Special Article

Extracranial Carotid Artery

Current Concepts of Diagnosis and Management

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Extracranial carotid artery disease is a frequent cause of transient ischemic attack (about 50%), but a much less common cause of cerebral infarction (about 15%). Transient ischemic attack almost invariably precedes strokes caused by extracranial carotid stenosis, but rarely heralds strokes that result from cardiogenic embolism or intracranial vascular disease. When extracranial carotid stenosis produces a transient ischemic attack or stroke, artery-to-artery embolism is the predominant mechanism.

Asymptomatic significant (>50%) carotid stenosis poses special clinical questions in patients scheduled to undergo general surgical or major cardiovascular operations. With general surgical procedures, there is no increased risk of stroke. With cardiovascular operations, however, there may be an increased risk of stroke in patients with critical (>90%) carotid stenosis or occlusion. When perioperative stroke occurs, the most common cause is embolism rather than focal hemodynamic change.

For symptomatic high-grade (>70%) extracranial carotid stenosis, carotid endarterectomy is the treatment of choice in patients who are not high-risk surgical candidates. Alternatively, for high-risk patients, new drugs such as ticlopidine appear quite promising, and percutaneous angioplasty may also prove effective.

Prevention of stroke must continue to be a major goal of national medical policy. Because cigarette smoking is the most important risk factor for extracranial carotid disease, more strenuous efforts must be directed toward eliminating this health risk.
(Texas Heart Institute Journal 1991;18:93-7)

In 1951, Fisher[1] elaborated upon the frequency with which extracranial carotid artery disease is associated with stroke. Since then, neurologists and vascular surgeons have focused on preventive treatment to avoid the disabling neurologic consequences. Because transient ischemic attack (TIA) frequently precedes stroke and provides time for successful medical or surgical intervention, attention has been directed toward correlating the symptoms of TIA with specific anatomic sites of involvement.

Most TIAs last for less than 15 minutes. Those involving the carotid distribution are characterized by transient monocular blindness (amaurosis fugax), aphasia, hemiparesis, and hemisensory loss. Amaurosis fugax is the most common TIA associated with extracranial carotid stenosis.[2] Hemispheric TIAs that last for more than an hour are not generally associated with carotid bifurcation disease.[3] Vertebrobasilar TIAs have protean manifestations, including crossed weakness, vertigo, diplopia, bilateral loss of vision, shifting numbness, transient global amnesia, and dysphagia. Symptoms such as homonymous hemianopia and dysarthria are not helpful in locating the site of involvement, and syncope is not usually an indication of extracranial carotid disease.

Because many strokes are not preceded by a TIA, preemptive surgery is frequently performed on patients with asymptomatic stenosis. This is a subject of considerable controversy.

In order to make informed decisions with regard to management options, physicians need to understand the pathogenesis of TIAs and strokes, as well as the natural history of extracranial carotid artery disease. Over the last few years, researchers have shed a great deal of light on these issues.

Etiology and Pathogenesis of Ischemic Stroke and Carotid Distribution TIA

To elucidate the causes of ischemic stroke in carotid and basilar artery distributions, Sacco and associates[4] recently reviewed 1,273 cases of stroke attributed to infarction and then assigned each case to 1 of 5 diagnostic categories. The tandem

Key words: *Angioplasty, transluminal; arterial occlusive diseases; atherosclerosis; carotid artery diseases; endarterectomy, carotid; cerebrovascular disorders; embolism; stroke; transient ischemic attack*

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Presented at the 20th anniversary symposium of the Texas Heart Institute, titled "Update Cardiology 1990," held 24-26 October 1990, at the Westin Galleria Hotel, Houston, Texas

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arterial pathology category constituted 5% of the cases; large-vessel atherosclerosis, 9%; cardiogenic embolism, 19%; lacunar infarction (presumed intracranial small-vessel disease), 27%; and infarction of unknown origin, 40%. When 138 of the 508 cases in the last category were reclassified on the basis of clinical findings, computed tomography, and angiography, 23% of the cases were attributed to large-vessel disease (15% involved extracranial carotid disease), 12% were due to lacunar infarction, and 66% were due to embolism from an undetermined source. A combination of tandem arterial pathology, large-vessel atherosclerosis, and infarctions of unknown cause (probably due to large-vessel disease) constitutes 16.7% of the total number of ischemic strokes. After subtraction of a small percentage of strokes resulting from basilar artery disease and large-vessel intracranial disease, the resulting proportion of ischemic strokes caused by carotid bifurcation stenosis is approximately 15%.

