REVIEW

CME CREDIT

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Carotid stenosis: Current strategies for choosing between medical and surgical management

ABSTRACT

The effectiveness of carotid revascularization depends on appropriate patient selection and balancing the expected benefits with the risks of treatment. Exceeding a rate of serious complications (strokes and deaths) of 5% for asymptomatic and 9% for symptomatic patients negates any benefit for carotid endarterectomy. Endovascular techniques such as stent-supported angioplasty will likely change the management approach for some patients with carotid occlusive disease. This paper contains the author's recommendations for choosing between medical and surgical management of carotid stenosis.

KEY POINTS

The best indication for carotid endarterectomy is to prevent ipsilateral carotid-territory ischemic stroke in patients with a recent transient ischemic attack or minor ischemic stroke due to severe atherosclerosis of the carotid bifurcation.

As the severity of carotid stenosis increases, so does the risk of having a stroke. As stroke risk increases, so does the benefit of surgery.

Whether noninvasive methods of measuring carotid stenosis are accurate enough to select patients for treatment achieve the same outcomes as the gold standard, angiography, remains to be proven.

Results of clinical trials to date do not justify screening for carotid occlusive disease in people without symptoms.

WHICH PATIENTS with carotid stenosis should undergo carotid endarterectomy, and which should receive medical therapy alone?

Carotid endarterectomy can be one of the most powerful therapies for preventing ischemic stroke. Yet it also can cause the very problem it is intended to prevent. Complicating matters further, the methods used to measure the degree of stenosis can provide different interpretations for the same lesion, and invasive tests carry some risk of stroke as well. In addition, carotid stenting is providing a new treatment option.

Clinical trials indicate that the benefit of carotid endarterectomy outweighs the risk—in specific groups of patients (TABLE 1). Therefore, candidates should be screened carefully, using the same criteria used in the clinical trials to achieve similar patient outcomes.

This article reviews the findings of these clinical trials and gives recommendations concerning indications for carotid endarterectomy, patient selection criteria, and the role of angioplasty and stenting.

BASIS FOR CURRENT MANAGEMENT GUIDELINES

The first randomized, controlled trial of carotid endarterectomy[1] began in 1959. A decade later, it reported that the operative morbidity and mortality from this procedure negated its benefit for all but those with unilateral symptomatic carotid stenosis.

TABLE 1

Is endarterectomy beneficial? Findings from major studies

STUDY	DEGREE OF STENOSIS	NUMBER NEEDED TO TREAT*	EVENT PREVENTED	TIME PERIOD
Patients with symptoms				
NASCET	70%–99%	6 10	Ipsilateral stroke Major stroke or death	2 years
ECST	70%–99%	15 20	Ipsilateral stroke Major stroke or death	3 years
NASCET	50%–69%	12 (men) 67 (women) 16 (men) 125 (women)	Ipsilateral stroke Major stroke	5 years
ECST	< 70%	No benefit	Ipsilateral stroke	> 4 years
NASCET	< 50%	No benefit	Ipsilateral stroke	5 years
VA	> 50% ≥ 70%	No benefit 26 (men)	Stroke or death Crescendo TIA or stroke	Terminated 1 year
Patients without symptoms				
CASANOVA	50%–90%	No benefit	Any stroke or death	3 years
VA	> 50%	No benefit	Any stroke or death	4 years
MACE		No benefit†		
ACAS	≥ 60%	17	Ipsilateral stroke or any perioperative stroke or death	5 years
ACST		Ongoing		

*The number of patients that would need to be treated to prevent one event
†Terminated because of excessive myocardial infarctions

Endarterectomy is beneficial for carotid stenosis of ≥ 50% (NASCET method) or ≥ 70% (ECST method)

Over the years, surgical and anesthetic techniques improved, as chronicled in nonrandomized case series, and the number of endarterectomies increased sevenfold to more than 100,000 per year by 1985. In 1988, the Rand report[2] expressed concerns about the appropriateness of surgical indications and the variation in complication rates. This report set the stage for seven randomized, controlled trials in the late 1980s,[3–13] which provided the data for the current guidelines.

Now, with more than 140,000 carotid endarterectomies performed each year and the new endovascular techniques of carotid angioplasty and stenting increasing in popularity, more patients than ever are being considered for treatment.

