Clinical Study
Is Near-Infrared Spectroscopy a Reliable Method to Evaluate Clamping Ischemia during Carotid Surgery?

Luciano Pedrini, Filippo Magnoni, Luigi Sensi, Emilio Pisano, Maria Sandra Ballestrazzi, Maria Rosaria Cirelli, and Alessandro Pilato

Operative Unit of Vascular Surgery, Department of Surgery, Maggiore Hospital of Bologna, 40133 Bologna, Italy

Correspondence should be addressed to Luciano Pedrini, luciano.pedrini@ausl.bologna.it

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1. Introduction

The European Society for Vascular and Endovascular Surgery (ESVS) guidelines [1] state that there is no evidence for the routine use of shunts during carotid endarterectomy (CEA) (grade A) and that both local and general anesthesia are safe (grade A). A critical issue confirms “there is insufficient evidence from RCTs to support or refute the use of routine or selective shunting during CEA.”

Italian SPREAD guidelines [2] regarding monitoring during CEA also state that there is little evidence to support specific monitoring in cases of selective shunting and that electroencephalography (EEG) combined with stump pressure (SP) measurement can reduce the number of shunts required without increased risk of perioperative stroke [3].

The European and Italian Society for Vascular Surgery guidelines do not include cerebral oximetry (CO) using near-infrared spectroscopy (NIRS) among methods for the evaluation of cerebral ischemia during CEA under general anesthesia (GA). Many authors do not recommend this monitoring, assuming many limits of this method, such as the wide range of baseline regional cerebral oxygen saturation (rSO2) values and lack of an absolute lower cut-off value. However, NIRS is widely used in cardiac, pediatric, neurosurgery and ICU for monitoring during and after operations [4]; moreover, it is used by anesthesiologists for the manipulation of blood pressure to optimize cerebral perfusion [5].

NIRS and its possible use in the evaluation of clamping ischemia has been reported in many papers [6]. Parameters reported by different available NIRS instruments are rSO2, changes in intracerebral saturation (CsO2), and tissue oxygen index (TOI) [7]. Parameters obtained using different tools are not comparable [8].

Firstly, we compared EEG and NIRS in a small sample of patients submitted to CEA under GA, showing a lowering of EEG records for decrease of rSO2 values between 13% and 25% over baseline and a flattening for decreases between 19% and 23% [9]. Then, in a sample of 248 patients, using a cutoff
of 15% baseline decrease, we recorded 99.59% reliability, sensitivity of 66.6%, and specificity of 100% [10].

In patients operated under local anesthesia (LA), Roberts observed the appearance of neurologic symptoms for decreases of rSO2 greater than 27% [11]. Using a 20% cut-off in patients operated under LA, Samra et al. [12] showed a sensitivity of 80% and specificity of 82%.

Since January 2000, we have routinely used NIRS with a 20% rSO2 decrease cut-off value for the decision to shunt patients submitted to CEA under GA.

The purpose of this study was to evaluate NIRS reliability in the prevention of cerebral clamping ischemia during CEA under GA, with persistent neurologic deficit at awakening, using a 20% rSO2 decrease as cutoff, if persistent more than 4 minutes, otherwise a 25% rSO2 decrease.

As there is no valuable gold standard, and as many recent papers compare their results to those obtained using the stump pressure measurement, we estimated diagnostic accuracy across the group, also comparing accuracy between NIRS and SP measurement.

2. Materials and Methods

In this study, we evaluated prospective data of all patients consecutively submitted to elective CEA between 2006 and 2008 for symptomatic and asymptomatic carotid stenosis. Patients who underwent routine shunting (due to large contralateral infarction at preoperative CT-scan and patients treated by junior surgeons), plus those treated for urgent CEA and under remifentanil anaesthesia, were excluded from analysis.

Preoperative evaluation included CT-angiography of supraortic and intracranial vessels and brain-CT. All patients were operated under GA, using standardized protocol with a combination of fentanyl and sevoflurane and supraortic and intracranial vessels and brain-CT.

Anesthesiologists and surgeons assessed clinical results at patient awakening, confirmed by an independent neurologist within 24–36 hours after the operation, before discharge. All patients with neurologic deficits or head shake underwent urgent CT-scan, repeated after 24 hours if symptoms persisted. In addition, patients with an intraoperative rSO2 decrease >20% for more than four minutes underwent CT scan before discharge.

The Local Research Ethics Committee granted approval for an observational study in consecutive patients treated for CEA.