What causes carotid distribution TIA? This entity has a different etiologic pattern than stroke. Studying 250 consecutive TIA patients, Bogousslavsky and colleagues[5] found that 47% had high-grade (>75%) carotid stenosis or ulceration appropriate to TIA and that 22% had emboligenic heart disease. The rest probably had intracranial vascular disease, especially small-vessel disease. Therefore, carotid bifurcation disease is a good predictor of TIA, but not necessarily of stroke (predicting about 50% of TIAs, but only about 15% of strokes).[4,5]

Artery-to-artery embolism has been indicated by much evidence to be the primary mechanism of carotid distribution TIA. In a case of transient monocular blindness (amaurosis fugax), Russell[6] observed such an embolism, which consisted of a mass of white material at the bifurcation of the central retinal artery. Subsequent pathologic studies disclosed that the retinal emboli consisted predominantly of platelets.[7] The role of embolization is indirectly confirmed by the inability of a superficial temporal-middle cerebral artery anastomosis to prevent a stroke or TIA.[8] Despite evidence that most TIAs have an embolic cause, a small percentage of patients probably have TIAs of hemodynamic origin, as manifested by positional neurologic deficits.[9]

Natural History

The natural history of asymptomatic extracranial vascular disease has been studied frequently by vascular surgeons and neurologists, but the results have been conflicting. In an early study by Humphries and colleagues,[10] 168 asymptomatic patients with >50% carotid stenosis were observed for as long as 12 years (average follow-up period, 32 months). One hundred thirty-six of the patients remained asymptomatic; 26 developed TIAs and successfully underwent carotid endarterectomy; 4 others had strokes, only 1 (0.6%) of which was unheralded by a TIA; and the remaining 2 patients developed vague, atypical neurologic symptoms that disappeared without treatment.

In a more recent prospective study,[11] in which 339 patients with significant (>50%) carotid stenosis were followed up for as long as 7 years, the annual risk of stroke without a premonitory TIA was 1%. The annual TIA rate was 2.5%. The major predictor of progressive symptomatic carotid disease was smoking, not hypertension.

In general, TIAs almost always precede strokes caused by carotid disease but are less likely to precede ischemic strokes that stem from cardiogenic embolism or intracranial vascular disease.

Should patients with severe carotid ulceration or asymptomatic high-grade carotid stenosis be considered at high risk? According to a recent review article,[12] ulceration does not increase the risk of either TIA or stroke. Intraplaque hemorrhage is common in symptomatic stenoses and is a good index of their severity, but is not a direct cause of TIA. In 1 study,[13] 38 patients with asymptomatic tight (>90%) carotid stenosis (receiving conservative medical treatment) were observed for a mean period of 4 years. The annual stroke rate was 1.7% without a preceding TIA and 4.2% with a preceding TIA. The cardiac death rate was 5.3% per year. Clearly, cardiac disease is the more serious problem in most of these patients.

The natural history of symptomatic carotid stenosis remains unclear. It has been the subject of few reports, because most of the affected patients undergo a carotid endarterectomy. In following up 45 high-risk medically treated patients for a mean period of 4 years, researchers[14] documented a maximal 10% ipsilateral infarct rate at the end of the 1st year and a 20% cumulative stroke rate at 5 years. The mortality rate of 5.6% per year was related primarily to cardiac deaths. No deaths were caused by ipsilateral cerebral infarction. These findings emphasize the fact that patients who are medically treated for symptomatic carotid stenosis are at high risk for cerebrovascular and cardiac events.

Risks of General and Cardiovascular Surgery

Asymptomatic carotid stenosis presents another special problem in patients scheduled to undergo general or cardiovascular surgery. To make an informed decision with regard to managing these patients, the physician must understand the mechanism of perioperative stroke.

In reviewing 24,500 general surgical procedures, Hart and colleagues[15] found that 12 patients had

suffered a cerebral infarction. Ten of these strokes had occurred during the immediate postoperative period, and only 2 were intraoperative. In 6 patients, the suspected mechanism was cardiogenic embolism; in 3 other patients, hypotension was a factor.

In another study,[16] 13 of 1,427 patients suffered a cerebral infarction associated with aortocoronary bypass. About half of these strokes were associated with cardiac arrhythmias and dilutional anemia. Two postoperative strokes were in the territory of a carotid stenosis documented by means of oculoplethysmography.

