

# Asymptomatic Carotid Stenosis: Screening and Management

Jonathan A. Grossberg, MD, N. Stevenson Potter, MD, PhD, and Mahesh V. Jayaraman, MD

**The management of asymptomatic carotid stenosis** can be a dilemma to the primary care physician. In this review, we hope to update the reader on current insights into asymptomatic carotid atherosclerosis.

Carotid stenosis is defined as the atherosclerotic narrowing of the proximal internal carotid artery exceeding 70% in severe cases and 50% in moderate cases. The prevalence of carotid stenosis in Western countries increases with age. A recent Western European population study placed the prevalence of moderate asymptomatic stenosis at 4.2% and severe stenosis at 1.7%. The prevalence was found to increase with age and be higher in males, with 12.5% of men being diagnosed with moderate stenosis.<sup>1</sup>

Fisher first described the pathophysiology of carotid atherosclerosis in 1951.<sup>2</sup> Since then it has increasingly been recognized as a risk factor and cause of stroke. A population based study of subjects older than 55 found that the presence of a severe carotid plaque burden increased the relative risk of a non-lacunar infarction in the anterior circulation by 3.2 times and increased the risk of a lacunar infarction by 10.8 times.<sup>3</sup> Accordingly, asymptomatic carotid stenosis has become an important cerebrovascular topic for the primary care physician.

## WHAT IS THE BEST SCREENING TEST FOR CAROTID ARTERY STENOSIS?

The diagnosis of asymptomatic carotid stenosis classically begins in the outpatient office. Many primary care physicians will examine patients for the presence of a carotid bruit, which is thought to signify turbulent blood flow across a stenotic plaque. While the Framingham Heart Study found that patients with a carotid bruit had double the stroke rate of controls, the majority of these strokes were in vascular territories unrelated to the stenosis.<sup>4</sup> Another large meta-analysis found a significantly increased risk of myocardial infarction and cardiovascular death in patients with a carotid bruit, thus

implying that the bruit is best used as a marker for total body atherosclerotic disease and not as a direct marker of carotid risk.<sup>5</sup> A recent cohort study examined the incidence of carotid bruit and clinically significant stenosis on carotid duplex and found that bruit auscultation had a sensitivity of 56% and a specificity of 98%. From the analysis of their data, the authors concluded that the auscultation was not sufficient to exclude stenosis, and further invasive testing should be considered in high-risk patients.<sup>6</sup>

Since physical exam has a low probability of diagnosing asymptomatic carotid stenosis, the diagnosis is often made through a variety of non-invasive radiological exams, namely **duplex ultrasonography (DUS)**, **computed tomographic angiography (CTA)**, and **magnetic resonance angiography (MRA)**. DUS is often the first screening test done due to its ease of use, lack of radiation or need for contrast material and cost. A review of non-invasive imaging found that DUS had an 86% sensitivity and 87% specificity for diagnosing clinically significant (>70%) stenosis.<sup>7</sup> One drawback of DUS is that it is operator dependent, and operator experience can affect the accuracy of results. In addition, the utility of DUS in screening patients without any risk factors for atherosclerotic disease is low, and screening the general population may not be cost-effective. Better results were found using MRA for the detection of clinically significant stenosis with a sensitivity of 95% and a specificity of 90%.<sup>7</sup> In another recent meta-analysis, CTA was found to have a sensitivity of 76% and a specificity of 94%. This study also found that contrast-enhanced MRA had the best sensitivity (94%) and specificity (93%) when compared to DUS, CTA, and non-contrast MRA.<sup>8</sup> One potential advantage of MRA over CTA is that dense calcification from some carotid plaque can limit luminal evaluation on CTA. While catheter angiography is the gold standard for evaluation of carotid stenosis, the cost, more invasive nature and potential

for neurologic complications have relegated it to a problem-solving role when significant discrepancies exist among the non-invasive imaging techniques. In patients with known carotid disease, the optimal interval for repeating DUS is unknown, but it is likely reasonable to repeat the study annually to monitor for interval change.

## HOW SHOULD A PATIENT WITH ASYMPTOMATIC CAROTID ARTERY STENOSIS BE FOLLOWED AND WHEN SHOULD THEY BE REFERRED FOR REVASCUARIZATION?

