Journal of Clinical Neuroscience 21 (2014) 406–411

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

Reduced middle cerebral artery velocity during cross-clamp predicts cognitive dysfunction after carotid endarterectomy

Joanna L. Mergeche [a], Samuel S. Bruce [b], E. Sander Connolly [b,c], Eric J. Heyer [a,c,*]

[a] Department of Anesthesiology, Columbia University, 630 West 168th Street, P&S Box 46, New York, NY 10032, USA
[b] Department of Neurological Surgery, Columbia University, New York, NY, USA
[c] Department of Neurology, Columbia University, New York, NY, USA

ARTICLE INFO

Article history:
Received 24 May 2013
Accepted 31 May 2013

Keywords:
Carotid endarterectomy
Cognition
Cognitive dysfunction
Transcranial Doppler

ABSTRACT

Transcranial Doppler (TCD) is a useful monitor that can be utilized during carotid endarterectomy (CEA). Cognitive dysfunction is a subtler and more common form of neurologic injury than stroke. We aimed to determine whether reduced middle cerebral artery (MCA) mean velocity (MV) predicts cognitive dysfunction and if so, whether a threshold of increased risk of cognitive dysfunction can be identified. One hundred twenty-four CEA patients were included in this observational study and neuropsychometrically evaluated preoperatively and 24 hours postoperatively. MCA–MV was measured by TCD and percentage of baseline during cross-clamp was calculated ($MV_{cross\text{-}clamp}/MV_{baseline}$). Patients with cognitive dysfunction had significantly lower MV during cross-clamp than those without cognitive dysfunction (33.1 ± 13.7 cm/s *versus* 39.6 ± 16.0 cm/s, $p = 0.02$). In the final multivariate model, each percent reduction in MV was significantly associated with greater risk of cognitive dysfunction (odds ratio [OR]: 0.05 [95% confidence interval {CI} 0.01–0.23], $p < 0.001$) while statin use was associated with lower risk (OR: 0.33 [95% CI 0.12–0.92], $p = 0.03$). Using receiver operator characteristic curve analysis, the Youden index identified 72% of baseline MV during cross-clamp as the cutoff of maximum discrimination. Significantly more patients with MV < 72% of baseline during cross-clamp exhibited cognitive dysfunction than patients with MV ⩾ 72% of baseline (74.1% *versus* 27.1%, $p < 0.001$). Reduced MCA–MV during cross-clamp is a predictor of cognitive dysfunction exhibited 24 hours after CEA. MCA–MV reduced to <72% of baseline, or a ⩾28% reduction from baseline, is the threshold most strongly associated with increased risk of cognitive dysfunction. These observations should be considered by all clinicians that utilize intraoperative monitoring for CEA.

1. Introduction

Transcranial Doppler (TCD) is a useful adjunct to the commonly used electroencephalographic (EEG) monitoring during carotid endarterectomy (CEA).[1–6] The incidence of perioperative stroke during CEA is very low,[2,7] but is generally attributed to either ischemia during cross-clamp of the carotid artery or emboli during reperfusion.[8] EEG is commonly used to prevent ischemic stroke by detecting significant hemispheric ischemia during the cross-clamp period. Previous studies have determined that TCD assessment of cerebral blood flow mean velocity (MV) through the middle cerebral artery (MCA) can detect ischemic as well as embolic events and can further reduce the risk of stroke.[4,9,10]

As the incidence of perioperative stroke is exceedingly rare, investigators are studying subtler forms of neurologic injury, like cognitive dysfunction, to improve the safety of this commonly performed procedure.[11–15] To our knowledge, however, no studies have determined whether TCD assessment of cerebral blood flow through the MCA can detect mildly ischemic conditions that are undetected by EEG and associated with cognitive dysfunction. Though less clinically momentous than stroke, postoperative cognitive dysfunction has significant implications for quality of life and early mortality.[16] Glial markers of neuronal injury are significantly elevated in CEA patients that exhibit cognitive dysfunction as early as 24 hours after CEA.[17] In our previous work, we documented that approximately a quarter of CEA patients exhibit cognitive dysfunction 24 hours after CEA.[18,19] Given the common occurrence and significance of cognitive dysfunction, determining if TCD parameters can predict cognitive dysfunction is not only interesting, but it can improve the neurologic safety of this commonly performed procedure.

The aim of this study was to determine whether TCD assessment of cerebral blood flow through the MCA during cross-clamp of the carotid artery can predict cognitive dysfunction 24 hours after CEA and if so, whether a threshold associated with increased

* Corresponding author. Tel.: +1 212 305 9072; fax: +1 212 305 8287.
E-mail address: ejh3@columbia.edu (E.J. Heyer).

0967-5868/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jocn.2013.05.010

risk of cognitive dysfunction can be identified. These findings could ultimately be utilized to improve the safety of this commonly performed procedure.

2. Methods

2.1. Patients, anesthesia and surgery

One hundred twenty-four patients were enrolled with written informed consent in this Institutional Review Board-approved observational single center study at Columbia University Medical Center (http://www.ClinicalTrials.gov NCT00597883). Patients eligible for inclusion in this observational study were those scheduled for elective CEA for high-grade carotid artery stenosis who were English-speaking, with no axis-I psychiatric disorders, with complete intraoperative TCD records, and complete neuropsychometric evaluation preoperatively and 24 hours postoperatively.

