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Near Infrared Spectroscopy Monitoring During Carotid Endarterectomy: Which Threshold Value is Critical?

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Objectives. *Retrospectively to verify which decreasing percentage in regional oxygen saturation (rSO_2) identified patients with good collateralisation during carotid artery cross clamp.*
Materials and methods. *During 594 endarterectomies under general anaesthesia the decreasing percentage from preclamp value to value detected in the first 2 min after clamping the CCA and/or ICA was calculated in real time. No temporary shunt was placed in any case. ROC analysis was performed to determine the optimal cut-off for rSO_2 decrease to identify the occurrence of neurological complications.*
Results. *A cut-off of 11.7% was identified as optimal. Sensitivity and specificity were 75% (95% CI 71–78) and 77% (95% CI 74–80), respectively. The cut-off of 20% had a lower sensitivity (30%) and a higher specificity (98%) to identify patients with complications, with positive and negative predictive value of 37 and 98%, respectively.*
Conclusions. *The study suggest that a relative decrease in rSO_2 of $<20\%$ from preclamp to early cross clamp value has a high negative predictive value, i.e. if rSO_2 does non decrease more than 20%, ischemia by hypoperfusion is unlikely and a shunt should not be necessary. Moreover, a relative decrease $>20\%$ may not always indicate intraoperative neurological complications.*

Key Words: Carotid endarterectomy; Cerebral oximetry; Cerebrovascular monitoring; Near-infrared spectroscopy.

Introduction

Carotid endarterectomy (CEA) is an established procedure in patients with high-grade carotid artery stenosis[1–3] but adverse outcomes are possible and must be kept to minimal levels. The complications reported in the NASCET[4] and ECST[1] studies, included a 5.8 and 7.5% major stroke rate and 2.1 and 3.2% mortality rate, respectively.

Hypoperfusion during clamping of the internal carotid artery can cause the development of a new stroke or can further aggravate existing damage caused by previous events. Therefore, maintaining adequate perfusion during the procedure is critical. Since routine placement of an intraluminal shunt carries its own risk of intimal damage or embolization,[5,6] selective shunting using a reliable monitoring technique should assure optimal intraoperative approach and avoid unnecessary shunting. But which monitoring technique is a reliable indicator for selective shunting during CEA under general anesthesia?

The Near-Infrared Refracted Spectroscopy (NIRS) has been advocated as a simple, non-invasive, continuous, real-time monitor during extracranial carotid surgery but reports comparing NIRS with other intraoperative monitors have indicated varying levels of agreement.[7–12] The major problem in using cerebral oximetry during CEA is that a critical regional oxygen saturation (rSO_2) threshold, below which neurological dysfunction would develop, remains to be defined. Therefore, the purpose of this retrospective study was to verify which decreasing percentage in rSO_2 from baseline-preclamp to value detected in the first 2 min after clamping the CCA and/or ICA in CEA under general anaesthesia could reliably identify patients without impending cerebral ischemia.

Materials and Methods

We analyzed the data about rSO_2 changes detected by

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cerebral oximetry during 594 CEAs performed under general anesthesia in Vascular Surgery and Neurosurgery Divisions, Department of Surgery, IRCCS Policlinico S. Matteo in Pavia between June 1996 and December 2002. All patients gave informed consent to participate in the study according to the guidelines approved by the Ethical Committee of IRCCS Policlinico S. Matteo in Pavia. All 594 patients had symptomatic high-grade carotid artery stenosis >70% with 39 contralateral ICA occlusion documented by preoperative Echo color Doppler and/or by angiographic evaluation. All of the CEA procedures were performed under general anesthesia induced using a standard balanced technique with remifentanil, midazolam and propofol repeated as necessary until loss of consciousness. After tracheal intubation anesthesia was maintained with remifentanil and sevoflurane. All patients were ventilated with 50% oxygen until reaching an end tidal carbon dioxide of 4.0–5.5 kPa, i.e. 30–41 mmHg. Mean blood pressure was kept within the range of +20% and −20% of the preoperative level by using ephedrine (5 mg/bolus) and vascular expansion with hetastarch.