DEFINING ISCHEMIC SYMPTOMS

In the clinical trials on which we base our recommendations, patients were admitted on the basis of whether they had ischemic symptoms, which were defined strictly and interpreted by specially trained neurologists.[4] Therefore, in deciding whether a patient might benefit from endarterectomy, physicians ought to apply the same definitions:

Transient ischemic attack (TIA)—the abrupt onset of unilateral motor or sensory disturbance, speech deficit, homonymous hemianopsia, or constructional apraxia (inability to reproduce a geometric figure) that conforms to a distinct focal, hemispheric pattern. By definition, a TIA must resolve completely within

24 hours, although the median duration is less than 15 minutes.

Transient monocular blindness (amaurosis fugax)—the abrupt onset of unilateral decreased visual acuity involving part or all of the visual field and resolving within 24 hours.

Minor stroke or retinal infarction—the above symptoms persisting more than 24 hours, but without resulting disability.

The trials included patients with both cortical and lacunar syndromes within the ipsilateral carotid territory, that is, the portion of the brain supplied by the stenotic carotid artery. Patients were excluded if they had only ill-defined symptoms such as nonspecific dizziness, vertigo, syncope, confusion, memory loss, isolated dysarthria, patchy numbness, or seizures, or if the event was more likely due to cardioembolism or intracranial stenosis.

IMAGING TESTS TO MEASURE CAROTID STENOSIS

Measuring carotid stenosis accurately is key, as the decision to treat medically or surgically is often based on the degree of stenosis.

Are noninvasive tests accurate enough?

Duplex ultrasonography is the preferred noninvasive screening test for patients with suspected extracranial carotid stenosis. It combines an anatomic image with Doppler ultrasonographic assessment of blood flow.

Doppler ultrasonography alone is a less-accurate alternative, but it costs less.

Magnetic resonance angiography (MRA) provides an extracranial vascular image within minutes with an accuracy comparable to that of Duplex ultrasonography. It is contraindicated in patients with implanted metal devices (eg, pacemakers, defibrillators) and certain other devices (vascular clips, stents, some cardiac valves). MRA is limited as a screening tool owing to its high cost; in addition, many patients cannot tolerate it because of claustrophobia.

Limitations of noninvasive tests. The clinical trials that found carotid endarterectomy to be beneficial used angiography to measure stenosis, not ultrasonography or MRA. Whether endarterectomy should be performed on the basis of noninvasive tests alone remains controversial,[14] because whether these tests measure the carotid stenosis accurately enough to select patients for treatment has not been studied in a clinical trial.

For example, MRA can overestimate the severity of stenosis, which would have the greatest impact on decision-making for moderate lesions. The accuracy of ultrasonography depends on operator skill, the equipment used, laboratory quality control, and the patient's anatomy. Ultrasonography is inherently inaccurate at the extremes of stenosis, and although missing mild stenosis may have little clinical significance, misinterpreting a severe stenosis with low flow as a complete occlusion can result in a serious error of not performing surgery on a patient who might benefit from it. Furthermore, ultrasound and MRA laboratories vary considerably in their validation methods and certification status and may not be able to reproduce a 6% false-positive error rate, which was the standard used in the Asymptomatic Carotid Atherosclerosis Study.[13]

Carotid angiography still poses some risk

Carotid angiography is the gold standard, and is the most commonly used diagnostic test for determining the degree of carotid artery stenosis. Intra-arterial digital subtraction techniques, smaller catheters, and arterial closure devices have made it a relatively safe procedure that can be performed on an outpatient basis, but 1% to 3% of patients still suffer serious complications such as stroke or life-threatening hemorrhage. This risk must be considered in any estimate of benefit vs risk of treatment.

Qualifying symptoms included hemiparesis and aphasia but not syncope

Two formulas for calculating stenosis

Two different methods for calculating the degree of angiographic stenosis were used in the major clinical trials (ie, the North American Symptomatic Carotid Endarterectomy Trial [NASCET][5,6] and the European Carotid Surgery Trial [ECST][7–9]; TABLE 2, FIGURE 1). These methods produce different results. Therefore, when interpreting imaging studies, clinicians need to know which technique was used for the reference standard so that they can refer to the appropriate clinical trial when they decide on a course of action.