### Medical Therapy

For the majority of asymptomatic patients with carotid stenosis the ideal treatment is a combination of risk factor modification and anti-platelet medication. The risk factors targeted are familiar to all clinicians and include hypertension, smoking, physical inactivity, obesity, hyperlipidemia, and glycemic control.

While a number of these risk factors can be modified through lifestyle changes, particular attention has been paid to pharmacological treatments for hyperlipidemia and hypertension and their direct effect on carotid atherosclerosis. It is well known that the use of statins to meet cholesterol goals reduces the risk of stroke, but there is also evidence that statins may impact carotid plaque itself.<sup>9</sup> A recent study reviewed the effect of statins on atherosclerotic burden by randomizing patients to low-dose versus high-dose statin therapy. All patients in the trial had a significant reduction in radiologic atherosclerotic burden by 12 months, and post-hoc analysis revealed that the change was more related to the low LDL level induced by statin therapy than to the medication itself.<sup>10</sup> Another more recent study found that statin use in symptomatic carotid patients was associated with a decreased incidence of negative plaque features on MR imaging. These negative plaque features are thought to be predictive of future cerebrovascular events and include intraplaque hemorrhage, necrotic

core, and a thin fibrous cap.<sup>11</sup> In addition, there is some evidence that certain anti-hypertensive medications can have positive effects on the morphology of carotid plaques. A more detailed review of the effect of various medications on plaque morphology is beyond the scope of this paper and can be found in the review by Daskalopoulou et al.<sup>12</sup> The literature, however, is not conclusive so the recommendation is that patients be treated with anti-hypertensive medications that best fit their other co-morbidities.

In addition to risk factor and lifestyle modifications, it is the consensus of the **American Stroke Association (ASA)** that patients with asymptomatic carotid stenosis be treated with aspirin.<sup>13</sup> While good data exist for recommending aspirin and other anti-platelet agents to patients with a history of an ischemic cerebrovascular or cardiovascular event, there are no adequate studies examining aspirin in patients with asymptomatic carotid stenosis.<sup>14</sup> This ASA recommendation for aspirin derives from the fact that nearly all trials comparing outcomes of medical management to surgical management for carotid stenosis treat patients with aspirin. While the ASA does give a class I evidence rating to the use of aspirin, there are no studies that provide class I data for the use of other antiplatelet agents in the management of asymptomatic carotid stenosis.

#### **Carotid Revascularization: Endarterectomy or Stenting**

The final potential treatment for asymptomatic carotid stenosis is the invasive option in the form of either surgical **carotid endarterectomy (CEA)** or **carotid angioplasty and stenting (CAS)**. The two keystone studies comparing endarterectomy to maximal medical management in asymptomatic patients found a small benefit of surgery when performed by an experienced surgeon with a low complication rate. The ACST examined asymptomatic patients with at least 60% stenosis on DUS and found a five-year stroke rate of 6.4% for patients treated with CEA versus 11.8% for patients under maximal medical management.<sup>15</sup> The ACAS study also evaluated asymptomatic patients with at least 60% stenosis and found similar results: patients treated surgically had a stroke or death rate of 5.1% compared to 11% for patients treated

with medical management.<sup>16</sup> As a result the ASA recommends endarterectomy in selected asymptomatic patients when performed by a surgeon with a <3% complication rate.<sup>13</sup> It should be noted that the patients in these trials were a highly selected group and there were many exclusion criteria that make the studies less generalizable. For example, patients with contralateral carotid occlusion were often excluded from these trials, as were patients with asymptomatic restenosis in the setting of prior carotid revascularization. In addition, the medical management arms of these trials were not standardized and often did not include current aggressive anti-hypertension and anti-hyperlipidemia pharmacological treatment.

