4. Screening for Asymptomatic Carotid Artery Stenosis

RECOMMENDATION

There is insufficient evidence to recommend for or against screening asymptomatic persons for carotid artery stenosis using the physical examination or carotid ultrasound. For selected high-risk patients, a recommendation to discuss the potential benefits of screening and carotid endarterectomy may be made on other grounds (see *Clinical Intervention*). All persons should be screened for hypertension (see Chapter 3), and clinicians should provide counseling about smoking cessation (see Chapter 54).

Burden of Suffering

Cerebrovascular disease is the third leading cause of death in the U.S., accounting for over 149,000 deaths in 1993.[1] Most stroke-related morbidity and mortality occur in older adults: 87% of all deaths and 74% of all hospitalizations occur in persons age 65 years or older.[2] Strokes can result in substantial neurologic deficits as well as serious medical and psychological complications. With an estimated prevalence of 3 million stroke survivors,[3] this illness places enormous burdens on family members and caretakers, often necessitating skilled care in an institutional setting. The direct and indirect costs of stroke in the U.S. have been estimated at $30 billion annually.[4] The principal risk factors for ischemic stroke are increased age, hypertension, smoking, coronary artery disease, atrial fibrillation, and diabetes.[4–7] Of these, the most important modifiable risk factors are hypertension and smoking.[8] Improved treatment of high blood pressure has been credited with the greater than 50% reduction in age-adjusted stroke mortality that has been observed since 1972 (see Chapter 3).

Population-based cohort studies have established that persons with carotid artery stenosis are at increased risk for subsequent stroke, myocardial infarction (MI), and death.[9,10] The risk of stroke is greatest for persons with neurologic symptoms such as transient ischemic attacks (TIAs), but is also increased in patients with asymptomatic lesions. The prevalence of hemodynamically significant carotid stenosis varies with age and other risk factors: population-based studies estimate that 0.5% of persons in their 50s and about 10% of those over age 80 have carotid stenosis greater than

50%.[11] The proportion of all strokes attributable to previously asymptomatic carotid stenosis seems to be small, however. In a study of 250 patients over age 60 with cerebral infarction, only 13% had ipsilateral carotid stenosis of 70% or greater.[12]

Accuracy of Screening Tests

Two methods are used to screen for carotid artery stenosis: clinical auscultation for carotid bruits and noninvasive studies of the carotid artery. Neck auscultation is an imperfect screening test for carotid stenosis. There is considerable interobserver variation among clinicians in the interpretation of the key auditory characteristics—intensity, pitch, and duration—of importance in predicting stenosis.[13] In addition, a cervical bruit can be heard in 4% of the population over age 40, but the finding is not specific for significant carotid artery stenosis. Between 40% and 75% of arteries with asymptomatic bruits do not have significant compromise in blood flow;[14] similar sounds can also be produced by anatomic variation and tortuosity, venous hum, goiter, and transmitted cardiac murmur.[13,15–17] Finally, hemodynamically significant stenotic lesions may exist in the absence of an audible bruit.[13,15,18] Using 70–99% stenosis on a carotid angiogram as a reliable standard, a carotid bruit has a sensitivity of 63–76% and a specificity of 61–76% for clinically significant stenosis.[19]

Persons with cervical bruits can be evaluated further with greater accuracy by noninvasive study of the carotid arteries. Older techniques (e.g., spectral analysis phonoangiography, continuous-wave or pulsed Doppler ultrasound, B-mode real-time ultrasound, oculoplethysmography, ophthalmodynamometry, periorbital directional Doppler ultrasound, and thermography) have been replaced largely by carotid duplex sonography which combines the capabilities of B-mode and Doppler ultrasound. A 1995 meta-analysis of 70 studies comparing the accuracy of noninvasive diagnostic tests to carotid angiography (the reference standard) concluded that carotid duplex, carotid Doppler, and magnetic resonance angiography (MRA) were equally effective in diagnosing carotid stenosis of 70% or greater: estimated sensitivity ranged from 83% to 86%, specificity from 89% to 94%.[20] Depending on the underlying population characteristics, the positive predictive value of carotid duplex ranges from 82% to 97%.[21] The performance of noninvasive tests for screening asymptomatic persons, however, has not been assessed in a prospective study. Although MRA seems to be quite sensitive and spares patients the risks of conventional angiography, it is unlikely to be a useful screening test due to costs (over $400) and inconvenience.[22]