In a series of 144 coronary artery bypass patients, Furlan and Craciun[17] observed 16 patients with >90% carotid stenosis, 1 of whom had experienced a postoperative stroke; the same series included 49 patients with carotid occlusion, 1 of whom had suffered an intraoperative stroke. These researchers showed that patients with critical carotid stenosis or occlusion may be at heightened risk of perioperative stroke, although this hypothesis was not proved unequivocally. Moreover, their findings cast doubt on the hypothesis that perioperative strokes are of hemodynamic origin, since the carotid occlusions were associated with a lower stroke rate than the high-grade carotid stenoses.

Carotid Endarterectomy

As evidence has accumulated concerning the natural history of extracranial carotid disease, surgeons have developed an aggressive approach. Between 1971 and 1982, the estimated number of carotid endarterectomies performed in the United States increased from 15,000 to 82,000.[18] By 1984, carotid endarterectomy was the 3rd most common operation performed in the U.S. (103,000 cases).

In 1986, a multicenter retrospective review[19] presented some enlightening statistics concerning 3,328 carotid endarterectomies performed at representative North American medical centers and community hospitals. These operations were associated with a 6% risk of stroke or death and a 2.5% risk of transient neurologic dysfunction. Depending on the institution, morbidity and mortality rates varied widely, from a low of 1.5% for minor strokes with no deaths to a high of 16% for major strokes with a 5% mortality rate. When carotid endarterectomy was combined with aortocoronary bypass, the combined major morbidity and mortality rate was 13.3%; the rate was 10.3% when carotid endarterectomy was combined with peripheral vascular surgery.

The above-noted data prompted a well-publicized review of the appropriateness of carotid endarterectomy.[20] A panel of experts, including an equal number of surgeons and medical specialists, reviewed a random sample of 1,302 Medicare patients in 3 geographic areas. The reason for carotid surgery was deemed to have been appropriate in 35% of the cases, equivocal in 32%, and inappropriate in 32%. The last group included patients who had undergone operations on arteries with <50% stenosis, on occluded arteries, or on the wrong side, as well as patients who had undergone operations despite high surgical risk.

As a result of these investigations, the American College of Physicians published a position paper in 1989,[21] which is summarized in Table I.

Medical Treatment

Because medical trials have focused on preventing strokes after TIAs regardless of cause, the results of such studies do not apply only to extracranial carotid artery disease. According to Toole and associates,[22] anticoagulation with warfarin probably reduces the incidence of recurrent TIA, but does not reduce the stroke rate. There is a consensus that, after TIA, aspirin reduces the stroke rate by 25% to 30%.[23] Hass and coauthors[24] compared aspirin to the new antiplatelet agent, ticlopidine,* in 3,069 high-risk patients

* Not yet approved for clinical use by the Food and Drug Administration of the United States Department of Agriculture.

TABLE I. Summary of the American College of Physicians' 1989 Position Paper on Carotid Endarterectomy

Acceptable Surgical Results
• <1% mortality for patients with TIAs
• <3% major morbidity for patients with TIAs
• <2% stroke morbidity for patients with asymptomatic disease
Indications for Carotid Endarterectomy
• Carotid distribution TIA
≥70% ipsilateral stenosis
≥50% ipsilateral stenosis plus a large ulceration
• Minor stroke, after a 1-month delay
≥70% ipsilateral stenosis
≥50% ipsilateral stenosis plus a large ulceration
• Possibly indicated for high-grade asymptomatic stenosis
• Possibly indicated for high-grade asymptomatic stenosis before cardiac surgery
Some Contraindications
• Vertebrobasilar TIA
• Ipsilateral carotid occlusion
• Multi-infarct dementia
• Major stroke
• Stroke in evolution (possibly contraindicated)

who had suffered either a TIA or a reversible ischemic neurologic deficit within 3 months of enrolling in the study. The stroke rate was 21% lower in the ticlopidine group. Chimowitz and coworkers[25] recently studied the mechanism of stroke in 47 patients receiving aspirin to determine which patients were unlikely to respond to this drug. These authors documented large-artery atherosclerosis in 40% of the cases (including 23% that involved extracranial carotid disease). Also documented were cardiogenic embolism in 32% and small-vessel disease (lacunar stroke) in 11%; the remaining strokes were of undetermined origin. Eighty-two percent of the patients with extracranial carotid disease and stroke had >90% stenosis or had occlusion. These findings suggest that aspirin is not effective for preventing strokes related to cardiogenic embolism, carotid occlusion, or critical carotid stenosis of >90%.

