Assessment of Asymptomatic Carotid Bruit

The term bruit refers to any noise detected on auscultation in the neck. The conventional method of auscultation is to use the bell of the stethoscope and listen over an area extending from the upper end of the thyroid cartilage to just below the angle of the jaw. The principal reason why bruits in the neck are matters of some concern is that they may reflect underlying occlusive carotid artery disease, which carries an increased risk of stroke.

In what follows, we outline a problem-oriented approach to the workup of patients found to have cervical bruits at the time of routine or focused vascular examination.

Clinical Evaluation

CAROTID BRUITS VERSUS OTHER CERVICAL SOUNDS

Clinical assessment begins with evaluation of the character of the bruit and examination of the precordium and the cervical structures. Carotid bruits must be distinguished from other sounds heard in the neck. Venous hums are relatively common, being reported in 27% of young adults. They tend to have a diastolic component, are louder when the patient sets or turns the head away from the side of auscultation, and disappear when the patient lies down or when the Valsalva maneuver is performed. Ejection systolic murmurs of cardiac origin may radiate into the neck, but generally, they are bilateral, are louder within the chest, and are less audible distally in the neck; the same is true of bruits arising in other intrathoracic vessels. No definitive clinical sign has yet been identified that clearly differentiates bruits from transmitted cardiac murmurs. On occasion, a bruit may be heard over the thyroid gland; however, this finding is extremely rare and is usually accompanied by thyromegaly and other features of autoimmune thyroid disease. In dialysis patients, a bruit may be generated by the increased flow resulting from the creation of an arteriovenous fistula in the forearm.

SYMPOTOMATIC VERSUS ASYMPTOMATIC CAROTID BRUITS

Transient ischemic attacks (TIAs) are defined as brief episodes of focal loss of brain function that can usually be localized to a specific portion of the brain supplied by a single vascular system. By arbitrary convention, such an ischemic episode is considered a TIA if it lasts less than 24 hours; a similar episode, in the absence of evidence of trauma or hemorrhage, is considered an ischemic stroke if it lasts more than 24 hours or causes death. Amaurosis fugax is a transient (< 24 hours) loss of vision in one eye or a portion of the visual field. If a patient with a carotid bruit has a history of any of these conditions in the ipsilateral eye or brain, then the bruit is regarded as neurologically symptomatic, and the relevant question at that point is whether the patient has significant carotid stenosis and may be a candidate for carotid endarterectomy on that basis. Given the substantial differences between the management of patients with symptomatic bruits and those with asymptomatic bruits, the distinction between these two patient groups is crucial.

The history is of critical importance in the diagnosis of TIA because most TIAs last less than 4 hours, which means that patients typically are not seen by physicians during the period of neurologic deficit. Patients should be specifically asked about transient focal problems with vision, language, facial paresis, dysarthria, and arm or leg numbness or weakness. A 1984 study reported good interobserver agreement (κ = 0.65) between clinicians diagnosing previous ischemic episodes. Assigning a probable neurologic territory to a TIA or stroke, however, proved more difficult: for TIAs, the interobserver agreement between two independent neurologists asked to distinguish between carotid and vertebrobasilar events was relatively poor (κ = 0.31). There is some evidence that using a standardized protocol for the diagnosis of previous ischemic episodes might improve this low interobserver agreement (e.g., to κ = 0.65 or κ = 0.77). Similar difficulties attend diagnosis of stroke by means of history and physical examination.

Many patients with a possible TIA or stroke will have undergone neurologic imaging. Such imaging is unhelpful if it yields negative results; however, in some cases, it reveals the presence of an infarct, thereby confirming the ischemic nature of the event and establish-

Table 1 Quantification of Interobserver Agreement*

<table>
<thead>
<tr>
<th>κ</th>
<th>Strength of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0.2</td>
<td>Poor</td>
</tr>
<tr>
<td>&gt; 0.2, ≤ 0.4</td>
<td>Fair</td>
</tr>
<tr>
<td>&gt; 0.4, ≤ 0.6</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt; 0.6, ≤ 0.8</td>
<td>Good</td>
</tr>
<tr>
<td>&gt; 0.8, ≤ 1</td>
<td>Very good</td>
</tr>
</tbody>
</table>

*Reliability (how closely an assessment agrees with another similar assessment on a second occasion or by a second observer) and validity (how closely the assessment agrees with another criterion or a gold standard) are the key properties of any assessment. When agreement between two observers is poor, the assessment in question, whether it is a physical finding, a clinical diagnosis, or an interpretation of a diagnostic test, is lacking in reliability; if more reliable methods are available, they should be considered instead. In clinical medicine, however, more reliable methods are not always available. When this is the case, the physician must use a relatively unreliable assessment as the best available alternative, while remaining aware of its limitations. κ is a statistical measure used to quantify agreement between two or more observers. It takes a value between 0 and 1, where 0 represents agreement no better than that expected by chance alone and 1 represents perfect agreement.
Assessment of Asymptomatic Carotid Bruit

Sound is carotid bruit
- Distinguish symptomatic bruits from asymptomatic bruits; the decision affects treatment.

Bruit is asymptomatic
- Perform vascular risk assessment, looking for vascular risk factors (e.g., ↑BP, ↑lipids, diabetes, smoking) and vascular disease (e.g., ischemic cardiac disease, peripheral vascular disease).
- Initiate modification of vascular risk. Determine subsequent management approach.

Bruit is symptomatic
- Perform prophylactic CE.

