Near-Infrared Spectroscopy Can Predict the Onset of Cerebral Hyperperfusion Syndrome after Carotid Endarterectomy

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Key Words

Near-infrared spectroscopy · Cerebral hyperperfusion syndrome · Carotid endarterectomy

Abstract

Background: Cerebral hyperperfusion syndrome (CHS) after carotid endarterectomy (CEA) is a potential life-threatening complication. Therefore, early identification and treatment of patients at risk is essential. CHS can be predicted by a doubling of postoperative transcranial Doppler (TCD)-derived mean middle cerebral artery blood velocity (V_{mean}) compared to preoperative values. However, in approximately 15% of CEA patients, an adequate TCD signal cannot be obtained due to an insufficient temporal bone window. Moreover, the use of TCD requires specifically skilled personnel. An alternative and promising technique of noninvasive cerebral monitoring is relative frontal lobe oxygenation ($r\text{SO}_2$) measured by near-infrared spectroscopy (NIRS), which offers on-line information about cerebral oxygenation without the need for specialized personnel. In this study, we assess whether NIRS and perioperative TCD are related to the onset CHS following CEA. **Methods:** Patients who underwent CEA under general anesthesia and had a sufficient TCD window were prospectively included. The V_{mean} and $r\text{SO}_2$ measured before induction of anesthesia were compared to measure-

ments performed in the first postoperative hour (ΔV_{mean} , $\Delta r\text{SO}_2$, respectively). Logistic regression analysis was performed to determine the relationship between ΔV and $\Delta r\text{SO}_2$ and the occurrence of CHS. Subsequently, receiver operating characteristic (ROC) curve analysis was used to determine the optimal cutoff values. Diagnostic values were shown as positive and negative predictive values (PPV and NPV). **Results:** In total, 151 patients were included, of which 7 patients developed CHS. The ΔV_{mean} and $\Delta r\text{SO}_2$ differed between CHS and non-CHS patients (median, interquartile range), i.e. 74% (67–103) versus 16% (–2 to 41), $p = 0.001$, and 7% (4–15) versus 1% (–6 to 7), $p = 0.009$, respectively. The mean arterial blood pressure did not change. Postoperative ΔV_{mean} and $\Delta r\text{SO}_2$ were significantly related to the occurrence of CHS [odds ratio (OR) 1.40 (95% CI 1.02–1.93) per 30% increase in V_{mean} and OR 1.82 (95% CI 1.11–2.99) per 5% increase in $r\text{SO}_2$]. ROC curve analysis showed an area under the curve of 0.88 ($p = 0.001$) for ΔV_{mean} and an optimal cutoff value of 67% increase (PPV 38% and NPV 99%), and an area under the curve of 0.79 ($p = 0.009$) for $\Delta r\text{SO}_2$ and an optimal cutoff value of 3% $r\text{SO}_2$ increase (PPV 11% and NPV 100%). The combination of both monitoring techniques provided a PPV of 58% and an NPV of 99%. **Conclusions:** Both TCD and NIRS measurements can be used to safely identify patients not at risk of developing CHS. It appears that NIRS is a good alternative when a TCD signal cannot be obtained.

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Background

Perioperative cerebrovascular complications of carotid endarterectomy (CEA) can be divided into intra- and postoperative complications, depending on the time of onset. Intraoperative adverse events, mostly caused by thromboembolic events or hypoperfusion [1], have significantly declined following the introduction of intraoperative cerebral monitoring [2–4], whereas the postoperative rate of cerebrovascular complications remained more or less stable with approximately 3% [2]. Besides local thrombosis at the level of the endarterectomy or thromboembolism, cerebral hyperperfusion syndrome (CHS) is an important postoperative complication.

CHS, defined as a cerebral hyperperfusion in addition to neurological symptoms, occurs in approximately 3–5% of patients undergoing a CEA procedure and is potentially life threatening [5].

When not recognized timely and treated adequately, CHS can lead to intracerebral hemorrhage, the most feared complication associated with a mortality of 40%, and therefore warrants early identification of patients at risk [6]. Currently, postoperative transcranial Doppler (TCD) monitoring is considered the gold standard in CHS prediction. A TCD value which is the double of preoperative middle cerebral artery (MCA) mean blood velocity (V_{mean}) is associated with onset of CHS in about 40% of patients and can reliably exclude patients at risk of developing CHS [7]. However, in 10–15% of CEA patients, an adequate TCD signal cannot be obtained because of an insufficient temporal bone window. At present, for this subgroup of patients, there is no reliable alternative monitoring tool to predict CHS. As a consequence, patients at high risk might be missed by the current monitoring strategy, while patients might be incorrectly identified as high risk for CHS leading to superfluous treatment and additional costs.