Several ongoing studies are comparing medical treatment to combined medical and surgical treatment for carotid artery disease. So far, approximately 1,100 patients have been enrolled in the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[26] but the population must reach 3,000 for statistical validity to be achieved. Several large medical centers are participating in this trial. An interim analysis[27] has disclosed that patients with high-grade (70% to 99%) symptomatic carotid stenosis definitely benefit from surgery. Three months after surgery, the risks of perioperative stroke and death are surpassed by the benefits of endarterectomy. As yet, no conclusion has been reached concerning the results of endarterectomy for those patients with moderate (30% to 69%) stenosis.

An older study, the Veterans Administration Cooperative Clinical Trial,[28] examines asymptomatic carotid stenosis and is still in progress. Patients with confirmed asymptomatic carotid stenosis of >50% have been randomly assigned to undergo either a carotid endarterectomy plus aspirin therapy or aspirin therapy alone. Approximately 450 patients have been enrolled, with a mean follow-up period of 4 years thus far. These patients have a high incidence of associated disorders such as coronary artery disease, hypertension, diabetes, and symptomatic peripheral vascular disease. To date, their surgical mortality is 1.9% and their stroke rate is 2.4%.[29] More results are expected to be published in 1991.

Percutaneous Transluminal Angioplasty

Carotid stenosis has been treated successfully with percutaneous transluminal angioplasty.[30-32] At the 1990 Toronto Stroke Workshop, Tsai[31] reviewed his experience with this method in 58 patients, 19 (33%) of whom showed no clinical benefit. Distal embolization has been reported after carotid transluminal angioplasty,[32] and the potential long-term benefit is questionable. This procedure may be more appropriate for treating the comparatively rare lesions that cause hemodynamic TIAs. It may also be more useful in treating proximal great-vessel disease, as seen in Takayasu's arteritis.

Risk Factors

Perhaps the most important approach to avoiding stroke is the prevention of carotid atheromatous disease. The major risk factors have been clearly identified. According to Crouse and associates,[33] these are age, hypertension, pack-years of cigarettes smoked, and coronary artery disease; the risk is inversely related to the high-density-lipoprotein cholesterol concentration, uric acid concentration, and Framingham Type-A score. According to a more recent report,[34] however, additional risk factors include male sex, diabetes mellitus, and an elevated systolic blood pressure. By far the strongest predictor of extracranial carotid artery disease is the duration of cigarette smoking. Were a 60-year-old person with a 40-year history of cigarette smoking to be compared with someone of the same age who had never smoked, the smoker's risk of developing severe extracranial carotid disease would be 3.5 times that of the nonsmoker.

Conclusion

There is an emerging consensus that extracranial carotid disease is responsible for nearly 50% of all TIAs in the carotid distribution, but for only about 15% of all ischemic strokes.[4,5] Cardiogenic embolism and intracranial vascular disease, combined, are far more important causes of ischemic stroke.

Patients who have significant (>50%) asymptomatic stenosis or occlusion and who undergo general or cardiovascular surgery have a negligible risk of perioperative stroke, because of satisfactory collateral vascular support. Possible exceptions may be cardiovascular surgery patients with critical (>90%) stenosis or <2-mm residual lumen. Perioperative stroke is usually a consequence of cardiogenic embolism rather than focal hemodynamic change.

Most physicians treating patients who have cerebrovascular disease advocate surgical treatment of symptomatic extracranial carotid stenosis if the patient is not a high-risk surgical candidate. Preliminary data from the NASCET study[27] confirm the benefit of carotid endarterectomy for patients with high-grade (≥70%) stenosis. With respect to patients with moderate (30% to 69%) stenosis, no conclusive results have yet been reported. Meanwhile, a new medication, ticlopidine, appears promising, and percutane-

ous angioplasty may prove effective for high-risk patients.

Prevention of stroke must continue to be the major thrust of national medical policy. Only over the past few years has it become clear that cigarette smoking is the primary risk factor for extracranial carotid disease. Although previous emphasis on the treatment of hypertension, diabetes, and hypercholesterolemia was not misplaced, these factors are clearly less important than smoking in the pathogenesis of extracranial carotid disease. Therefore, more strenuous efforts must be directed toward eliminating this health risk.

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