3. Statistical Analysis

Data was analyzed using SPSS statistics version 17.0 for Windows (SPSS Inc. Chicago, Ill, USA). Categorical data was analyzed using Chi square or Fisher’s exact test where appropriate. Differences in mean values of age, SP, and CO in both patient groups (those who required a shunt and those who were not shunted) were evaluated by 2-tailed t-Student test for unpaired samples. Mean rSO2 trend during surgery was evaluated using a 2-tailed t-Student test for paired samples. Relationships between rSO2 and SP were analyzed using
Pearson’s correlation test (two tails). Data were tested for normality using the Kolmogorov-Smirnov test.

For assessment of the accuracy of cerebral oximetry in discriminating ischemic from nonischemic patients, we performed receiver operating characteristic (ROC) analysis.

Reliability was also calculated determining true and false positives and negatives, positive predictive value (PPV), and negative predictive value (NPV) in subgroup of nonshunted patients, using specificity and sensitivity tests. Data is presented as mean (or median) ± SD. Probability values < 0.05 were considered statistically significant.

4. Results

A total of 473 cases were reviewed: 305 males (64.5%) mean age 73.3 ± 7.3 (range 50–86); 333 were asymptomatic for the ipsilateral hemisphere, but 70 of these had ischemic lesions in the ipsilateral hemisphere at cerebral CT-scan. Overall brain CT scan presented ipsilateral preoperative ischemic lesions in 162 (34.2%) patients. Detailed patient characteristic data is reported in Table 1. No strokes or deaths were reported in the postoperative period.

Three patients (all women), operated for mono- and bilateral stenosis, presented transient neurologic symptoms (TIA) at awakening: patients no. 1 and no. 3 required extended clamping time. In case one we inserted a shunt between the common and external carotid artery, as it was impossible to perform a carotid reconstruction with an intraluminal shunt in the normal position. rSO2 increased, but remained lower than 20% overall for 17 minutes subdivided into three periods of three, eight, and six minutes, respectively. The patient awoke slowly with uncertain neurologic deficits but recovered after a few minutes. In case three the shunt did not work due to distal kinking. On awakening she demonstrated mild paresis of the hand but recovered after 30 minutes. Patient no. 2 had very low SP and basal rSO2, quickly recovered to 47% after shunt insertion; low perfusion lasted three minutes before shunting and for a further three minutes after shunt removal. At awakening the patient showed paresis of the upper limb which recovered within one hour. All patients had a decrease >25% which lasted for two—five minutes, none had changes at brain CT-scan, and none presented new neurologic symptoms (see Table 2).

5. Monitoring Evaluation

In general rSO2 decreased after carotid clamping (C1), but in some patients it spontaneously increased after clamping due to carotid bulb baroreflex. Clamping induced a significant decrease of mean rSO2 value (P < 0.0001) in both patient groups. Mean rSO2 increased slightly over base soon after declamping (D1-D2-D3). No difference was noted in rSO2 after trial clamping (when performed) and definitive clamping.

After declamping we observed an immediate increase of rSO2; one minute after declamping, mean values were similar to base, but significantly slightly higher (P < 0.002) (Tables 3 and 4). In 12 cases, prevalently nonshunted patients, with delta rSO2 < 20% (5 cases) and >20% (7 cases), we observed a temporary rSO2 increase considered as an instrumental sign of hyperperfusion.

The shunt significantly increased mean rSO2 one minute after insertion (P < 0.0001), even though mean data remained significantly lower than baseline (P < 0.0001) (see Table 4).

One hundred and four patients reached a delta rSO2 greater than 20% and only 46 greater than 25%. SP was <50 mmHg in 172 cases. An intraluminal shunt was inserted in 41 cases as some rSO2 decreases lasted for less than two minutes or arose during carotid suture.

Relationships between SP and C1 values were not significant; in fact there was a weak but significant inverse relationship between SP and delta-rSO2 (−0.273; P < 0.0001). Evaluating the differences between two categories of SP (<50 mmHg and ≤50 mmHg) and delta rSO2 using two cut-off values, a significant difference emerged between the two parameters using both a delta rSO2 cut-off of 20% (P < 0.002) and 25% (P = 0.016, Fisher’s exact test).

Twenty-four patients presented rSO2 lower than 40% during clamping with a further five lower than 30%. Two symptomatic patients, at awakening, reached 28% and 27% during clamping, respectively, while the lowest value of other symptomatic patients was 49%. (See Table 2.)

6. Reliability

Using the ROC curve analysis, we calculated the sensitivity and specificity of many different threshold reductions of rSO2 in detecting neurologic deficits after carotid endarterectomy. Plotting these thresholds on a graph of sensitivity versus, 1—specificity in order to find that with the best performance we found, for a >25% reduction from baseline value, a sensitivity of 100% and a specificity of 90.6% (CI (95%) 0.934–0.997). The shape of the curve is very square indicating excellent performance of cerebral oximetry in preventing neurologic deficits (Figure 1). The lower rSO2 value did not result predictive (AUC 0.075, SE 0.059, CI (95%) 0–1).