TABLE 2

Comparison of two methods used to measure carotid stenosis

ANGIOGRAPHIC % STENOSIS		CALCULATED CROSS-SECTIONAL AREA (%)
NASCET METHOD*	ECST METHOD†	
90	97	99
80	91	96
70	85	91
60	80	84
50	75	75
40	70	64
30	65	51

*North American Symptomatic Carotid Endarterectomy Trial[5,6]; see FIGURE 1
†European Carotid Surgery Trial[7–9]; see FIGURE 1

TABLE 3

Risk factors for perioperative complications from carotid endarterectomy

Neurologic
- Deficit within past 24 hours
- Stroke within past 7 days
- Crescendo transient ischemic attack
- Global cerebral ischemia
- Stroke evident on computed tomography
- Left-sided disease

Angiographic
- Contralateral carotid occlusion
- Siphon stenosis
- Stenosis > 3 cm distal
- Stenosis > 5 cm proximal
- Bifurcation at C2
- Intraluminal thrombus
- Irregular, ulcerated plaque

Medical
- Age > 70 years
- Coronary artery disease
- Hypertension
- Severe peripheral arterial disease
- Chronic obstructive pulmonary disease
- Severe obesity
- Diabetes mellitus

ADAPTED FROM REFERENCES 18 AND 19

COMPLICATIONS OF CAROTID ENDARTERECTOMY

Stroke is the most feared complication of carotid endarterectomy, as stroke prevention is the primary goal of surgery.

In contemporary clinical trials, the 30-day stroke rate for patients undergoing carotid endarterectomy was higher by 2 to 5 percentage points than for those not undergoing surgery, with a 1% to 2% risk of death.

After surgery, keep the systolic blood pressure below 150 - 160 mm Hg

Ischemic events

Minor cerebral ischemic symptoms are often due to embolism of plaque or platelet-fibrin debris, and major stroke can be due to embolism or carotid thrombosis.

Cerebral hemorrhage

Intracerebral hemorrhage is an uncommon complication of carotid endarterectomy (occurring in < 1% of patients), but is often fatal. It is attributed to cerebral hyperperfusion due to abnormal cerebral autoregulation. Risk factors for hemorrhage include a recent cerebral infarction, correction of a severe stenosis, and postoperative hypertension.

As a preventive measure, antihypertensive therapy is started postoperatively to keep systolic pressures less than 150 to 160 mm Hg. If a patient develops postoperative focal seizures or an ipsilateral throbbing headache that improves with sitting, which are symptoms that can precede a hemorrhage by hours or days, we prefer to reduce the blood pressure by an additional 10% to 20% with antihypertensive agents that do not produce cerebral vasodilation (eg, labetalol).

Predictors of risk

Surgical complication rates can vary by as much as 10-fold on the basis of neurological, angiographic, and risk factors. Sundt et al[15] described a set of risk factors (TABLE 3) and used them to divide of group of 1,176 patients into four grades. The incidence of stroke or death in the four grades was as follows:

- Grade 1 (neurologically stable, no angiographic or medical risk factors)—0.9%
- Grade 2 (neurologically stable, angiographic risk but no medical risk)—1.7%
- Grade 3 (neurologically stable, major

Two methods of measuring the severity of carotid stenosis

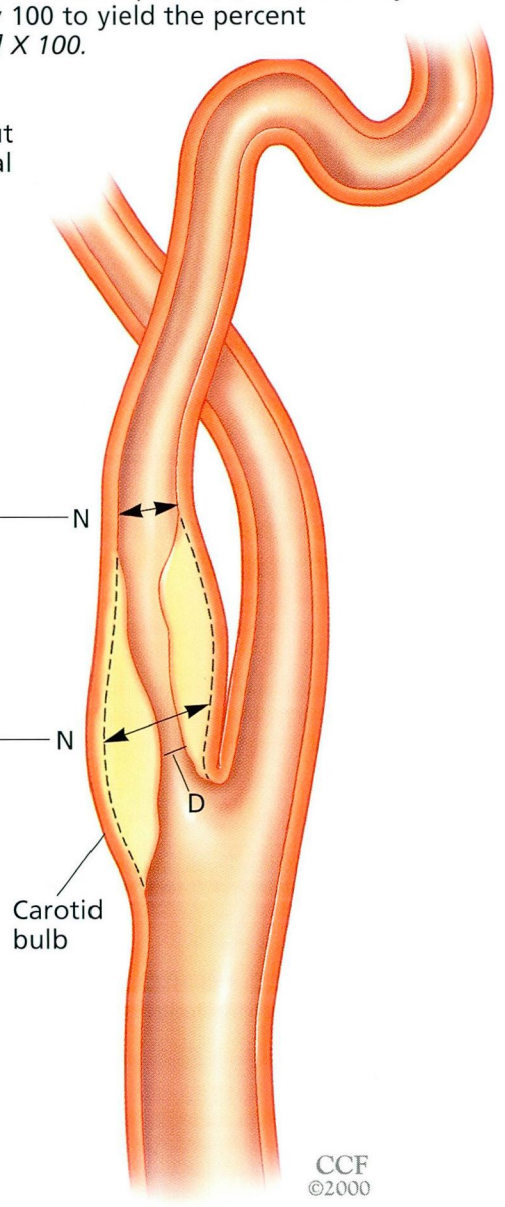
The two major clinical trials that evaluated the efficacy of carotid endarterectomy used different methods of calculating the severity of stenosis on carotid angiograms. The two trials were the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST).

