Low-Grade Carotid Stenosis
Implications of MR Imaging

Mahmud Mossa-Basha, MD[a,*], Bruce A. Wasserman, MD[b]

KEYWORDS

• MR imaging • Carotid vessel wall imaging • Low-grade carotid stenosis • Stroke

KEY POINTS

- Luminal imaging techniques do not adequately evaluate extracranial carotid atherosclerotic plaque burden and characteristics in patients with low-grade carotid stenosis.
- Although multiple randomized controlled trials have not indicated an advantage to surgery over medical management in the low-grade stenosis population, there is an associated risk of stroke.
- Plaque features such as intraplaque hemorrhage, fibrous cap rupture, and ulceration, among others, confer an increased risk of stroke in low-grade stenosis.
- Considering that atherosclerosis is a systemic disease, vessel wall MR imaging can help determine the culprit lesion in the setting of cryptogenic stroke.
- Carotid vessel wall MR imaging can be helpful in identifying likelihood of plaque and its associated risk in other vascular beds that are not as easily imaged.

INTRODUCTION

Stroke is the second most common cause of mortality and a leading cause of morbidity worldwide. Approximately 80% of strokes are presumed to be ischemic in etiology, with 20% to 30% arising from extracranial carotid atherosclerosis.[1] In the setting of extracranial carotid artery disease, the decision to treat symptomatic patients surgically or with carotid artery stenting has traditionally relied on the degree of luminal stenosis on catheter angiography based on the results of randomized controlled trials.[2,3] Pooled data from the trials showed a 16% absolute reduced 5-year risk of future stroke events in patients with 70% or greater stenosis undergoing carotid endarterectomy in comparison with medical management.[4]

Over the past 10 years, however, investigation has placed less emphasis on the degree of stenosis and more on plaque features that confer lesion vulnerability. These vulnerable plaque features support the hypothesis, as in coronary artery disease, that many cerebral infarctions result from plaque rupture and distal embolization or acute occlusion, and not long-standing hypoperfusion.[5–9] Multiple studies have provided evidence that plaques resulting in moderate stenosis can rupture and result in acute ischemic events.[10–12] Barnett and colleagues[13] indicated a significantly increased 5-year risk of ipsilateral stroke ($P = .045$) in patients with 50% to 69% stenosis treated medically (22.2%) compared with those treated surgically (15.7%). For those with less than 50% stenosis in the North American Symptomatic Carotid Endarterectomy Trial (NASCET), the stroke rate was lower in the surgical group relative to the medically managed group, although

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[a] Division of Neuroradiology, University of Washington Medical Center, University of Washington School of Medicine, 1959 Northeast Pacific Street, Box 357115, Seattle, WA 98195, USA; [b] Russell H. Morgan Department of Radiology and Radiological Sciences, Johns Hopkins School of Medicine, 367 East Park Building, 600 North Wolfe Street, Baltimore, MD 21287, USA
* Corresponding author.
E-mail address: mmossab@uw.edu

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this did not reach statistical significance (14.9% vs 18.7%, $P = .16$). According to pooled data from the randomized control trials,[4] the 5-year reduction in ipsilateral stroke rate was 4.6% for surgical patients with moderate (50%–69%) stenosis. There was no benefit in stroke rate for patients with 30% to 49% stenosis between the surgical and medical management groups, whereas there was increased risk of stroke in the surgical group for those with less than 30% stenosis (absolute risk reduction −2.2%, $P = .05$).[4,14,15] The European Carotid Surgical Trial[9] reported a 1.3% rate of ipsilateral ischemic stroke lasting longer than 7 days in patients with symptomatic mild (0%–29%) stenosis during a 3-year follow-up (0.43% per year). Fritz and Levien[16] reported an 8.6% rate of ipsilateral ischemic events during a 2-year follow-up of 35 symptomatic patients with low-grade carotid stenosis or ulcerated plaque on medical management. In the setting of carotid atherosclerosis, including lesions resulting in low-grade carotid stenosis, there may be other lesions ipsilateral to the symptomatic side including aortic and intracranial plaques. Plaque-component characterization can provide important information to help stratify the likelihood that the carotid plaque is indeed the culprit lesion so that an appropriate treatment strategy can be implemented, including resection of the low-grade lesion. With moderate or severe carotid stenosis the associated plaques are presumed to be the culprits, and the randomized controlled trials have indicated the value of surgical intervention. The overestimation of stroke risk by contemporary standards in the medically managed groups for these trials that predate statin treatment suggests potential overtreatment of high-grade stenosis by surgery, and MR vessel wall imaging might also help to stratify high-grade lesions for a more appropriate balance of medical versus surgical treatments.

Although the rate of stroke in low-grade extracranial carotid stenosis differs based on the aforementioned trials, these trials have indicated that the benefit of surgery in low-grade stenosis may not improve the outcome over medical management when surgical risks are taken into consideration. However, these trials are based on narrowing to guide surgical management, which cannot stratify the risk of rupture for low-grade lesions and identify those at high enough risk to benefit from endarterectomy, and for this reason plaque characterization by MR imaging can potentially play an important role. Furthermore, despite a lower risk of stroke from low-grade carotid plaque compared with high-grade lesions, the chance for stroke from low-grade plaque cannot be discounted when considering the high prevalence of this disease. The occurrence of low-grade carotid stenosis in elderly populations is frequent, as 75% of men and 62% of women older than 64 years had carotid stenosis on ultrasonography in the Cardiovascular Health Study,[17] whereas only 7% of men and 5% of women had stenosis greater than 49%.

MODIFICATIONS IN MEDICAL MANAGEMENT

Since the publication of the trials for evaluation of disease management based on luminal stenosis, there have been significant changes to the optimal medical management regimen that have modified stroke risk in medically managed patients. 3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins), a class of cholesterol-lowering drugs, have become a staple of atherosclerosis-related stroke management. The Stroke Prevention by Aggressive Management in Cholesterol Levels Investigators (SPARCL)[18] randomized 4731 patients with prior stroke or transient ischemic attack (TIA) (between 1 and 6 months from the event), no known coronary heart disease, and low-density lipoprotein cholesterol (LDL-C) between 100 and 190 mg/dL to 80 mg atorvastatin therapy or placebo. The 5-year absolute reduction in risk of major cardiovascular events was 3.5% (hazard ratio [HR] 0.8, 95% confidence interval [CI] 0.69–0.92; $P = .002$) with no significant difference in mortality rates. Of the 4731 randomized patients, 4278 were evaluated for carotid disease, and of those 1007 were found to have carotid stenosis.[19] By randomization to the atorvastatin group, the incidence of any cardiovascular events was reduced by 42% relative to placebo (HR 0.58; 95% CI 0.46–0.73; $P<.00001$). The risk of cerebrovascular events (TIA or stroke) was reduced by 34% in the atorvastatin group (HR 0.66, 95% CI 0.5–0.89; $P = .005$). The risk of undergoing carotid revascularization was reduced by 54% (HR 0.44, 95% CI 0.24–0.79; $P = .006$). The Heart Protective Study Collaborative Group[20] randomized 20,536 patients in the United Kingdom with coronary artery disease, other occlusive artery disease, or diabetes mellitus to 40 mg simvastatin or placebo groups, and found a significant reduction in fatal and nonfatal stroke risk in the statin group (4.3% vs 5.7%, $P<.0001$). For the first occurrence of major vascular events, there was a 24% reduction in the event rate (19.8% vs 25.2%, $P<.0001$). Hegland and colleagues[21] evaluated 230 patients with 318 carotid arteries with at least 40% carotid stenosis on carotid ultrasonography without occlusion or referral for carotid revascularization. Of