When to perform transcranial Doppler to predict cerebral hyperperfusion after carotid endarterectomy?

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Summary   Cerebral hyperperfusion syndrome (CHS) after carotid endarterectomy (CEA) is a potential life-threatening disease. Identification of patients at risk for CHS commonly takes place with use of intra-operative transcranial Doppler (TCD), but is associated with both false positive and false negative results. We aimed to determine the diagnostic value for predicting CHS, by adding a TCD measurement in the early post-operative phase after CEA.

We retrospectively included 72 patients who underwent CEA between January 2004 and August 2010 and in whom both intra- and post-operative TCD of the ipsilateral middle cerebral artery monitoring were performed. Twelve patients (17%) had an intra-operative mean blood flow velocity (V_{mean}) increase >100% and 13 patients (18%) a post-operative V_{mean} increase of >100%. In 5 patients (7%) CHS was diagnosed; 2 of those had an intra-operative V_{mean} increase of >100% and all 5 a post-operative V_{mean} increase >100%. This results in a positive predictive value of 17% for the intra-operative and 38% for the post-operative measurement.

In conclusion, a post-operative increase of the mean velocity in the ipsilateral middle cerebral artery of >100% as measured by TCD is superior to an intra-operative velocity increase, for the identification of patients at risk for the development of CHS after CEA.
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Introduction

Cerebral hyperperfusion syndrome (CHS) after carotid endarterectomy (CEA) is a potential life-threatening disease. It is defined by a combination of symptoms, including headache, vomiting, neurological deficit or seizures, and at least a doubling of pre-operative cerebral blood flow. CHS can occur during the first few days up to four weeks after CEA in 1−3% of patients [1]. If not recognized and treated adequately in time (i.e., strict blood pressure control), hemorrhagic stroke may occur, which subsequently leads to death in up to 40% of patients [2].

The generally accepted definition of post-operative cerebral hyperperfusion in the context of CEA is defined as an increase in cerebral blood flow (CBF) of >100% over baseline [3]. This occurs in approximately 10% of CEA patients [4] and has been associated with a tenfold higher risk for post-operative intra-cerebral hemorrhage in patients operated under general anesthesia [3,5]. Changes in CBF are correlated with changes in the mean blood velocity (V_{mean}) in the ipsilateral middle cerebral artery (MCA) as measured with TCD [6,7]. Currently, during CEA under general anesthesia, an increase in V_{mean} of >100% three minutes after declamping the ICA, compared to the pre-clamping V_{mean} is the most commonly used predictor of CHS [2,8−10]. However, intra-operative TCD monitoring is associated with both false negative and false positive results [2,11]. Therefore, a more precise method is needed to predict which patients are at risk for CHS [12].

This study aimed to assess the predictive values of TCD monitoring regarding the development of CHS, by introducing an additional TCD measurement in the first two post-operative hours.

Methods

Patients who underwent CEA between January 2004 and August 2010 in the St. Antonius Hospital, Nieuwegein, The Netherlands, were retrospectively included. All patients who underwent CEA for a high degree ICA stenosis and in whom both intra- and post-operative TCD monitoring were performed were included.

Surgery was performed under general anesthesia and all patients received the same anesthetic regimen. An intra-luminal shunt was used selectively in case of EEG asymmetry or a decrease of >60% of V_{mean} measured by TCD [13].

For the TCD registration, a pulsed Doppler transducer (Pioneer TC4040, EME, Überlingen, Germany), gated at a focal depth of 45−60 mm, was placed over the temporal bone to insonate the main stem of the MCA ipsilateral to the treated carotid artery. The TCD transducer was fixed with a head frame and V_{mean} was recorded continuously.

V_{mean} values at the following time points were used for further analysis. For the pre-operative V_{mean} ($V1$), a TCD measurement was performed 1−3 days prior to operation. During operation, the pre-clamping V_{mean} ($V2$) was registered 30 s prior to carotid cross-clamping. The post-declamping V_{mean} ($V3$) was determined three minutes after declamping. An additional post-operative V_{mean} ($V4$) was measured within the first 2 h after surgery on the recovery ward. The intra-operative increase of V_{mean} was defined

Table 1 Patient characteristics.

Patient characteristics	$N = 72$; mean $\pm$ SD
Age (years)	68.4 ($\pm$ 10.1)
Gender (male)	53 (74%)
Site (right)	36 (50%)
Symptomatic	62 (86%)
Shunt use	22 (31%)
Post-operative hypertension	19 (26%)
Cerebral hyperperfusion syndrome	5 (7%)

and calculated as $(V3 − V2)/V2 \times 100$. For calculating the post-operative increase of V_{mean} the following formula was used $(V4 − V1)/V1 \times 100$. The positive (PPV) and negative predictive values (NPV) of both intra-operative and post-operative increase of V_{mean} were calculated.

