

Reporting Standards for Carotid Artery Angioplasty and Stent Placement

Randall T. Higashida, MD, Philip M. Meyers, MD, Constantine C. Phatouros, MD, John J. Connors III, MD, John D. Barr, MD, David Sacks, MD, for the Technology Assessment Committees of the American Society of Interventional and Therapeutic Neuroradiology and the Society of Interventional Radiology

J Vasc Interv Radiol 2004; 15:E1-E24

CEREBROVASCULAR disease is the third leading cause of death in the United States (1,2). Approximately 750 000 people have a stroke annually, costing an estimated \$45 billion in treatment and lost productivity (3,4). Carotid occlusive disease is responsible for 25% of these strokes (5). Large population-based studies indicate that the prevalence of carotid stenosis is approximately 0.5% after age 60 and increases to 10% in persons older than age 80 years. The majority of cases are asymptomatic (6–8). Surgical carotid endarterectomy is currently the accepted standard of treatment for revascularization of extracranial carotid occlusive disease (9). This has been validated by multiple, randomized, controlled trials that have demonstrated its efficacy over best medical therapy. However, in the past several years, carotid artery stenting has emerged as a potential therapeutic alternative to carotid endarterectomy

for the treatment of atherosclerotic carotid artery disease. The future status of this endovascular approach will be determined by randomized trials directly comparing carotid artery stenting to endarterectomy, as well as by the potential for further innovation and improvement in endovascular devices, techniques, and safety. Comparisons of carotid stenting and endarterectomy are difficult because of differences in patient selection, the use of case series rather than randomized controlled trials for stenting, differences in definitions of outcomes and complications, and observer bias. The suggested reporting standards for carotid endarterectomy have not been uniformly followed up for surgical trials and not used in trials of carotid stenting (10). It is the purpose of this document to standardize reporting of carotid stent trials and recommend trial designs so that carotid stenting and endarterectomy may be fairly compared. This document is a consensus statement of the Technology Assessment Committees of the American Society of Interventional and Therapeutic Neuroradiology and the Society of Interventional Radiology.

CAROTID ENDARTERECTOMY

In 1953, DeBakey performed the first successful carotid endarterectomy for the treatment of an occluded cervical carotid artery (11). In 1954, Eastcott performed the first successful carotid endarterectomy in which the circulation to the brain was intentionally interrupted to remove a stenotic plaque (12,13). Despite only anecdotal evi-

dence of efficacy, ≈1 million carotid endarterectomies were performed worldwide between 1974 and 1985 (14,15). There was a temporary decline in the mid 1980s, when a number of critical reports suggested unacceptable rates of perioperative stroke or death (16–21), and a high rate of endarterectomy performed for inappropriate indications (22). Rates of carotid endarterectomy in the United States and Canada have again increased since the publication of favorable, well constructed clinical studies, beginning in 1991 with the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (23,24). In 1996, ≈130 000 carotid endarterectomies were performed in the United States; twice that of 1991; in 2000, it was estimated that 174 000 carotid surgeries were performed (25). Because endarterectomy is considered the gold standard of carotid revascularization, the major trials that document its safety and efficacy are summarized by the following text.

Randomized Trials of Symptomatic Patients

North American Symptomatic Carotid Endarterectomy Trial.—The North American Symptomatic Carotid Endarterectomy Trial (NASCET) was conducted at 106 centers in the US and Canada and analyzed 2885 patients with symptomatic carotid stenosis that were stratified into 2 groups: 30% to 69% stenosis (2226 patients) (25) and 70% to 99% stenosis (659 patients) (23). The degree of

Received December 12, 2003; accepted January 14, 2004.

From University of California (R.T.H.), San Francisco; Columbia University (P.M.M.), New York, NY; Royal Perth Hospital (C.C.P.), Australia; Miami Cardiac and Vascular Institute (J.J.C.), Fla; Mid-South Imaging and Therapeutics (J.D.B.), Memphis, Tenn; The Reading Hospital and Medical Center (D.S.), West Reading, Pa. **Address correspondence** to Philip M. Meyers, 710 W 168th St, Neurological Institute, New York, NY 10032. E-mail pmm2002@columbia.edu

This article is being copublished in the May 2004 issues of *Stroke* (*Stroke* 2004;35:e112-e133.) and the *Journal of Vascular and Interventional Radiology*.

