EVALUATION OF AN INTRAOPERATIVE ALGORITHM BASED ON NEAR-INFRARED REFRACTED SPECTROSCOPY MONITORING, IN THE INTRAOPERATIVE DECISION FOR SHUNT PLACEMENT, IN PATIENTS UNDERGOING CAROTID ENDARTERECTOMY

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Abstract

Background: We evaluated whether the use of an intraoperative algorithm based on cerebral oximetry with near-infrared refracted spectroscopy (NIRS) monitoring, could aid in the intraoperative decision for shunt placement, in patients undergoing carotid endarterectomy (CEA).

Methods: In this prospective, randomized, controlled study were included 253 patients who underwent CEA under general anesthesia. They were randomly allocated in Group A (n = 83) using NIRS monitoring and the suggested algorithm, Group B (n = 84) using NIRS monitoring without the algorithm and Group C (n = 86) who served as controls. Shunt placement criterion for Group A and B was 20% drop in ipsilateral regional saturation from the baseline value recorded before surgery. Primary endpoint of the study was to evaluate the use of the intraoperative algorithm based on NIRS monitoring, in the intraoperative decision for shunt placement, in patients undergoing carotid endarterectomy. Additionally, we examined whether this might affect the rate of postoperative neurologic deficits.

Results: When compared with Group A, Group B and Group C had 3.7 times (99% c.i 1.5-9.5) and 70.6 times (99% c.i. 15-724.3) respectively, greater likelihood of having a shunt placed. When compared with Group B, Group C had 19.4 times (99% c.i. 4.3-191.2) greater likelihood of having a shunt placed. Regarding the rate of postoperative neurologic deficits no significant difference was found between the three groups.

Conclusions: The use of a specific algorithm based on NIRS monitoring, in patients undergoing CEA, may aid in the intraoperative decision for shunt placement.

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Introduction

Hypoperfusion during carotid endarterectomy (CEA) due to clamping of the internal carotid artery may result in cerebral ischemia or further aggravate a preexisting brain damage[1-4]. The complications reported in the NASCET and ECST studies, included a 5.8% and 7.5% major stroke rate and 2.1% and 3.2% mortality rate, respectively[1,3]. Previous studies have showed the risks for postoperative neurologic deficits during common carotid artery (CCA) cross clamping and embolic events due to vascular surgical manipulations[5,6]. Vascular surgeons estimate the risk adequacy of the collateral flow by measuring the stump pressure[7-10]. Recently, the introduction of cerebral Near-Infrared Refracted Spectroscopy (NIRS) monitoring has been associated with shorter recovery and hospital stay in noncardiac surgery[11] and with a decrease in major organ dysfunction after cardiac surgery[12]. Furthermore, Denault et al. have suggested an algorithm based on NIRS monitoring to optimize cerebral oxygenation during surgery[13]. However, there are not extensive studies for the intraoperative use of NIRS and/or NIRS based intraoperative strategies during carotid endarterectomy. In this prospective study, we evaluated whether the use of an intraoperative algorithm based on NIRS monitoring, could aid the intraoperative decision for shunt placement, in patients undergoing carotid endarterectomy.