Effectiveness of Early Detection

The rationale for testing for carotid artery stenosis is that persons with asymptomatic stenoses are not only at increased risk for cerebrovascular

disease,[11,12] but that early detection can reduce morbidity due to cerebrovascular disease. According to this rationale there are several benefits to early detection of asymptomatic carotid stenosis. An awareness of the diagnosis might motivate patients to modify other risk factors (e.g., high blood pressure, smoking, physical inactivity). Performing carotid endarterectomy in some individuals might prevent subsequent cerebral infarction distal to the obstruction. Finally, antiplatelet drugs (aspirin and ticlopidine) might reduce stroke risk in asymptomatic individuals with carotid artery stenosis. No study has specifically compared a strategy of screening and early intervention in asymptomatic persons to intervening only in symptomatic patients (e.g., those with TIAs). The first symptom of carotid stenosis in some patients may be an irreversible stroke, however. A number of studies have examined whether interventions in asymptomatic persons can reduce the subsequent incidence of fatal and nonfatal stroke.

A bruit over the carotid artery is a fair indicator of vascular disease but a poor predictor that ischemic stroke will occur in its arterial distribution. The proportion of persons with asymptomatic bruits who will experience stroke is small: the annual incidence of stroke ipsilateral to a bruit and unheralded by TIAs is only 1–3%.[9,10,16,23–25] Higher grades of stenosis (assessed by sonography) are associated with increasing risk of neurologic events, rising to 5–7% per year with high-grade stenosis or total occlusion.[26,27] However, in those persons who will suffer a stroke, the degree of carotid stenosis does not always predict the risk of cerebral infarction,[16,23,28] or its location.[11,12] Carotid artery lesions may be less a predictor of atherothrombotic strokes than of generalized atherosclerotic disease; persons with carotid artery disease are considerably more likely to die from ischemic heart disease than from a cerebrovascular event.[9,10]

One of the major justifications for screening is the belief that carotid endarterectomy for high-grade, asymptomatic lesions detected through screening can prevent stroke. Three studies published before 1987 reported improved outcomes after endarterectomy. These studies provide poor quality evidence because they included previously symptomatic patients, were convenience samples derived from surgeons' practices, had inconsistent measurement criteria, or did not randomly assign patients.[17,29,30] Four more recent randomized trials have compared aspirin with endarterectomy in patients with asymptomatic carotid artery stenosis. The first study comparing aspirin alone with endarterectomy alone[31] enrolled only 71 patients before it was terminated due to excess MI in the surgical group; no conclusions could be drawn regarding the effectiveness of endarterectomy for preventing stroke.[32] The second study, the 1991 European CASANOVA trial, randomized 410 patients with moderately severe stenosis (.50% but ,90%) to treatment with aspirin/dipyridamole or aspirin/dipyridamole plus surgery.[33] The protocol was complex: some patients in both groups had contralateral symptoms, patients with stenosis

greater than 90% were excluded, and 72 patients received therapy appropriate for the other group (more in the group randomized to surgery). There were no differences in the numbers of neurologic events and deaths between the two groups. The power of the study, however, was insufficient to exclude a clinically important benefit in the surgical group.[33] A third study, published in 1993, randomized 444 older veterans (mean age 64) with 50% or greater carotid stenosis to aspirin plus carotid endarterectomy or aspirin therapy alone. Patients who underwent carotid endarterectomy had lower rates of ipsilateral neurologic events, the primary endpoint: the combined incidence of TIAs, transient monocular blindness, and stroke was 8% in the surgery group versus 21% with aspirin only (p , 0.001), during an average follow-up of 48 months. The two groups had similar outcomes, however, using a combined endpoint of stroke or death from any cause. The power of the study was insufficient to exclude up to a 20% reduction in stroke in the surgically treated group.[34] The generalizability of this study was limited by the lack of female subjects and by the excessive morbidity and mortality in both groups (over 40% incidence of stroke or death in both groups over the 4-year follow-up).