© 2004 American Heart Association, Inc. With permission from the American Heart Association, Inc.

DOI: 10.1097/01.RVI.0000128205.10925.8E

carotid stenosis was determined by the ratio between the luminal diameter at the point of greatest stenosis and the normal artery beyond the carotid bulb. The eligibility requirements for the NASCET were strictly defined. Patients with symptoms within 120 days of randomization were considered symptomatic. Patient exclusion criteria included a previous ipsilateral endarterectomy; an intracranial lesion that was more severe than the surgically accessible lesion; no angiographic visualization of both carotid arteries and their intracranial branches; or lung, liver, or renal failure. Temporary exclusion criteria included uncontrolled diabetes mellitus, hypertension or unstable angina pectoris; myocardial infarction within the previous 6 months; contralateral carotid endarterectomy within the previous 4 months; signs of progressive neurological dysfunction; or a major surgical procedure within the previous 30 days. These patients could be included if the disorder responsible for their ineligibility resolved within 120 days of their qualifying cerebrovascular event. Neurological classification was performed 30 and 90 days after the procedure with strokes (any new focal neurological deficit lasting >24 hours) categorized as disabling (modified Rankin score ≥ 3) or non-disabling. If sufficient functional recovery occurred within 90 days, then the stroke could be reclassified from disabling to nondisabling (26).

The authors reported a 5.8% incidence of perioperative stroke and death (0.6%) in the endarterectomy group. The inclusion of perioperative myocardial infarction (0.9%) increased the complication rate to 6.7% (23). There was an unequivocal benefit of surgery over best medical management in symptomatic patients with a severe carotid stenosis of $\geq 70\%$. Surgical intervention reduced the 2-year risk of any ipsilateral stroke in the medical group from 26% (annual event rate of 13%) to 9% in the surgical group, thus yielding an absolute risk reduction of 17%. Therefore, for every 100 patients undergoing surgery, 17 nonfatal strokes or deaths were prevented over a 2-year period. However, this risk reduction was not equal for all patients. The benefit was twice as great

in patients with a stenosis of 90% to 99% as it was in those with a stenosis of 70% to 79%. At 8-year follow-up, the risk of an ipsilateral disabling stroke was 6.7%; of any ipsilateral stroke was 15.2%; of any stroke was 29.4%; and of any stroke or death was 46.6%. Therefore, despite the durability of endarterectomy in preventing an ipsilateral disabling stroke, the risk of any stroke or death over the ensuing 8 years was nearly 50% (25).

The benefits of carotid endarterectomy in patients with symptomatic moderate stenoses of 30% to 69%, over a mean follow-up of 5 years, have also been reported. For patients with a stenosis of 50% to 69%, the 5-year rate of any ipsilateral stroke was 15.7% in the surgical group versus 22.2% in the medical group; an absolute risk reduction from any ipsilateral nonfatal or fatal stroke of 6.5% (1.3% per annum). However, among patients with 30% to 49% stenosis, the 5-year rate of any ipsilateral stroke was 14.9% for surgical patients versus 18.7% for medically treated patients, an insignificant risk reduction. The perioperative rate of disabling stroke and death was 2% (25).

The surgical and medical complication rates for all patients ($n=1415$) undergoing carotid endarterectomy as part of the NASCET (30% to 99% symptomatic stenosis) have been reported (27,28). The overall rate of perioperative stroke and death (1.1%) was 6.5%. Five baseline variables were predictive of statistically significant increased surgical risk: hemispheric versus retinal transient ischemic attack as the qualifying event, left-sided procedure, contralateral carotid occlusion, ipsilateral ischemic lesion on CT scan, and irregular or ulcerated ipsilateral plaque. The incidence of perioperative wound complications was 9.3% and cranial nerve damage was 8.6% (27). Cardiovascular complications occurred in 8.1% of patients undergoing endarterectomy. Cardiovascular complications included myocardial infarction (1.2%), congestive heart failure (1.2%), and hypotension (2.1%). Patients with a history of myocardial infarction, angina pectoris, or hypertension were at significantly higher risk. Medical complications resulted in a pro-

longed hospitalization in $\approx 30\%$ of cases (28).