An alternative approach is perioperative monitoring of the frontal lobe oxygenation of the brain (rSO_2) with near-infrared spectroscopy (NIRS). This technique may be a promising alternative cerebral monitoring technique since it is easy to apply, applicable in all patients and relatively low in costs. However, the existing evidence on perioperative use of NIRS in relation to the onset of CHS is limited [8].

In the present study, we questioned whether NIRS could be used for identification of patients at risk of developing CHS. Therefore, we prospectively gathered NIRS-measured rSO_2 before, during and after CEA and related NIRS and TCD to the development of CHS following CEA.

Methods

Patients

This study was designed as a single-center cohort study. Patients who underwent CEA between February 2009 and June 2011 in the University Medical Center Utrecht and had a temporal window suitable for TCD monitoring were prospectively included. The severity of the carotid artery stenosis on preoperative imaging by computed tomography angiography or magnetic resonance angiography was categorized on a 4-point scale: <50%, 50–70%, 70–99% stenosis or occlusion.

Measurements (fig. 1)

One day before surgery, baseline oscillometric blood pressure (BP) and bilateral V_{mean} were measured. Baseline rSO_2 was determined bilaterally before induction of anesthesia and continued till the end of surgery. Peroperatively and in the recovery ward, intra-arterial BP was monitored through a catheter (1.1 mm ID, 20 gauge) placed in the radial artery. Intraoperative V_{mean} monitoring was started after induction, but before incision, and continued till the end of surgery. Postoperative TCD and NIRS measurements were performed for a period of 20 min in the first postoperative hour.

Transcranial Doppler

For measurement of the V_{mean} in the MCA, a pulsed Doppler transducer (DWL Multidop X4, Sipplingen, Germany) gated at a focal depth of 45–60 mm was placed over the temporal bone to insonate the main stem of the ipsilateral MCA and V_{mean} was recorded continuously.

Near-Infrared Spectroscopy

The rSO_2 measurement was performed using Invos Cerebral Oximeter (Somanetics Corporation, Troy, Mich., USA) with the aid of two sensors placed on the forehead.

Intraoperative Management

After application of routine monitoring devices (ECG and pulse oximetry), induction of anesthesia was achieved with sufentanil (0.3–0.7 $\mu\text{g}/\text{kg}$), propofol (0.5–2.0 mg/kg) and rocuronium (0.3–0.5 mg/kg). Anesthesia was maintained using sevoflurane, with a minimum alveolar concentration of 0.5–1. Before cross-clamping the carotid artery, 5,000 U of heparin was given intravenously.

The CEA was performed by an experienced vascular surgeon or by a vascular trainee under supervision in a standardized way. An intraluminal shunt was used selectively in case of electroencephalographic (Micromed Inc., Treviso, Italy) asymmetry.

Postoperative Management

Postoperatively, patients stayed in the recovery ward for continuous BP monitoring for at least 6 h. After the postoperative NIRS and TCD measurements had been performed, patients with a systolic BP >160 mm Hg, a BP of 20% above the preoperative BP, a postoperative V_{mean} >100% compared to preoperative V_{mean} , or an absolute V_{mean} >120 $\text{cm}\cdot\text{s}^{-1}$ with or without symptoms were treated with intravenous infusion of labetalol (5–20 $\text{mg}\cdot\text{h}^{-1}$) to decrease BP and/or V_{mean} . After 6 h, patients were moved to the general ward. However, if BP was not controlled appropriately or if signs of CHS were present during the 6-hour time frame in the

Table 1. Patient characteristics of all patients and according to the onset of CHS