---

## **The question often facing the primary care physician dealing with asymptomatic carotid stenosis is when to refer for invasive treatment and when to treat medically.**

---

While the evidence for CEA in carotid stenosis is well established, the data involving CAS is only beginning to emerge. The most significant recent publication is the CREST trial, which randomized both symptomatic and asymptomatic patients to either CEA or CAS. Looking at both symptomatic and asymptomatic patients, the trial found that CEA and CAS were statistically equivalent in the composite rate of stroke, myocardial infarction, and death at four years. Where the two differed, however, was in a higher rate of peri-procedural myocardial infarction with CEA and a higher rate of stroke with CAS. For the asymptomatic subgroup, there was a non-statistically significant trend towards lower stroke and death rate at four years in the CEA group, and the writers noted the effect of stroke on quality of life. The CREST trial lacks a medication-only asymptomatic subgroup.<sup>17</sup> There are a

number of similar trials comparing endarterectomy to carotid artery stenting that go beyond the scope of this paper. On the basis of the early trials, the ASA recommends that CAS be considered only in patients with symptomatic stenosis who have either a medical or surgical condition that makes surgery high risk (such as prior CEA, radiation therapy to the neck, or significant co-morbidities to surgery).<sup>13</sup> Despite this recommendation, a recent study detailed that in New York and Florida, nearly 92% of CAS performed were for asymptomatic disease.<sup>18</sup> In addition, many of the same critiques of the CEA trials (such as patient selection and variable medical management of the non-operative arm) can be applied to the stenting trials, which make recommending CAS for the modern asymptomatic patient a difficult decision.

#### **How should asymptomatic carotid stenosis be treated?**

The question often facing the primary care physician dealing with asymptomatic carotid stenosis is when to refer for invasive treatment and when to treat medically. A recent article in *Stroke* by Abbot attempted to answer the question by reviewing the stroke rate of patients with asymptomatic carotid stenosis in published studies over a two-decade span. The study found that with the advances in modern medical therapy, the stroke rate of patients with asymptomatic carotid stenosis treated medically overlaps that of the patients treated surgically in the above-detailed studies.<sup>19</sup> After analyzing the raw study data, Abbot found that the risk of ipsilateral stroke was 1.5% per year in the patients undergoing CEA in ACAS and 2.3% for the patients treated with maximal medical treatment in the same study. Abbot compared those ACAS rates published in 1995 with the ASED and SMART trials, published over the past 5 years, which found annual ipsilateral stroke rates of 0.6%-1.2% in asymptomatic patients managed medically.<sup>19,20,21</sup> These conservative management stroke rates are similar to the recent CREST trial which found a 4.5% four year risk of ipsilateral stroke for patients treated with CAS and a 2.7% four year risk of stroke for patients treated with CEA.<sup>17, 19</sup>

In addition, Abbot's study found that medical management is three to eight

times more cost-effective than surgical management. This study suggests that the best treatment for most patients with asymptomatic carotid stenosis is the medical treatment detailed above: aggressive treatment of risk factors such as smoking, hyperlipidemia, hypertension, and glyce-mic control, combined with anti-platelet therapy, such as aspirin. The author does indicate that her numbers are based on a regression analysis and that there is no study that directly measures the impact of best medical practice on stroke rates in asymptomatic carotid stenosis.<sup>19</sup>

### SHOULD ASYMPTOMATIC CAROTID DISEASE BE SCREENED FOR?

Given the questions regarding stroke rates in asymptomatic disease for medi-cally treated patients, perhaps the bigger question is whether carotid atherosclerotic disease should be screened for with DUS. A large trial of over 5000 asymptomatic individuals analyzed with DUS found that increased carotid intima and media thickness was significantly associated with an increased risk for myocardial infarction and stroke.<sup>22</sup> Even in patients with known peripheral artery disease or coronary disease, screening for carotid disease with DUS should be considered. While the results of screening might not result in referral for carotid revasculariza-tion, they do provide valuable insight into the patient's overall atherosclerotic plaque burden, a "window into their arteries."