Risk of carotid stenosis is high
- Risk factors include ↑age, ↑BP, smoking, peripheral vascular disease.
- Assess risk of stroke.

Risk of carotid stenosis is low
- Assess risk of carotid stenosis.

Risk associated with CE is low (Goldman class I or II)

Assess risk of carotid stenosis.

Risk of stroke is high
- Risk factors include age > 70, male sex, ↑BP, ↑lipids, diabetes, smoking, ischemic cardiac disease, peripheral vascular disease.
- Consult patient preferences regarding surgical treatment.

Risk of stroke is low

Patient prefers surgical management
- Determine presence and degree of carotid stenosis with duplex ultrasonography and carotid angiography.

Patient prefers medical management

Severe stenosis is present
- Perform prophylactic CE.

Moderate stenosis is present
- Reevaluate with duplex ultrasonography every 1–2 yr unless patient status changes.

Minimal or no stenosis is present
Sound is venous hum, radiating cardiac murmur or intrathoracic bruit, or thyroid bruit

Patient is to be assessed as candidate for carotid endarterectomy (CE)
Determine level of risk associated with procedure.

Risk associated with CE is high (Goldman class ≥ III)

Patient is to be managed conservatively

Continue modification of vascular risk.
Educate patient regarding symptoms and signs of stroke.
Carry out nonsurgical follow-up.
Re-refer patient promptly if he or she ever becomes symptomatic.
ing its location. For a bruit to be regarded as symptomatic on the basis of imaging studies, at least one infarct must be seen in the appropriate ipsilateral anterior vasculature.

It is evident that distinguishing between symptomatic and asymptomatic bruits on clinical grounds may be difficult; nonetheless, it is worthwhile to make the effort because the risk of stroke in the asymptomatic population is quite different from that in the symptomatic population. For example, whereas the Asymptomatic Carotid Atherosclerosis Study (ACAS), which included patients believed on clinical grounds to be neurologically asymptomatic, reported an overall stroke rate of 6.2% at 2.7 years in its medically managed group,19 the North American Symptomatic Carotid Endarterectomy Trial (NASCET), which included patients assessed as neurologically asymptomatic (i.e., with a history of amaurosis fugax, TIA, or minor stroke), reported a stroke rate of 26% at 3 years in its medically managed group.16

In determining whether a unilateral bruit is symptomatic or asymptomatic, the physician should concentrate primarily on ischemic deficits in the ipsilateral hemisphere (i.e., those causing focal contralateral motor or sensory deficits) and ipsilateral amaurosis fugax. However, symptoms referable to the contralateral carotid artery, even if no bruit is heard on that side, might prompt evaluation of the patient for symptomatic carotid stenosis on the contralateral side. The absence of a bruit by no means excludes the diagnosis: carotid bruits are absent in 20% to 35% of patients with high-grade stenosis of the internal carotid artery.17 In the NASCET subgroup in which the physical finding of a carotid bruit was compared with angiographic imaging of the carotid system, the presence of a focal ipsilateral carotid bruit had a sensitivity of 63% and a specificity of 61% for high-grade (70% to 99%) stenosis; the absence of a bruit did not significantly change the probability of significant stenosis in this population (pretest 52%, posttest 40%).18

Workup of patients with symptomatic bruits is beyond the scope of this chapter. Accordingly, the ensuing discussion focuses on assessment of patients with asymptomatic bruits.

VASCULAR RISK ASSESSMENT

Vascular diseases and other vascular risk factors are common in patients with asymptomatic carotid bruits. Hypertension is twice as common in patients who have bruits as in those who do not;19 smoking, ischemic heart disease, and peripheral vascular disease are also more prevalent.20,21 Consequently, detection of a bruit should prompt a thorough vascular risk assessment. Standard vascular risk factors—hypertension, hyperlipidemia, diabetes, and smoking—can be integrated into risk profiles for particular patients by using either the New Zealand risk tables (http://www.nzgg.org.nz/library/gl_complete/bloodpressure/appendix.cfm) or the formula and spreadsheets provided by Anderson et al.22,23 The probability of stroke for various follow-up periods may be quantified by using the Framingham stroke-risk profile.24 From age, systolic blood pressure, diabetes, smoking, cardiovascular disease, atrial fibrillation, and left ventricular hypertrophy, probability of stroke may be calculated for men and women according to a point system.24

Smoking cessation should be recommended to all patients,25-27 and hypertension should be controlled (BP < 140/90).28-31 Depending on a patient’s individual risk profile, dietary and pharmacologic management of hyperlipidemia may also be warranted.32-34 Diabetic control should be optimized.35,36

Patients should be asked specifically about any concurrent vascular disease—in particular, symptoms suggestive of ischemic heart disease or of claudication or rest pain. In patients with established vascular disease, the risk that future vascular events (e.g., coronary-related death, myocardial infarction [MI], new angina, stroke, TIA, new congestive heart failure, or peripheral vascular syndrome) will occur in the next 5 years is greater than 20%.22,37 In such patients, consultation of formulas or tables is unnecessary, and all modifiable risk factors should be aggressively managed (target BP < 140/90; target ratio of total cholesterol to high-density lipoprotein [HDL] cholesterol < 4).22

A meta-analysis of randomized, controlled trials showed that aspirin reduced the risk of subsequent stroke, MI, and death from vascular events for patients who had previously experienced a cerebrovascular event, MI, or unstable angina.38 Other meta-analyses of randomized, controlled trials39,40 were unable to confirm the effectiveness of aspirin in preventing cerebrovascular events in asymptomatic patients or in patients with TIAs or strokes of noncardiac (and presumably vascular) origin41; however, one randomized, controlled trial involving hypertensive patients at modest vascular risk found that aspirin reduced the risk of vascular events, if not the risk of stroke.42 In the absence of contraindications, we recommend that aspirin be considered for all patients who have established vascular disease elsewhere and for all patients who have a bruit in association with any vascular risk factors.

