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The Efficacy of Near-Infrared Spectroscopy Monitoring in Carotid Endarterectomy: A Prospective, Single-Center, Observational Study

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Abstract

There has been no gold standard for intraoperative monitoring in carotid endarterectomy (CEA) till now. The purpose of the current study was to investigate the value of near-infrared spectroscopy (NIRS) monitoring in CEA and explore the thresholds for intraoperative cerebral hypoperfusion. Eighty-four consecutive patients who underwent CEA surgery in Xuan Wu Hospital of Capital Medical University from August 2015 to June 2016 were enrolled in this study. All patients were intraoperatively monitored by transcranial Doppler ultrasonography (TCD) and NIRS. Regional oxygen saturation (rSO_2) monitored by NIRS and blood flow velocity of the middle cerebral artery (V-MCA) monitored by TCD were continuously recorded. Correlation analysis was conducted for NIRS and TCD monitoring values. Intraoperative shunting was performed in five patients according to the TCD monitoring results and surgeon preference. During clamping of the carotid artery, the Pearson correlation index between rSO_2 and V-MCA was 0.581 ($P<0.001$). A cut-off of 12.3% decrease of rSO_2 was identified as the optimal threshold for intraoperative hypoperfusion indicated by TCD monitoring, when the sensitivity and specificity were 74.6% and 91.7%, respectively, with a 0.609 Kappa value. Physical examination immediately after operation showed no ischemic injury occurred, and no death and stroke occurred during the postoperative hospitalization. Our study demonstrated that NIRS could serve as a favorable monitoring tool during CEA. A 12.3% decrease of rSO_2 could be adopted as a reliable threshold for intraoperative cerebral hypoperfusion.

Keywords

carotid endarterectomy, near-infrared spectroscopy, transcranial Doppler ultrasonography, hypoperfusion

Introduction

Thanks to developments in cell translation techniques and stem cell therapy, the prevention and treatment of ischemic stroke has made significant progress in recent years[1–4]. It is well known that carotid endarterectomy (CEA) is an ideal treatment for middle to high-grade carotid artery stenosis[5,6]. However, perioperative stroke induced by intraoperative embolism and hemodynamic impairment negates the benefit of surgery. Embolism is usually induced by dissection, shunt insertion, and clamp release. Intraoperative cerebral hypoperfusion often occurs during carotid clamping in patients whose collateral circulation is poorly developed. Timely recognition and placement of shunt could relieve this kind of intraoperative hemodynamic impairment. The recognition of hypoperfusion depends to a large extent on effective monitoring. On the other hand, postoperative cerebral hyperperfusion syndrome (CHS) resulting from the significantly increased cerebral blood flow and impaired cerebral autoregulation could bring about fatal stroke[7].

A series of monitoring tools have been adopted in CEA during the last century. The monitoring techniques were mainly adopted for the indication for selective shunting, and for the assessment of risk of postoperative CHS[8]. Among all

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monitoring techniques, the awake test under regional anesthesia may be the most reliable method[9]. However, many patients cannot tolerate the trauma of CEA under regional anesthesia, and the awake test has no effect on the assessment of postoperative cerebral perfusion, so few surgeons practice this methodology. Transcranial Doppler (TCD) and near-infrared spectroscopy (NIRS) have become the most widely used monitoring tools in recent years. TCD is adopted as the gold standard for intraoperative monitoring in many centers, and regional oxygen saturation (rSO_2) monitored by NIRS can also effectively evaluate the regional blood flow. However, the threshold of drop in rSO_2 during carotid clamping for intraoperative hypoperfusion has still not been agreed[10]. This prospective study was conducted to investigate the threshold of intraoperative cerebral hypoperfusion.

