Background—Carotid endarterectomy is the most common surgical procedure used to treat stenosis of the extracranial precerebral carotid artery. Data from several randomized controlled trials are available to help guide its use in specific patient subgroups. Carotid angioplasty with stenting is also being performed, and clinical trials comparing this procedure with carotid endarterectomy are in progress.

Summary of Report—For patients with symptomatic high-grade (ie, 70% to 99%) stenosis, carotid endarterectomy is associated with an overall benefit (risk ratio estimate for the combined end point of nonfatal stroke, nonfatal myocardial infarction, or death, 0.67; 95% CI, 0.54 to 0.83). The benefit is more modest for patients with less severe stenosis (ie, 50% to 69%) and may vary with specific patient characteristics. Selected patients with asymptomatic carotid stenosis may also benefit from the operation, but it needs to be performed with very low complication rates, which can be difficult to achieve in clinical practice. Several studies of angioplasty, angioplasty with stenting, and more recently angioplasty with stenting and a so-called distal protection device have also been performed. The technology involved continues to evolve rapidly, presenting a challenge for the design and conduct of clinical trials.

Conclusions—Surgical intervention for extracranial carotid stenosis remains a major potential therapeutic modality for the prevention of stroke in selected patients. Endovascular approaches continue to be evaluated in ongoing trials. (Stroke. 2003;34:2767-2773.)

Key Words: angioplasty ■ carotid endarterectomy ■ carotid stenosis ■ stents

Carotid endarterectomy is the most commonly performed surgical procedure for patients at risk for hemispheric ischemic stroke. Although its use is based on the results of several clinical trials, treatment decisions for individual patients are often based on post hoc subgroup analyses and extrapolation. The advent of endovascular approaches for the treatment of carotid disease provides another potential mode of intervention and is the subject of ongoing clinical trials. Candidates for either procedure include persons with symptoms referable to the ipsilateral carotid circulation and those with an asymptomatic stenosis, detected either incidentally or on the basis of the results of a specific screening test.¹⁻³

Carotid Endarterectomy: Summary of Primary Clinical Trial Data

Symptomatic Carotid Artery Stenosis
There have now been at least 5 completed randomized controlled trials of carotid endarterectomy for patients with symptomatic extracranial carotid artery stenosis. The Joint Study of Extracranial Arterial Disease was published 30 years ago.⁴ In addition to including a high proportion of patients (42%) with vertebrobasilar artery distribution symptoms, the trial had several other methodological limitations in relation to current standards. A second trial was halted prematurely because of high postoperative morbidity in surgical patients.⁵ These studies will not be considered further.

High-Grade Symptomatic Carotid Artery Stenosis
The interim results of 3 trials (North American Symptomatic Carotid Endarterectomy Trial [NASCET],⁶ European Carotid Surgery Trial [ECST],⁷ and Veterans Affairs Cooperative Symptomatic Carotid Stenosis Trial [VACS]⁸) became available in 1991. The degree of carotid stenosis was angiographically determined in each study, but the way in which it was measured varied. NASCET and VACS calculated the percent stenosis by dividing the residual luminal diameter by the luminal diameter of a distal portion of the same vessel where the walls of the vessel became parallel. ECST divided the residual luminal diameter by the estimated normal diameter of the artery at that level. Because of this difference, 48% of patients classified as having “severe” (ie, >70% to 99%)
stroke by ECST-type criteria would be reclassified as “moderate” (ie, >40% to 69%) by NASCET/VACS-type measurements. From the standpoint of clinical decision making, it is important to use the method employed in NASCET when applying NASCET data to individual patients.

Although published more than a decade ago, when best medical therapy differed considerably from current practice, these studies are relied on to guide present-day clinical decisions. A meta-analysis reviewed the differences in patient characteristics among the trials and supported the efficacy of the procedure among patients with >70% to 99% symptomatic stenosis (risk ratio estimate [RR] for a combined end point of nonfatal stroke, nonfatal myocardial infarction [MI], or death=0.67; 95% CI, 0.54 to 0.83). There were no significant overall differences in outcome rates among the trials, and benefits were similar for men and women when the results were analyzed together (on the basis of NASCET and ECST [VACS did not include women], RR=0.58; 95% CI, 0.45 to 0.74 for men; RR=0.84; 95% CI, 0.57 to 1.25 for women). However, the studies were not sufficiently powered to detect a difference between men and women. ECST found no benefit for endarterectomy in patients with symptomatic mild (0% to 29%) carotid stenosis, and there is no evidence that the operation is efficacious in this group of patients. Table 1 summarizes data from NASCET.