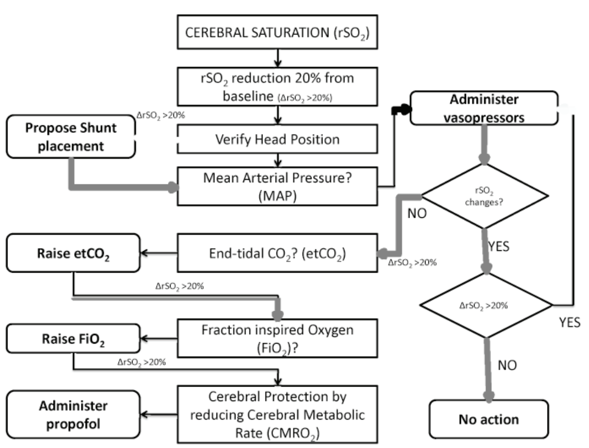
Methods

This prospective, controlled, randomized study was conducted in two Greek institutions from December 2007 to January 2010, and included 253 patients American Society of Anesthesiologists physical status II-III, aged 42-82 years who underwent carotid endarterectomy. The study was in conformation with the principles outlined in the Declaration of Helsinki and was approved by the Institutional Ethics Committee. The criteria for carotid endarterectomy were symptomatic carotid artery stenosis greater than 70% and asymptomatic carotid artery stenosis greater than 80% with coexisting risk factors[14]. The degree of stenosis was evaluated by means of vascular ultrasound and invasive angiography. Preoperatively, all patients underwent a complete clinical neurologic evaluation followed by a brain computed tomography (CT) scan.

Anesthetic management was standardized. Anesthesia was induced with fentanyl and propofol. Neuromuscular blockade was achieved with cisatracurium. Maintenance was with remifentanil infusion, sevoflurane in oxygen and nitrous oxide. Heparin 100U/kg was administered five minutes before carotid cross clamping (CCC). Stump pressure was measured using a transducer system connected to 22G catheter. Thirty minutes before emergence morphine was administered for postoperative analgesia.

Standard monitoring in all patients included electrocardiography (ECG), end tidal carbon dioxide ($EtCO_2$), invasive blood pressure (IBP) and pulse oximetry (SpO_2). Patients were randomly allocated by using closed envelopes into three groups. In the first and second group (group A and group B respectively), in addition to the above mentioned monitoring, cerebral oximetry with near-infrared refracted spectroscopy (INVOS 4100, Somanetics Inc., Troy MI) was used. Patients in the third group (Group C) underwent routine CEA without INVOS monitoring and served as control group. In groups A and B, the cerebral oximetry sensors (rSO_2) were placed on the forehead over the eyebrows monitoring the ipsilateral and contralateral hemispheres. Baseline rSO_2 values were obtained before induction and without any medication administered and from that point continuous recording every 10 seconds was established. Cerebral oximetry changes were recorded when the patient entered the operating room without any medication (T1), 2min before CCC (T2), 2min after CCC (T3), 2min after end of patching during reperfusion (T4), 10min after reperfusion (T5) and after emergence (T6). The change from the baseline (ΔrSO2) taken before induction was recorded in percentage. The rSO_2 values were recorded as averages. A 20% drop from the baseline was considered as a cutoff value for ischaemia and the surgeon was notified. This value has been well established from previous studies[15-17]. During the above time points vital signs (MAP, HR, $EtCO_2$) were recorded in all patients. Patients in group A were managed according to the algorithm developed by Denault et al[13] for patients undergoing cardiac surgery, which was adjusted for patients undergoing carotid surgery by our team (Fig. 1). On the other hand, in patients of group B cerebral oximetry values were recorded but anesthesia management was not based upon the aforementioned algorithm. Patients who exhibited new neurologic deficits postoperatively that persisted for more than 24 hours underwent a follow-up brain CT scan.

Fig. 1
The suggested intraoperative algorithm based on cerebral oximetry with near-infrared refracted spectroscopy



Primary end point of the study was to evaluate whether the use of the intraoperative algorithm based on NIRS monitoring might affect the intraoperative decision for shunt placement, in patients undergoing carotid endarterectomy. Additionally, the possible effect of the above algorithm upon the rate of postoperative short-term neurologic deficits was examined.

Statistical Analysis

Categorical variables were evaluated by two-tailed Fisher exact tests, with odds ratio estimates for 2 x 2 tables being conditional maximum likelihood estimates. Continuous variables were evaluated by two-tailed Welch's t tests, with natural logarithms of ratios being taken. Because three statistical assessments were performed for many variables, alpha was adjusted such that null hypotheses were rejected when $P < 0.5/3 \approx 0.015$. Power analysis was performed with Power And Precision™ (Biostat, Inc., Englewood, NJ). Other statistical analyses were performed on R2.10.1 (R Development Core Team (2009). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org).

All remaining analyses had results that might have been due to chance ($P > 0.015$, for each analysis); power analysis revealed all would have been able to detect moderate sized differences. Seventy patients per patient group detects as significant moderately-sized differences for χ^2 tests of 2 x 2 contingency tables and two-tailed t tests in 81% of studies with alpha = 0.01.