Variable	All patients (n = 151)	CHS (n = 7)	Non-CHS (n = 144)	p value
Male gender	117 (78)	5 (71)	112 (78)	0.695
Right side	63 (42)	3 (43)	60 (42)	0.950
Median age (IQR), years	70 (64–78)	59 (54–69)	70 (64–78)	0.079
History of CEA				
Ipsilateral	1 (1)	0	1 (1)	0.825
Contralateral	17 (11)	1 (14)	16 (11)	0.795
Symptomatic indication	133 (88)	6 (86)	127 (88)	0.843
Degree of ipsilateral stenosis				
50–70%	9 (6)	1 (14)	8 (6)	0.341
>70%	142 (94)	6 (86)	136 (94)	
Degree of contralateral stenosis				
<50%	72 (48)	2 (29)	70 (49)	0.300
50–70%	25 (17)	1 (14)	24 (17)	0.869
70–99%	24 (16)	2 (29)	22 (15)	0.348
Occlusion	19 (13)	1 (14)	18 (13)	0.889
Unknown	11 (7)	1 (14)	10 (7)	0.465
Peroperative shunt use	17 (11)	2 (29)	15 (10)	0.138
Perioperative stroke	4 (3)	0	4 (3)	0.655
Perioperative transient ischemic attack	1 (1)	0	1 (1)	0.825
Postoperative hypertension	32 (21)	7 (100)	25 (17)	<0.001
Death <30 days	1 (1)	0	1 (1)	0.825

Figures in parentheses are percentages, unless otherwise determined.

recovery ward, patients were transferred to the medium care unit for continuous monitoring and intravenous therapy.

Definition of CHS

CHS was defined as the postoperative occurrence of headache, confusion, seizures, focal neurological deficits or an intracranial hemorrhage, in addition to TCD-registered postoperative cerebral hyperperfusion (>100% increase of the preoperative V_{mean} or an absolute $V_{\text{mean}} > 120 \text{ cm} \cdot \text{s}^{-1}$).

Data Analysis

The BP signal and the envelope curve of the TCD spectrum were A/D converted at 100 Hz, while bilateral frontal lobe $r\text{SO}_2$ was determined at 0.14 Hz. To calculate the mean arterial blood pressure (MAP) and V_{mean} , the diastolic pressure or velocity, respectively, was multiplied by 2 and added to the systolic pressure or velocity. Subsequently, the results were divided by 3.

A 30-second averaged value of MAP, V_{mean} and $r\text{SO}_2$ was calculated at the following time points: baseline, preclamping, post-clamping and postoperative. Subsequently, relative differences between baseline and postoperative MAP, V_{mean} and $r\text{SO}_2$ and between pre- and postclamping MAP, V_{mean} and $r\text{SO}_2$ were defined as ΔMAP , ΔV_{mean} and $\Delta r\text{SO}_2$ respectively.

Statistical Analysis

Data are presented as median and interquartile range (IQR). The Wilcoxon signed rank test was used to compare the different

measurements. To calculate the differences between CHS and non-CHS patients, the Mann-Whitney U test was used. A p value <0.05 was considered significant. To determine the relationship between ΔV_{mean} and $\Delta r\text{SO}_2$ and outcome, logistic regression analysis was performed. The optimal cutoff point of both ΔV_{mean} and $\Delta r\text{SO}_2$ in relation to the onset of CHS was chosen using the receiver operating characteristic (ROC) curve and Youden's index (sensitivity + specificity – 1). Predictive values are shown as positive predictive value (PPV) and negative predictive value (NPV).

Results

Patient Characteristics (table 1)

Within the study time frame, 294 patients underwent CEA. Because of logistic reasons, 151 of these patients were included in this study, with a median age of 70 years (IQR 64–78). The 30-day death/stroke rate was 3%. One patient died 13 days after surgery, because of vegetative endocarditis, without cerebrovascular complications. Seven patients (5%) developed CHS, none of them suffering focal neurological sequelae and all 7 patients fully recovered. All CHS patients developed hypertension prior to the development of CHS.

Fig. 1. Time frame. At the following time points, MAP (mm Hg), V_{mean} ($\text{cm}\cdot\text{s}^{-1}$) and $r\text{SO}_2$ (%) were recorded and calculated. At baseline, MAP was measured using an oscillometric (osc.) method. Transition from white turns to gray indicates anesthetizing of the patient. $n = 151$; data are shown as median (IQR). Baseline

values: 1 day before surgery. Preclamping values: averaged value of a 30-second measurement, 30 s before preclamping. Postclamping values: averaged value of 30-second measurement, 3 min after declamping. Postoperative values: averaged value of 30-second measurement, in the first postoperative hour.

Hemodynamic and Cerebral Measurements (fig. 1; tables 2, 3)

Intraoperatively, MAP decreased from 95 mm Hg (85–104) before cross-clamping the carotid artery to 88 mm Hg (IQR 78–96 mm Hg) ($p < 0.001$) after declamping. V_{mean} increased from 48 $\text{cm}\cdot\text{s}^{-1}$ (IQR 42–59) to 55 $\text{cm}\cdot\text{s}^{-1}$ (IQR 42–67), $p < 0.001$. Three patients had an intraoperative ΔV_{mean} of $>100\%$; none of them developed CHS. $r\text{SO}_2$ did not change significantly after declamping the carotid artery.

