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Evaluation of Carotid Endarterectomy with Sequential MR Perfusion Imaging: A Preliminary Report


BACKGROUND AND PURPOSE: Current indications for carotid endarterectomy are determined by balancing the relative risks of surgery with the benefits of reduced risk of subsequent stroke. Our purpose was to use MR perfusion imaging to assess patients being considered for carotid endarterectomy and to monitor sequential changes in MR perfusion characteristics after surgery. In particular, we wished to determine whether this technique could be used to detect changes that might be related to post–carotid endarterectomy hyperemia.

METHODS: We used a single-section gradient-recalled echo sequence to investigate 14 patients being examined before possible surgery for carotid artery disease. In the 12 patients in whom carotid endarterectomy was performed, sequential studies were performed 3 to 5 days after surgery and at 3 months. Analysis of bolus-arrival-time (BAT) images was performed.

RESULTS: Significant delays in preoperative BAT images of 0.89 seconds (range, 0.05 to 3.22 seconds) were apparent between hemispheres. Excluding the two patients with contralateral internal carotid artery (ICA) occlusion, early arrival, possibly indicating postoperative hyperemia, was seen in five patients immediately after carotid endarterectomy but resolved within 3 to 5 months after surgery.

CONCLUSION: MR perfusion imaging shows differences in BAT between hemispheres in patients with ICA stenosis. Changes in perfusion characteristics after carotid endarterectomy are complex, and early BAT on the operative side can occur soon after endarterectomy in over half those patients without an occluded contralateral vessel. The significance of these findings with regard to patient outcome and risk of postoperative hyperemia requires further investigation.

Carotid endarterectomy has been shown to be effective in reducing the prevalence of stroke and mortality in persons with severe (>70%) carotid stenosis (1). Its efficacy may be due to the normalization of cerebral blood flow (CBF), to improvement in cerebrovascular reserve (2–4), and/or to reduction in the formation of emboli from carotid plaque. There is, however, little evidence as to whether changes in microvascular perfusion lead to clinical improvement.

Newly developed dynamic MR imaging techniques can assess cerebral perfusion (5) using conventional MR systems and may delineate ischemic tissue. The observation of widespread abnormalities in bolus arrival time (BAT) and relative cerebral blood volume (rCBV) in territories with normal T2-weighted MR characteristics indicates that this technique may define at-risk territories in patients with carotid artery disease (6).

Current indications for carotid endarterectomy are determined by the need to balance the relative risks of surgery with the benefits of a reduced risk of subsequent stroke. In recent large-scale trials, the perioperative stroke rate was a key determinate in defining the degree of carotid stenosis that would benefit from carotid endarterectomy as compared with medical management. Hemorrhagic stroke, which may be related to postoperative hyperemia, is a significant problem and occurs in approximately 0.6%
of carotid endarterectomies (7). The overall perioperative mortality and morbidity of carotid endarterectomy is about 5.8% in skilled hands (1). Any method that can be used to predict which patients will be at increased risk of post–carotid endarterectomy hyperperfusion and possible stroke may ultimately reduce the postoperative stroke rate.

The aim of this study was to use MR perfusion imaging to assess patients being evaluated for possible carotid endarterectomy and to monitor changes in MR perfusion characteristics soon after surgery and again at 3 months. In particular, we wished to determine whether this method could detect changes that might be related to postoperative hyperemia.

**Methods**

Fourteen patients, referred for the investigation of likely carotid stenosis, were studied prospectively. All MR imaging and perfusion studies were carried out at 1.5 T. Five series were obtained as follows. Sagittal T1 localizer images were acquired with parameters of 200/9/1 (TR/TE/excitations), a 25-cm field of view (FOV), and a 256 × 128 matrix. Single-section fast spin-echo T2-weighted (3000/17,85/1) images were obtained with an echo train length of 8, a 22-cm FOV, 8-mm-thick sections, no gap, and a 256 × 256 matrix. MR gradient-recalled echo perfusion images were acquired with parameters of 34/22.0/75, a flip angle of 20°, a 22-cm FOV, a 256 × 128 matrix, and a section thickness of 10 mm. Forty perfusion images were obtained at 3.25-second intervals. After 10 baseline images were obtained, gadopentetate dimeglumine, in a bolus of 0.2 mmol/kg of body weight, was administered by one of two investigators as a rapid hand injection through an antecubital vein followed by a bolus of normal saline. The duration of the bolus injection was 6 to 8 seconds.