In both methods, the difference between the "normal" diameter (N) and the residual lumen diameter at its narrowest point (D) is divided by the normal diameter and multiplied by 100 to yield the percent stenosis: *Percent stenosis = [(N – D) / N] X 100.*

Both NASCET and ECST define D (the narrowest point) the same way but differ in how they define N (the normal diameter). This can lead to different stenosis measurements for the same lesion (see TABLE 2).

The NASCET method defines normal as the diameter just distal to the carotid bulb (not the bulb itself nor a region of poststenotic dilatation). In this example, the stenosis is 46% by the NASCET method.

The ECST method defines normal as the estimated diameter of the carotid bulb as it was before the disease narrowed the lumen. In this example, the stenosis is 75% by the ECST method.



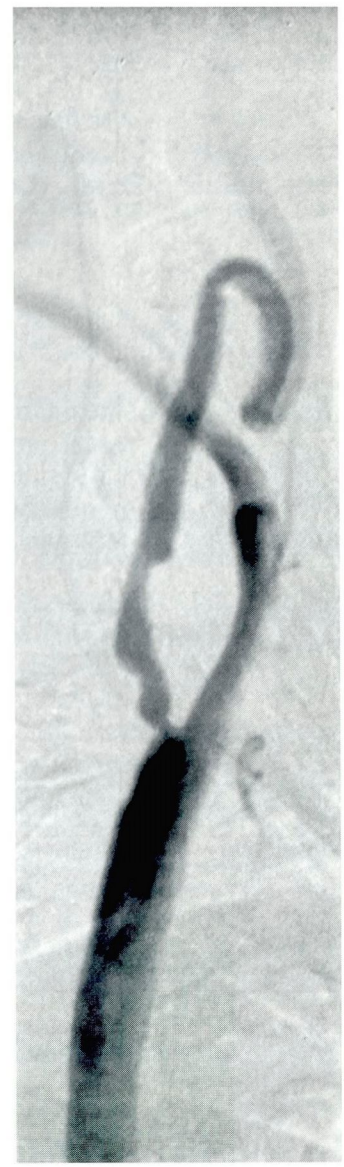


FIGURE 1

medical risks with or without angiographic risks)—3.1%
- Grade 4 (neurologically unstable)—8.1%.

Myocardial infarction

The mortality rate from myocardial infarction is 3% to 5% per year in patients with symptomatic or asymptomatic carotid artery disease, and myocardial infarction therefore needs to be considered when anticipating the risk of a surgical procedure. In the ACAS trial,[13] nearly half of the deaths were due to acute myocardial infarction or other cardiac disease, whereas only 9% were due to stroke.

Cranial nerve injury

Cranial nerve injury is a frequent complication of endarterectomy, occurring in 3% to 9% of cases. It is manifested as asymmetric grimacing, hoarseness, or dysphagia. The mandibular branch of the facial nerve and the greater auricular, superior laryngeal, hypoglossal, and glossopharyngeal nerves are vulnerable.