Routine monitoring included ECG, direct radial artery blood pressure, pulse oximetry and capnography. As a general rule, during all operations, intravenous heparin (5000 IU) was given before clamping. Details of the principles of cerebral oximetry used by INVOS 3100-A and INVOS 4100-SSA have been previously described.[13,14]

Data collection

The numerical rSO_2 readings were recorded at 10 or 20-second intervals and stored on floppy disk for off-line data analysis at a later time. The numerical values of rSO_2 in each patient were calculated following these criteria.

Mean preclamp. The mean value in the last 2 min after clamping the ECA and before clamping the CCA. This value was considered the baseline value.

Early lowest cross-clamp. The mean of the two lowest documented values in the first 2 min after clamping the CCA and/or ICA.

Mean cross-clamp. The mean value detected in cross clamp phase, i.e. from clamping CCA and ICA to clamp complete removal.

Lowest cross-clamp. The lowest value detected in cross clamp phase.

Mean post-clamp. The mean of the values in the first 10 min post-clamp, i.e. after clamp removal.

Duration of carotid cross-clamp time was recorded for each patient. Because intersubject variability in rSO_2 numerical values was noticed in many other studies,[10,12,15] to allow comparison of rSO_2 changes in any phase of CEA among all patients with varying absolute values, the recorded rSO_2 data was normalized by calculating a decreasing or increasing percentage change from baseline to other value according to the following formula.

Percent change = [(mean preclamp − value in other phase)/mean preclamp] × 100.

Adopting the same formula it was possible to calculate the increasing or decreasing percentage change in rSO_2 reading in each other period or phase of operation in all patients. It is worthy of remark that the most recent device shows the variations on the screen in continuous and real time.

All patients were tested after extubation for development of a new neurological deficit. Patients who had a neurological deficit with complete recovery within 24 h were classified as having sustained a TIA, while those with neurological deficit persisting for more than 24 h were classified as having sustained a stroke.

Statistical analysis

Descriptive statistics were computed as mean and standard deviation (SD) for continuous variables and as absolute and relative frequencies for categorical variables.

Relative changes from baseline of rSO_2 were computed for the various groups of patients, with decrease >20% or decrease <20%, occluded or not-occluded, together with their 95% confidence intervals (95% CI).

The independent role of contralateral occlusion was also evaluated by including this parameter into the model. Huber–White robust standard errors were calculated to account for intra-patient correlation over time. For post-hoc comparisons paired and unpaired t tests were used to contrast measures over time.

Finally, the role of a series of possible prognostic factors in predicting neurological complications was assessed by means of a logistic model. The odds ratio (OR) and its 95% CI was calculated to assess the strength of the association. ROC analysis was performed to determine the optimal cut-off (with highest sensitivity and specificity) for rSO_2 decrease to identify the occurrence of neurological complication in patients without shunt placement. Stata 7 (StataCorp, College Station TX) was used for computation. A 2-sided *p*-value was retained for statistical significance. For post-hoc comparisons, nominal *p*-values were corrected according to Bonferroni correction.

Results

Baseline

The baseline characteristics of the 594 patients, i.e. age, sex, side, contralateral occlusion and rSO_2 mean value, are shown in Table 1.

Changes in time

rSO_2 mean values over time (and 95% CIs) are shown in Table 2. For statistical analysis, two different models were fitted depending on the measurements considered in time. In the first case rSO_2 measurements included: baseline (preclamp); early lowest; mean cross clamp; and mean post declamp. In the second case rSO_2 measurements included: baseline (preclamp); early lowest; mean lowest cross clamp; and mean post declamp.

Both regression models were statistically significant ($p < 0.0001$) and showed rSO_2 values to depend on time ($p < 0.001$). Once having accounted for time, the presence of a contralateral carotid occlusion had no additional role in determining rSO_2 ($p = 0.9$ in both models). After Bonferroni correction all intraoperative rSO_2 values appeared to be significantly different from baseline and from each other ($p < 0.01$ in both models). Baseline and mean post declamp values were comparable.

Perioperative neurological complications

Neurological complications occurred in 20/594 (3.4%). It is useful to highlight that sixteen patients (2.7%) showed an early (the mean of the two lowest documented values in the first 2 min after clamping the CCA and/or ICA) drop in rSO_2% above 20%. Six patients (37.5%) with a decrease >20% had neurological complications as compared to 14 (2.4%) with a decrease <20% ($p < 0.0001$). The presence of contra lateral occlusion has independent negative effect after accounting for levels of rSO_2% in time. Level of rSO_2% also proved to be an independent predictor of neurological complications, while contralateral occlusion was not (Table 3).