Analysis was performed using the WinFun software package (developed by Mike Hayball, Department of Radiology, University of Cambridge) on a conventional personal computer. Images were constructed, pixel by pixel, of BAT, and elliptical regions of interest (ROIs) were chosen in comparable contralateral middle cerebral artery (MCA) territories so that relative delays between hemispheres could be calculated. The ROIs were drawn as large as possible while maintaining symmetry, including the gray and white matter, and avoiding any area of infarction. The software simultaneously displayed both an original image from the perfusion sequence and a calculated image. The ROIs were drawn on both images, making it easier to exclude areas with abnormalities or artifacts. Dual-display images were also obtained of BAT and enhancement. The time-signal data were initially converted into a signal-change curve using the following formula: Signal change = −Klog (S/S0), where K is an arbitrary constant, S is the signal, and S0 is the average signal before injection of contrast medium. This generated a curve with a positive peak, to which a gamma variate function was fitted (8). In our examples, K = 1000. The BAT was calculated as the peak of the gamma variate function, fitted to the curve using the Levenberg-Marquardt method (9). This was performed on a pixel-by-pixel basis, and the mean and standard deviation within each ROI were used to provide 95% confidence limits. Relative interhemispheric delays were calculated using the side of eventual, or contemplated, carotid endarterectomy as the reference. A positive delay was equivalent to a delay in BAT on the side of carotid endarterectomy relative to the contralateral hemisphere.

Studies were performed 1 to 13 days before endarterectomy, 3 to 5 days afterward, and 3 months later in the same anatomic plane. All patients had confirmatory preoperative conventional catheter X-ray angiography. MR perfusion studies were analyzed by investigators who were blinded to the side of carotid endarterectomy. Statistical significance was defined as P = .05 using Student’s t-test. Approval was obtained from the Local Research Ethics Committee of Addenbrooke’s Hospital.

**Results**

Of the 14 patients studied, four were women and 10 were men; the mean age was 71 years (range, 51 to 81 years). Two patients did not undergo carotid endarterectomy: one (case 13) because of complete internal carotid artery (ICA) occlusion shown by MR angiography and confirmed by X-ray angiography, and the other (case 14), who had nonlateralizing clinical symptoms, because of delayed BAT in the hemisphere contralateral to the diseased carotid, caused by MCA branch occlusions. One patient withdrew from the immediate postoperative study because of claustrophobia. Thus, 11 patients underwent pre- and postendarterectomy studies, nine of whom had late studies (repeated at 3 months or beyond). BAT images were calculated and are presented as interhemispheric delays relative to the side of carotid endarterectomy. The average number of pixels in the ROIs was 1249 (range, 270 to 2023). Data sets from two patients (cases 9 and 11) were of technically poor quality owing to moving artifacts.

**Preoperative Studies**

All 12 patients with adequate data sets had relative preoperative delays in BAT between hemispheres of 0.89 seconds (range, 0.05 to 3.22 seconds), P = .019 (see Table). Among the seven patients with unilateral severe (>70%) carotid stenosis, the delay was on the side of maximal stenosis in six patients. The remaining patient (case 4) had trivial early arrival of 0.05 ± 0.08 seconds (mean ± SD). One patient (case 13) had unilateral carotid occlusion with a normal contralateral vessel. In two patients with bilateral disease, the delay in BAT was on the side of carotid occlusion. In two patients who had unilateral severe disease with contralateral occlusions there was relatively early BAT ipsilateral to the side of surgery. Representative images are shown in Figure 1. Figure 2 shows BAT images in another patient.