The importance of hospital endarterectomy volume

MI is the most common cause of death in patients with asymptomatic carotid stenosis

The results achieved in the "real world" may not be the same as those achieved in clinical trials, in which protocols restricted the types of patients, surgeons, and institutions. For example, in Ohio Medicare beneficiaries undergoing carotid endarterectomy in 1993 and 1994, complication rates were inversely related to hospital volume.[16] For patients without symptoms, the 30-day rate of death or stroke warranting hospitalization was 0% at high-volume hospitals vs 4.9% at low-volume hospitals. For patients with TIAs, the rate was 4.6% at high-volume hospitals vs 9.8% at low-volume hospitals. As complication rates higher than 5% for asymptomatic patients and 9% for symptomatic patients negate any benefit for endarterectomy, a knowledge of surgeon-specific and hospital-specific outcome data is essential.[17]

THREE TRIALS OF TREATING SYMPTOMATIC CAROTID ARTERY STENOSIS

Three randomized trials examined the safety and efficacy of carotid endarterectomy for symptomatic carotid artery stenosis:
- The North American Symptomatic Carotid Endarterectomy Trial (NASCET)[5,6]
- The European Carotid Surgery Trial (ECST)[7–9]
- The Veterans Administration Symptomatic Trial (VA 309).[4]

The results (primarily from the first two trials) indicate that the best use of carotid endarterectomy is to prevent ipsilateral carotid-territory ischemic stroke in patients with a recent TIA or minor ischemic stroke due to severe atherosclerosis of the carotid bifurcation.

North American Symptomatic Carotid Endarterectomy Trial

Starting in 1987, NASCET randomized patients with carotid-territory TIA or nondisabling ischemic stroke within 3 months and ipsilateral internal carotid stenosis of 30% to 99%.

How stenosis was measured. The degree of stenosis was determined by comparing the angiographic residual lumen diameter at the narrowest point with the lumen diameter of normal vessel just distal to the carotid bulb. This "NASCET method" is the standard for measuring carotid stenosis and differs importantly from other methods (TABLE 2, FIGURE 1).

The severity of carotid stenosis was stratified as either moderate (30% to 69% stenosis) or severe (70% to 99% stenosis).

Treatment. Patients were randomized to receive "best medical management" (including antiplatelet therapy) either alone or with surgery.

Benefit in patients with severe (70%–99%) symptomatic carotid stenosis. The study was prematurely terminated in patients with 70% to 99% stenosis after an interim analysis demonstrated a statistically significant benefit in favor of surgery.[5] At 2 years in this group, the rate of any type of ipsilateral stroke was 9% in patients who underwent carotid endarterectomy vs 26% in those who received medical therapy alone—a 17% reduction in absolute risk and a 65% relative risk reduction. Endarterectomy also reduced the risk of major or fatal ipsilateral stroke from 13.1% to 2.5% (an 81% relative risk reduction).

As the severity of carotid stenosis increased, so did the risk of having a stroke, and as stroke risk increased, so did the benefits of surgery. Ipsilateral ischemic stroke was reduced by 12% in patients with 70% to 79% stenosis, 18% in patients with 80% to 89% stenosis, and 26% in patients with 90% to 99% stenosis. The overall risk of any stroke or death was also significantly reduced, from 32.3% to 15.8% (a 51% relative risk reduction) at 2 years.

Nine prospectively selected risk factors identified patients at high risk of stroke with medical therapy alone (TABLE 4). Of patients with more than six of these risk factors, 39% had an ipsilateral stroke within 2 years.

Benefit in patients with high-moderate (50%–69%) symptomatic carotid stenosis. In 1998, when results in 2,226 patients with moderate symptomatic carotid stenosis were published along with the long-term follow-up results in patients with severe symptomatic carotid stenosis,[6] the relationship between the degree of carotid stenosis, risk of stroke, and expected benefit from carotid endarterectomy continued to hold true.

Carotid endarterectomy for high-moderate (50% to 69%) symptomatic carotid stenosis also reduced the rate of any ipsilateral stroke from 22.2% to 15.7% (a 6.5% absolute risk reduction and a 29% relative risk reduction) at 5 years, but the statistical significance was marginal ($P = .045$).

Within this subgroup, characteristics associated with a greater benefit from endarterectomy included male gender, a recent stroke (rather than a TIA), recent hemispheric symptoms (rather than retinal symptoms), and failure of aspirin therapy at a dosage of 650 mg or more per day.

No benefit in patients with low-moderate (30%–49%) symptomatic carotid stenosis. Endarterectomy did not benefit those with low-moderate (30% to 49%) symptomatic carotid stenosis: the rate of any ipsilateral stroke at 5 years was not significantly different among those who had surgery (14.9%) compared with those who received medical therapy alone (18.7%).[6]

Perioperative stroke morbidity and mortality. At 30 days, 5.8% of patients with severe carotid stenosis who underwent endarterectomy had either had a stroke or died, compared with 3.3% of patients receiving medical therapy alone. In the endarterectomy group, the rate of major stroke or death was 2% and the mortality rate was less than 1%.