Table 1. Baseline characteristics

Characteristics	$N = 594$
Age in years (mean (SD))	70.4 (6.7)
Male (*N*, %)	415 (70%)
Left carotid (N, %)	313 (53%)
Contralateral occlusion (*N*, %)	39 (7%)
rSO_2% (mean (SD))	67.9 (6.8)

ROC analysis

In the group of 594 patients the rSO_2 decrease ranged from 44 to 0 (median 9) and by ROC analysis a cut-off of 11.7% was identified as optimal to identify patients with/without neurological complication. Five patients (1.1%) with a decrease <11.7 had neurological complications as compared to 15 (10.2%) with a decrease ≥11.7% ($p < 0.0001$). Sensitivity and specificity for the cut-off of 11.7% were 75% (95% CI 71–78) and 77% (95% CI 74–80), respectively. The area under the ROC curve indicated good discrimination ability and was 0.80 (95% CI 0.65–0.94). The positive and negative predictive values were 10 and 99%, based on complication prevalence in the group of 3.4%.

However, the impact of a drop >20% is clinically relevant: a drop >20% was associated with neurological complications (three stroke, three TIA) in 6/16 patients (37%), while a drop ≤20% was associated with neurological complications (three stroke, 11 TIA) only in 14/578 patients (2%) ($p < 0.0001$). In 3/6 patients with stroke on awakening the decrease from baseline to early lowest cross clamp is >20%.

Reliability of cut-off <20% at NIRS monitoring

Specificity and sensitivity, as well as the predictive values based on data prevalence were computed to assess the ability of a critical cut-off in rSO_2 to predict the uselessness of shunting or to predict neurological complications.

We observed a high rate of true negative cases resulting in both high specificity and negative predictive value of the <20% cut-off in identifying patients with good cerebral perfusion by collateralisation. The cut-off of 20% had a lower sensitivity (30%) but a higher specificity (98%) to identify patients with complications, with positive and negative predictive values of 37 and 98%, respectively.

Discussion

It is firmly stated that the relative change in rSO_2 rather than the absolute number are a more reliable indicator of the ischemic threshold to establish the need for a shunt. As reported by others utilizing this device[8,16–19] the definition of 'normal values' for rSO_2 is highly questionable because of the wide variation of preclamp baseline saturation. Like the variability

Table 2. rSO_2 values over time

rSO_2 measurement	$N = 594$	
	Mean (SD)	% Change from baseline (95% CI)
Baseline*,†	67.9 (6.8)	–
Early lowest*,†	62.1 (7.2)	−8.5 (−8.9; −8.1; 9.3)
Mean crossclamp*	62.5 (6.9)	−7.9 (−8.4; −7.5)
Mean lowest crossclamp†	59.5 (7.2)	−12.4 (−12.9; −12.0)
Mean post declamp*,†	67.7 (6.7)	–

*Model 1: time effect $p < 0.0001$. For post-hoc comparisons see text.
†Model 2: time effect $p < 0.0001$. For post-hoc comparisons see text.

found in jugular venous oxygen saturation in healthy volunteers[20] rSO_2 has been found to exhibit a similar but even wider variability. The results of our study confirmed the variability of this parameter and the necessity to focus attention on individual changes of rSO_2 and to normalize the preclamp value to make easier the calculation of the percentage decrease. On the other hand, the newer devices show the relative decrease from baseline in real time on the screen. The aim of our investigation was to evaluate the reliability of NIRS as a new form of neurological monitoring during CEAs under general anesthesia. At this point, there is little evidence to support the use of one form of monitoring over another in selecting patients requiring a shunt.[21]

The true 'gold standard' of CEA monitoring is the neurological examination in the awake patient and other methods of monitoring are unnecessary. However, loco-regional anesthesia is not always appropriate. We evaluated the reliability of NIRS during CEA under general anesthesia using comparisons between our data relative to sensitivity and specificity and perioperative morbidity with the homologous data reported by other authors adopting continuous EEG monitoring. Somatosensory evoked potentials[9–12,22] or transcranial Doppler in the same conditions or with the neurologic examination in the awake patient.[7,13]