**Postoperative Studies**

Three of the six patients with less than severe (<70%) contralateral ICA disease had early BAT on the side of carotid endarterectomy 3 to 5 days after surgery. At 3 months, only the two patients with contralateral ICA stenosis had early BAT ipsilateral to the side of surgery. Of the two patients with unilateral ICA disease, one (case 2) had early arrival immediately after carotid endarterectomy, and the other (case 3) had some improvement in delay times postoperatively. Among the patients with bilateral, nonocclusive ICA disease without evidence of early BAT at 3 months, three had sustained improvement in BAT (cases 1, 3, and 6), and three had worsening of the ipsilateral BAT (cases 2, 4, and 5) at 3 months. Two of
these patients (cases 2 and 5) had signs of early arrival immediately after carotid endarterectomy.

There was no postoperative mortality or significant morbidity. A review of the postoperative T2-weighted images revealed small new areas of hyperintensity ipsilateral to the side of carotid endarterectomy in four of the 11 patients (cases 1, 2, 5, and 10). None of these lesions were clinically apparent. No T2-weighted changes were found in the hemisphere contralateral to the carotid endarterectomy.

**Discussion**

Our study indicates that cerebral MR perfusion imaging may be a promising and sensitive marker of carotid disease. In all patients with symptomatic unilateral carotid disease, maximal delays were ipsilateral to the side of endarterectomy (the preoperative results in patient 4 most likely being within statistical error). The mean asymmetry in BAT between hemispheres of 0.89 seconds compares well with the results obtained by Nighoghossian et al (10), who found an average difference in mean transit time (MTT) of 1.15 seconds in 12 patients with unilateral carotid stenosis. In our study, the two patients with early BAT preoperatively had contralateral ICA occlusions. Excluding those patients with preoperative ICA occlusions, five (71%) of seven patients were shown to have early BAT ipsilateral to carotid endarterectomy soon after surgery.

MR perfusion imaging has been used to assess relative CBF and rCBV in patients with carotid artery stenosis (10, 11). Previous investigators have shown either increased rCBV ipsilateral to carotid stenosis (11) or no significant asymmetry between hemispheres (10). MTT has, however, been shown to be significantly delayed ipsilateral to the side of carotid stenosis (10). The relationship between the degree of ICA stenosis and CBF is complex, with some studies showing some relationship (12) and others showing no relationship (2). Because the majority of patients had bilateral disease in our study, it is not possible to evaluate the data from this preliminary series in terms of whether a correlation exists between the degree of ICA stenosis and BAT abnormalities.

Patients are currently examined macrovascularly with duplex sonography or MR angiography, and frequently proceed to X-ray angiography before surgery. Other techniques for assessing cerebral perfusion, such as positron emission tomography (PET), xenon CT, or dynamic contrast-enhanced CT (13), are either not readily available or require the use of ionizing radiation. Although recent developments in the use of echo-planar perfusion techniques can achieve much improved temporal resolution, our method is able to show differences between hemispheres, in keeping with previous work by Nighoghossian et al (10) and Reith et al (14).

Early BAT after carotid endarterectomy may be an indication of hyperperfusion, a phenomenon that has been well described (15–17) and is thought to be ischemic in origin, owing to its relationship with carotid cross-clamping time (2) and associated intraoperative electroencephalographic changes (18, 19). Patients with post–carotid endarterectomy hyperperfusion syndrome are at risk of intracerebral hemorrhage (20). Naylor and Ruckley (16) described three variables in the understanding of this syndrome: rec-
Fig. 1. Dual display of bolus arrival time (BAT) and enhancement in an 81-year-old man (case 1) with 99% stenosis of the left ICA and minimal contralateral disease.

A, Before carotid endarterectomy, clear asymmetry is noted between hemispheres with both delayed arrival and reduced enhancement in the left MCA territory.

B, Corresponding display of signal intensity changes with time shows clear BAT delay on the side of eventual carotid endarterectomy (CE) as compared with the contralateral region of interest (Ref).

C, Postoperative dual display shows improvement in perfusion characteristics.

Fig. 2. Case 6: 74-year-old woman with 99% stenosis in right ICA and 50% stenosis in left.