In patients with moderately severe carotid stenosis, 6.7% of those who underwent endarterectomy had either had a stroke or died by 30 days, compared with 2.4% of those receiving medical therapy. In the endarterectomy group, the major stroke rate was 1.6% and the mortality rate was 1.2%. The net increase in 30-day risk with carotid endarterectomy for patients with moderate symptomatic stenosis was 4.3% for any stroke or death and 2% for disabling stroke or death.

Characteristics that doubled the risk of perioperative stroke or death included:

TABLE 4

Risk factors for stroke with best medical therapy alone: NASCET*

Patients with severe (70% to 99%) stenosis
- Age > 70 years
- Male gender
- Hypertension
  - Systolic pressure > 160 mm Hg
  - Diastolic pressure > 90 mm Hg
- Neurologic symptoms within past 31 days
- History of stroke
- Carotid stenosis greater than 80%
- Plaque ulceration
- History of one or more of the following:
  - Smoking
  - Hypertension
  - Myocardial infarction
  - Congestive heart failure
  - Diabetes mellitus
  - Claudication
  - Hyperlipidemia

Patients with moderate (50% to 69%) stenosis
- Male gender
- Recent stroke (rather than transient ischemic attack)
- Hemispheric symptoms (rather than retinal symptoms)
- Failure of aspirin therapy (650 mg or more per day)

*North American Carotid Endarterectomy Trial

- Contralateral carotid occlusion
- Evidence of ipsilateral cerebral infarct on computed tomographic scan or magnetic resonance imaging
- Left-sided carotid disease
- Diabetes
- Diastolic blood pressure above 90 mm Hg
- Absence of a history of myocardial infarction or angina
- Taking less than 650 mg of aspirin per day.

Neither age nor gender was associated with a doubling of this risk.

In patients with symptomatic carotid stenosis greater than 50%, the risk of ipsilateral stroke was highest immediately after the initial ischemic event and declined gradually to 3% per year within 2 to 3 years with medical therapy alone. In contrast, risk dropped rapidly to 2% per year within 10 days of carotid endarterectomy. If patients with symptomatic carotid stenosis escaped recurrent symptoms for 2 or 3 years after the index ischemic event, they had little to gain from having subsequent surgery.

Carotid stenosis is a powerful predictor of cardiovascular events

European Carotid Surgery Trial (ECST)

The ECST[7–9] began in 1981 and allowed individual physicians to enroll patients with a TIA or nondisabling stroke within 3 months if there was "substantial uncertainty" about which treatment they should receive. This unique and inexpensive enrollment method allowed for a heterogeneous group based on individual physician preference. In all, 2,518 patients were enrolled.

How stenosis was measured. Like NASCET, ECST determined the degree of carotid stenosis by angiography, but the method of measurement differed in that the residual lumen diameter at the narrowest point was compared to an estimated diameter of the carotid bulb prior to disease. This method overestimates the stenosis compared to the NASCET method, an important point to remember when comparing the results of the clinical trials (**TABLE 2, FIGURE 1**). The investigators stratified patients by severity of carotid stenosis: less than 30%, 30% to 69%, and 70% to 99%.

Benefit in severe stenosis. Carotid endarterectomy was beneficial only for patients with severe (70% to 99%) symptomatic carotid stenosis[7]: at 3 years, the rate of any ipsilateral stroke or death was 16.8% in the medical group vs 10.3% in the surgical group, a 39% reduction. The rate of disabling or fatal ipsilateral stroke was 11% in the medical group vs 6% in the surgical group, a 45% reduction. The perioperative rate of stroke or death was 7.5%, which included a rate of major stroke or death of 3.7%.

No benefit in mild or moderate stenosis. For patients with mild (< 30%) symptomatic carotid stenosis, the rate of any ipsilateral stroke at 3 years was so small that any surgical risk outweighed any potential benefit. The rate of any ipsilateral stroke or death at 4 years was not significantly different in patients with moderate (30% to 69%) symptomatic carotid stenosis who underwent carotid endarterectomy (16.6%) vs medical therapy alone (12.7%).[8]

The investigators concluded that carotid endarterectomy was indicated for patients with greater than 80% carotid stenosis, which translates to 60% stenosis by the NASCET method.[9]

Veterans Administration Symptomatic Trial

The Veterans Administration Symptomatic Carotid Stenosis Trial (VA 309)[4] began in 1988 and entered only 197 patients (3.8% of 5,000 screened) before the publication of NASCET and ECST prompted its termination. There was no significant difference in the rates of stroke and death between medical and surgical treatment in men with greater than 50% carotid stenosis who had symptoms of cerebral or retinal ischemia within 3 months. Statistical significance was achieved only by adding crescendo TIA into the end point, and all of the benefit occurred in patients with at least 70% stenosis.