**Mild to Moderate Symptomatic Carotid Artery Stenosis**

Both NASCET and the ECST continued to recruit patients with more moderate grades of stenosis after the initial results in patients with high-grade disease were published. Table 1 summarizes the overall results of NASCET by degree of stenosis for the outcome of any ipsilateral stroke. There is a mild benefit in favor of endarterectomy for patients with moderate-grade (eg, 50% to 69%) stenosis. However, on the basis of subgroup analyses, the benefit of carotid endarterectomy for these patients was not uniform. As shown in Table 2, men, nondiabetics, and those having nondisabling stroke versus transient ischemic attack (TIA) had benefit. The lack of benefit in women with 50% to 69% stenosis may be related to their relatively low stroke risk with medical treatment.

**Pooled Analysis of Symptomatic Carotid Endarterectomy Trials**

A pooled analysis of final data from NASCET, ECST, and VACS remeasured the degree of stenosis from ECST using the method employed in the other 2 trials. In the earlier meta-analysis, outcome events were redefined as necessary so that the data could be combined. Overall, 7.1% of patients had strokes or died within 30 days of the operation. Surgery increased the 5-year risk of ipsilateral ischemic stroke in patients with <30% stenosis (absolute risk increase=2.2%; P=0.05), had no effect in those with 30% to 49% stenosis (absolute risk reduction [ARR]=3.2%; P=0.6), had marginal benefit in those with 50% to 69% stenosis (ARR=4.6%; P=0.04), and was of greatest benefit in patients with >70% stenosis but without near occlusion (ARR=16%; P<0.001). In those with near occlusion, there was trend toward benefit at 2 years (ARR=5.6%; P=0.19) but no benefit at 5 years (absolute risk increase=1.7%; P=0.9). It was noted that the results for patients with near occlusion are difficult to interpret because the numbers of patients and outcomes were small. Overall, 22 patients (95% CI, 12 to 80) with 50% to 69% stenosis and 6 (95% CI, 5 to 9) with >70% stenosis (but less than near occlusion) had to have the operation to prevent 1 ipsilateral stroke, operative stroke, or death over 5 years. For those with >70% stenosis, maximum benefit was reached by 3 years, with the event curves becoming largely parallel thereafter (up to 8 years).

**NASCET Post Hoc Analyses**

There have been numerous secondary publications based on post hoc analyses of NASCET data. These analyses must be viewed as only exploratory because of potential group imbalances and limited statistical power. Nonetheless, they provide insights that may help clinicians attempting to apply the trial results to their patients.

**Ulceration**

The NASCET investigators found that symptomatic patients with an ulcerative plaque in the setting of a high-grade

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### TABLE 1. Efficacy of Carotid Endarterectomy for Moderate to Severe Grade Stenosis—NASCET

<table>
<thead>
<tr>
<th>Stenosis (%)</th>
<th>CEA</th>
<th>Control</th>
<th>AR</th>
<th>RRR</th>
<th>NNT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%–49%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>678</td>
<td>690</td>
<td></td>
<td></td>
<td></td>
<td>0.16</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>14.9%</td>
<td>18.7%</td>
<td>3.0%</td>
<td>3.7%</td>
<td>0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Crude annual rate</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>P</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NNT</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>50%–69%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>430</td>
<td>428</td>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>15.7%</td>
<td>22.2%</td>
<td>3.1%</td>
<td>4.4%</td>
<td>0.16</td>
<td>&lt;0.001</td>
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<tr>
<td>Crude annual rate</td>
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<tr>
<td>P</td>
<td>0.05</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>NNT</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70%–99%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>325</td>
<td>331</td>
<td></td>
<td></td>
<td></td>
<td>0.91</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>13.0%</td>
<td>26.0%</td>
<td>2.6%</td>
<td>5.2%</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>Crude annual rate</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
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<td></td>
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<tr>
<td>NNT</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

CEA indicates carotid endarterectomy; NNT to prevent 1 event over 5 years.
stenosis were at particularly high stroke risk. However, these individuals would already be candidates for the operation solely on the basis of the degree of stenosis. There remain little data from prospective randomized studies to help determine whether symptomatic patients with ulcerated lesions and less severe degrees of stenosis have increased benefit compared with those with similar degrees of narrowing but no ulceration.