All patients received general anesthesia with standard hemodynamic and temperature monitoring, as previously described.[18] No patients received blood transfusions. The surgical technique, anesthetic management, and indications for CEA have remained constant at this institution, as previously described.[18–21]

2.2. Cognitive measures

All patients were examined with an extensive battery of neuropsychometric tests ⩽24 hours preoperatively and 24 hours postoperatively. The neuropsychometric tests evaluate four cognitive domains – verbal memory (Controlled Oral Word Association Test, Hopkins Verbal Learning Test, and/or Buschke Selective Reminding Test), visuo-spatial organization (Rey-Osterrieth Complex Figure Copy and Recall), motor function (Grooved Pegboard and/or Finger Tapping Test), and executive action (Halstead-Reitan Trials A and B).

Similar to previous studies,[18–20,22,23] Z-scores were generated based on a surgical reference group's performance to account for practice effect, trauma of surgery, general anesthesia, and the overnight hospital stay experience. The surgical reference group was composed of 124 age- and sex-matched patients ⩾60 years of age undergoing lumbar level laminectomy or microdiscectomy on ⩽2 levels without fusion, no tumor/cyst, or blood loss necessitating transfusion. These patients experience similar surgical and anesthetic times as well as a similar general anesthetic. The mean difference score of the surgical reference group was subtracted from the difference score for the CEA patient and then divided by the standard deviation of the surgical reference group ($[\text{Difference}_{\text{CEA}} - \text{Mean Difference}_{\text{Reference}}]/\text{Standard Deviation}_{\text{Reference}}$). Therefore, each test was evaluated in units of standard deviation (SD) of the surgical reference group's change in performance.

CEA patient domains were evaluated to account for both focal and global/hemispheric deficits: (1) ⩾2 SD worse performance than the reference group in two or more cognitive domains or (2) ⩾1.5 SD worse performance than the reference group in all four cognitive domains. The details of each neuropsychometric test and their respective scoring rubrics are described in great detail in previous works.[18,19,21,24,25] The surgical reference group was only used to generate Z-scores; therefore, the surgical reference patients were not included in any other analysis or reported otherwise in this study.

A variety of factors affect the risk of cognitive dysfunction after CEA, but only age >75 years, diabetes mellitus, and statin use have been previously shown to significantly and independently affect the risk.[23,26] Other factors that might also affect the risk, but have not been shown to independently do so, were evaluated as well. These included sex, years of education, body mass index, history of smoking, hypertension, extensive peripheral vascular disease, previous myocardial infarction, previous coronary bypass-grafting, symptomatic history of transient ischemic attack or stroke, operative side, and duration of cross-clamp.

2.3. EEG

All patients were monitored intraoperatively with a 16 channel XL-Tek EEG (Natus Medical Inc., San Carlos, CA, USA) bipolar "double-banana" montage[27] using the nomenclature of the International 10–20 electrode placement system with either an Electro-Cap (Electro-Cap International Inc., Eaton, OH, USA) (n = 83) or microelectrodes (Rhythmlink, Columbia, SC, USA) (n = 41). Intraoperative monitoring for cerebral ischemia was performed by board certified neurologists. No patients included in this study experienced significant intraoperative ischemia detected by EEG that required shunt placement. No patients included in this study had a perioperative stroke.

2.4. TCD

An ST-3 TCD machine (Spencer Technologies, Seattle, WA, USA) was used for all patients. A 2 MHz probe was applied over the thinnest portion of the squamous component of the temporal bone on the operative side of the head. The MCA was insonated at an approximate depth of 50 mm from the scalp. A Marc 600 Headframe (Spencer Technologies) was used to hold the probe in place for the duration of the surgery. The primary TCD parameter evaluated in this study was MCA–MV measured in units of cm/s. Pulsatility index (PI) was also recorded to document a surrogate marker of cerebrovascular distal resistance. Prospective recordings were obtained at baseline, pre-clamp, clamp, 30 seconds post-clamp, pre-release, release, 5 minutes post-release, and 15 minutes post-release. Patients had baseline MV and PI values recorded prior to incision. During cross-clamp of the carotid artery, MV and PI were recorded at several time points, but the values utilized in this study are the values recorded after perfusion stabilized and remained constant during the cross-clamp period; immediately after cross-clamp, the MV often takes seconds to minutes to stabilize as cerebrovascular distal resistance, reflected as PI, decreases to compensate for the reduced blood flow (Fig. 1). The stabilized MV during cross-clamp was then divided by the MV at baseline ($MV_{\text{cross-clamp}}/MV_{\text{baseline}}$) to provide the percentage of remaining MCA blood flow velocity and presumptive blood flow. TCD records were also evaluated for high-intensity transient signals (HITS) to account for potential embolic or micro-embolic events during reperfusion.[28]

2.5. Statistical analysis

Statistical analysis was performed using R environment for statistical computing (R Development Core Team, Vienna, Austria). Multivariate imputation by chained equations (mice) with fully conditional specification was used in the event of missing data.[29] Five imputations were performed, with predictive mean matching for continuous variables and logistic regression for categorical variables. The R package mice (R Development Core Team)[30] was used to perform the imputation and pooled analyses.

For univariate analyses, Student's *t*-test, Wilcoxon rank sums test, Fisher's exact test, Pearson's χ^2 test and simple logistic regression were used where appropriate. A multiple logistic regression model was constructed to identify independent predictors of cognitive dysfunction within 24 hours. All factors with $p < 0.20$ in simple univariate logistic regression were entered into the final model. Model fit and calibration were confirmed with the likelihood ratio