A, Bolus arrival time (BAT) image shows delays in the right hemisphere preoperatively.

B, Corresponding graph of preoperative changes in signal intensity with time from the MCA territories.

C, The 3- to 5-day postoperative study shows an improvement in BAT, particularly in the posterior parietal region.

D, On the 3-month postoperative study, some deterioration in the postoperative changes is noted, although improvement is still significant relative to preoperative status.
ognition of vulnerable patients; definition of the temporal relationship among cerebral hemodynamics, cerebral autoregulation, postoperative hypertension, and onset of symptoms; and investigation of the microcircuital changes that result in cerebral edema, infarct extension, and, ultimately, hemorrhage. Although none of our patients had evidence of postoperative hemorrhage, over half may have been at risk, either immediately after surgery or during the subsequent 3 months.

Data concerning changes in CBF after carotid endarterectomy are variable, both in the short (19–23) and long (2) term, with studies reporting increased (4, 12, 19, 22, 24, 25), decreased (25), and no (19, 22, 25–27) changes in CBF after surgery. Hartl et al (27) demonstrated that while carotid endarterectomy had no significant effect on CO$_2$ reactivity across all patient groups, improvements were seen in those patients with clear asymmetry in CO$_2$ reactivity before surgery. Bishop et al (2) showed that while CBF, as measured with xenon-133, returned to preoperative surgery. Bishop et al (2) showed that while CBF, as measured with xenon-133, returned to preoperative levels by 6 months after carotid endarterectomy, CO$_2$ reactivity continued to improve. This improvement is significant, as CO$_2$ reactivity is regarded as a satisfactory method of assessing hemodynamic reserve (28, 29) and is a predictive factor for stroke (30). While unilateral changes in CO$_2$ reactivity are perhaps more common (31, 32), bilateral improvement in CO$_2$ reactivity has also been demonstrated 3 months after carotid endarterectomy (3) and 6 months after carotid angioplasty (33). In addition, there is evidence of ischemia prior to carotid endarterectomy in some patients when assessed with proton MR spectroscopy (34).

Araki et al (21) reported Doppler flow velocity changes after carotid endarterectomy in patients with more than 75% stenoses, but no changes in patients with less than 75% stenoses. Substantial reductions in external carotid artery blood flow have also been shown after carotid endarterectomy (35). Using PET, Powers et al (36) failed to establish that abnormal hemodynamics associated with ICA stenosis significantly increased the risks of subsequent stroke. More recent work has clearly shown that subgroups of patients with carotid artery stenosis, in whom autoregulation is significantly impaired, do exist (37).

There is increasingly compelling evidence that the most cost-effective strategy for the investigation of symptomatic carotid stenosis is the routine use of MR angiography and duplex sonography, supplemented by X-ray angiography for cases with disparate results (38). Recent guidelines established by the American Heart Association for the investigation of transient ischemic attacks and minor stroke also advocate consideration of the use of CT angiography (39). The emerging understanding of the importance of identifying subgroups of patients who are at increased risk after carotid endarterectomy, or patients who might potentially enjoy a greater benefit from surgery (3), produces challenges for the development of optimal imaging regimens. MR perfusion imaging may provide just such a role. While the benefits of carotid endarterectomy are increasingly well defined via assessment of degree of extracranial ICA stenosis (1), it is of some concern that up to 18% of carotid endarterectomies performed in one region were clearly inappropriate using the NASCET criteria, and a further 49% were of uncertain necessity (40). Barnett et al (41), however, continue to suggest caution regarding the robustness of current studies in their ability to define specific groups who would benefit from carotid endarterectomy.

Conclusion

This study shows that the susceptibility weighted MR perfusion sequence is sensitive to differences in BAT between hemispheres in patients with ICA stenosis. In addition, it shows that changes in MR perfusion characteristics after carotid endarterectomy are complex, but that early BAT ipsilateral to the side of surgery can occur postoperatively. The significance of these findings with regard to patient outcome and risk of post-carotid endarterectomy hyperemia requires further investigation.

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References