Materials and Methods

Study Design

This was a prospective, observational study. All recruited patients were continuously monitored by TCD and NIRS during operation under general anesthesia. The rSO_2 was monitored by NIRS (Cas Medical Systems, Inc, Branford, Connecticut, USA), and velocity of middle cerebral artery (V-MCA) was monitored by TCD (The Elicacompany, ShenZhen, China). The NIRS probes were placed on the bilateral forehead, monitoring the anterior cerebral artery (ACA) blood velocity. Two time points when remarkable hemodynamic change occurs were selected for analysis: (1) when the carotid artery was clamped; (2) when cerebral perfusion stabilized after declamping of the carotid artery. At each time point, percentage changes of both monitoring values from baseline were calculated for further analysis. All patients had signed the informed consent, and the study was approved by our Institutional Review Board.

Inclusion Criteria

1. Age from 20 to 80 years old;
2. Symptomatic patients who were diagnosed with a 50% stenosis of internal carotid artery (ICA) or asymptomatic patients who were diagnosed with a 70% ICA stenosis by preoperative digital subtraction angiography (DSA);
3. Transparency of the temporal bone window of patients for the continuous TCD monitoring during operation;
4. Patients who signed the informed consent of current study.

Exclusion Criteria

1. Patients who could not tolerate the surgical or anesthetic process due to systematic diseases;
2. Patients who were concomitant with pulmonary diseases that influence the oxygen saturation monitored during operation, such as pneumonia, asthma, and chronic obstructive pulmonary disease.

Table 1. Monitoring Values during Operation.

	T_1	T_2	T_3
V-MCA	V_1	V_2	V_3
rSO_2	R_1	R_2	R_3
MAP	M_1	M_2	M_3

T_1: Time when preclamping of carotid artery after general anesthesia which was recorded as baseline reference;
T_2: Time after clamping of the carotid artery;
T_3: Time after declamping of carotid artery and stabilization of cerebral perfusion;
V-MCA: Velocity of middle cerebral artery;
rSO_2: Regional oxygen saturation;
MAP: Mean arterial blood pressure

Clinical Definitions

1. Intraoperative cerebral hypoperfusion was defined by TCD monitoring values: V-MCA decreased more than 50% compared with the baseline value after clamping of the carotid artery;
2. Postoperative hyperperfusion was recorded when the V-MCA increased more than 100% compared with the baseline value after declamping of the carotid artery;
3. CHS was recorded if patients developed mental disorders, seizures, or focal neurological deficits after operation, accompanied with or without brain edema or hemorrhage on computed tomography or magnetic resonance imaging (MRI).

Intraoperative Monitoring and Selective Shunting

Patients in the current study were operated under general anesthesia by three experienced neurosurgical specialists. Patients were continuously monitored by TCD and NIRS throughout their operation. The blood pressure would be moderately increased if V-MCA decreased more than 50% after clamping the carotid artery so as to improve the cerebral perfusion and to avoid intraoperative cerebral infarction. Shunting was conducted based on the TCD monitoring results and the surgeon's discretion.

Data Collection

Three time points were selected: the time of preclamping of the carotid artery after general anesthesia was recorded as baseline reference T_1; the time after clamping of the carotid artery was recorded as T_2; the time after declamping of the carotid artery and stabilization of cerebral perfusion was recorded as T_3. Relevant monitoring values (V, r) combined with mean arterial blood pressure (MAP, M) at each point of time were recorded, as shown in Table 1.

Table 2. Baseline Information of Patients in Current Study.

Characteristics	Number(%)
Gender	
Male	69(82.1%)
Female	15(17.9%)
Age	63.0 ± 8.7
Morbidities	
Severe stenosis of contralateral ICA	29(34.5%)
Hypertension	66(78.6%)
Diabetes mellitus	32(38.1%)
Coronary heart disease	25(29.8%)
Smoking history	44(52.4%)

Statistical Analysis

Continuous variables are presented as the mean ± standard deviation, and categorical variables are presented as the percentages. One-way analysis of variance (ANOVA) was performed for the comparison of rSO_2 at different time points, followed by post hoc analysis for inter-group difference. Based on TCD monitoring values, sensitivities and specificities for monitoring of intraoperative cerebral hypoperfusion by NIRS were calculated. The best cutoff of rSO_2 decrease for the detection of intraoperative hypoperfusion was explored by the receiver operating characteristics (ROC) curves. The correlation between NIRS and TCD monitoring results was evaluated by the Pearson correlation analysis, based on the percent changes from baseline reference of each monitoring value. All statistical analyses were performed by the SPSS software (Version 27.0, IBM Corporation, New York, USA). P<0.05 was considered statistically significant.