The Asymptomatic Carotid Artery Study (ACAS),[35] funded by the National Institutes of Health, recently reported final results that provide stronger evidence of the benefit of endarterectomy for asymptomatic stenoses.[36] This multicenter study randomized 1662 patients with asymptomatic stenoses greater than 60% (mean stenosis 73%) to endarterectomy plus aspirin or to aspirin alone. Most patients (87%) were over age 60, and more than two thirds had coronary heart disease. The trial was stopped after a median follow-up of 2.7 years. The estimated 5-year risk for ipsilateral stroke or perioperative stroke or death was 5.1% for surgical patients and 11% for medically treated patients, a reduction in cumulative risk of 53% (95% confidence interval, 22 to 72). The absolute reduction in the combined incidence of major ipsilateral stroke, major perioperative stroke, or perioperative death, however, was considerably smaller (estimated 5-year risk of 3.4% in the surgery group vs. 6% in the medical group), not statistically significant (p = 0.13), and evident only in the fifth year of follow-up. Subgroup analyses suggest that endarterectomy may be less effective in women than in men (17% vs. 66% reduction in 5-year event rate), possibly due to higher perioperative complication rates (3.6% in women vs. 1.7% in men); neither of these differences between genders was statistically significant, however. The medical centers participating in this trial had been rigorously evaluated for the quality of patient management, and only surgeons with a perioperative complication rate of less than 3% among asymptomatic patients were allowed to participate.[37] Published studies have reported a perioperative mortality ranging from 1% to 3%,[33,34,38–40] and a perioperative stroke rate ranging between 2% and

10%, depending on patient characteristics and surgical expertise.[13,33,34,39–44] In six prospective trials of endarterectomy published after 1990, perioperative complication rates (stroke and death combined) range from 3% to 8%.[38] Complication rates seem to be lower in asymptomatic patients than in symptomatic patients, however.[38,40] A fifth trial of surgery versus medical management for asymptomatic carotid artery stenosis is still in progress.[11]

Antiplatelet therapy with aspirin or ticlopidine offers a second possible intervention to reduce the risk of stroke in patients with asymptomatic carotid artery stenosis. Clinical trials have demonstrated a benefit of aspirin in reducing stroke among symptomatic patients (i.e., in persons with TIAs or stroke),[45–48] but observed no benefit on stroke in a large trial in asymptomatic physicians (prevalence of carotid disease unknown).[49] Among patients with asymptomatic carotid disease, who have a lower risk of ischemic events than do symptomatic patients, chronic aspirin therapy may not provide sufficient benefits to justify the documented risks of hemorrhagic complications (see Chapter 69). A multicenter prospective study comparing aspirin to placebo in asymptomatic patients with >50% carotid stenosis found no difference in stroke rates.[50] Ticlopidine is an alternative to aspirin in patients with risk factors for gastrointestinal hemorrhage, aspirin intolerance, and in patients who continue to have vascular events despite aspirin therapy, but its use is limited by high cost and small risk of neutropenia (approximately 1%).[51,52] The efficacy of ticlopidine in patients with asymptomatic carotid artery stenosis is not known.

Reducing serum lipids may slow the progression of carotid atherosclerosis and reduce clinical events. In a randomized trial enrolling patients with moderately elevated levels of LDL cholesterol (130–190 mg/dL) and early carotid atherosclerosis diagnosed by B-mode ultrasound, lovastatin induced regression of atherosclerosis and reduced total cardiovascular events compared to placebo.[52a] Lipid-lowering drug therapy has not been examined specifically for treatment of advanced carotid stenosis, but is generally recommended for patients with high cholesterol and symptomatic vascular disease, based on its ability to reduce coronary heart disease mortality (see Chapter 2). No controlled studies have examined changes in the behavior of patients (e.g., smoking cessation or dietary modification) on learning the results of carotid artery examinations.