ASYMPTOMATIC CAROTID STENOSIS: FOUR TRIALS

The value of carotid endarterectomy for people with asymptomatic carotid stenosis is far less clear than for people with symptomatic narrowing. Three randomized trials[10–12] of endarterectomy for asymptomatic carotid stenosis produced negative or inconclusive results, and one had positive results.[13]

Carotid Artery Stenosis with Asymptomatic Narrowing: Operation vs Aspirin study

The Carotid Artery Stenosis with Asymptomatic Narrowing: Operation vs Aspirin (CASANOVA) study[10] randomized 410 patients with 50% to 90% asymptomatic internal carotid artery stenosis. Patients with greater than 90% stenosis, a recent myocardial infarction, or other severe medical diseases were excluded. The rates of stroke or surgical death were virtually identical in the medical and surgical groups, but 17% to 20% of the patients never received the intended treatment, and almost as many underwent bilateral endarterectomy.

Veterans Administration Asymptomatic Carotid Stenosis trial

The Veterans Administration Asymptomatic Carotid Stenosis trial (VA 167)[11] randomized 444 patients with greater than 50% asymptomatic carotid stenosis, and recommended a dose of 1,300 mg aspirin daily as part of "best medical therapy." Carotid endarterectomy did not reduce the rates of stroke or stroke and death, and statistical significance was achieved only by adding transient neurological events to the end point. The mortality rate at 4 years was 33%—considerably higher than in other trials, with coronary artery disease the prime determinant of operative mortality.

Mayo Asymptomatic Carotid Endarterectomy study

The Mayo Asymptomatic Carotid Endarterectomy (MACE) study[12] was designed to compare medical therapy (aspirin 80 mg daily) vs carotid endarterectomy without aspirin for asymptomatic high-grade carotid stenosis. The trial was terminated early with 71 patients entered, after 22% of the surgical patients had myocardial infarctions. Although no patient suffered a major stroke or died, the excess of myocardial infarctions and TIAs in the surgical group was attributed to the withholding of aspirin.

The Asymptomatic Carotid Atherosclerosis Study

The Asymptomatic Carotid Atherosclerosis Study (ACAS)[13] randomized 1,662 patients with 60% or greater internal carotid artery stenosis to best medical therapy (including aspirin 325 mg daily) with or without carotid endarterectomy. Although cerebral angiography was not required, ultrasound laboratories were required to undergo rigorous standardization and certification procedures to establish their own "cutpoint" predictive of 60% or greater stenosis. For the 63% of patients who went on to angiography, fewer than 5% had less than the required 60% stenosis, and 58% had 70% or greater stenosis.

In patients with asymptomatic carotid stenosis of 60% or greater, carotid endarterectomy significantly reduced the 5-year rate of any ipsilateral stroke, any perioperative stroke, or death from 11% to 5.1% (a 5.9% absolute and 53% relative risk reduction). However, surgery did not reduce the overall rate of major or disabling events, and benefit was only apparent for men. Any surgical benefit for women was negated by an excess of angiographic and perioperative complications.

Importance of medical management highlighted

As nearly half of the cerebrovascular events in asymptomatic patients are due to lacunar or cardioembolic stroke, the role of medical management becomes as important as contemplating a surgical referral.[18] The Asymptomatic Carotid Surgery Trial (ACST)[19] of 3,200 patients should provide further guidance in the use of medical therapy vs surgery in asymptomatic patients.

