could be grounds for criticism. However, we believe the use of MMSE is justified, because of simplicity, and also because reduction of MMSE by 2 or more points below baseline in repeat testing is strong evidence of cognitive decline [13].

Cognitive dysfunction was observed preoperatively and persisted postoperatively in 6 patients with baseline rSO_2 < 50. Among patients with normal baseline rSO_2, three patients developed intraoperative desaturation, had postoperative MMSE ≤23, experienced postoperative agitation and were treated successfully with medications.

Overall, we did not observe any correlation between low baseline rSO_2 values or intraoperative desaturations and outcome (postoperative agitation or confusion, duration of hospital stay). Our results are in agreement with a study by Casati *et al*, which showed prolonged hospital stay in patients who developed intraoperative cerebral desaturations that went untreated [8]. Last, our study showed that patients with baseline rSO_2 < 55 required significantly more medications for agitation, but length of hospital stay did not differ between patients who did *vs* those who did not need treatment for agitation.

CONCLUSION

Our findings show that low preoperative baseline cerebral rSO_2 values are common in elderly patients with hip fractures, correlate with lower preoperative hematocrit, hemoglobin and arterial SpO_2 values and are associated with peri-operative cognitive dysfunction. Published data suggest that a multi-factorial perioperative treatment program including preoperative oxygen supplementation, intravenous fluid resuscitation and arterial oxygen saturation monitoring may reduce the incidence of delirium in elderly hip fracture patients [24], but the value of cerebral oximetry monitoring has not been established and deserves further study. We suggest that cerebral oximetry is a useful tool for monitoring elderly patients undergoing surgery for hip fractures, and could be a meaningful end-point for protocols designed to protect the central nervous system in the perioperative period. Large prospective clinical studies are needed to evaluate the benefits, if any, of monitoring cerebral oximetry in elderly patients undergoing orthopedic surgery, and validate whether this technology can contribute to improved preoperative patient preparation, fewer episodes of cerebral desaturation, less cognitive dysfunction and perhaps improvement in other outcome variables.

ETHICAL APPROVAL AND INFORMED CONSENT

This study was approved by the Institution Ethics Committee. Written informed consent was obtained from all patients who participated in the study.

ACKNOWLEDGEMENT

Declared none.

CONFLICT OF INTEREST

This work was supported solely by Department funds. All authors state that they do not have any conflicts of interest to report.

ABBREVIATIONS

ASA	=	American Society of Anesthesiologists
ET	=	End Tidal
Hb	=	Hemoglobin
Hct	=	Hematocrit
MAP	=	Mean Arterial Pressure
MMSE	=	Mini Mental State Examination
POCD	=	Postoperative cognitive dysfunction
rSO_2	=	regional oxygen saturation
SpO_2	=	Pulse Oximetry

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Regional cerebral saturation versus transcranial Doppler during carotid endarterectomy under regional anaesthesia

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Background and objective **The aim of this study was to compare a cerebral oximeter with transcranial Doppler (TCD) as a neurological monitor in patients undergoing carotid endarterectomy under regional anaesthesia.**

Methods **Forty patients were enrolled for this prospective study. We recorded every adverse neurological event after arterial clamping and variations in parameters evaluated by the two monitoring systems in order to determine whether there was any correlation between TCD data and those obtained by regional cerebral saturation, the timing of detection of the adverse event in both clinical examination and instrumental data and the presence of any false positives or negatives in any of the two monitoring systems.**

Results **Shunting was necessary in eight patients, following clinical signs of a neurological deficit during clamping. In these patients, a significant reduction in TCD values and regional cerebral saturation values from baseline was recorded. We observed a drastic reduction in TCD values in four patients during clamping (6 ± 5 versus $41 \pm 4\,cm\,s^{-1}$) that was not associated with any neurological deficit or reduction in regional cerebral saturation values (51 ± 4 versus $54 \pm 7\%$). Instrumental detection of a neurological deficit anticipated the clinical observation of about 5–10 s.**

Conclusion **We observed a greater reliability with the cerebral oximeter than with TCD in our patients. *Eur J Anaesthesiol* 26:643–647 © 2009 European Society of Anaesthesiology.**

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Keywords: carotid endarterectomy, cerebral oximeter, local anaesthesia, transcranial Doppler

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Introduction

Carotid endarterectomy (CEA) is considered an effective and well tolerated treatment for carotid stenosis greater than 70%, particularly if patients are symptomatic [1,2]. Nevertheless, this surgery is associated with a risk of perioperative stroke of 2–7.5% [1,3]. In order to minimize this risk, intraoperative cerebral monitoring is used to detect inadequate cerebral perfusion and to identify the need for shunting during carotid clamping.