European Carotid Surgery Trial.—The results of The European Carotid Surgery Trial (ECST), another large, multicenter, randomized controlled trial, were in accordance with the NASCET after adjustment for the different methods used to calculate the angiographic degree of carotid stenosis (29–31). The ECST method of calculating angiographic stenosis used an approximation of the normal carotid bulb diameter as the denominator rather than the distal cervical internal carotid artery, which was used in the NASCET, and resulted in overestimation of narrowing compared with the NASCET.

The ECST enrolled 3024 patients with symptomatic carotid stenosis stratified into 3 groups: 0% to 29%, 30% to 69%, and 70% to 99% stenosis, with a mean follow-up of 6.1 years. The ECST demonstrated that endarterectomy reduced the Kaplan-Meier 3-year risk of major stroke or death in patients with a symptomatic stenosis of $\geq 80\%$ ($\geq 60\%$ as measured by the NASCET method) from 26.5% in the control group, with an annual event rate of 8.8%, to 14.9% in the surgical group, thus giving an absolute risk reduction of 11.6% at 3 years. The rate of nonfatal stroke, defined as symptoms lasting >7 days or death (1.3%) from surgery was 7%. The ECST did not specify rates of nonstroke surgical complications such as cranial nerve injury or cardiac events (31,32).

Veterans Affairs Cooperative Carotid Trial.—The Veterans Affairs Cooperative Symptomatic Carotid Stenosis Trial (VA-CSP-309) was a third randomized trial evaluating endarterectomy in symptomatic carotid stenosis, but it was prematurely terminated when the NASCET and ECST data were released (33). The VA-CSP-309 study enrolled 189 male patients, with a mean follow-up of 11.9 months, and demonstrated an absolute risk reduction for stroke or crescendo transient ischemic attacks of 11.7% in men with a carotid stenosis >50% who underwent endarterectomy (17.7% for stenosis >70%). They reported a perioperative surgical stroke and death rate of 5.5%. Among the 3 perioperative deaths, none was caused by ischemic stroke.

Randomized Trials of Asymptomatic Patients

Asymptomatic Carotid Atherosclerosis Study.—The only large, well-constructed, randomized, controlled trial published to date comparing surgical endarterectomy with medical therapy in asymptomatic carotid stenosis is the Asymptomatic Carotid Atherosclerosis Study (ACAS), which enrolled 1662 patients at 39 centers with a median follow-up of 2.7 years (34). As in the NASCET, the inclusion criteria for the ACAS were stringent. Patients were excluded from the ACAS because of previous cerebral infarction; previous endarterectomy with restenosis; previous extracranial-to-intracranial bypass; any disorder that could seriously complicate surgery or prevent continuing participation over 5 years; long-term anticoagulation therapy; or a surgically inaccessible lesion.

Patients in the medical control group received 325 mg aspirin per day. Some authors have suggested this does not represent optimum medical therapy (the recommended dose in the NASCET was 1300 mg per day), because high-dose aspirin, ticlopidine, and aspirin combined with warfarin may be more effective (35). The ACAS reported an actuarial estimated 5-year risk, with a mean follow-up of only 2.7 years, for ipsilateral stroke and any perioperative stroke or death in patients with a carotid stenosis of $\geq 60\%$, of 5.1% for surgical patients versus 11%, with an annual event rate of 2.2% for medically treated patients, and yielded an absolute risk reduction of 5.9%. Therefore, over a 5-year period, ≈ 1 stroke per year was prevented for every 85 patients undergoing endarterectomy. However, the absolute risk reduction for disabling ipsilateral stroke was only 2.6%, which doubles the number of endarterectomies needed to prevent 1 ipsilateral disabling stroke compared with any ipsilateral stroke. This result was obtained with a very low 30-day perioperative stroke and death (0.1%) rate of 2.3%; 52% of these complications attributable to strokes were caused by diagnostic cerebral angiography (arteriography stroke rate of 1.2%). Stratification of data revealed no significant reduction in risk of

stroke or death for females undergoing endarterectomy. Furthermore, no correlation between benefit and degree of stenosis was demonstrated.