$\Delta r\text{SO}_2$ did not differ between patients with and without an intraoperative ΔV of $>100\%$. Intraoperative ΔMAP , ΔV_{mean} and $\Delta r\text{SO}_2$ did not differ significantly between patients who did or did not develop CHS.

Postoperatively, MAP decreased from 102 mm Hg (IQR 93–110) preoperatively to 84 mm Hg (IQR 76–99) after surgery ($p = 0.001$), while V_{mean} increased from 55 $\text{cm}\cdot\text{s}^{-1}$ (IQR 45–65) to 65 $\text{cm}\cdot\text{s}^{-1}$ (IQR 53–79), $p < 0.001$, in combination with a stable $r\text{SO}_2$, being 70% (IQR 65–76) versus 71% (IQR 65–75), $p = 0.340$.

Pre- and postoperative MAP did not differ between CHS and non-CHS patients. However, patients who developed CHS had both a larger ΔV_{mean} and a larger $\Delta r\text{SO}_2$ than patients without CHS [74% (IQR 67–103) vs. 16% (IQR –2 to 41) and 7% (IQR 4–15) vs. 1% (IQR –6 to 7), $p < 0.01$, respectively].

Six patients had a postoperative ΔV_{mean} of $>100\%$, 4 patients had a postoperative V_{mean} of $>120 \text{ cm}\cdot\text{s}^{-1}$ and 2

patients had both. Two of these 12 patients developed CHS. Patients with a postoperative ΔV_{mean} of $>100\%$ or a postoperative V_{mean} of $>120 \text{ cm}\cdot\text{s}^{-1}$ had a higher $\Delta r\text{SO}_2$, i.e. 8% (IQR 2–15), than patients who had not, i.e. 0% (IQR –5 to 6), $p = 0.019$. The MAP did not change postoperatively compared to preoperative measurements.

Logistic Regression Analysis (table 4)

Univariate analysis demonstrated that both postoperative ΔV_{mean} [odds ratio (OR) 1.40 (95% CI 1.02–1.93) per 30% increase] and postoperative $\Delta r\text{SO}_2$ [OR 1.82 (95% CI 1.11–2.99) per 5% increase] were related to the development of CHS postoperatively.

ROC Curve Analysis (fig. 2)

Based on ROC curve analysis an increase in V_{mean} of 67% was identified as the cutoff value most related to the onset of CHS, with an area under the curve of 0.88 ($p = 0.001$). With this cutoff value, a PPV of 38% and an NPV of 99% were found (table 5). A cutoff value of 2% $r\text{SO}_2$ increase with an area under the curve of 0.79 ($p = 0.009$) had a PPV of 11% and an NPV of 100%. As shown in table 5, a combination of both monitoring techniques provides a PPV of 58% and an NPV of 99%. Of all 15 patients with $\Delta V_{\text{mean}} > 67\%$, 9 patients had a $\Delta r\text{SO}_2 > 2\%$.

Table 2. Intraoperative (Δ Intra) and postoperative (Δ Post) relative changes in MAP, mean MCA blood velocity (V_{mean}) and frontal lobe oxygenation ($r\text{SO}_2$) for all patients who developed CHS separately and their symptoms

Patient No.		Baseline	Preclamping	Postclamping	Post CEA	Δ Intra %	Δ Post %	Symptoms
1	$r\text{SO}_2$, %	72	62	68	74	9.0	3	Dysphasia and headache on 3rd postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	35	42	37	59	-12	69	
	MAP, mm Hg	110	132	64	114	-52	4	
2	$r\text{SO}_2$, %	70	68	67	74	-1	6	Dysphasia and confusion on 5th postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	77	68	70	86	3	12	
	MAP, mm Hg	109	96	96	116	0	6	
3	$r\text{SO}_2$, %	63	77	76	69	-3	10	Headache on 1st postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	39	47	59	79	26	103	
	MAP, mm Hg	115	110	81	64	-26	-44	
4	$r\text{SO}_2$, %	67	72	71	72	-1	7	Headache on 1st postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	35	28	26	71	-1	103	
	MAP, mm Hg	93	69	86	91	25	-2	
5	$r\text{SO}_2$, %	75	68	71	87	3	16	Headache and hypertension on 1st postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	88	73	82	153	-12	74	
	MAP, mm Hg	119	111	83	115	-25	-3	
6	$r\text{SO}_2$, %	75	80	82	88	3	17	Headache and hypertension on 6th postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	76	75	90	127	20	67	
	MAP, mm Hg	100	100	96	107	-4	7	
7	$r\text{SO}_2$, %	64	54	67	66	24	3	Headache and vomiting on 1st postoperative day
	V_{mean} , $\text{cm}\cdot\text{s}^{-1}$	67	62	103	120	66	79	
	MAP, mm Hg	97	146	102	100	-30	3	