It is controversial which cerebral monitor is best for intraoperative neurological monitoring during CEA. Many devices have been used [somatosensory evoked potentials [4], jugular bulb oxygen saturation [5], stump pressure [6], bispectral index [7], electroencephalography [8] and transcranial Doppler (TCD) [9]], but there is no neurological monitoring able to determine an acute cerebrovascular flow inadequacy that needs shunting with certainty. The cerebral oximeter [In-Vivo Optical Spectroscopy (INVOS) Cerebral Oximeter; Somanetics Troy, Michigan, USA] is a monitoring system based on near-infrared spectroscopy (NIRS) principles that uses bilateral frontal sensors to measure regional cerebral oxygen saturation (rSO_2) to monitor any discrepancies between oxygen delivery and request [10]. The aim of this study was to evaluate rSO_2 compared with TCD as a neurological monitor in patients undergoing CEA under regional anaesthesia.

Methods

Forty patients were enrolled in the study. Each patient signed an informed consent form. The protocol was approved by the University Committee of Paride Stefanini Department, Policlinico Umberto I, Rome. All patients were asymptomatic with a high-degree carotid artery stenosis (>70%) and were scheduled to undergo CEA under regional anaesthesia. No enrolled patients had significant contralateral carotid stenoses.

An ipsilateral cervical plexus block (deep and superficial) was performed according to Germain using ropivacaine 0.25% (10 ml for each root) for the deep plexus block (roots C2, C3 and C4) and ropivacaine 0.125% (20 ml) for the superficial plexus block.

Each patient underwent the following monitoring: continuous ECG with ST-segment analysis, invasive arterial pressure measured by a radial artery cannula, continuous peripheral oxygen saturation (Sp_{O_2}), rSO_2, mean blood flow velocity in the middle cerebral artery (mMCAv) with TCD (Pioneer TC 4040; Nicolet Biomedical, Madison, Wisconsin, USA) and neurological status (loss of strength of contralateral handgrip, dysarthria and impaired consciousness). TCD monitoring was performed by a technician during the whole duration of the surgery. Data were recorded continuously during clamping and every 5 min during the other phases of surgery.

Fifty per cent oxygen was administered to each patient using a face mask in order to increase Sp_{O_2}. When necessary, norepinephrine ($0.01–0.2\,\mu g\,kg^{-1}\,min^{-1}$) and nitroglycerine ($0.25–1\,\mu g\,kg^{-1}\,min^{-1}$) were administered to maintain adequate systemic arterial pressure.

If a neurological deficit occurred during carotid clamping, a sodium thiopental bolus ($1–1.5\,mg\,kg^{-1}$) and respiratory assistance with 100% oxygen were administered for cerebral protection; in these patients after carotid declamping, an 18% mannitol bolus ($0.25\,g\,kg^{-1}$) was administered to avoid cerebral oedema caused by reperfusion.

We considered as significant an mMCAv reduction over 50% from baseline (preclamping value) or an absolute mMCAv value under $10\,cm\,s^{-1}$ [11], whereas for rSO_2 a reduction of more than 20% from baseline or an absolute value under 45% was considered significant [12]. We recorded any adverse neurological event after clamping and any reduction in mMCAv and rSO_2 in order to determine whether there was a correlation among them, the delay in detection of the adverse event in both clinical examination and instrumental data and the presence of any false positives or negatives in either of the two monitoring systems.

To correlate TCD and rSO_2 data, we used the Bravais–Pearson linear correlation coefficient in which an r^2 value of more than 0.7 was considered to be significant. A Bland–Altman analysis was used to assess the level of agreement between the two methods to compare the two monitoring systems. To validate rSO_2 and TCD ability to predict the occurrence of acute cerebrovascular flow inadequacy during clamping, we used probability theory according to Bayes theorem; we calculated specificity, sensitivity, positive predictive value, negative predictive value and accuracy, and we compared the proportions between the procedures. Statistical results were calculated with SPSS10.0 (SPSS Inc., Chicago, Illinois, USA), and a P value of less than 0.05 was considered statistically significant.