INDICATIONS FOR SURGICAL INTERVENTION

The absolute risk of stroke is increased in the presence of a carotid bruit. In population-based studies, the annual risk of stroke was 2.1% (95% confidence interval [CI], 0.6 to 8.5)19,20,43,44 for persons who had a carotid bruit and 0.86% (95% CI, 0.8 to 0.9) for those who did not.19,43,44 These figures represent an absolute risk increase for stroke of 1.24% a year and a relative risk for stroke of 2.4. The mean patient age in these studies was approximately 65 years, and sex distribution and prevalence of risk factors for atherosclerotic disease were similar in patients with bruits and those without bruits. Even after adjustment for age, sex, and the presence of hypertension, the presence of a carotid bruit remained an independently significant variable, with a relative risk of 2.0.19

Table 2 Annual Risk of Stroke

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Annual Risk of Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population without bruits, age &gt; 60 yr19,43,44</td>
<td>0.86% (95% CI, 0.8–0.9)</td>
</tr>
<tr>
<td>Population with bruits, age &gt; 60 yr19,20,43</td>
<td>2.1% (95% CI, 0.6–6.5)</td>
</tr>
<tr>
<td>Male population without bruits, age &gt; 60 yr19,24</td>
<td>0.9% (95% CI, 0.1–3.0)</td>
</tr>
<tr>
<td>Male population with bruits, age &gt; 60 yr19</td>
<td>8.0% (95% CI, 0.2–38.0)</td>
</tr>
<tr>
<td>Female population without bruits, age &gt; 60 yr24</td>
<td>2.0% (95% CI, 0.8–4.2)</td>
</tr>
<tr>
<td>Female population with bruits, age &gt; 60 yr19</td>
<td>2.4% (95% CI, 0.7–5.5)</td>
</tr>
</tbody>
</table>

Table 3 Prevalence of Carotid Stenosis in Patients with Bruits and in Healthy Volunteers

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Prevalence of Carotid Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population with cervical bruits</td>
<td>58% (95% CI, 55–60)</td>
</tr>
<tr>
<td>&gt; 35% stenosis20,56-58,119</td>
<td>21% (95% CI, 18–24)</td>
</tr>
<tr>
<td>&gt; 60%–75% stenosis56-58</td>
<td>5.1% (95% CI, 2.6–9.0)</td>
</tr>
<tr>
<td>Healthy volunteers*</td>
<td>1.5% (95% CI, 0.2–5.3)</td>
</tr>
</tbody>
</table>

*In healthy volunteers, the incidence of asymptomatic carotid stenosis is significantly correlated with age (P < 0.01) and with the presence of hypertension (P < 0.005).
Given the low absolute risk of stroke in asymptomatic patients with bruits [see Table 2], the low prevalence of surgically relevant stenosis in patients with bruits [see Table 3], and the small (and only marginally statistically significant) absolute benefit of carotid endarterectomy in patients with asymptomatic stenosis,45,46 we and others47-51 do not believe that further investigation with a view to carotid endarterectomy is mandatory in the asymptomatic population. Many surgeons may prefer to manage these patients conservatively, reevaluating them promptly if they become symptomatic [see Discussion, below]. Other surgeons may wish to pursue a more interventional strategy with selected patients, in which case further evaluation with an eye to surgical treatment depends on the presence of the following key findings in a given patient: (1) low risk associated with carotid endarterectomy, (2) relatively high risk of carotid stenosis, and (3) high risk of stroke if carotid stenosis is documented. In addition, the patient’s preferences should be consulted: no patient should be subjected to further evaluation who is not prepared to undergo surgical treatment if such management is recommended. Patients who, on the basis of any of these criteria, are not suitable candidates for intervention will not benefit from imaging studies and should be managed medically.

Finally, surgeons and centers who are contemplating offering prophylactic carotid endarterectomy for asymptomatic stenosis should be able to document that their rates of stroke or perioperative death for this procedure are lower than 3% [see Table 4]. When complication rates exceed this threshold, the value of carotid endarterectomy becomes negligible, and surgeons may find themselves doing more harm than good.45,46

**Low Risk Associated with Carotid Endarterectomy**

In NASCET and ACAS, patients were excluded if they had coexisting medical disease likely to produce significant mortality and morbidity (e.g., cardiac valvular or rhythm disorders, uncontrolled hypertension or diabetes, unstable angina pectoris, or MI in the previous 4 months)16; accordingly, the results of these trials are not generalizable to patients who have such conditions. Further evidence for the impact of operative risk on outcomes is provided by a retrospective review of 562 patients who underwent carotid endarterectomy for symptomatic and asymptomatic disease in a large community hospital.52 For patients in Goldman class I or II,53 the overall rate of death or nonfatal MI was 2% (95% CI, 1.1 to 3.9), whereas for patients in class III or IV, the corresponding figure was 21% (95% CI, 9.2 to 39.9) [see Table 5].