Table 3. Intraoperative and postoperative relative increase in MAP (Δ MAP), mean MCA blood velocity (ΔV_{mean}) and frontal lobe oxygenation ($\Delta r\text{SO}_2$) in patients who developed CHS and those who did not

	Intraoperative, %			Postoperative, %		
	Δ MAP	ΔV_{mean}	$\Delta r\text{SO}_2$	Δ MAP	ΔV_{mean}	$\Delta r\text{SO}_2$
All	-7 (-16 to 3)	7 (-5 to 29)	0 (-3 to 4)	-15 (-26 to -3)	17 (0-44)	1 (-5 to 7)
CHS (n = 7)	-26 (-30 to 0)	13 (-6 to 25)	3 (-1 to 9)	3 (-3 to 6)	74 (67-102)	7 (4-15)
Non-CHS (n = 144)	-7 (-16 to 3)	7 (-5 to 30)	0 (-4 to 4)	-16 (-27 to -3)	16 (-2 to 41)	1 (-6 to 7)
p value	0.174	0.846	0.246	0.058	0.001	0.009

Data are shown as median (IQR).

Discussion

In this study, we evaluated the relationship between changes in both $r\text{SO}_2$ and V_{mean} during CEA and the development of postoperative CHS. We showed that both $r\text{SO}_2$ and V_{mean} were more increased in patients who did develop CHS than in those who did not. Both measurements could independently relate to the occurrence of CHS. Based on our results, the combination of TCD and

NIRS seems to most reliably select patients at risk for the development of CHS, while NIRS monitoring alone can safely exclude patients at risk of developing CHS.

Exclusion of patients being at risk of developing CHS is essential as treatment of patients in the early phase can potentially prevent life-threatening symptoms [6]. Several risk factors have been proposed to be associated with the occurrence of CHS, including longstanding hypertension, poor collateral flow high-grade ipsilateral steno-

Fig. 2. ROC curves comparing the postoperative increases in relative frontal lobe oxygenation (rSO_2 ; dark line) measured using NIRS and TCD-derived mean MCA blood velocity (V_{mean} ; light line) for prediction of CHS following CEA.

sis and contralateral carotid occlusion, but no clear preoperative prediction model exists today [5]. Moreover, both a reduced cerebral blood flow and cerebral vasoreactivity have been shown to be independently related to the onset of CHS [9, 10]. Increases in cerebral blood flow can be measured using SPECT [11, 12]; however, as this method has several disadvantages including high procedural costs, TCD increase is currently mostly used as a surrogate for cerebral blood flow measurements.

We recently observed that TCD measurements in the postoperative phase more precisely predict the onset of CHS than intraoperative TCD measurements [7]. We attributed this finding to the influence of the administered anesthetic agents during the intraoperative measurement. To avoid the influence of anesthetics on the measurements, we used the same time frame in the current study and compared the preoperative and postoperative awake values.

As described elsewhere, the value of NIRS related to the onset of CHS has been promising, but the evidence is poor since there are no clearly defined rSO_2 cutoff values [8]. Ogasawara et al. [13] compared declamping rSO_2 with pre-clamping values and found a significant correlation between rSO_2 increases after declamping and the onset of

Table 4. Univariate predictors of the development of CHS

Variable	OR	95% CI
Male gender	1.40	0.26–7.56
Right side	1.05	0.23–4.86
Age	0.93	0.86–1.01
History of CEA		
Ipsilateral	0	
Contralateral	1.33	0.15–11.79
Symptomatic indication	0.80	0.09–7.08
Degree of ipsilateral stenosis		
50–70%	2.83	0.30–26.45
>70%	0.13	0.04–3.30
Degree of contralateral stenosis		
<50%	0.42	0.08–2.25
50–70%	0.83	0.10–7.24
70–99%	2.22	0.41–12.16
Occlusion	1.17	0.13–10.26
Unknown	2.23	0.24–20.41
Peroperative shunt use	3.44	0.61–19.30
Intraoperative ΔV_{mean} , per 1% increase	1.00	0.98–1.02
Intraoperative ΔrSO_2 , per 1% increase	1.10	0.92–1.19
Postoperative ΔV_{mean} , per 1% increase	1.01*	1.00–1.03
Postoperative ΔrSO_2 , per 1% increase	1.13*	1.02–1.25
Postoperative ΔV_{mean} , per 30% increase	1.48*	1.08–2.03
Postoperative ΔrSO_2 , per 5% increase	1.82*	1.11–2.99

Statistically significant predictors of CHS are indicated by an asterisk.