Recommendations of Other Groups

Although auscultation of the carotid arteries is widely considered a routine component of the physical examination, the Canadian Task Force on the Periodic Health Examination[53] recommended against screening for bruits in asymptomatic persons, based on the poor sensitivity and specificity of cervical bruits as an indicator of significant carotid stenosis. The American

Academy of Family Physicians recommends auscultation for carotid bruits in people age 40 and older with risk factors for cerebrovascular or cardiovascular disease, those with neurologic symptoms (e.g., TIA) or those with a history of cardiovascular disease;[54] this policy is currently under review. The 1988 guidelines of the American College of Physicians recommend that patients with asymptomatic bruits should not have further diagnostic testing but should be educated about potential symptoms of a TIA in the carotid circulation.[55] In 1988, an ad hoc multidisciplinary consensus panel involved in designing the ACAS study recommended a baseline noninvasive study of the carotid arteries in persons considered at high risk for extracranial carotid arterial disease.[56] In 1992, the Ad Hoc Committee of the Joint Council of the Society for Vascular Surgery and the North American Chapter of the International Society for Vascular Surgery recommended that patients with asymptomatic carotid artery stenosis greater than 75% who are otherwise healthy and have a projected life expectancy more than 5 years should be considered for surgery if the operative morbidity and mortality rates are less than 3%.[57]

Discussion

The effectiveness of routine screening and intervention to reduce morbidity from asymptomatic carotid artery disease remains uncertain. The most effective interventions to prevent stroke are smoking cessation and the identification and treatment of hypertension. Although screening will detect some patients with asymptomatic high-grade carotid lesions who may benefit from endarterectomy, such patients account for only a small proportion of all strokes. In addition, there are several reasons to be cautious about undertaking widespread screening in asymptomatic persons on the basis of the current evidence:[11,38,58] the risk of major stroke ipsilateral to stenotic lesions is relatively low without surgery (approximately 1% per year); the absolute reduction in major stroke and death due to surgery over 5 years in ACAS was small and not conclusive; surgery may result in other nonfatal complications (cranial nerve injury, MI, etc.); and the low complication rate of the ACAS-selected surgeons is not likely to reflect the typical risk of endarterectomy in the community. If complication rates of surgery are higher or underlying risk of stroke lower than reported for the ACAS study, the risks of surgery for asymptomatic carotid artery disease may outweigh the benefits. Routine screening will also subject some patients without significant carotid disease to the risks of angiography (1% risk of stroke), due to occasional false-positive results of carotid ultrasound.

As a result, it is not yet clear whether widespread screening in the primary care setting will be an effective way to reduce morbidity and mortality from stroke. Noninvasive testing for carotid artery stenosis is expensive (over $150 for carotid duplex or Doppler ultrasound);[20] the cost of screen-

ing 50% of the population over age 60 in the U.S. has been estimated at over $7 billion.[58] Auscultation for bruits involves little direct expense and may detect a majority of patients with severe stenosis, but the costs of follow-up testing of all patients with asymptomatic bruits could be substantial. Revised cost-effectiveness analyses of various screening and treatment strategies for asymptomatic carotid disease are under way. Patients most likely to benefit from screening are older men (over age 60) who have other risk factors for stroke, no contraindications to major surgery, and access to high-quality vascular surgery centers. Evidence regarding the effectiveness of antiplatelet drugs for asymptomatic persons is not yet sufficient to make a recommendation.

CLINICAL INTERVENTION

There is insufficient evidence to recommend for or against screening asymptomatic persons for carotid artery stenosis, using physical examination or carotid ultrasound ("C" recommendation). A recommendation may be made on other grounds to discuss the potential benefits of screening with high-risk patients (e.g., persons over age 60 at high risk for vascular disease), provided that high-quality vascular surgical care is available (surgical morbidity and mortality less than 3%). These other grounds include the increased prevalence of significant carotid disease, and the possible long-term benefit of endarterectomy in patients with asymptomatic stenosis greater than 60% when performed by qualified surgeons. Patients should be screened and counseled about other risk factors for cerebrovascular disease as discussed in other chapters (see Chapters 3 and 54).

The draft update of this chapter was prepared for the U.S. Preventive Services Task Force by Stephen Tabet, MD, MPH, Alfred O. Berg, MD, MPH, and David Atkins, MD, MPH.

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