Reliability was also calculated in the group of 433 patients nonshunted or with nonfunctioning shunts, including the patient with the shunt in the external carotid artery. Using a delta cutoff of 25%, reliability, sensitivity, specificity, PPV and NPV were 95.38%, 100%, 95.36%, 9% and 100% respectively. When using a 20% cutoff they were 82.67%, 100%, 82.83%, 2.26% and 100% respectively.

Using an SP of 50 mmHg as cutoff in the same group, reliability, sensitivity, specificity, PPV, and NPV were 36.6%, 66%, 47%, 0.6%, and 99.4%, respectively.

7. Discussion

Endarterectomy under GA needs cerebral monitoring to avoid ischemic deficits and/or the routine use of shunts. EEG is the most studied neurophysiologic technique which shows functional deficit when blood flow is <20 mL/100 g/min; however, we know that cerebral damage occur at a flow of <6–10 mL/100 g/min. EEG also presents some disadvantages
Table 1: Patient characteristics and analysis of the difference between the groups in relation to shunting and symptoms at awakening.

| Characteristics          | Num./mean %/SD | Not shunted | Shunted | P  | Asympt. | Sympt. | P     |
|--------------------------|----------------|-------------|---------|----|---------|--------|-------|
| Patients                 | 473            | 432 41      | 470 3   |    |         |        |       |
| Sex                      |                |             |         |    |         |        |       |
| M                        | 305            | 279 26      | 305 0   | NS | 0       | 0.0044 |
| F                        | 168            | 155 15      | 165 3   |    |         |        |       |
| Age                      | 73.3 7.4       | 73.3 ± 7.4  | 73.3 ± 7.4 | NS | 73.3 ± 7.3 | 74.6 ± 9 | NS   |
| Symptoms                 |                |             |         |    |         |        |       |
| none                     | 333 70.4       | 305 28      | 332 1   |    |         |        |       |
| TIA                      | 46             | 42 4        | 45 1    |    |         |        |       |
| ocular                   | 11             | 9 2         | 11 0    |    |         |        |       |
| VB/borderline            | 30             | 27 3        | NS 30 0 | NS |         |        |       |
| m-stroke                 | 32             | 27 5        | 31 1    |    |         |        |       |
| stroke                   | 21             | 20 1        | 21 0    |    |         |        |       |
| Contralat. stenosis      |                |             |         |    |         |        |       |
| None                     | 311 65.7       | 291 20      | 310 1   |    |         |        |       |
| >70%                     | 134 28.3       | 123 11      | <0.0001 | 132 | 2       | NS     |       |
| Occlusion                | 28             | 18 10       | 28 0    |    |         |        |       |
| Positive CT scan         |                |             |         |    |         |        |       |
| Ipsilateral only         | 60             | 52 8        | 59 1    |    |         |        |       |
| Bilateral               | 102            | 94 8        | NS 101 1 | NS |         |        |       |
| Contralat. only          | 42             | 37 5        | 42 0    |    |         |        |       |
| Monitoring               |                |             |         |    |         |        |       |
| T0                       | 64.8 ±9.8      | 64.4 ± 10.3 | NS 64.9 ± 9.7 | 50.6 ± 14.4 | 0.012 |
| Delta-rSO\textsubscript{2} | 13.5 ±9.8     | 12.3 ± 8.7  | <0.0001 | 13.4 ± 9.7 | 32.4 ± 5.4 | <0.001 |
| Stump pressure           | 59.8 ±23.13    | 61.9 ± 22.6 | 38.6 ± 16.1 | <0.0001 | 59.6 ± 23.1 | 52.3 ± 28.5 | NS   |

Table 2: Characteristics of patients with TIA’s at awakening.

| N | Age | carotid lesion | Bain CT | Preop. symptoms | Stump press. | rSO\textsubscript{2} | Shunt | 20 | Time > 25 |
|---|-----|----------------|---------|-----------------|--------------|----------------------|-------|----|----------|
|   | 84  | BS             | Omo     | Ctr | TIA | mmHg | T0 | C1 | Min | Delta (%) | min | Min |
| 1 | 66  | MS             | −       | −   | Asympt. | 50 67 | 62 49 | 26.87 | ECA | 3 + 8 + 6 | 5    |
| 2 | 74  | BS             | +       | +   | mStroke | 82 45 | 35 28 | 37.78 | NF  | 2 + 1    | 2 + 1 |