Lam *et al*.[23] compared the sensitivity and specificity of EEG and SEPs as a monitor of cerebral ischemia during CEAs with general anesthesia, without use of a shunt even if electroencephalography or SEPs changes are observed. They concluded that the relative sensitivity and specificity for EEG and SEPs in detecting postoperative stroke was 50 and 92% for EEG and 100 and 94% for SEPs, respectively. Sbarigia *et al*.[22] compared SEPs with an objective cerebral monitoring technique during CEA under local anesthesia: the results show that SEPs is associated with a 2% false negative rate. Moreover, the time needed for evoked potentials to return to normal after shunting limits their usefulness in verifying effective shunting.

Our data are strictly similar to those referred by Samra *et al*.[7] in awake patients and state that a rSO_2 decrease ≤20% indicates that shunt placement is not necessary. But our data also shows that a decrease >20% does not always predict neurological symptoms. If the reduction of cerebral oxygen saturation only persists for a short time, it may be tolerated without symptoms. In the study of Samra *et al*.[7] in 99 patients undergoing 100 CEAs with regional anesthesia monitoring the rSO_2 using the INVOS cerebral oximeter, the cut-off value of 20% resulted in a sensitivity of 80% and in a specificity of 82.2%. The false-positive rate using this cut-off point in the study by Samra *et al*.[7] was 66.7% and the false negative rate was 2.6% providing a positive predictive value of 33.3% and a negative predictive value of 97.4%. In our study a 20% decrease in rSO_2 had a 98% negative predictive and a 37% positive predictive value. Exactly the same data reported by Samra in CEAs under loco-regional anesthesia. A cut-off of 25–27% reduction in rSO_2 could reduce the false positive rate as reported by Roberts KW *et al*.[15] i.e. could reduce the number of patients requiring a shunt, but it could increase the rate of neurological complications.

A deeper analysis of data collected in those 16 cases with a decrease >20% showed that in patients without neurological dysfunction (six cases) the decrease >20% was limited to comparison of preclamp value vs early lowest cross-clamp while in the other cases with neurological dysfunction (10 cases) the decrease >20% persisted throughout the cross-clamp phase. Thus the duration of decrease in rSO_2 is also an important factor determining the neurological effect. It is not surprising that reduction of cerebral oxygen saturation persisting for a short time may be tolerated without permanent cerebral sequelae.

Table 3. Prognostic factors for neurological complications (multivariate model)

		Neurological complications (N, (%))	OR	95% CI	p
rSO_2%		*	0.95	(0.92–0.98)	0.001
Controlateral occlusion	No	130 (4%)			
	Yes	15 (4%)	0.5	(0.1–2.2)	0.358

Model $p = 0.0003$; *overall mean: 63.9 (SD 7.7).

According to the above reported data, in some cases a shunt is unnecessary even if the decrease in rSO_2 is $>20\%$. In practice, the surgeon wants to know immediately after clamping the CCA if hypoperfusion is detected or not and whether a shunt is really necessary or not. Therefore, the value to take into account is the early lowest cross clamp value detected in the first 2 min after clamping the CCA and/or ICA. In the early phases of clamping the rSO_2 may fluctuate due to auto regulation. Thus for correct decision making, the surgeon should wait until 2 min after clamping, the required time for auto regulation.

There are some limitations to the use of NIRS. Firstly, embolic insult is a significant factor in determining patient outcome and no published studies have demonstrated that NIRS can detect emboli. On the other hand, neither EEG nor SEP can detect emboli and also transcranial Doppler has many problems about the detection of emboli. Additionally, NIRS is highly regional in nature and monitoring is limited to a small but critical area of the watershed between the middle and anterior cerebral arteries territories. Also SEPs explore the somatosensory cortex alone rather than exploring the whole cortical area. Besides, the amplitude of SEPs and EEG is reduced by drugs that depress brain metabolism commonly used for general anesthesia: it could make difficult to evaluate the changes of amplitude of the neurophysiologic signal during surgery. NIRS is not affected by drugs. However, when considering other factors such as the great ease of use, the rapidity of measurement and the fact that NIRS offers a continuous, real time and non-invasive means for the assessment of cerebral cortical oxygenation, we conclude that NIRS is a useful means of monitoring hypoperfusion during CEA.

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