Results

Patient Information

For this study 84 consecutive patients were enrolled, among which 29 cases were simultaneously associated with ICA severe stenosis or occlusion. According to preoperative DSA, collateral circulation was poorly developed in 41 patients. Some 23 patients complained about transient ischemic attack (TIA) and 47 patients suffered from stroke before operation, with the remaining 14 patients asymptomatic. Baseline information of all 84 patients is given in Table 2.

Efficacy of Monitoring of Intraoperative Cerebral Hypoperfusion by NIRS and Correlation between NIRS and TCD Monitoring Value

After clamping the ICA, cerebral hypoperfusion occurred in 14(16.6%) patients, whose V-MCA decreased more than 50% compared with baseline value. Only five among them received intraoperative shunting according to the surgeon's decision. During clamping, the rSO_2 and V-MCA, respectively, decreased 6.5 ± 5.4% and 27.0 ± 13.5% from baseline values. The NIRS monitoring value had significant positive correlation with TCD monitoring value (Pearson correlation coefficient was 0.581, P<0.001). According to the ROC analysis, the area under ROC curve (AUC) was 0.929 (95%CI 0.865–0.994, P<0.001), and the optimal cutoff value for intraoperative cerebral hypoperfusion was rSO_2 decreasing by 12.3% (Fig. 1). The sensitivity, specificity, false negative rate, false positive rate, diagnostic accordance rate, positive predictive value, and negative predictive value were 64.3%, 90.0%, 35.7%, 10.0%, 85.7%, 56.3%, and 92.6%, respectively, and the diagnostic Kappa value was 0.570, P<0.001. The accuracy of NIRS versus TCD monitoring is shown in Table 3.

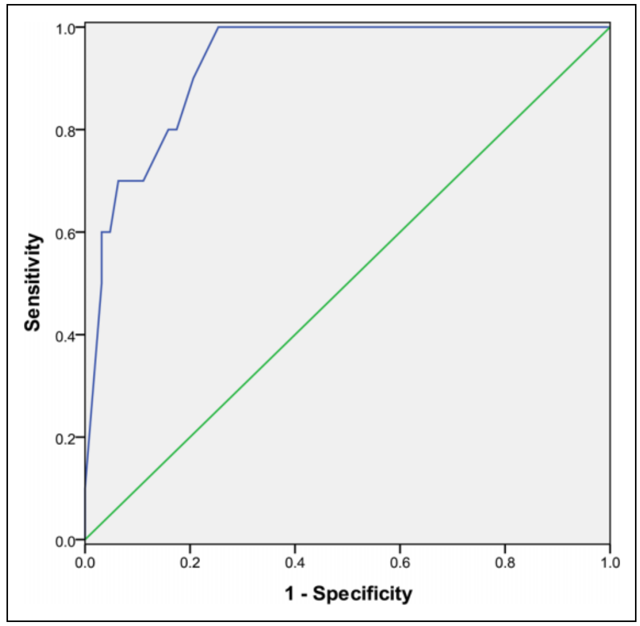

Fig. 1. ROC curve of NIRS monitoring for intraoperative hypoperfusion.

Table 3. Accuracy of NIRS vs. TCD Monitoring for Intraoperative Cerebral Hypoperfusion.

	V-MCA decrease ≥50%		
rSO_2 decrease ≥12.3%	+	-	Total
+	9	7	16
-	5	63	68
Total	14	70	84

The rSO_2 during the Surgical Process

The rSO_2 value ipsilateral to operative side before clamping was 68.1 ± 6.7, slightly lower than that of contralateral side (71.2 ± 5.7, P=0.215). A significant drop of rSO_2 value occurred immediately after carotid clamping, and then it gradually increased and approached the baseline value after

Table 4. rSO_2 at Different Time Points During Operation.