Retinal Versus Hemispheric Symptoms

Patients with amaurosis fugax may be at lower stroke risk than those with hemispheric TIA. In NASCET, the 2-year risk of ipsilateral stroke in patients with an approximate 75% stenosis was 11.2% after amaurosis fugax versus 37.4% after a hemispheric TIA. Stroke rates increased with increasing degrees of stenosis after either event (17.8% versus 60.0% for retinal versus hemispheric TIA with an approximate 85% stenosis and 28.9% versus 96.3% with a 95% stenosis). Although the risk of ipsilateral stroke remains high in patients presenting with amaurosis fugax, the risk appears higher in those presenting with hemispheric TIA and similar degrees of carotid stenosis.

Collaterals

The presence of angiographically defined collaterals was associated with a lower risk of stroke (11.3% with collaterals versus 27% without collaterals; \( P = 0.005 \)) and TIA (19.1% versus 36.1%; \( P = 0.008 \)) among medically treated patients over 2 years. The perioperative risk of stroke was 1.1% versus 4.9% and the 2-year risk of stroke was 5.9% versus 8.4% among surgically treated patients with and without collaterals, respectively (neither difference was statistically significant).

Stroke Subtype

To avoid confounding the results, patients with potential cardiac sources of emboli (eg, atrial fibrillation) were excluded from the clinical trials. Approximately 40% of NASCET patients had “lacunar” syndromes. Although traditionally thought to be due to intracranial “small-vessel” disease, these syndromes may have a variety of causes, including cardiogenic or artery-to-artery embolization. The rates of ipsilateral stroke were reduced with carotid endarterectomy from 25% to 10% (66% risk reduction; \( P = 0.002 \)) in those with nonlacunar syndromes, from 16% to 8% (53% risk reduction; \( P = 0.22 \)) in those with possible lacunar syndromes, and from 26% to 17% (35% risk reduction; \( P = 0.53 \)) in those with probable lacunar syndromes. Because of sample size limitations and because this represents a post hoc analysis, patients with lacunar syndromes need to be investigated for ipsilateral carotid stenosis if they are otherwise surgical candidates.

Tandem Lesions

Patients with a high-grade intracranial stenosis ipsilateral to an extracranial carotid artery stenosis were excluded from NASCET. Intracranial atherosclerotic disease was detected on angiography in one third of patients. The infracranial portion of the vessel was affected 7 times more frequently than the supraclanoid portion or the proximal anterior or middle cerebral arteries. Table 3 presents the 3-year risk of ipsilateral stroke in patients with or without noncritical intracranial atherosclerotic disease. Non–high-grade intracranial stenosis further increases the risk of stroke in patients with ipsilateral extracranial disease. The numbers needed to treat are lower with both increasing degrees of extracranial stenosis and the presence of ipsilateral intracranial disease, suggesting that carotid endarterectomy is of benefit even in the setting of a noncritical intracranial tandem lesion.

Ipsilateral Intracranial Aneurysms

Only 3.1% of NASCET patients had an unruptured intracranial aneurysm. One of the 25 patients having endarterectomy ipsilateral to an unruptured aneurysm had a subsequent subarachnoid hemorrhage 6 days later and died. The site of bleeding was not identified at postmortem evaluation. None of the 23 patients with a small unruptured aneurysm ipsilateral to carotid stenosis who were treated medically had a subarachnoid hemorrhage. Although the numbers are quite small, it was concluded that endarterectomy should generally not be precluded by the presence of an ipsilateral small unruptured aneurysm.

Endarterectomy in the Elderly

NASCET (but not ECST or VACS) was limited to patients aged <80 years. Data from randomized controlled studies regarding the efficacy of carotid endarterectomy in symptomatic patients aged >75 years are limited. A meta-analysis of 36 published studies found that age >75 years was associated with a 36% increase in perioperative risk of stroke or death (found in 10 studies; odds ratio = 1.36; 95% CI, 1.09 to 1.71). However, at least 1 study reported that endarterectomy could be safely performed even in octogenarians. Clinical judgment remains essential when deciding whether to recommend any octogenarian for surgery. In particular, the decision maker needs to consider the patient’s life expectancy when estimating the risk of ipsilateral stroke if the carotid stenosis is left untreated and balance that rate against the risk of operative complications.