Table 1
Demographic and clinical characteristics

	Group A (n = 83)	Group B (n = 84)	Group C (n = 86)	P-values Fisher exact test, two-tailed		
				A vs B	A vs C	B vs C
Gender (M/F)	57/26	68/16	60/26	0.20	0.87	0.12
		Mean (range)				
Age (yrs)	69.1 (50-82)	68.3 (48-80)	68.4 (48-81)	0.28	0.28	0.40
BMI (kg/m^2)	27.7 (23.1-33.1)	26.9 (21.5-33.8)	28.2 (22-33.1)	0.15	0.31	0.0057
		N (%)				
Hyperlipidemia	42/83 (50.6%)	41/84 (48.8%)	40/86 (46.5%)	0.71	0.3	0.56
Hypertension	45/83 (54.2%)	47/84 (55.9%)	46/86 (53.4%)	0.68	0.85	0.65
Diabetes mellitus	21/83 (25.3%)	21/84 (25%)	24/86 (27.9%)	0.87	0.7	0.71
Coronary artery disease	32/83 (38.5%)	31/84 (36.9%)	33/86 (38.3%)	0.7	0.75	0.7
Hemodialysis	4/83 (4.8%)	5/84 (5.9%)	5/86 (5.8%)	0.85	0.88	0.88

Table 2
Preoperative neurologic status

	Group A (n = 83)	Group B (n = 84)	Group C (n = 86)
Asymptomatic	56/83 (67.4%)	56/84 (66.7%)	58/86 (67.4%)
Symptomatic	27/83 (32.5%)	27/84 (32.1%)	27/86 (31.3%)
Stroke	11/83 (13.2%)	13/84 (15.4%)	14/86 (16.2%)
TIAs	9/83 (10.8%)	10/84 (11.9%)	10/86 (11.6%)
Amaurosis fugax	7/83 (8.4%)	5/84 (5.9%)	4/86 (4.6%)

Differences between groups were not statistically significant (Fisher's test), TIAs: Transient Ischemic Attacks.

Results

Patients were randomly allocated to three groups: group A (n = 83) and group B (n = 84) in which NIRS monitoring was applied and group C (n = 86) in which only standard anesthesia monitoring was used (control group). There were no differences between groups with respect to demographic and clinical characteristics (Table 1). There were not statistically significant differences in the preoperative neurologic status between the three groups (Table 2).

Table 3 shows data from the monitoring of intraoperative vital signs. MAP values taken two minutes after the opening of the CCA (T4) were decreased in all groups as compared to values taken two minutes before CCA cross clamp (T2). Chronological alterations in MAP between the above two time points (MAP T4/T2 ratios) were significantly increased in both groups A and B as compared to controls, which means that accordingly there was a smaller amount of reduction in MAP values in groups A and B as compared to controls (Table 3). $EtCO_2$ values taken two minutes after the opening of the CCA (T4) were increased in groups A and B, while decreased in controls, as compared to values taken two minutes before CCA cross clamp (T2) (Table 3). Finally, chronological alterations in rSO_2 values between two minutes after CCA cross clamp and two minutes before CCA cross clamp, as described by the rsO2 T3/T2 ratio, showed an increase of the above ratio in group A as compared to group B (Table 3).

Table 4 describes significant differences concerning shunt placement that were recorded between groups. Specifically, patients in groups B and C exhibited 3.7 times (99% c.i 1.5 - 9.5) and 70.6 times