Results

Characteristics of studied patients are presented in Table 1. Each patient was treated successfully, and no major complications were recorded in the postoperative period.

Table 1 Characteristics of patients

Sex (male/female)	29/11
Age (years)	77 ± 8 (64–90)
Weight (kg)	75 ± 6 (65–90)
Height (cm)	170 ± 3 (162–174)
Carotid stenosis (%)	83 ± 7 (70–90)
Operative time (min)	128 ± 25 (95–180)
Clamping time (min)	36 ± 7 (24–52)

Characteristics are reported as numbers (patients and sex). Age, weight, height, carotid stenosis, operative time and clamping time are reported as mean values ± SD and range.

The mean operative time was 128 ± 25 min (range 95–180 min). Mean clamping time was 36 ± 7 min (range 24–52 min) (Table 1). Mean rSO_2, TCD, arterial pressure and heart rate values are described in Table 2.

The Bayesian indices are reported in Table 3. Surgical technique was the same for each patient (CEA). The artery suture was performed using a synthetic patch in 14 patients, by simple suture in 21 patients and by means of a by-pass in five patients.

A shunt was necessary in eight patients (20%) because of neurological deficits during clamping. In this period, a drastic reduction in TCD values (baseline: 32 ± 8 versus clamping: $8 \pm 4\,cm\,s^{-1}$) and rSO_2 values (baseline: 62 ± 5 versus clamping: $32 \pm 3\%$) was recorded (Fig. 1). During clamping, we observed a mean mMCAv reduction of $73.5 \pm 16\%$ and a mean rSO_2 reduction of $24.7 \pm 2.6\%$ from baseline values. Instrumental detection of a neurological deficit anticipated the clinical observation of about 5–10 s.

We observed a drastic reduction of mMCAv in four patients after clamping (clamping: 6 ± 5 versus baseline: $41 \pm 4\,cm\,s^{-1}$) that did not correspond to any neurological deficit nor to a reduction in rSO_2 values (clamping: 51 ± 4 versus baseline: $54 \pm 7\%$) (Fig. 2). In these cases, we observed a mean mMCAv reduction of $59 \pm 8\%$ and a mean rSO_2 reduction of $7.6 \pm 3.4\%$ from baseline values. In the remaining 28 patients, during clamping, we observed a mean reduction of mMCAv of $18.7 \pm 8.7\%$ and a mean rSO_2 reduction of $7.9 \pm 3.9\%$ from baseline values.

From the data obtained, rSO_2 had a sensitivity of 100% and a specificity of 100% in detecting early neurological

Table 2 Regional cerebral oxygen saturation and mean flow velocity in middle cerebral artery values

	T_0	T_1	T_2	T_3	T_4	T_5
rSO_2 (%)	65 ± 7	65 ± 8	62 ± 9	63 ± 10	69 ± 8	68 ± 8
mMCAv ($cm\,s^{-1}$)	32 ± 12	38 ± 12	29 ± 14	26 ± 10	32 ± 12	33 ± 8
mAP (mmHg)	100 ± 26	103 ± 18	113 ± 12	99 ± 12	94 ± 16	91 ± 25
HR (bpm)	73 ± 20	74 ± 16	74 ± 15	80 ± 13	82 ± 13	75 ± 16

Data are reported as mean values ± SD. bpm, beats per minute; HR, heart rate; mAP, mean arterial pressure; mMCAv, mean flow velocity in middle cerebral artery; rSO_2, regional cerebral oxygen saturation; T_0, basal time; T_1, preclamping time; T_2, clamping time; T_3, predeclamping time; T_4, declamping time; T_5, final time.

Table 3 Bayesian indices

Indices	INVOS	TCD	*P*
Sensitivity	1	1	NS
Specificity	1	0.8	0.02
Positive predictive value	1	0.6	0.0001
Negative predictive value	1	1	NS
Accuracy	1	0.9	0.04

INVOS, in-vivo optical spectroscopy; NS, not significant; TCD, transcranial Doppler.

deficit during clamping, whereas TCD had a sensitivity of 100% and a specificity of 80%. No statistically significant correlations were observed between TCD relative changes and rSO_2 relative changes (from baseline values to clamping values) with an r^2 of 0.4943 (Fig. 3).