All patients with post-operative hypertension, i.e. blood pressure (BP) >160 mmHg systolic (absolute), >20% above the pre-operative BP, or BP risen above the individual restriction in patients with an intra-operative V_{mean} increase >100%, underwent strict individualized BP control during the early post-operative period with intravenous labetalol (first choice) or clonidine (second choice).

CHS was diagnosed if the patient developed headache, confusion, seizures, intracranial hemorrhage or focal neurological deficits in the presence of post-operative cerebral hyperperfusion (defined as >100% increase of the pre-operative V_{mean}) after a symptom-free interval.

Results

Of the 560 patients undergoing CEA during the time of the study, 72 (13%) received both intra- and post-operative TCD monitoring and were included for the present analysis. See Table 1 for patient characteristics. The majority of patients were symptomatic (86%). About a third of the patients required the use of an intra-luminal shunt because of either EEG asymmetry or a decrease of >60% of V_{mean} measured by TCD.

Twelve patients (17%) had an intra-operative V_{mean} increase >100%. Post-operatively, V_{mean} increase >100% was found in the 13 patients (18%).

During all TCD measurements no significant increase in BP was found after declamping compared to the pre-clamping systolic BP or when the post-operative measurement was compared to the pre-operative systolic BP.

Of all 72 patients, 19 patients (26%) developed post-operative hypertension and 5 patients (7%) suffered from CHS. All patients with CHS had hypertension during the post-operative phase. The overall 30-day rate of death/stroke was 1%.

TCD measurements and clinical outcome

Of 12 patients with an intra-operative increase of V_{mean} >100%, 2 patients developed CHS. On the other hand, in 60 patients who had an intra-operative increase less than 100%, 3 patients suffered from CHS. This results in a PPV of 17% (2/12) and NPV of 95% (57/60) in the prediction of CHS (Table 2).

Table 2 Cross tables for predictive values of intra- or post-operative TCD measurements for the occurrence of CHS.

	CHS+	CHS−	PPV (%)	NPV (%)
Intra-operative increase				
>100%	2 (3%)	10 (14%)	17	95
<100%	3 (4%)	57 (79%)		
Post-operative increase				
>100%	5 (7%)	8 (11%)	38	100
<100%	0 (0%)	59 (82%)		

CHS+: number of patients who developed CHS (%); CHS−: number of patients who did not develop CHS (%); PPV: positive predictive value (%); NPV: negative predictive value (%).

With respect to the post-operative TCD measurements 5 of the 13 patients with at least a doubling of post-operative V_{mean} developed CHS. In the subgroup of 59 patients with a post-operative increase of less than 100% CHS did not occur. This results in a PPV of 38% (5/13) and a NPV of 100% (59/59) for the development of CHS.

Discussion

In the present retrospective study, as previously published, an increase in V_{mean} measured with post-operative TCD is superior in predicting the development of CHS to the commonly used increase in V_{mean} measured three minutes after declamping versus pre-clamping value [12]. The PPV of the post-operative measurement in the prediction of CHS is more than two times higher than the PPV of the intra-operative measurement (38% and 17% respectively). Moreover, absence of doubling of the V_{mean} at the post-operative measurement completely excluded the development of CHS (NPV 95% vs. 100% for the intra-operative and post-operative measurements, respectively). Therefore, with post-operative measurement fewer patients will be treated unnecessarily by strict intravenous antihypertensive medication. These observations need confirmation in larger patients cohorts, with special focus on the optimal threshold of post-operative CHS prediction.

In our study, only 5 of all patients developed CHS. The low incidence of CHS hampers the interpretation of our results. However, the incidence in our group of patients (7%) is relatively high compared to other series. This might be explained by the fact that in our referral hospital a selected group of patients with relatively severe hemodynamic compromise are treated, which is also reflected in the relatively high number of patients in whom a shunt was used (31%). In addition, data were collected retrospectively, and were more likely to be complete (i.e., including post-operative measurements) in patients with an intra-operative V_{mean} increase of >100%, or in patients who developed post-operative hypertension. However, prospectively collected data in another large vascular training hospital show similar results and thus confirm our findings [12]. A multicenter prospective study to optimize the post-operative TCD-measurements will start in 2012.

Conclusion

Besides the commonly used intra-operative TCD monitoring, additional TCD measurement in the early post-operative phase is useful to predict CHS in patients that underwent CEA under general anesthesia. By measuring V_{mean} in the post-operative instead of only in the intra-operative phase, both the positive and negative predictive value of TCD for development of CHS after CEA can be improved. Therefore, we recommend a baseline measurement before the administration of anesthetics and a post-operative measurement within two hours after surgery.

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