Veterans Affairs Cooperative Study.—The Veterans Affairs Cooperative Study (VA-CSP-167), a smaller multicenter trial that enrolled 444 males with asymptomatic carotid stenosis $\geq 50\%$, failed to demonstrate a statistically significant difference in the combined rate of stroke or death between the endarterectomy and medical groups at a mean follow-up of 47.9 months. The authors concluded that a modest effect could not be excluded because of the relatively small sample size. The 30-day perioperative rate of permanent stroke or death was 4.7%, which included a 0.4% stroke rate from diagnostic cerebral angiography (36). As in NASCET and ACAS patients undergoing endarterectomy for symptomatic carotid stenosis of $\geq 70\%$, cardiac-related deaths were the most frequent cause of mortality in the endarterectomy patients (23,34).

European Carotid Surgery Trial.—The European Carotid Surgery Trial (ECST) also reported on the risk of stroke in the distribution of the asymptomatic carotid artery in 2295 patients stratified into 4 categories of carotid stenosis: 0% to 29% ($n=1270$); 30% to 69% ($n=843$); 70% to 99% ($n=127$); and occluded ($n=55$). During a mean follow-up of 4.5 years, the 3-year Kaplan-Meier risks for ipsilateral stroke and fatal stroke were 2.1% and 0.3%, respectively. The 3-year risk of ipsilateral stroke for patients with an asymptomatic, severe (70% to 99%) carotid stenosis was 5.7%. This was significantly less than the 17.1%, 3-year ipsilateral stroke risk for ECST patients with a symptomatic, severe, carotid stenosis treated medically, and not significantly greater than the 3.1%, 3-year ipsilateral stroke risk for a severe, symptomatic, carotid stenosis after successful endarterectomy.

Given the modest benefit results of the asymptomatic endarterectomy trials and the low annual event rates associated with asymptomatic carotid stenosis, the cost-effectiveness of performing surgical endarterectomy for asymptomatic carotid stenosis has been questioned (37). The results of a second, large, multicenter, random-

ized trial examining endarterectomy in asymptomatic carotid stenosis, The Asymptomatic Carotid Surgery Trial (ACST), currently in progress, are awaited (38).

Mayo Asymptomatic Carotid Endarterectomy Study.—The Mayo Clinic undertook a randomized controlled trial to compare the effects of carotid endarterectomy with medical treatment. Over 30 months of recruitment, 71 patients were randomized and 87 patients who were eligible but unrandomized were included in the follow-up protocol. The total ipsilateral perioperative stroke and death rate was 0% in the randomized group and 3% in the nonrandomized group. The major stroke and death rate was 0% for both groups. Too few cerebral ischemic events occurred to compare the efficacy of endarterectomy with low-dose aspirin for asymptomatic carotid stenosis. However, the trial was prematurely terminated because there was a significantly high number of myocardial infarctions and transient ischemic events in the surgical group compared with the medical group (39).

Nonrandomized Studies

Innumerable case series of carotid endarterectomy have been published. A systematic review of the risk of stroke and death caused by endarterectomy for symptomatic carotid stenosis was performed by Rothwell et al (40). The authors analyzed 51 studies since 1980, including the NASCET, and reported an overall perioperative risk of stroke and/or death of 5.64%. The overall death rate was 1.62%, with the risk of a fatal stroke (0.86%) slightly exceeding the risk of a non-stroke death (0.7%). The authors noted there was significant heterogeneity in the reported stroke and mortality rates between studies. Surgical series in which neurological outcome assessment was independently adjudicated by neurologists reported significantly higher risks of stroke and death (41).