Timing of Surgery

Consideration of carotid endarterectomy is appropriately delayed after large hemispheric strokes to determine the patient’s level of recovery and to avoid the hyperperfusion-related injury that was found in studies performed in the 1960s. Another NASCET subgroup analysis compared 42 patients with 70% to 99% carotid stenosis and a nondisabling
stroke operated on between 30 days with 58 patients operated on after 30 days (range, 33 to 117 days). The perioperative stroke rate was 4.8% in the early group versus 5.2% in the delayed group (P=1.00), with no perioperative deaths. This is particularly important in view of a more recent study showing that the risk of stroke is approximately 11% over the first 90 days after TIA, with 85% occurring over the first month. There is no reason to delay surgery in these patients.

**Perioperative Platelet Antiaggregants**

In NASCET, the risk of perioperative stroke or death was 1.8% for those taking 650 to 1300 mg of aspirin versus 6.9% for those taking 325 mg daily, suggesting a benefit with higher aspirin doses. The Aspirin and Carotid Endarterectomy (ACE) trial subsequently randomized 2849 patients to receive 81, 325, 650, or 1300 mg of aspirin daily after carotid endarterectomy. The primary analysis compared the 2 high-dose groups with the 2 low-dose groups. The 30-day rates of stroke, MI, or death were lower in those given the lower doses of aspirin (Table 4). None of the other available platelet antiaggregants have been tested in the perioperative period.

**Asymptomatic Carotid Artery Stenosis**

There have been 3 randomized trials of endarterectomy for patients with asymptomatic extracranial carotid artery stenosis. A Mayo Clinic study included 71 randomized and 87 nonrandomized patients. Surgically treated patients were not given aspirin. There were no major strokes or deaths in either group. However, MI occurred in 9% of those in the medical arm versus 26% of those in the surgical arm (P=0.002), reinforcing the importance of treating patients with cerebrovascular disease with platelet antiaggregants.

A Veterans Affairs Cooperative Study included patients with >50% asymptomatic stenosis. Combined perioperative and angiographic risk was 4.7%. There was a significant 38% risk reduction for the primary combined end point of ipsilateral TIA, transient monocular blindness, and stroke over 2 years. Although the risk of stroke was decreased by 50% in the patients who had endarterectomy, the difference between the groups was not statistically significant. However, the study was not powered to detect this subgroup difference.

The largest study completed to date, the Asymptomatic Carotid Atherosclerosis Study (ACAS), evaluated the efficacy of endarterectomy in patients with a >60% diameter reduction in asymptomatic carotid stenosis. Patients were aged 40 to 79 years and had a >5-year life expectancy. Approximately 30% of patients had other cerebrovascular symptoms. The event rate in surgically treated patients for the primary end point (ipsilateral stroke, perioperative stroke, or death) was 5.1% over 5 years. This included a 1.2% risk of angiography-related complications among the 424 patients undergoing postrandomization angiograms and a 1.1% surgical risk (2.3% aggregate perioperative stroke risk). The corresponding rate in medically treated patients was 11% (55% risk reduction; 2%/y rate reduced to 1%/y; number needed to treat=17; P=0.004).

**ACAS Subgroups**

With acknowledgment of the limitations of subgroup analyses, data are available from ACAS to address 4 additional questions of clinical importance: efficacy of prophylactic endarterectomy in women, benefit in asymptomatic patients (as distinct from asymptomatic vessels), relationship between the degree of asymptomatic stenosis and surgical benefit, and benefit in patients with contralateral occlusion. Table 5 shows the percentages of ipsilateral strokes, perioperative strokes, or deaths with the use of 5-year Kaplan-Meier estimates. The relative lack of benefit in women was ascribed to their higher perioperative complication rate (3.6% versus 1.2% in men) combined with a relatively lower event rate with medical treatment. There was a 46% risk reduction in patients who never had cerebrovascular symptoms. There was no evidence of increasing efficacy with increasing degrees of stenosis; however, cerebral angiography was not mandatory in patients randomized to medical therapy.