"Best medical therapy" in the clinical trials was often poorly described but generally included aspirin. Patients also underwent evaluation and treatment for hypertension, hyperlipidemia, diabetes mellitus, and cigarette smoking, as indicated by the individual physician's discretion. Future trials will also have to consider statin therapy, which was recently demonstrated to induce regression of carotid plaque by 10 to 60 μm/year.[20]

'Best medical therapy' was not well defined but generally included aspirin

CAROTID ANGIOPLASTY AND STENTING

Over the last decade, endovascular techniques of angioplasty and stenting have evolved into

a viable option for patients with surgically inaccessible stenoses and with stenoses due to radiation damage or prior endarterectomy. Aggregate data from single-center studies report technical success in more than 90% of patients; complications include a 3% risk of major stroke, a 1% risk of death, and an 8% risk of any stroke or death.[21]

Primary angioplasty of extracranial and intracranial carotid stenoses is complicated by a 5% risk of dissection, an 8% risk of embolism, and a 15% rate of restenosis. With the addition of stents, the rates of dissection and restenosis have been reduced to less than 5%.[22]

Since endovascular techniques can be performed without anesthesia, they would be an ideal nonsurgical option for patients at increased anesthetic risk due to significant cardiac or pulmonary disease. However, endovascular manipulation of the carotid bulb can produce bradycardia, hypotension, or asystole, and acute myocardial events and hemorrhage requiring transfusion have been reported. Long-term durability is, as yet, uncertain and emergency or delayed surgical repair may be more difficult or not feasible because of the presence of a stent.

Surgeon expertise and hospital volume affect complicaton rates

In the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS),[23] 560 patients were randomized between 1992 and 1997 to undergo angioplasty (26% with stenting), surgery, or medical therapy if not appropriate for surgery. Most patients had a greater than 80% stenosis, and fewer than 5% were asymptomatic. The rate of stroke and death was identical for the 253 patients who underwent carotid endarterectomy and for the 251 patients who underwent angioplasty: 10% in both groups. At 1 year of follow-up, restenosis of greater than 70% was rare in endarterectomy patients but was present in 21% of angioplasty patients, likely related to the low rate of stent-supported angioplasty. At 3 years of follow-up, there was no significant difference in the rates of ipsilateral stroke, disabling stroke, or death.

Results operator-dependent

Although techniques and devices for endovascular approaches are improving, results remain operator-dependent. We must be wary of being seduced by the "oculostenotic reflex," that enthusiastic response by clinicians to the appearance of a large, smooth arterial lumen after endovascular treatment.[24] Outcomes data from anticipated clinical trials such as the Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) and the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) will clarify the respective roles of endovascular approaches in contemporary surgical or medical management of carotid artery stenosis.[25]

RECOMMENDATIONS

Patients with symptoms

Two large, well-executed clinical trials indicate which patients with recent carotid-territory TIA or nondisabling ischemic events should undergo carotid endarterectomy.[5–9] Specifically:

- **Patients with 70% to 99% stenosis** (as measured by the NASCET method) should be recommended to undergo surgery
- **Patients with 50% to 69% stenosis** may benefit from surgery, although the benefit is less (Factors that predict a greater chance of long-term benefit include male gender, recent stroke rather than TIA, recent hemispheric symptoms rather than retinal symptoms, and failure of aspirin therapy at 650 mg or more daily.)
- **Patients with less than 50% stenosis by the NASCET method or less than 80% by the ECST method** should be managed medically.

Patients without symptoms

For patients with asymptomatic carotid stenosis of 60% or greater (by the NASCET criteria), carotid endarterectomy offers modest benefit, based on the results of a single, well-executed clinical trial.[13] My recommendations:

- Prophylactic endarterectomy can be offered for men who have 60% to 99% asymptomatic stenosis, a high functional status, a good 5-year life expectancy, and a low surgical risk.
- Women with asymptomatic carotid steno-

sis of 60% to 99% may also benefit from endarterectomy, but the risks of surgery and angiography need to be tightly controlled.

- Elderly or high-risk surgical patients and patients with less stenosis should be managed medically and carefully educated regarding the symptoms of cerebral ischemia.
- The clinical trial results do not justify population screening of people without symptoms.
- The benefits of carotid endarterectomy are seen only when the procedure can be performed with stroke morbidity and mortality complication rates no higher than 5%.

Patients with coronary artery disease

For all patients, carotid stenosis is a powerful predictor of coronary artery disease, and cardiovascular mortality accounts for a substantial proportion of adverse outcomes. However, the clinical trials excluded patients with coronary artery disease warranting revascularization; therefore, definitive trials are needed to address the special circumstances of high-risk patients with concomitant disease.

Carotid stent-supported angioplasty

The rapidly evolving endovascular techniques of carotid angioplasty and stenting will likely change our approach for some patients with carotid occlusive disease, and clinical trials are needed to compare outcomes with current standard medical and surgical approaches.

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