Monitored parameter	T_1	T_2	T_3
MAP(mmHg)	94.7 ± 7.8	104.5 ± 13.2	92.2 ± 9.3
Ipsilateral rSO_2	68.1 ± 6.7	63.3 ± 6.7	72.0 ± 6.2
Contralateral rSO_2	71.2 ± 5.7	70.4 ± 6.1	71.7 ± 6.0
P	0.215	<0.001	0.472

T_1: Time when preclamping of carotid artery after general anesthesia which was recorded as baseline reference;
T_2: Time after clamping of the carotid artery
T_3: Time after declamping of carotid artery and stabilization of cerebral perfusion.

Table 5. Subgroup Analysis of rSO_2 at Different Time Points Among Patients with Contralateral ICA Severe Stenosis or Without.

	Ipsilateral rSO_2 (N_1=29)	Ipsilateral rSO_2 (N_2=55)	P
T1	66.8 ± 6.1	68.8 ± 6.6	0.531
T2	62.5 ± 6.5	63.7 ± 6.7	0.620
T3	71.1 ± 6.1	72.5 ± 6.2	0.547

T_1: Time when preclamping of carotid artery after general anesthesia which was recorded as baseline reference;
T_2: Time after clamping of the carotid artery.
T_3: Time after declamping of carotid artery and stabilization of cerebral perfusion.
N_1: Patients concomitant with contralateral ICA severe stenosis.
N_2: Patients without contralateral ICA severe stenosis.

carotid declamping. The rSO_2 value of the contralateral side stayed relatively stable during operation. The variation trend of the rSO_2 value at different time points is shown in Table 4. Moreover, we performed subgroup analysis of rSO_2 at different time points among patients with contralateral ICA severe stenosis or without. We found that the rSO_2 of patients with contralateral ICA severe stenosis was insignificantly lower than patients without it (Table 5). As a result, we believe that NIRS is equally useful in ICA stenosis patients and patients without stenosis.

Patient Outcome

No stroke or death occurred after operation in the current study. Brain MRI rechecked after operation showed that fresh infarction of the ipsilateral hemisphere developed in 16 patients (19.0%), but all were asymptomatic.

Discussion

Therapeutic measures for ischemic stroke include medical treatment, interventional therapy, ischemic preconditioning, and surgical strategy[11,12]. As an important treatment for symptomatic severe stenosis of ICA[13–15], the benefit of CEA has been limited by the perioperative complications. Temporary cerebral hypoperfusion and potential ischemic injury during cross-clamping may occur in some patients, especially in those without well-developed collateral circulation. Intraoperative shunting is the most effective measure for the prevention of cerebral hypoperfusion during carotid clamping. However, it may on the other hand result in intraoperative embolism or damage of the vessel wall. Moreover, a large retrospective study indicated that intraoperative shunting may increase the long-term restenosis rate after CEA[16]. There is no guideline for intraoperative shunting to date; some surgeons advocate routine shunting for fear of the serious risk of cerebral hypoperfusion[17,18]. Because most patients with chronic stenosis of ICA usually develop sufficient collateral circulation, other surgeons are in favor of selective shunting[19–21]. Selective shunting based on intraoperative monitoring results is recommended by many surgeons.

Several monitoring techniques have been suggested over the years to solve this problem, yet none of them has been accepted as the standard method. Electroencephalography (EEG) can indirectly reflect cerebral blood flow during CEA, but the monitoring information is always influenced by anesthetic depth and temperature changes. Furthermore, EEG monitoring results are to a great extent dependent on the experience of monitoring personnel, resulting in a relatively high false positive rate[22,23]. TCD can continuously monitor blood flow velocity in the MCA, but it cannot objectively reflect cerebral perfusion. Furthermore, utilization of TCD is greatly restricted because no suitable temporal bone window exists in about 15% patients[24]. As a traditional monitoring technique, the sensory evoked potential (SEP) is also used for monitoring of brain function by stimulating peripheral nerves. Nevertheless the SEP is not only time-consuming but also susceptible to anesthetic depth, and it cannot monitor the function of whole hemisphere[25]. As for the stump pressure, it cannot continuously monitor the cerebral blood flow (CBF)[26,27].