A subgroup analysis was also performed for ACAS patients with an asymptomatic carotid stenosis contralateral to a carotid occlusion. Medically treated patients with a contralateral occlusion were less likely to have a stroke than those without a contralateral occlusion (3.5% versus 11.7%; P=0.011). The event rates among surgically treated patients with (5.5%) and without (5.0%) a contralateral occlusion were similar. Therefore, this post hoc analysis found no benefit for surgery in those with a contralateral occlusion. This lack of benefit was not due to increased surgical risk (the 30-day postoperative event rates were similar in patients with [2.3%] and without [2.2%] contralateral occlusion).
Application to Clinical Practice

The application of ACAS data to clinical practice has been controversial. The operation was recommended in scientific statements from the American Heart Association, provided that it could be conducted within acceptable limits of morbidity (<3%). However, it was not recommended in a Canadian consensus statement. This is related in part to the low (relative to symptomatic patients) stroke risk with medical therapy and a perceived high or uncertain risk of perioperative complications (see below). The lack of an identifiable higher-risk ACAS subgroup makes case selection difficult. Some observational studies suggest that the rate of stroke may be higher in those patients with progressing stenosis compared with those with stable disease and higher in those with more severe stenosis.

The cost-effectiveness of carotid endarterectomy for asymptomatic stenosis varies considerably among studies, on the basis of assumptions underlying the analyses including patient age, event and complication rates, costs of surgery and stroke, and whether the screening tests are included. In addition, technical issues (eg, discount rates, inflationary factors) need to be considered. For asymptomatic patients, the cost per quality-adjusted life year varies from $8484 (benefit, 1998 US dollars) to no benefit (ie, not cost-effective). However, given the limitations of the analyses, cost-effectiveness data need to be interpreted with care and are difficult to use for patient management. Decision makers considering carotid endarterectomy for asymptomatic patients must take into account the patients’ willingness to accept the perioperative risk in comparison with their anticipated long-term benefit.

Importance of Surgical Risk

The benefit of carotid endarterectomy in comparison to medical therapy alone is highly dependent on surgical risk. Complication rates significantly higher than 4% to 6% in patients with high-grade symptomatic stenosis or 3% in those with asymptomatic stenosis can eliminate the benefit of the operation. Sundt and coworkers developed a system for grading the risk of endarterectomy based on preoperative factors. A modified version of the Sundt index was validated in a study of carotid endarterectomies performed at 12 academic medical centers.

Although a variety of preoperative patient-related factors may affect the risk of carotid endarterectomy, surgical volume and the skill of the surgeon are critical. In recognition of this, the randomized controlled trials included careful surgeon selection and ongoing monitoring. Observed perioperative morbidity and mortality are often higher when performed outside of the setting of a clinical trial, even in centers that participated in randomized studies. Therefore, knowledge of an individual surgeon’s complication rate is critical. Surgical series report perioperative complication rates of approximately 3%, but community-based surveys have reported combined morbidity and mortality rates of 6% to 20%. One of the more recent studies assessing the utilization of endarterectomy in 10 states found stroke rates varying from 2.3% to 6.7% and mortality rates ranging from 0.5% to 2.5% for patients having the operation for asymptomatic disease.

Despite the central role of complication rates for surgical decisions and clear evidence that morbidity and mortality rates can be higher than recommended in guideline statements, a survey found that <20% of physicians knew the perioperative complication rates of their hospital for carotid endarterectomy. A second study surveyed the surgery program directors of medical centers in the United States. Approximately 20% indicated that their programs were not systematically monitoring carotid endarterectomy complication rates. Ongoing audits of surgical complication rates need to be performed to provide these essential data. However, these estimates are likely to be statistically unstable in low-volume centers.

Stroke Prevention After Endarterectomy

It is important to recognize that 20% of patients undergoing endarterectomy for symptomatic disease subsequently have strokes related to other etiologies. Carotid endarterectomy represents only 1 mode of reducing stroke risk in patients with TIA or nondisabling stroke. Therefore, whether symptomatic or asymptomatic, these patients need to be fully evaluated for other potential treatable causes of stroke.

Carotid Angioplasty and Stenting

Endovascular treatment of extracranial carotid artery stenosis has been performed for over a decade. Potential advantages over carotid endarterectomy include avoiding a surgical incision and its complications, including cranial nerve palsies and wound hematomas. Endovascular treatment is being used in many centers for patients who present a technical challenge for endarterectomy, such as postradiation vasculopathy, restenosis after previous endarterectomy, and surgically inaccessible lesions. It has also been argued that endovascular approaches do not require general anesthesia and may require shorter (or even no) hospitalization, potentially reducing costs. However, many surgeons perform endarterectomy under local anesthesia, and 24-hour hospitalizations are possible. Most importantly, prospective controlled data comparing the relative risks and benefits of endovascular approaches compared with the established carotid endarterectomy remain limited.