### REFERENCES

- de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: system-atic review and meta-regression analysis. *Stroke*, 2009;40:1105-13.
- Fisher M. Occlusion of the internal carotid ar-tery. *AMA Arch Neurol Psychiatry*, 1951;65:346-77.
- Hollander M, Bots ML, Del Sol I, et al. Carotid plaques increase the risk of stroke and subtypes of cerebral infarction in the asymptomatic eld-erly: the Rotterdam study. *Circulation*, 2002; 105:2872-7.
- Wolf PA, Kannel WB, Sorlie P, McNamara P. As-ymptomatic carotid bruit and risk of stroke. The Framingham study. *JAMA*, 1981;245:1442-5.
- Pickett CA, Jackson JL, Hemann BA, Atwood JE. Carotid bruits as a prognostic indication of cardiovascular death and myocardial infarction: a meta-analysis. *Lancet*, 2008;371:1587-94.
- Ratchford EV, Jin Z, Di Tullio MR, et al. Carotid bruit for the detection of hemodynami-cally significant carotid stenosis: the Northern Manhattan study. *Neurol Res*, 2009;31:748-52.
- Nederkoorn PJ, van der Graaf Y, Hunink MG. Duplex ultrasound and magnetic resonance angiography compared to digital subtraction angiography in carotid artery stenosis: a sys-tematic review. *Stroke*, 2003;34:1324-32.
- Wardlaw JM, Chappell FM, Best JJ, et al. Non-invasive imaging compared to intra-arterial angiography in the diagnosis of symp-tomatic carotid stenosis: a meta-analysis. *Lancet*, 2006;367:1503-12.
- Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet*, 2005;366:1267-78.
- Corti R, Fuster V, Fayad ZA, et al. Effects of aggressive versus conventional lipid-lowering therapy by simvastatin on human athero-sclerotic lesions: a prospective, randomized, double-blind trial with high-resolution mag-netic resonance imaging. *J Am Coll Cardiol*, 2005;46:106-12.
- Kwee RM, van Oostenbrugge RJ, Prins MH, et al. Symptomatic patients with mild and moder-ate carotid stenosis: plaque feature at MRI and association with cardiovascular risk factors and statin use. *Stroke*, 2010;41:1389-93.
- Daskalopoulou SS, Daskalopoulos ME, Perrea D, et al. Carotid artery atherosclerosis: what is the evidence for drug action? *Curr Pharm Des*, 2007;13:1141-59.
- Goldstein LB, Adams R, Alberts MJ, et al. Primary prevention of ischemic stroke: A Guideline From the American Heart Asso-ciation/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Coun-cil; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Stroke*, 2006;37:1583.
- Antithrombotic Trialists' Collaboration. Col-laborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ*, 2002;324:71-86.
- Halliday A, Mansfield A, Marro J, et al. Preven-tion of disabling and fatal stroke by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet*, 2004;363:1491-502.
- Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA*, 1995;273:1421-8.
- Brott TG, Hobson RW, Howard G. Stenting versus endarterectomy for treatment of carotid artery stenosis. *NEJM*, 2010;363:11-23.
- Steppacher R, Csikensz N, Eslami M, et al. An analysis of carotid artery stenting proce-dures performed in New York and Florida (2005-6): procedure indication, stroke rate, and mortality rate are equivalent for vascular surgeons and non-vascular surgeons. *J Vasc Surg*, 2009;49:1379-85.
- Abbott AL. Medical (Nonsurgical) interven-tion alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. *Stroke*, 2009;40:573-83.
- Abbott AL, Chambers BR, Stork JL, et al. Em-bolic signals and prediction of ipsilateral stroke or transient ischemic attack in asymptomatic carotid stenosis: A multicenter prospective co-hort study. *Stroke*, 2005;36:1128-33.
- Abbott AL, Chambers BR, Stork JL, et al. Em-bolic signals and prediction of ipsilateral stroke or transient ischemic attack in asymptomatic carotid stenosis: A multicenter prospective co-hort study. *Stroke*, 2005;36:1128-33.
- O'Leary DH, Polak JF, Kronmal RA, et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *NEJM*, 1999;340:14-22.

Jonathan A. Grossberg, MD, is a Resi-dent in Neurosurgery at the Warren Alpert School of Medicine of Brown University.

N. Stevenson Potter, MD, PhD, is an Assistant Professor of Neurology and Neurosurgery at the Warren Alpert School of Medicine of Brown University, and a critical care neurologist at Rhode Island Hospital.

Mahesh V. Jayaraman, MD is Assistant Professor of Diagnostic Imaging and Neuro-surgery at Rhode Island Hospital, and is the director of Interventional Neuroradiology at Rhode Island Hospital.

### Disclosure of Financial Interests

The authors and/or their spouse/significant others have no financial interests to disclose.

### CORRESPONDENCE

N. Stevenson Potter, MD, PhD  
593 Eddy Street, APC-650  
Providence, RI 02903  
phone: (401) 444-8362  
fax: (401) 444-8366  
e-mail: npotter2@Lifespan.org