Table 4 Necessary Criteria for Offering an Intervventional Approach to Selected Patients with Carotid Bruits

<table>
<thead>
<tr>
<th>Center-specific criteria</th>
<th>Surgeon-specific criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Either DUS is documented to have a &gt; 90% PPV for stenosis &gt; 50% on angiography and is used alone or DUS has a lower PPV and is used as a screening test only, and angiography in patients with cerebrovascular disease has a documented complication (stroke or death) rate of around 1%</td>
<td>Perioperative rate of stroke or death is &lt; 3% for carotid endarterectomy</td>
</tr>
</tbody>
</table>

DUS—duplex ultrasonography  PPV—positive predictive value

Given that 50 prophylactic carotid endarterectomy would have to be performed to prevent one stroke over the subsequent 3-year period (i.e., the number needed to treat [NNT] is 50), it is clearly unacceptable to perform this procedure in a population facing a 21% incidence of MI or death, in which for every 5 patients undergoing the operation, one would experience an MI or die (i.e., the number needed to harm [NNH] is only 5). Further consideration of prophylactic carotid endarterectomy in patients for whom the procedure carries a high risk is not warranted.

**High Risk of Carotid Stenosis**

Cohort45,54-60 and population-based19,61,62 studies suggest that patients with asymptomatic carotid bruits are more likely to have significant carotid stenosis if they are older, are hypertensive, smoke, or have advanced peripheral vascular disease. In one study, hemodynamically significant stenosis (i.e., > 50%) was found by means of ultrasonography in 32% of patients scheduled to undergo peripheral vascular procedures but in only 6.8% of those scheduled to undergo coronary artery bypass grafting (CABG).63 (All figures for degree of stenosis in this chapter are determined according to the formula used in NASCET [see Table 6 and Figure 1].)

Further consideration of carotid endarterectomy may be warranted in patients with vascular risk factors or known peripheral vascular disease; in the absence of these findings, the risk of significant carotid stenosis is low. Further evaluation is unnecessary for patients who are younger, do not smoke, are not hypertensive or diabetic, and are not known to have peripheral vascular disease.

**High Risk of Stroke**

Within the group of patients with asymptomatic carotid stenosis, there is only limited direct evidence for the existence of subgroups of patients at higher risk for stroke. Men seem to be at higher risk for stroke than women are: in the medical arm of ACAS, the incidence of stroke or death at 2.7 years was 7.0% (95% CI, 4.9 to 9.4) for men and 4.9% (95% CI, 2.7 to 8.0) for women. Gender-related differences aside, however, identification of other subgroups at higher risk relies on extrapolation of data from other populations at risk for artery-to-artery embolism. Data from NASCET indicate that for symptomatic patients with greater than 70% carotid stenosis, the presence of a higher number of identifiable clinical risk factors (age > 70 years; male sex; systolic or diastolic hypertension; the occurrence of a cerebrovascular event within the preceding 31 days; the occurrence of a more serious cerebrovascular event, namely, stroke rather than a TIA or amaurosis fugax; smoking; MI; congestive heart failure; diabetes; intermittent claudication; or hyperlipidemia) was associated with a higher annual stroke risk. For patients with zero to three risk factors, the annual stroke risk was 6.6%; for those with four or five, 9.2%; and for those with six or more, 15.8%. Data from the same study indicate that among patients with a contralateral asymptomatic stenosed carotid artery, patients with zero to three risk factors have an annual stroke risk of 1.4% in the territory of the asymptomatic stenosis; those with four or five, 2.8%; and those with six or more, 3.8%.64
Obesity is another risk factor for stroke. Some 60% of patients who experience a stroke before 65 years of age have a body mass index greater than 24 kg/m^2. This finding, in conjunction with a history of smoking, was found to predict 60% of strokes in men in this age group.

Patients with carotid bruits who do not have significant systemic risk factors or other vascular disease are at low absolute risk for stroke and are unlikely to benefit from carotid endarterectomy; hence, further investigation is not warranted. Patients with numerous (i.e., six or more) clinical risk factors [see Table 7] are at relatively high risk for stroke, and it is in this population that most of the benefit from carotid endarterectomy is likely to be concentrated.

**Investigative Studies**

The purpose of investigation of asymptomatic neck bruits is to identify persons with significant carotid stenosis who are at increased risk for cerebrovascular disease and who are likely to benefit from carotid endarterectomy. In the absence of other significant findings, cervical bruits are not sufficiently predictive of significant carotid stenosis or ischemic stroke to be useful in selecting candidates for noninvasive imaging. Noninvasive testing is a reasonable step in patients with the characteristics listed above, but routine screening of all patients with asymptomatic carotid bruits is not warranted.

**Duplex Ultrasonography**

Duplex ultrasonography (DUS) should be performed bilaterally. A meta-analysis conducted in 1995 found that for detecting greater than 50% stenosis (determined by means of angiography, the gold standard), DUS had a sensitivity of 91% (95% CI, 89 to 94) and a specificity of 93% (95% CI, 88 to 95). Given a disease prevalence of approximately 41% in patients referred for DUS, these findings translate into a positive predictive value of 90% and an accuracy of 92%. A subsequent prospective study of patients (both symptomatic and asymptomatic) in whom carotid endarterectomy was being considered reported a sensitivity of 100% and a specificity of 98% for greater than 60% stenosis, with a positive predictive value of 99%.

At centers where DUS has been internally validated in comparison with angiography and where this level of performance has been documented, the surgeons may choose to proceed to surgery without angiography. At centers where DUS is less reliable, however, it should be regarded as a screening test, and angiography should be performed when DUS suggests greater than 50% stenosis.