The Bland–Altman analysis (Fig. 4) indicates that the 95% limits of agreement between the two methods ranged from −63.5 to 18.6. The two methods do not consistently provide similar measures because there is a level of disagreement that includes clinically important discrepancies. No changes were observed between presurgical and postsurgical neurological status in any patient.

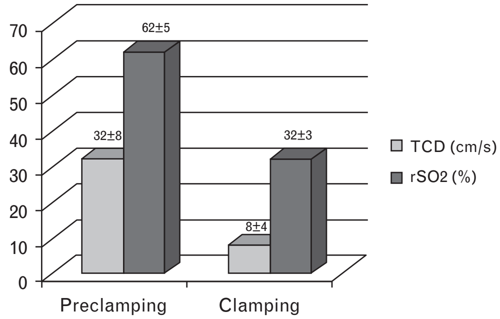
Discussion

In this small prospective study, we investigated the relationships among TCD and cerebral oximetry and neurological deficit during CEA carried out under regional anaesthesia. We found that rSO_2 was more closely related to the neurological events than TCD.

TCD allows continuous and noninvasive measurement of cerebral mean blood flow velocity and the identification of microemboli in the mean cerebral artery. However, there is controversy about the reliability of TCD as a monitor during CEA: Belardi *et al.* [13] as well as McCarthy *et al.* [11] concluded from their studies that TCD is not reliable in predicting the necessity for shunting, whereas Cao *et al.* [14] concluded in their study that assuming a decrease of mMCAv greater than 70% from baseline as the criterion to identify the need for shunting, a sensibility of 83% and a specificity of 96% can be reached.

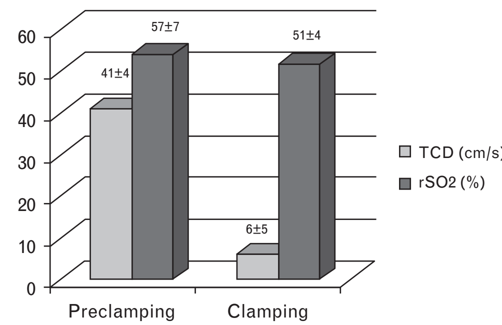
The cerebral oximeter INVOS uses NIRS to continuously and noninvasively monitor rSO_2. This technique has been studied for about two decades, but its use and reliability in neurological monitoring is still under investigation. The cerebral oximeter consists of a potentially useful methodology to identify objectively cerebral ischaemia, to identify the necessity for shunting and to provide an evaluation about shunt functioning during CEA. rSO_2 changes reflect the variation in cerebral perfusion that can be revealed during CEA [15,16]. Significant desaturation indicates haemodynamic ischaemia below the region examined

Fig. 1



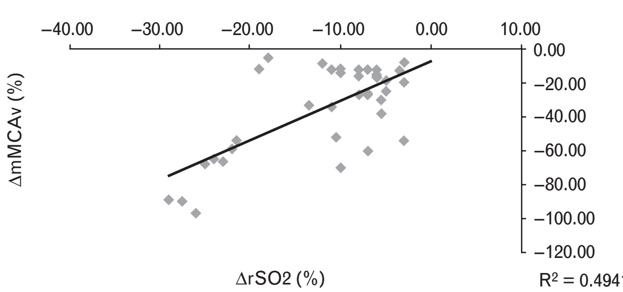
Mean transcranial Doppler and regional cerebral oxygen saturation values during preclamping and clamping in the eight patients who had neurological deficit during clamping (real positives). TCD values are reported as $cm\,s^{-1}$, rSO_2 values are reported as %. rSO_2, regional cerebral oxygen saturation; TCD, transcranial Doppler.