MS: monolateral stenosis, BS: bilateral stenosis, omo: omolateral brain, ctc: contralateral brain CT, ECA: shunt inserted in external carotid artery for technical reason, NF: not functioning, time: time length delta-rSO\textsubscript{2} >20%/25% recorded consecutively in two or more steps of the operation.

as its use requires the presence of a neurologist and has other limits due to anesthetic drugs and its inability to highlight ischemic complications of the subcortical and internal capsule area [13]. One review shows an incidence of false positives of between 8% and 13% while false negatives range between 5% and 50% [14]. False negatives are often associated to lacunar infarct [15], under LA reaching up to 40.6% [16] and are particularly dangerous.

The incidence of ischemic complications due to carotid clamping is fortunately low; therefore, it is difficult to find significant data for each monitoring tool.

Cerebral oximetry by NIRS is the latest monitoring proposed; it has been criticized for the wide range of values in normal conditions and for the lack of a sure cut-off value. Moreover, there are many confounding factors that may change rSO\textsubscript{2}, such as modification of systemic oxygen saturation and blood pressure, bronchodilatation, and so forth, but these same factors could also modify brain perfusion during LA with an increase of neurologic symptoms. As these factors can be quickly modified by the anesthesiologist, with consequent return to normality, we did not take them into account. Otherwise, all medications used for GA influence all neurophysiologic monitoring. Notwithstanding these criticisms, many studies confirm NIRS reliability. When compared with SSEP, NIRS showed a greater rSO\textsubscript{2} decrease in patients with flattening of potentials [17]. Studies obtained using INVOS showed good relationships between NIRS, jugular bulb venous oxygen saturation (S\textsubscript{J}O2), and trans-cranial Doppler (TCD) [18]. To date, the proposed cut-off for NIRS ranges between a 15% and 25% reduction over baseline.

Samra et al. [12] using a cutoff of 20%, in patients operated under LA, recorded a sensitivity of 80% and a specificity of 82% concluding that using a cutoff greater than 20%, NIRS
Figure 1: ROC curve of delta rSO2. Area under the curve 0.966, SE 0.016, CI (95%) 0.934–0.997.

Table 3: Mean values of rSO2 recorded in the different steps of operation compared to mean T0 values. P = P value (two-sided) t-Student test for paired samples.

| rSO2 values | Mean | SD | P    |
|-------------|------|----|------|
| T0          | 64.85| 9.8| <0.0001|
| T1          | 59.44| 10.3|<0.0001|
| C1          | 59.34| 10.4|<0.0001|
| L- rSO2     | 56.29| 10.3|<0.0001|
| D1          | 65.42| 10.3| 0.064 |
| D2          | 66.38| 34.3| N.S.  |
| D3          | 64.61| 9.7 | N.S.  |

Table 4: Mean values of rSO2 recorded in the two groups of shunted and not shunted patients.

| Time | Shunted Mean | SD | Not shunted Mean | SD | P    |
|------|-------------|----|------------------|----|------|
| T0   | 64.41       | 10.31| 64.89            | 9.76|      |
| T1   | 53.88       | 10.842| 59.99            | 10.12|      |
| C1   | 52.37       | 11.467| 64.53            | 10.27|      |
| S1   | 59.27       | 12.994|                |     |
| S2   | 51.46       | 11.567|                |     |
| D1   | 63.88       | 11.122| 65.73            | 9.87|      |
| D2   | 62.80       | 15.302| 65.26            | 9.84|      |
| D3   | 64.15       | 11.421| 64.69            | 9.55|      |

has a sensibility and specificity similar to EEG and SSEP, with a low incidence of false negatives but a high incidence of false positives.

Another study [19], also performed under LA, comparing NIRS, TCD, SP, SSEP, with neurologic surveillance, found as cutoff: a 20% decrease of basal rSO2, a 48% decrease of TCD, 40 mmHg of SP, 50% decrease of SSEP and a lower rSO2 value of 59%.

This data contrasts with the results of another study which showed that cerebral saturation lower than 54–56.1% and a decrease greater than 15.6–18.2% predicts neurological impairment [20].

A recent study reported the relationship between prolonged rSO2 desaturation and cognitive changes, showing impairment below a rSO2 threshold of 50% [21].

In our sample, mean lowest rSO2 value was 56.3 ± 10.2 (95% CI 55.4–57.2, range 20–91), and the median value was 57%. However, 298 patients had an L-rSO2 < 59, 194 patients <54 and five <30; only two of these were symptomatic at awakening. We also performed studies on cognitive changes; however, these modifications were not included as part of this particular study.