**Table 5: Cardiac Risk Assessment**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Goldman</th>
<th>Detsky</th>
<th>Eagle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 70 yr</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>MI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 mo</td>
<td>10</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>&gt; 6 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic, abdominal, or thoracic</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 wk</td>
<td>11</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 1 wk</td>
<td>7</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>ECG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhythm other than sinus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5 PVC/min</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Poor medical status†</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

**Risk of Perioperative Cardiac Events**

<table>
<thead>
<tr>
<th></th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–12 (class I, II)</td>
<td>0–15</td>
<td>16–30</td>
<td>1–2</td>
</tr>
<tr>
<td>&gt; 25 (class III)</td>
<td>&gt; 30</td>
<td>&gt; 30</td>
<td>≥ 3</td>
</tr>
</tbody>
</table>

*The Goldman cardiac risk index is a multifactorial index of cardiac risk in patients undergoing noncardiac surgery. Modifications have been proposed by Detsky, who included angina and institutional-specific perioperative cardiac event rates in the model. The Eagle index is another risk index based on five clinical variables. Despite the lack of consensus regarding the relative merits of these tools for preoperative cardiac risk assessment, stratification of patients into risk categories is helpful in assessing the risk and benefits of a procedure such as carotid endarterectomy.*

\[ P_{O2} < 60 \text{ mm Hg}; P_{CO2} > 50 \text{ mm Hg}; K^+ < 3 \text{ mmol/L}; \text{ serum } \text{HCO}_3^- < 20 \text{ mmol/L}; \text{ serum urea } > 18 \text{ mmol/L}; \text{ abnormal ALT}; \text{ signs of chronic liver disease}; \text{ bedridden from cardiac causes}. \]

CHF—congestive heart failure  MI—myocardial infarction  PVC—premature ventricular contraction
periodically. Since 1990, four prospective studies71-74 have addressed the question of the risks associated with angiography in patients with atherosclerotic cerebrovascular disease. When the data from these studies were pooled, the risk of permanent neurologic deficit or death was 1.1% (95% CI, 0.6 to 2.0).75 In ACAS, the 1.2% of patients in the intervention arm who experienced stroke or died after angiography accounted for 40% of the strokes and deaths attributable to surgical intervention.15 Angiographic complication rates significantly worse than these will adversely impact the risk-benefit ratio associated with surgical intervention. Centers that consistently record relatively high angiographic complication rates should not offer evaluation for and surgical treatment of asymptomatic carotid disease.

Management

CAROTID ENDARTERECTOMY

At this point in management, it is reasonable to offer surgical treatment of asymptomatic disease to patients with greater than 50% stenosis. ACAS15 and two meta-analyses45,46 that included other trials of surgical therapy for asymptomatic carotid stenosis documented a small and marginally statistically significant benefit from prophylactic carotid endarterectomy in asymptomatic patients with greater than 50% to 60% carotid stenosis. Because the absolute benefit is small, we do not consider it obligatory to pursue the diagnosis or to offer an invasive strategy in patients identified solely on the basis of an asymptomatic bruit; however, patients possessing all the characteristics listed earlier [see Indications for Surgical Intervention, above] probably constitute a group that is particularly able to benefit from surgical intervention. Patients with higher degrees of stenosis are at higher risk for stroke and are therefore most likely to benefit.76-79

The degree of stenosis and the presence or absence of plaque ulceration may modify the final decision for or against operative management [see Discussion, Subgroup Analyses for Potential High-Risk Factors, below].

In May 2004, the United Kingdom Medical Research Council Asymptomatic Carotid Surgery Trial (ACST) collaborative group reported the results of a prospective, randomized trial of carotid endarterectomy in asymptomatic patients.80 More than 3,000 patients were randomly assigned either to undergo immediate carotid endarterectomy or to be placed on indefinite deferral. In the patients referred for immediate carotid endarterectomy, one half underwent endarterectomy within 1 month of referral, 88% underwent endarterectomy within 1 year. Combining the rate of perioperative events and nonperioperative strokes, the 5-year results indicate a stroke rate of 6.4% in the group undergoing immediate carotid endarterectomy, as compared with 11.8% in the deferral group. These findings are strikingly similar to the ACAS findings. However, the ACST found a similar benefit for women. In addition, in the ACST, no difference was found in the degree of stenosis and the benefit of surgery—an interesting observation, because one would expect that greater degrees of stenosis would be associated with greater risk of stroke. This finding may be explained either by the fact that duplex ultrasound was the sole imaging criterion or that plaque morphology plays a greater role in determining stroke risk than degree of stenosis. Furthermore, unlike previous studies, many of the patients in the ACST were receiving lipid-lowering drugs and other antiplatelet agents. As Barnett pointed out in his discussion of the ACST article, the perioperative stroke rate must be low for the results of this study to be generalized.81 In the ACST, the risk of stroke or death within 30 days of undergoing carotid endarterectomy was 3.1%.

Technical details of carotid endarterectomy are discussed elsewhere [see 6.9 Surgical Treatment of Carotid Artery Disease].