Most of the data regarding the performance of endovascular carotid procedures are based on case series, surveys, and enrollment of patients in voluntary registries. By the year 2000, >5210 procedures involving 4757 patients were reported worldwide, with a technical success of 98.4%. Overall, there were 139 TIA and 129 minor strokes (2.72%), 71 major strokes (1.49%), and 41 deaths (0.86%) within a 30-day postprocedure period. The combined minor and major stroke and procedure-related death rate was 5.07%. Restenosis rates after carotid stenting were 1.99% and 3.46% at 6 and 12 months, respectively. These types of studies are subject to reporting and other types of biases. The same type of procedural data based on independent audits that was reviewed for carotid endarterectomy has not been performed for endovascular approaches.

There have been at least 5 randomized trials comparing carotid angioplasty with or without stenting with the established standard, carotid endarterectomy. One study begun in
the United Kingdom was halted after only a few patients were enrolled because of very high complication rates in the endovascularly treated patients and other methodological issues.48

The multicenter Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) included patients with carotid stenosis with (90%) or without symptoms within the prior 6 months.59 Patients were enrolled on the basis of the uncertainty principle (ie, the investigator had to be uncertain which procedure was preferable in a given patient). Carotid endarterectomy was performed in 253 patients, with 251 having endovascular treatment. Suitable stents became available during the course of the study but were used in only 26% (n=55) of the procedures. Periprocedural stroke and death rates were higher than in previously cited trials of endarterectomy but were similar for endovascular treatment and surgery (10.0% versus 9.9%). The endovascular approach was less frequently associated with cranial neuropathy (0% versus 8.7%), less frequently associated with major neck or groin hematoma (1.2% versus 6.7%), but more frequently associated with severe restenosis at 1 year (14% versus 4%), with similar overall rates of ipsilateral stroke over 3 years (however, fewer than half of the patients remained free of events and available for follow-up after 2 years, thereby diminishing the study’s power to detect a difference). How the use of stents might affect the restenosis rate remained uncertain, and the relatively high perioperative complication rates in both groups were a cause of concern in this study.

A third multicenter trial compared endovascular treatment with carotid endarterectomy in which all of the endovascularly treated patients had stent placement.50 The results of this study were presented in preliminary form in 2001 and suggested a higher rate of stroke with angioplasty/stenting (at 1 year, 12.2% of stent patients had an ipsilateral stroke versus 3.6% in the endarterectomy group; P=0.022). Part of this was attributed to the “learning curve” for endovascular treatment. The full study report has not yet been published. In contrast, a single-center randomized trial comparing angioplasty and stenting (n=53) with endarterectomy (n=51) in patients with >70% symptomatic carotid artery stenosis found the 2 procedures to be equivalent.51 A single patient having endarterectomy died, and a single patient treated endovascularly had a TIA. Although promising, the generalizability of the results of this single-site study is uncertain, and the sample size is too small to reliably determine whether the procedures are equivalent.

The advent of distal protection devices to capture embolic material during angioplasty/stenting has the potential to decrease the risk of embolic stroke during the procedure.52 The Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) study compared endarterectomy with stenting, including the use of a distal embolic protection device, for the treatment of patients with moderate to severe carotid stenosis who also had comorbid conditions that might increase the risk of surgery. This study was also presented in abstract form at the 55th Annual Meeting of the American Academy of Neurology in 2003, but the full report has not yet been published. The study included both symptomatic and asymptomatic patients. The 30-day major adverse event rate (stroke, MI, or death) was 5.8% (9/156) for endovascularly treated patients versus 12.6% (19/151) for those having carotid endarterectomy (P=0.05). These periprocedural complication rates were higher in both groups than the 3% rate for asymptomatic patients recommended in the current American Heart Association guideline statement.1

The Carotid Revascularization Endarterectomy Versus Stent Trial (CREST) is currently in progress and compares the 2 techniques.53 However, the procedure continues to evolve from a technical standpoint, and several other studies are also in progress. New stents are rapidly being developed, and a variety of distal protection devices are being introduced. These constantly changing technologies present a critical challenge for clinical trial design.

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Extracranial Carotid Artery Stenosis
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