Table 3
Intraoperative monitoring data

	Group A (n = 83)	Group B (n = 84)	Group C (n = 86)	P-values Welch's t test, two-tailed, on logs		
	Log mean (range)			A vs B	A vs C	B vs C
MAP T3/T2	0.85 (0.6-1.14)	0.87 (0.54-1.2)	0.83 (0.65-1.1)	0.57	0.31	0.11
MAP T4/T2	0.86 (0.58-1.2)	0.96 (0.74-1.4)	0.78 (0.57-1.35)	< 0.001	0.002	< 0.001
MAP T5/T2	0.81 (0.6-1.27)	0.92 (0.65-1.3)	0.77 (0.6-1.04)	< 0.001	0.07	< 0.001
HR T3/T2	0.97 (0.68-1.9)	1.0 (0.66-1.5)	0.96 (0.65-1.5)	0.39	0.76	0.20
HR T4/T2	1.01 (0.75-1.7)	1.03 (0.57-1.5)	0.98 (0.6-1.5)	0.50	0.46	0.19
HR T5/T2	1.01 (0.75-1.5)	1.0 (0.60-1.5)	1.04 (0.8-1.6)	0.85	0.36	0.30
etCO2 T3/T2	1.03 (0.90-1.2)	1.01 (0.92-1.1)	0.95 (0.8-1.2)	0.015	< 0.001	< 0.001
etCO2 T4/T2	1.05 (0.94-1.4)	1.02 (0.92-1.1)	0.93 (0.8–1.0)	0.006	< 0.001	< 0.001
etCO2 T5/T2	1.03 (0.9-1.3)	1.03 (0.97-1.1)	0.90 (0.8–1.0)	0.87	< 0.001	< 0.001
rSO_2 T3/T2	0.91 (0.73-1.1)	0.85 (0.6-1.1)	§	< 0.001	§	§
rSO_2 T4/T2	1.04 (0.9-1.2)	1.02 (0.82-1.2)	§	0.11	§	§
rSO_2 T5/T2	1.04 (0.9-1.2)	1.03 (0.83-1.2)	§	0.43	§	§

MAP: mean arterial pressure, HR: heart rate $etCO_2$: end-tidal carbon dioxide, rSO_2: cerebral oximeter measured regional hemoglobin saturation in cerebral tissue ipsilateral to the operated carotid artery. MAP, HR, et CO2 and rSO_2 ratios reference ratios of measurements taken at different time points: T2 - two minutes before common carotid artery cross clamp; T3 - two minutes after common carotid artery cross clamp; T4 - two minutes after opening common carotid artery; T5 - ten minutes after opening common carotid artery. § rSO_2 values were not recorded in the control group.

(99% c.i. 15 - 724.3), respectively, greater likelihood of having a shunt placed, as compared with patients in group A. When compared with Group B, Group C had 19. 4 times (99% c.i. 4.3 - 191.2) greater likelihood of having a shunt placed.

Table 4
Intraoperative shunt placement

Shunt	Not placed	Placed	p-value Fisher's exact test
Group C	0 (0%)	86 (100%)	<0.001
Group A	60 (72.3%)	23 (27.7%)	<0.001
Group B	34 (40.5%)	50 (59.5%)	<0.001

There were no significant differences between the three groups regarding postoperative neurologic deficits (Table 5). Thirty two out of the total 253 patients (12.6%) experienced neurologic deficits postoperatively and only 13 out of the total 253 patients (5.1%) suffered a permanent deficit confirmed by a CT scan as an ischemic region. Finally, seven out of the total 253 patients (2.7%), (group A n = 1, group B n = 2 and group C n = 4) exhibited evidence of cardiovascular ischemia, as assessed by clinical and laboratory examinations; while 2 out of the total 253 patients (0.8%), one in group B and one in group C, expired due to cardiovascular events, postoperatively.

Table 5
Postoperative neurologic deficits between groups

Neurologic deficit	Group A	Group B	Group C	P-value Fisher's exact test
No	73 (87.9%)	73 (86.9%)	75 (87.3%)	0.89
Yes	10 (12.1%)	11 (13.1%)	11 (12.7%)	

Discussion

We demonstrated that the use of an intraoperative algorithm based on NIRS monitoring, in patients undergoing carotid endarterectomy, may aid in the intraoperative decision for shunt placement. The latter during carotid endarterectomy is a surgical practice that may minimize the risk of perioperative cerebral ischemia[18]. However, definite benefits from this intraoperative practice have not been published yet. Additionally, there is no consensus whether routine shunting is superior to selective shunting during carotid endarterectomy[19].