PATIENT EDUCATION

All patients with asymptomatic carotid bruits, whether they are undergoing prophylactic endarterectomy or not, should be carefully advised regarding the symptoms and signs of stroke, TIAs, and amaurosis fugax and should be strongly encouraged to seek urgent medical attention if such problems arise. Patients who experience one of these untoward events should undergo full reevaluation for stroke risk factors (e.g., hypertension, hyperlipidemia, diabetes, smoking, and atrial fibrillation); in the absence of atrial fibrillation (which

Table 6 Conversion between Different Methods of Measuring Degree of Carotid Stenosis

<table>
<thead>
<tr>
<th>Method</th>
<th>Minimal</th>
<th>Moderate</th>
<th>Severe</th>
<th>Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECST*</td>
<td>24%–57%</td>
<td>58%–69%</td>
<td>70%–81%</td>
<td>82%–99%</td>
</tr>
<tr>
<td>NASCET</td>
<td>0%–29%</td>
<td>30%–49%</td>
<td>50%–69%</td>
<td>70%–99%</td>
</tr>
<tr>
<td>CC method†</td>
<td>35%–56%</td>
<td>57%–61%</td>
<td>62%–80%</td>
<td>81%–99%</td>
</tr>
</tbody>
</table>

*Conversion from ECST to NASCET was done according to the following formula: ECST % stenosis = 0.6(NASCET % stenosis) + 40.127
†The relation of the NASCET method to the CC method is linear, with a ratio of 0.62 between the distal internal carotid diameter and the common carotid diameter.117

Figure 1 Carotid angiography remains the gold standard for determining the extent of carotid arterial disease. Several methods of reporting angiographically defined stenosis have been described in the literature.115 The most commonly used methods are those adopted by the NASCET and ECST investigators, though the so-called common carotid (CC) method has its advocates as well.116,117
Table 7  Risk Factors for Stroke128,129

<table>
<thead>
<tr>
<th>Age &gt; 70 yr</th>
<th>Smoking (or history of smoking)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>&gt; 80% carotid stenosis</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>Presence of ulceration</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Ischemic heart disease†</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Peripheral vascular disease</td>
</tr>
</tbody>
</table>

*Defined as systolic BP > 160 mm Hg or diastolic BP > 90 mm Hg.
†MI or CHF.

should prompt consideration of prophylactic anticoagulation82-84), a change in antiplatelet therapy should be considered. Both ticlopidine85 and clopidogrel86 are more effective than aspirin in preventing stroke. (Ticlopidine is associated with reversible but severe neutropenia in fewer than 1% of cases; accordingly, monitoring for this complication is indicated.)

If a patient who is a surgical candidate experiences a TIA or stroke as a result of an ischemic event in the carotid region in the absence of atrial fibrillation, he or she must be promptly referred back to the vascular surgeon. This possibility should be clearly explained to patients once the initial evaluation is complete and they have been referred back to their primary care physicians. Patients referred back to a vascular surgeon under these circumstances should then be regarded as having symptomatic carotid disease. A subgroup analysis of patients with symptomatic stenosis reported that carotid endarterectomy performed soon after a nondisabling stroke was not associated with a significantly higher operative complication rate than endarterectomy performed 30 days or longer after a stroke.75 Performing endarterectomy early reduces the risk period for recurrent stroke and may therefore increase the potential benefit of the intervention; the usual approach is to perform the procedure within a week or two of a patient’s first neurologic event.

Management of cardiovascular risk factors and concurrent vascular disease should continue. In the absence of concurrent vascular disease, patients may be referred back to the family practitioner, internist, or cardiologist in place of specific surgical follow-up.

FOLLOW-UP OF PATIENTS WITH LOWER-GRADE STENOSIS

Carotid stenosis progresses in about one quarter of patients with asymptomatic carotid stenosis monitored with DUS over a 2-year period.87 In a population of asymptomatic patients with bruits who were referred to a vascular laboratory, 282 stenotic carotid arteries (average stenosis, 50%) were followed for 38 ± 18 months. Progression of stenosis, defined as an increase in degree of stenosis to 80% or beyond, occurred in 17% of arteries, and 2% became completely occluded. Progression was associated with an increase in stroke risk of 4.9% at 1 year, 16.7% at 3 years, and 26.5% at 5 years. In comparison, the estimated stroke risk in an asymptomatic population of patients with 50% to 79% stenosis was 0.85%, 3.6%, and 5.4% for the same three periods (P = 0.001).76

Although carotid stenosis, once identified, tends to progress over time,20,54,76,88 the data are currently insufficient to permit recommendation of routine ultrasonographic or other surveillance for all patients with neck bruits outside a research setting. In our view, reevaluation every 1 to 2 years with noninvasive diagnostic tests is a reasonable approach to patients (1) who are already known to have greater than 50% stenosis, (2) who do not undergo surgery, and (3) who are at high risk for stroke, are surgical candidates, and are not averse to surgery.

Discussion

Epidemiology

In cross-sectional and population-based studies, the overall prevalence of greater than 75% carotid stenosis has been low. A 1992 study reported a 2.3% prevalence in men and a 1.1% prevalence in women; there was a significant (P < 0.0001) increase with age with each decade from 65 years to beyond 85 years, but there were no significant differences between men and women.62 In the Framingham study population, the incidence of greater than 50% stenosis was 8% (95% CI, 6.5 to 9.8).61 In a study of healthy volunteers, the incidence of greater than 50% stenosis was 5.1% (95% CI, 2.6 to 9.0) in patients 70 years of age or older and 1.5% (95% CI, 0.2 to 5.3) in younger patients.89

The pooled risk of greater than 60% to 75% stenosis in patients with carotid bruits referred for noninvasive vascular evaluation at an average age of 65 years is reported to be 21% (95% CI, 18 to 24),46-58 which is three to four times the prevalence expected on the basis of population-based studies. Thus, five persons with neck bruits must be screened to detect one patient with moderate to severe carotid stenosis. The absolute benefit of surgery is small and of borderline statistical significance. In ACAS, as noted (see above), the relative risk reduction for an ipsilateral major stroke or perioperative death over a 2.7-year period was 36.5% (95% CI, 27.5 to 47.1), the absolute risk reduction was 2.3% (95% CI, 0.2 to 7.0), and the NNT was 43 (95% CI, 14 to 500); the number of patients that would have to be screened with DUS to prevent one stroke over a 3-year follow-up period was 250 (95% CI, 70 to 2,500).

