The Effect of Carotid Endarterectomy on Cerebral Blood Flow and Cognitive Function

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Background: The effect of carotid endarterectomy on cognitive function is not fully understood. This study aims to characterize changes in cerebral blood flow after carotid endarterectomy and to determine if patients with improvement in cerebral blood flow have improved cognitive function after endarterectomy. *Methods:* Cerebral blood flow was measured preoperatively and 1 month postoperatively using phase contrast magnetic resonance angiography. Preoperative flow impairment was defined as ipsilateral flow at least 20% less than contralateral flow. Improvement in flow was defined as an absolute increase of at least 0.10 in flow ratio from pre- to postoperative assessments. Patients underwent cognitive testing preoperatively and at 1, 6, and 12 months postoperatively. *Results:* Twenty-four patients with unilateral carotid stenosis were enrolled from 3 sites. Preoperative internal carotid artery (ICA) and middle cerebral artery (MCA) flow impairment was observed in 50% and 22% of patients, respectively. Patients with preoperative flow impairment had an average of 0.25 and 0.16 absolute improvement in flow ratio in the ICA and MCA vessels, respectively; this was statistically significant for patients with baseline ICA flow impairment ($P < .01$). One hundred percent of patients with improvement in MCA flow had a significant improvement in attention compared to 56% of patients without MCA flow improvement ($P = .06$). Clinically significant improvements in all 4 cognitive domains were observed at 1 year ($P < .01$). *Conclusions:* Patients with baseline impairment of MCA blood flow were more likely to experience improvement in flow after revascularization. Improvement in MCA blood flow was associated with greater cognitive improvement in attention and executive functioning. **Key Words:** Carotid artery stenosis—carotid endarterectomy—cerebral blood flow—cognitive outcomes.

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Approximately 795,000 people in the United States suffer from a new or recurrent stroke each year, with an estimated 20% to 30% of these strokes resulting from carotid stenosis.[1,2] Carotid revascularization procedures including carotid endarterectomy (CEA) and percutaneous carotid angioplasty and stenting (CAS) have been shown to prevent strokes.[2-5] The effect of carotid revascularization on cognitive outcome is controversial. While some studies have shown cognitive improvement after carotid revascularization,[6,7] others have shown no change or even cognitive decline.[8,9] Both cerebral emboli and hyperperfusion mechanisms have been put forward as possible explanations for cognitive decline after revascularization.[10-14]

Evidence from several studies suggests that impaired cerebral blood flow caused by carotid stenosis may contribute to baseline cognitive impairment.[15] There are limited data from transcranial Doppler (TCD) measurements of the middle cerebral artery (MCA) with hypercapnic challenge, suggesting that some patients with limited cerebrovascular reserve resulting from carotid stenosis might experience improved cognitive function after carotid revascularization, presumably from the restoration of cerebral blood flow.[16] Previous techniques for assessing cerebral blood flow in patients with carotid stenosis have been limited because of the invasiveness of the technique or the lack of a quantitative approach.[17] We have used noninvasive phase contrast quantitative magnetic resonance angiography (qMRA) technology[18-24] to assess cerebral blood flow before and after CEA in patients with asymptomatic and symptomatic unilateral carotid stenosis. We report the effect of improved blood flow on cognitive function. By stratifying populations of patients with carotid stenosis in terms of degree of flow impairment, we hope to better understand which patients stand to benefit cognitively from carotid revascularization procedures.

Methods

Institutional review board approval was obtained for the clinical protocol at 3 institutions. All data were centrally managed at the Wallace Clinical Trials Center in Greenwich, Connecticut. Patient data were deidentified before leaving the treating institution to protect patient confidentiality in compliance with the Health Insurance Portability and Accountability Act (HIPAA).

Study Population

Patients with significant (>60%) carotid artery stenosis who were surgical candidates for carotid revascularization were prospectively enrolled over a 4-year period at 3 sites (2005-2009). Symptomatic status was defined as a recent transient ischemic episode referable to the ipsilateral hemisphere without evidence for acute infarction. Patients with bilateral disease, a history of acute stroke or history of a major stroke, dementia, major depression, or previous ipsilateral carotid surgery were excluded. All patients underwent carotid revascularization using CEA performed under general anesthesia with selective usage of shunting only when electroencephalographic (EEG) changes occurred during the cross-clamp period.

qMRA

Patients underwent phase contrast qMRA preoperatively and 1 month postoperatively. Quantitative cerebral blood flow values were generated using a qMRA software package, which is currently commercially available (VasSol, Chicago, IL). Quantitative blood flow rates were calculated for both the ipsilateral and contralateral internal carotid artery (ICA) and middle cerebral artery (MCA) vessels.

Flow compromise was assessed using a simple ratio (ipsilateral flow/contralateral flow) of the vessel flow rates as described previously.[25] For this analysis, preoperative flow impairment was defined as an ipsilateral flow at least 20% less than contralateral flow (flow ratio $\leq$0.8). Improvement in flow after carotid revascularization was defined as an absolute increase of at least 0.10 in the flow ratio from preoperative to 1 month postoperative assessments.

CEA

All patients underwent general endotracheal anesthesia in order to perform CEA. Surface EEG monitoring was performed throughout the procedure. The common, internal, and external carotid vessels were identified in all cases. Intravenous heparin (5000 IU) was administered 5 minutes before cross-clamping all major vessels. After all vessels were cross-clamped, selective usage of shunting was used at the discretion of the operating surgeon if ipsilateral or global EEG changes were observed. Endarterectomy was performed as previously described.[26]

Cognitive Outcomes

Patients underwent neuropsychological testing covering 4 cognitive domains: attention (Trail Making A), executive functioning (Trail Making B), language/verbal fluency (FAS), and memory/new learning (Hopkins Verbal Learning Test [HVLT]). Tests were administered preoperatively and 1 month, 6 months, and 1 year postoperatively. A clinically meaningful difference was defined as $\geq$10% improvement over baseline scores for the Trail Making A, Trail Making B, Verbal Fluency, and HVLT tests.

Statistical Analysis

Continuous variables were compared using the Student *t* test, and paired observations, such as mean preoperative ICA flow impairment versus postoperative ICA flow impairment, were compared using a paired *t* test. Categorical variables were analyzed with the Chi-square and Fisher exact tests, as appropriate, and paired proportions were compared with the McNemar test. The binomial test of equality of proportions was used to test if the proportion experiencing postoperative flow improvement was significantly different from 0.5. $P < .05$ (2-sided) was considered statistically significant. Analyses were conducted with SAS (version 9.2; SAS Institute, Cary, NC) and STATA (version 11; StataCorp, College Station, TX).

Results

A total of 24 patients with unilateral carotid stenosis (13 right and 11 left) were enrolled in this pilot study.