The present data suggested that in patients in whom an intraoperative algorithm based on NIRS monitoring was used (group A), the rate of shunt placement was reduced as compared to patients in whom even though NIRS monitoring was applied the specific algorithm was not utilized (group B). Additionally, no significant differences between the three groups concerning the rate of postoperative neurologic deficits were recorded. Postoperatively, 12.6% of patients presented with new neurologic deficits, and only 5.1% of patients were diagnosed with permanent deficits. These findings are in agreement with the NASCET and ECST studies[1,2].

During surgery the identification of possible hypoperfusion may aid in the intraoperative decision for the necessity of shunt placement. Intraoperative stroke accounts for 15–20% of the perioperative strokes, due to hypoperfusion during cross-clamping or thromboembolism[20,21]. Intraoperative neurological deficit is most often associated with carotid artery dissection or clamp release (83%) and only rarely (17%) with cross-clamping[22].

Mental status evaluation during carotid cross-clamping in the awake patient remains the gold standard with which other methods of monitoring should be compared[23,24]. Monitoring of the conscious patient provides a unique opportunity to determine the time of onset of a neurological deficit and to deduce the likely cause[25,26]. In patients under general anesthesia monitoring with electroencephalography (EEG) is oftentimes applied[27], however this method can not reliably detect cerebral ischaemia and therefore provide a clear guide to shunting. Recent data reported a 82% rate of shunting in patients who underwent CEA under general anesthesia[28], which is significantly higher compared with the 28.4% recorded rate in our patients in whom the specific intraoperative algorithm based on NIRS monitoring was used.

Cerebral oximetry with near-infrared spectroscopy (NIRS) allows for continuous monitoring of changes in cerebral oxygenation (rSO_2) through adhesive sensors on the patients' forehead[16,29,30]. NIRS was evaluated under regional anesthesia in patients undergoing CEA by previous studies (16, 31). In these studies rSO_2 values showed an intersubject variability in the pre-clamp period. Specifically, Samra et al[16] considered a decrease in rSO_2 of 20%, or an absolute reading of less than 50%, as indicative of cerebral ischaemia, resulting in a false-negative rate of 2.6% and a false-positive rate of 66.7%. Roberts et al[31] used a decrease of ≥ 27% in rSO_2 as indication for a shunt and had no false-negative or false-positive results in 45 patients. A possible explanation was the shorter duration of cross-clamping, and it was demonstrated that permanent sequelae result from a combination of both the magnitude and duration of ischaemia[31].

Our study implemented the use of NIRS monitoring along with a series of interventions such as intraoperative adjustments of MAP, CO2, FiO2 and pertinent modifications in the depth of anesthesia in order to provide a safe guide for shunting.

In the present study a 20% drop in rSO2 was used as a cutoff value indicative of cerebral ischemia, which is comparable to previous reports[16,31]. Interestingly, we found that chronological alterations in between and two minutes before CCA cross clamp, as described by the rsO2 T3/T2 ratio, showed an increase of the above ratio in group A as compared to group B. Hence, two minutes after CCA cross clamp rSO_2 values were increased in group A as compared to group B. This might be attributed to the fact that intraoperative adjustments of MAP, CO2, FiO2 and pertinent modifications in the depth of anesthesia, according to the suggested algorithm, were applied only in patients of group A. However, no significant differences in the rate of new neurologic deficits were recorded between the study groups postoperatively. Therefore placement of shunt may not be of the major criteria to avoid neurological complications. It may be the patient's integrity of circle of Willis and collateral circulation to compensate the acute ischemia during carotid cross clamp. From this point of view cerebral oximetry with near-infrared spectroscopy may be a useful and effective monitoring.

Our study exhibits several limitations. First, 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 even the usage of transcranial Doppler is rather problematic in detecting emboli[32-34]. 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.

Conclusions

We found that the use of an intraoperative algorithm based on NIRS monitoring, in patients undergoing carotid endarterectomy, may aid in the intraoperative decision for shunt placement. However, no significant effect of the above method upon the rate of postoperative neurologic deficits was observed.

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