Economic Considerations

A cogent argument in favor of pursuing a surgical strategy in at least some patients was made by a 1997 economic analysis,90 which demonstrated that although prophylactic endarterectomy in patients with asymptomatic carotid stenosis did not reduce societal costs appreciably, it was nonetheless, at a cost of $8,000/quality-adjusted life year (QALY), within the range of many interventions considered by society to be cost-effective. It should be pointed out, however, that this economic analysis addressed only carotid endarterectomy in patients with identified carotid stenosis, not screening strategies for patients with bruits, and consequently did not consider costs associated with investigation and follow-up to the point of recommendation for or against carotid endarterectomy in the broader group of patients with bruits. These costs would alter the economic analysis substantially, and if they are included, it is far from clear whether the resulting overall cost/QALY would still be acceptable. To date, no trial or economic analysis of a screening strategy has been published.

Screening Issues

For the reasons previously discussed, we do not feel justified in recommending routine screening for patients with asymptomatic carotid bruits. Given the available evidence, we believe that such patients may reasonably be managed in either of two ways. One choice is simply to conclude that screening patients with carotid bruits as possible candidates for carotid endarterectomy has not
been proved to be a useful intervention and to concentrate instead on general vascular risk reduction. The other, which is appropriate in centers where noninvasive or invasive diagnostic tests reach acceptable standards with an acceptable degree of risk and where the procedure is done by surgeons whose documented perioperative stroke and death rates are less than 3%, is to take a selective approach that addresses various issues related to stroke risk, cardiac risk, and patient preferences before noninvasive tests are ordered.

**Subgroup Analyses for Potential High-Risk Factors**

Given the small absolute risk reduction reported by ACAS and by the two meta-analyses of all asymptomatic carotid stenosis trials, it would be useful to be able to identify one or more high-risk groups within the broader group of patients identified as having stenosis.

**SEX**

ACAS included a subgroup analysis addressing the effect of sex on ability to benefit from surgery: the absolute reduction in the risk of perioperative stroke or death or ipsilateral stroke at 2.7 years was 3.6% (95% CI, 1.1 to 9.9) for men and 0.5% (95% CI, 0.01 to 2.7) for women.

**DEGREE OF STENOSIS**

In asymptomatic patients stratified according to their ultrasonographically determined degree of stenosis, the risk of stroke is low both for patients with less than 30% stenosis (4% cumulative event rate at 3 years) and for those with 30% to 74% stenosis (9% cumulative event rate at 3 years); it is highest for those with greater than 75% stenosis (21% cumulative event rate at 3 years). The European Carotid Surgery Trialists (ECST) study, using angiographic data from the asymptomatic carotid arteries of 2,295 patients, reported that the Kaplan-Meyer estimate of stroke risk at 3 years was only 2% and remained low (< 2%) when patients with less than 79% stenosis were considered; stroke risk increased to 9.8% for patients with 70% to 79% stenosis and to 14.4% for those with 80% to 99% stenosis. In a population of patients referred to a vascular laboratory with asymptomatic carotid stenosis on DUS who were followed for a mean of 38 months, the incidence of stroke was 2.1% in patients with 50% to 79% stenosis and 10.4% in those with greater than 80% stenosis.

In ACAS, there were too few strokes to permit subgroup analysis of the effect of degree of stenosis on ability to benefit from carotid endarterectomy. In both ECST and NASCET, however, higher degrees of stenosis in symptomatic patients were consistently observed to be associated with higher stroke risk as well as with greater ability to benefit from surgical treatment.

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>Relative Risk Reduction or Increase</th>
<th>Absolute Risk Reduction or Increase</th>
<th>Number Needed to Treat or Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>70%–99%</td>
<td>RRR, 48% (95% CI, 27–63)</td>
<td>ARR, 6.7% (95% CI, 3.2–10)</td>
<td>NNT, 15 (95% CI, 10–31)</td>
</tr>
<tr>
<td>50%–69%</td>
<td>RRR, 27% (95% CI, 5–44)</td>
<td>ARR, 4.7% (95% CI, 0.8–8.7)</td>
<td>NNT, 21 (95% CI, 11–125)</td>
</tr>
<tr>
<td>≤ 49%</td>
<td>RRI, 20% (95% CI, 0–44)</td>
<td>ARI, 2.2% (95% CI, 0–4.4)</td>
<td>NNIH, 45 (95% CI, 22–∞)</td>
</tr>
</tbody>
</table>

**PLAQUE ULCERATION AND PLAQUE STRUCTURE**

At present, there are no subgroup analyses examining the effect of plaque ulceration on the ability of asymptomatic patients to benefit from surgical treatment. In NASCET, however, when symptomatic patients with 70% to 99% stenosis were considered, those with angiographic evidence of plaque ulceration were at higher risk for stroke than those without ulceration and derived greater benefit from surgery. Angiography had a sensitivity of 46% and a specificity of 74% in the detection of ulcerated plaques, with a positive predictive value of 72%. A 1994 study reported that when ulceration was detected with B-mode imaging in patients with asymptomatic carotid stenosis, the incidence of silent cerebral infarction detected by magnetic resonance imaging was 75%, compared with an incidence of 25% when ulceration was absent.

