From Case Study to Prospective Study

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Atherosclerosis remains a major cause of death in industrialized countries. Our understanding of the natural course of the disease and of the effects of intervention is mainly based on autopsy studies and on studies in animal models. This has primarily been because of the lack of good tools to image plaque components in vivo. Indeed, even in animal studies, analysis of plaque components has occurred for the most part ex vivo by histologic sections and dedicated staining techniques. In vivo visualization of the atherosclerotic plaque and its components (calcifications, fibrocellular tissue, lipid core, hemorrhage, and thrombus), particularly in humans, will further elucidate the disease process and the effect of various types of interventions, and subsequently will have important clinical implications.

The severity of stenosis in the carotid artery is a well-known predictor of cerebral infarction and is currently the main parameter used in deciding between carotid intervention (endarterectomy or stent placement) and pharmacologic intervention. Plaque morphology is considered an additional, independent predictor of cerebral infarction: plaques containing a necrotic lipid core covered by a thin fibrous cap (known as unstable or vulnerable plaque) are prone to rupture, releasing thromboembolic particles to the brain. Therefore, noninvasive, in vivo assessment of plaque components in the carotid artery would be useful in therapy determination.

Carotid stenosis of a severity that warrants surgical or endovascular treatment is found in 10 to 20% of all patients with transient ischemic attack (TIA) or ischemic stroke. Atrial fibrillation occurs in 5% to 10% of these patients and small vessel disease in 25%. In the remaining patients, moderate carotid atherosclerosis with low-grade stenosis is probably an important causative prognostic factor, but this has not been systematically studied. Indeed, prediction of recurrent stroke lacks precision, probably because we lack simple, reliable, and valid indicators of moderate carotid atherosclerosis. Noninvasive analysis of plaque morphology could fill this gap.

Until recently, angiography and ultrasound were the most common methods of analyzing atherosclerotic disease. Angiography provides information on the degree of stenosis but probably because we lack simple, reliable, and valid indicators of moderate carotid atherosclerosis. Noninvasive analysis of plaque morphology could fill this gap.

Two existing noninvasive imaging modalities—magnetic resonance imaging (MRI) and computed tomography (CT)—are able to detect atherosclerotic disease and to image different plaque components. Because of its superior contrast resolution, MRI has the potential to provide more detailed information on the morphology of the atherosclerotic plaque than CT. Previous in vitro validation studies have shown that MRI differentiation of calcifications, fibrocellular tissue, lipids, and intraplaque hemorrhage is possible. This makes MRI an important modality for plaque morphology imaging.

In their article, Wasserman and colleagues provide a review of (1) current knowledge about clinical implications of low-grade stenosis (<50% to 70%) of the carotid bifurcation and (2) the evidence available for focusing on plaque structure and composition instead of degree of stenosis as predictor of neurologic events. The authors stress the importance of plaque size and certain plaque features as predisposing factors to events. However, they admit that most data on the relationship between plaque features and events are from coronary studies rather than carotid studies. Whether these data also apply to carotid plaque must still be shown. MRI allows us this opportunity.

For these reasons, the most important part of the paper is the case report presenting sequential MRI of a carotid artery with atherosclerotic plaque and low-grade stenosis. Previous MRI studies of the carotid artery addressed the issue of validation of the MRI findings with histologic sections as the gold standard. These studies only included patients scheduled for carotid endarterectomy, thus with high-grade stenoses, so that specimens would be available for histology. Low-grade stenoses have as yet only been studied to monitor pharmacologic interventions.

Now that MRI analysis of the morphology of atherosclerotic plaques has been validated, a new phase of clinical application is ahead: evaluating the predictive value of atherosclerotic plaque characteristics in stroke patients or patients with an increased risk of atherosclerotic disease. Wasserman et al have begun this phase with the current case report.

The case report describes the feasibility of sequential MRI evaluation of carotid atherosclerosis. Sequential MRI is expected to reveal alterations in plaque size and plaque composition. Future studies will reveal the determinants of plaque features and alterations in plaque composition, and the effect of pharmacologic intervention. In addition, the case
Report describes the role of MRI-assessed plaque features in medical decision-making.

The authors had several arguments for a carotid endarterectomy in their patient with low-grade stenosis, of which the most important was repeated hemispheric ischemic events in the presence of an atherosclerotic lesion in the carotid bifurcation with absence of other etiologies. Whether the presence of certain plaque features justifies surgical intervention must be demonstrated in larger prospective studies, which will determine the significance of MRI-assessed plaque features for stroke risk.

Such studies will prove whether the concept of vulnerable plaque is applicable to carotid atherosclerosis. If so, a randomized, controlled trial is necessary to decide if surgical intervention is beneficial in patients with MRI-assessed vulnerable plaques in the carotid artery.

In conclusion, evaluation of carotid atherosclerosis with MRI has become mature. Large prospective studies have become mandatory.

References

Key Words: atherosclerosis MRI
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Stroke. 2005;36:2337-2338; originally published online October 20, 2005;
doi: 10.1161/01.STR.0000185665.15738.60
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/36/11/2337