Table 5. Diagnostic cross-table for the number of patients that developed CHS after CEA correctly diagnosed by NIRS and/or TCD measurements

	CHS+	CHS–	Sens. %	Spec. %	PPV %	NPV %
Monitoring technique						
NIRS+	7 (5)	59 (39)	100	58	11	100
NIRS–	0 (0)	82 (5)				
TCD+	6 (4)	10 (7)	86	93	38	99
TCD–	1 (1)	131 (9)				
Combined monitoring techniques						
TCD+, NIRS+	6 (4)	3 (2)	86	98	67	99
TCD–, NIRS–	0	74 (49)	0	54	0	10
TCD+ or NIRS+	7 (5)	64 (4)	100	46	10	100

Figures in parentheses are percentages. The cutoff points used are determined after analysis of the ROC curve; it was a 2% increase for NIRS measured frontal lobe oxygenation (ΔrSO_2) and a 67% increase for TCD-measured MCA blood velocity (ΔV_{mean}).

Sens. = Sensitivity; Spec. = specificity.

CHS. However, in their study, only 1 patient developed CHS. Komoribayashi et al. [14] also used intraoperatively measured NIRS values. They found a significant association between cerebral hyperperfusion, patients without clinical symptoms, and a reduced rSO_2 during clamping as compared to preclamping values. Moreover, the association between intraoperative ischemia and cerebral hyperperfusion following CEA has been shown previously [15].

Our study has several limitations. Firstly, early antihypertensive treatment of patients at risk might have prevented the later development of CHS. In 12 patients, cerebral hyperperfusion was observed (ΔV_{mean} of $>100\%$, or a postoperative V_{mean} of $>120 \text{ cm}\cdot\text{s}^{-1}$), but only in 8 of these patients an increase in rSO_2 of $>2\%$ was found. Nevertheless, the other 4 patients did not develop CHS. This might be explained by the use of antihypertensive therapy in the selected patients. It is thought that patients with a high-degree carotid stenosis have an impaired cerebral autoregulation. As in these patients the cerebrovascular resistance is reduced and the V_{mean} (as a surrogate measure of the cerebral blood flow) has become BP dependent [16], antihypertensive treatment might have prevented the later development of CHS in these patients. However, in our analysis, we assumed that all hypertensive patients would have developed CHS (worst case scenario). In such a scenario, the magnitude of the ORs remained similar, and therefore we feel that the treatment of hypertension of patients whose blood pressure rose did not affect our findings. Therefore, we conclude that the use of antihypertensive medication has not influenced our results. Secondly, the utility of TCD was limited by the need for a sufficient bone window; moreover, TCD measurements required experienced personnel. NIRS can partly compensate for the disadvantages of TCD, since it is easy to apply and can be performed in all patients. Nevertheless, the interindividual and intraindividual baseline variability is high [17]; therefore, we correlated outcome to the relative and not the absolute change in rSO_2 . Further-

more, the reproducibility of NIRS measurements has previously been questioned [17]. To reduce the interindividual variation, we used NIRS as a trend monitor and to reduce the intraindividual variation, we did not remove the sensor between the end of surgery and the measurement in the recovery room.

The third and most relevant limitation of our study is the limited number of cases. Because of the small number of patients who develop CHS following CEA, this number is not easy to expand. Therefore, we used a limited number of predictors and no adjustment for multiple testing was made. Where the small numbers limited the precision of our estimates, it is unlikely that it affected the validity of our findings.

Based on our results, we conclude that NIRS is a reliable monitoring technique to exclude patients at risk of developing CHS. Furthermore, for the detection of patients at risk of developing CHS, the combination of NIRS and TCD monitoring provides the highest predictive value. However, as increase in the number of cases is needed to confirm our results, it is too premature to recommend a widespread application of use for the detection of patients at risk of developing CHS. Nevertheless it strengthens us to continue the evaluation of both NIRS and TCD and we added NIRS to our standard cerebral monitoring protocol.

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Disclosure Statement

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