It has also been suggested that carotid plaques of differing structures may have different embolic potentials. DUS can distinguish between fibrous plaques (which are highly echogenic) and plaques with high concentrations of lipid and necrotic material (which are echolucent). Echolucent plaques are more frequently associated with neurologic symptoms and computed tomography–proven cerebral infarction. Interobserver reliability for plaque echosounding, however, seems to be highly variable, ranging from good (κ = 0.79) for greater than 70% stenosis to average (κ = 0.51) for greater than 40% stenosis to poor (κ = 0.29) for greater than 80% stenosis. A 1994 report found no correlation between the presence or type of symptoms and plaque structure as determined by DUS. The true importance of carotid plaque echomorphology and surface characteristics as predictors of cerebrovascular events remains to be defined.

**CONTRALATERAL DISEASE**

It has been suggested that the presence of contralateral carotid disease is a risk factor for future cerebrovascular events. In NASCET patients with greater than 70% stenosis, contralateral occlusion significantly increased the benefit of surgery with respect to the incidence of stroke or death, but contralateral high-grade stenosis did not.

**ASYMPTOMATIC CEREBRAL INFARCTION**

The presence of areas of asymptomatic cerebral infarction ipsilateral to the area of carotid stenosis on head CT may identify patients who would benefit from surgery. In asymptomatic patients with carotid stenosis, the incidence of silent strokes demonstrated by CT has been reported to be 10% in patients with 35% to 50% stenosis on DUS, 17% in those with 50% to 75% stenosis, and 30% in those with greater than 75% stenosis. The incidence of silent cerebral infarctions demonstrated by MRI in the same type of population has been reported to be 42%, increasing to 75% for greater than 50% stenosis. Use of CT and MRI of the brain in risk strati-
fication of patients with asymptomatic carotid stenosis is controversial and currently is not advised.

CONCLUSIONS

Although only limited data on patients with asymptomatic stenosis are available, we believe that consideration of sex, degree of stenosis, and possibly the presence of plaque ulceration may be helpful in making the final decision on whether to offer carotid endarterectomy to these patients; at present, plaque morphology is insufficiently reliable to be a useful guide to clinical management.

Special Situations

RESTENOSIS OR PREVIOUS CAROTID SURGERY

Patients who have previously undergone carotid surgery have been excluded from most studies of asymptomatic patients; when they have been included in trials addressing symptomatic stenosis, they have experienced increased rates of perioperative complications.16,50 Patients in whom restenosis occurs after an earlier carotid endarterectomy should be advised against surgery while they remain asymptomatic.15 It is therefore unnecessary to follow patients with ultrasonography after carotid endarterectomy if no symptoms develop.

PREOPERATIVE ASSESSMENT FOR CORONARY ARtery BYPASS GRAFTING

Some 20% to 30% of patients undergoing assessment for CABG are found to have carotid bruits,49,104 and 5% to 20% have greater than 50% stenosis on DUS105-107 or ocular plethysmography.108 In asymptomatic patients with carotid stenosis who are undergoing CABG, there is no direct evidence favoring prophylactic carotid endarterectomy either before or in conjunction with CABG. Cohort studies including symptomatic and asymptomatic carotid stenosis indicate that patients undergoing CABG and carotid endarterectomy in the same operation have a stroke rate of 6% (95% CI, 4.6 to 7.8), an MI rate of 4.6% (95% CI, 3.1 to 6.5), and a mortality of 4.7% (95% CI, 3.4 to 6.4).109 For cohorts in which carotid endarterectomy was performed before CABG, the stroke rate is 3.2% (95% CI, 2.1 to 4.5), the MI rate is 5.2% (95% CI, 3.6 to 6.9)—a non-significant increase—and the mortality is 4.7% (95% CI, 3.4 to 6.4).109 For cohorts in which CABG was done first and carotid stenosis was treated on its own after the cardiac procedure, the stroke rate is 3.5% (95% CI, 1.0 to 9.0), the MI rate is 2% (95% CI, 0.2 to 6.0), and the mortality is 0.8% (95% CI, 0.02 to 4.8).110-112

We recommend against a combined surgical approach in patients with asymptomatic carotid stenosis. Given the equivalent stroke rate and the lower MI rate and mortality, we believe that the preferred strategy in patients with bruits is first to proceed with CABG if indicated and then to determine whether the patient should be further evaluated as a candidate for carotid endarterectomy in the same manner as other elective patients would be.

Effect of Center-Specific Variations on Risk-to-Benefit Ratio

In ACAS, 1.2% of the overall 2.7% perioperative stroke rate was accounted for by strokes occurring after angiography. Centers where ultrasonography has been documented to have high predictive values may avoid this risk by proceeding directly from ultrasonography to surgery. If these complications had been avoided in ACAS, the absolute risk reduction would have been more substantial: 3.43% (95% CI, 1.1 to 9.9), corresponding to an NNT of 29 (95% CI, 1 to 80). The true perioperative combined stroke and death rate achieved in this study was 1.5%, a result that is definitive of excellence in the surgical management of carotid endarterectomy and that constitutes a useful quality assurance measure for centers and individual surgeons.

Issues for the Future

It is possible, perhaps likely, that in the future, magnetic resonance angiography67 and three-dimensional CT angiography,113,114 together with DUS, will replace angiography as preferred imaging methods for diagnosing internal carotid artery stenosis. As for surgical treatment and screening, further data on patients with asymptomatic carotid stenosis are necessary before definitive recommendations can be made.

References


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Acknowledgment

Figure 1 Laurie Grace.