NIRS is based on measuring the oxyhemoglobin fraction in the microvasculature under the cerebral cortex; it can continuously and noninvasively monitor the cerebral oxygen saturation of target brain tissue, indirectly reflecting CBF during CEA, so it has been adopted as a monitoring tool in many centers[28]. Multiple monitoring by NIRS and EEG has produced satisfactory results[29], and correlation between NIRS and TCD monitoring values has also been confirmed[30,31]. Yet the NIRS monitoring value may be disturbed by extracranial oxygen metabolism, and is susceptible to the influence of blood pressure and arterial oxygen saturation. The reliability of NIRS monitoring for intraoperative cerebral hypoperfusion still needs further research for verification. On the other hand, the optimal threshold for selective shunting during CEA is still debated.

In this prospective study, TCD was set as a gold standard for intraoperative monitoring because of its advantages in the real-time measurement of V-MCA. Among the 14 patients in which V-MCA decreased more than 50% during clamping, only five received shunting because the other nine cases had well-developed collateral circulation as shown on the preoperative DSA. After carotid clamping, the ipsilateral

rSO_2 immediately decreased, significantly lower than baseline value, whereas rSO_2 of the contralateral side had no significant change.

Among the 14 patients whose V-MCA decreased more than 50% during clamping, rSO_2 in nine of them decreased more than 12.3%, resulting in a 35.7% false negative rate. The relatively high negative rate could be explained in three aspects. First, as we all know, TCD mainly measures the blood flow velocity of MCA, while NIRS monitors the oxygen saturation of the frontal cortex, mainly supplied by ACA. Second, the NIRS monitoring value might have been influenced by oxygen metabolism of extracranial origin, combined with the influence of changes in blood pressure and arterial oxygen saturation. Third, cerebral perfusion in some patients might be compensated by the blood flow from the anterior communicating artery, so there might be no evident change of rSO_2 in spite of the significant decrease of V-MCA. Generally speaking, the two monitoring parameters are not physiologically the same.

On the other hand, among 70 patients whose V-MCA decreased less than 50%, rSO_2 in seven cases dropped more than 12.3%, resulting in a 10% false positive rate. We believe the heterogeneity of hemodynamics and difference of compensatory capacity in CBF among the patient population might be the reason for the false positive rate.

Our study indicated that the sensitivity and specificity of NIRS monitoring for intraoperative hypoperfusion were 64.3% and 90.0%, resulting in a strong consistency with TCD monitoring results (Kappa=0.570, $P<0.001$). The ROC analysis confirmed that rSO_2 decreasing by 12.3% could most effectively predict the intraoperative hypoperfusion. There existed five false negative cases, but no intraoperative ischemic brain injury occurred, even though only one patient received intraoperative shunting. Subsequently, we advocate that NIRS could accurately detect intraoperative hypoperfusion during carotid clamping, and reliably indicate for selective shunting.

Conclusions

NIRS is not only convenient and economic, but could continuously and noninvasively monitor oxygen saturation in real time. Our study revealed that NIRS monitoring results were strongly consistent with TCD monitoring values, and a 12.3% decrease of rSO_2 could be adopted as a reliable threshold for intraoperative cerebral hypoperfusion. It could serve as a good substitute for TCD in CEA monitoring for patients without satisfactory temporal bone windows.

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Ethical Approval

This study was approved by Comite Etico de Investigacion(CEI).

Statement of Human and Animal Rights

This article contains human studies approved by the local CEI.

Statement of Informed Consent

Written informed consent was obtained from all patients in this study.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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