Fig. 2



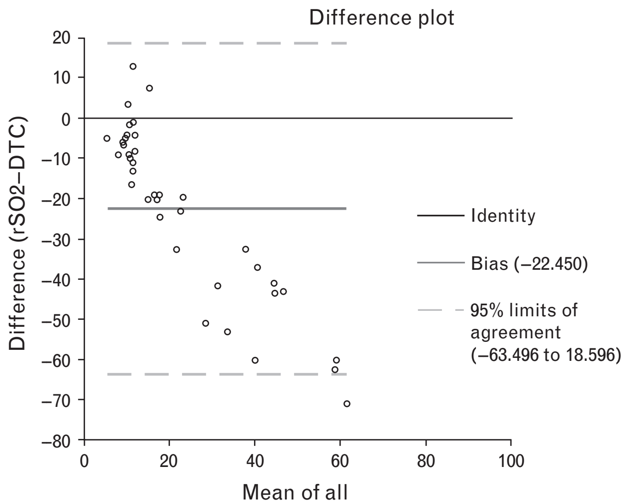
Mean transcranial Doppler and regional cerebral oxygen saturation values during preclamping and clamping in the four patients who had a decrease in transcranial Doppler values without a decrease in regional cerebral oxygen saturation values and without neurological deficit (false positives). TCD values are reported as $cm\,s^{-1}$, rSO_2 values are reported as %. rSO_2, regional cerebral oxygen saturation; TCD, transcranial Doppler.

Fig. 3



Linear correlation between mean flow velocity in middle cerebral artery relative changes and regional cerebral oxygen saturation relative changes (from baseline values to clamping values). mMCAv, mean flow velocity in middle cerebral artery; rSO_2, regional cerebral oxygen saturation.

Fig. 4



Bland–Altman plot between mean flow velocity in middle cerebral artery relative changes and regional cerebral oxygen saturation relative changes (from baseline values to clamping values). (Correlation absolute difference versus average = 0.90; bias = −22.450; 95% confidence interval = −29.148 to −15.752; standard error = 3.3113; *t* statistic = −6.78; $P < 0.0001$). rSO_2, regional cerebral oxygen saturation; TCD, transcranial Doppler.

by the spectroscopy sensors [17]. It should be remembered that, although the sensors monitor the frontal lobes, the sensorimotor strip is further posterior. However, clinical evidence supports the association between cerebral ischaemia and an rSO_2 decrease greater than 20% from baseline [12]. This then provides a simple method to identify the necessity for shunting and to evaluate the functioning of the shunt.

In some controlled studies of CEA, changes of 20–30% in rSO_2 were shown to correlate with changes in the neurological status of the patient. In these studies, rSO_2 values lower than 50% were correlated with a high likelihood of an adverse outcome. In addition, patients who had pre-existing diseases appeared to be less tolerant to low rSO_2 values [12,18–20].

Recent studies tried to evaluate the efficacy of TCD and INVOS to predict the need for shunting in patients undergoing CEA, but the results were controversial: Grubhofer *et al.* [21] found a false positive rate of 13% using a decrease in rSO_2 values greater than 13% from preclamping values; Fassidias *et al.* [22] concluded that INVOS appeared to be a satisfactory device for monitoring adequacy of cerebral perfusion and oxygenation during CEA in comparison with TCD; Moritz *et al.* [6] concluded that TCD, NIRS and stump pressure measurements provided similar accuracy for the detection of cerebral ischaemia during carotid surgery.

In our study, we observed a good association of TCD with clinical evaluation, even if we observed four false positives. This is probably due to the principal defect: operator dependence. A disappearing TCD signal could be explained through: inability to obtain a sufficient signal quality, the Doppler probe dislodging intraoperatively, a different source of the signal other than the MCA or the presence of arterial vessel abnormalities or collaterals that could perfuse the brain parallel to the MCA.

We observed, instead, a significant reduction (>20%) in rSO_2 values in those patients who showed a neurological deficit. In addition, neither false positives nor false negatives were observed. TCD does not seem to be an adequate device to identify the need for shunting during carotid clamping. Its use, because of its low specificity, may indicate shunting even in patients who have a good haemodynamic compensation during cross clamping, subjecting them to the risks associated with this surgical technique.

In this small study, INVOS was shown to be sensitive and specific in identifying an inadequate cerebral oxygenation. However, this device does not detect emboli that account for the majority of neurological deficits in these patients.

Conclusion

Although the number of observations was small, we observed a statistically significant improved specificity with INVOS rSO_2 than with TCD. rSO_2 represents a promising monitor during CEA and merits further evaluation in patients under general anaesthesia.

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