In a study including 594 patients operated under GA without shunting, the best cutoff was 11.7%, with a sensitivity of 75% (95% CI 71–78) and a specificity of 77% (95% CI 74–80). A cutoff of 20% showed a lower sensitivity (30%) but a higher specificity (98%) in identifying complications, with a PPV of 37% and a NPV of 98% [22].

In another recent study under LA, the cut-off drop indicating the need for shunt was 19%, with a sensitivity of 100%, a specificity of 98%, a PPV of 82%, and a NPV of 100% [23].

Brain perfusion is modified by head position, blood pressure, and heart and respiratory rate, plus autoregulatory response (also in GA) or by administration of vasoactive drugs. For this reason, it is difficult to compare results obtained under LA with those obtained under GA. Moreover, we agree with Gough [24] and McClearly et al. [25] about the impossibility of applying criteria for shunt insertion under GA derived by CEA under LA.

As we know that neurological deficit follows a persistent flow decrease, we introduced a variable “time” in the shunt decision. On this basis, we decided to evaluate the diagnostic accuracy of this monitoring for an rSO2 decrease greater than 20% or 25%, in the prevention of cerebral clamping ischemia during CEA. A single center study avoided the bias linked to multiple surgical and anesthesiological staff.

In our sample, using NIRS to identify the need for shunt, we did not observe any strokes. The three TIA occurred in patients with a delta-rSO2 greater than 25%; patients no. 1 and no. 3 presented a very low rSO2 value after clamping; SP indicated the need for shunt only in patient no. 2.

NIRS allowed us to monitor modifications of cerebral oximetry during all surgery phases, from anesthesia to head positioning and awakening. Utilizing this tool, we used a shunt in 41 (8.7%) of patients; based on the initial rSO2 value, the number patients with indication to shunting would have been 30 but in the other 11 patients CO decreased during surgery without correction by anesthetic management. Here NIRS was useful in showing delayed rSO2 reduction leading to shunt insertion also in these patients. Furthermore, it was useful to alert promptly of shunt malfunction. Using a delta rSO2 cutoff ≥ 15%, 20%, 25%, and 30%, we would have used a shunt in 185, 107, 47, and 22 patients, respectively. Using SP at 50 mmHg cutoff (derived
by our previous experiences), we would have used a shunt in 172 cases or in 102 cases using a cutoff of 40 mmHg.

The reliability of NIRS in our sample was high (95.38%), with a sensitivity of 100% and a specificity of 95.36%. The number of false positives was 4.6% using NIRS with rSO2 cutoff of 25% against 44.6% using SP. The lack of false negatives with CO in our study, even using a 25% decrease as cutoff, offers an important safety benefit.

Lee et al. [26] showed a relationship between rSO2 decrease and SP ($r = -0.57, P = 0.002$); however in our sample this relationship was very weak ($r = -0.26, P < 0.0001$).

Evaluation of our postdeclamping data is very useful. Generally we observed a prompt rSO2 increase (within 5 seconds), slightly higher than baseline. In patients with a preserved baroreflex, systemic blood pressure decreased with the secondary lowering of CO. The absence of an increase may be related to carotid thrombosis or hemodynamic failure. Significantly high values can be predictive of hyperperfusion [27]. In our sample we observed only 12 (2.5%) cases of temporary hyperperfusion that induced a strict control of systemic blood pressure.

8. Conclusions

It is not possible to show functional changes under GA without using EEG and/or SSEP (with the reported limits) as can done under LA or GA with remifentanil conscious sedation, being only possible to show transient or permanent neurologic deficits at awakening.

For this reason, the purpose of our monitoring was to prevent TIAs and strokes related to carotid clamping, without routine shunting and to demonstrate the suitability of the cutoff. This protocol did not include a routine postoperative neuroimaging; however, we performed a CT-scan in all patients showing any symptoms or at risk, without evidence of new ischemic areas.

The results of this study suggest that during CEA, under GA, monitoring of cerebral oxygenation by NIRS is a reliable method, using a cutoff of 25% or a cutoff of 20% for prolonged hyperperfusion. The absence of false negatives confirms its safety. Based on our study sample, we are unable to propose a lower value as cutoff for shunting; however, it is certainly lower than those proposed under LA. In consideration of data reported by Slater et al. [21], we agree that there is need for further study of this complication in CEA.

In conclusion, NIRS cannot exclude ischemic damages due to embolism during carotid preparation or after declamping, which can only be showed by TCD, a useful tool particularly in teaching hospitals. Our study also does not provide information about clamping ischemia not followed by neurologic deficits at awakening, which are not important if they are not responsible for cognitive deficits, as suggested by some studies.

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