Rothwell et al performed a similar systematic review comparing the risk of stroke and death caused by carotid endarterectomy, performed by the same surgeons in the same institutions, for symptomatic versus asymptomatic stenosis (42). The authors analyzed 25 studies since 1980 and

reported an overall perioperative risk of stroke and/or death for asymptomatic lesions of 3.35%. This risk estimate was significantly lower than for symptomatic lesions (5.18%) and consistent across virtually all studies.

Results from randomized trials may not be generalizable to the results of treatment in clinical practice. Wennberg et al assessed the perioperative mortality among 113 300 Medicare patients undergoing carotid endarterectomy during 1992 to 1993 in "trial hospitals" (those participating in NASCET and ACAS, n=86), and "nontrial hospitals" (nonfederal institutions performing endarterectomy n=2613), looking at all patients treated rather than those selected for a trial (43). The perioperative mortality rate was 1.4% at trial hospitals compared with 2.5% at low-volume (≤ 6 procedures/year) nontrial hospitals.

High-Risk Patients.—NASCET, ACAS, and the VA Cooperative studies excluded patients with significant comorbid illnesses such as lung, liver, or renal failure, unstable angina, and recent myocardial infarction. Therefore, the complication rates reported in these studies may be lower than the rates achievable when all patients are included. Wennberg et al (43), as noted, found that the perioperative mortality rate at NASCET trial hospitals was 1.4% when all patients were included, compared with 0.6% in NASCET patients. Similar findings were reported by Lepore et al (44), who found that NASCET/ACAS trial-eligible patients had a perioperative stroke and death rate of 1.5% compared with 3.6% for trial-ineligible patients (45). However, according to Dorros, these "high-risk" patients were excluded from the NASCET, not because the surgical outcomes may have been adversely influenced but primarily because attendant comorbidities could have potentially contaminated the outcome data (46). The ASA and carotid endarterectomy (ACE) trial was a randomized trial of high- versus low-dose aspirin at the time of endarterectomy (47). Patients were not excluded based on comorbidities; therefore, the data are likely to reflect the patient selection found in standard medical practice rather than selecting only the patients at lowest risk. Both symptomatic (n=1292) and

Table 1
Sundt's Classification System Based on Retrospective Analysis of 3111 Consecutive Carotid Endarterectomy Patients

Sundt's Class (49)	Criteria for Classification	Combined Surgical Morbidity (Mortality), %
I	Neurologically stable, no major medical/angiographically defined risk, with unilateral/bilateral ulcerative-stenotic disease	0.9
II	Neurologically stable, no major medical risks, with or without angiographic risks	1.7
III	Neurologically stable, major medical risks, with or without angiographic risks	3.7 (1.3)
IV	Neurologically unstable, with or without medical/angiographic risks	8.1 (2.9)
V	Acute internal carotid artery occlusion, progressive neurological deficit within 6 h of examination	Not included in study
VI	Recurrent symptomatic carotid stenosis	Not included in study

asymptomatic (n=1512) patients were treated. Most patients had a carotid stenosis $>70\%$ diameter. Among symptomatic patients, there was a 6.4% rate of perioperative stroke (minor or major) or death but only 2.8% rate of perioperative major stroke or death (48). Among asymptomatic patients, the rate of any perioperative stroke or death was 4.6%.

A retrospective analysis by Sundt, in which 3111 consecutive endarterectomy patients were stratified into 6 risk classes according to neurological status, comorbid conditions, and angiographic variables, revealed a very low major complication rate (permanent stroke, myocardial infarction, or death) for class I and II patients, whereas class IV patients had an 8.1% risk and 2.9% mortality (Tables 1, 2) (49,50). Factors correlating with an increased surgical morbidity and mortality included unstable neurological status; the presence of comorbid conditions; age older than 70; and contralateral internal carotid artery occlusion.

Estes et al followed a random sample of 22 165 Medicare beneficiaries, who underwent carotid endarterectomy between 1988 to 1990, until the year 1992. They identified patients with acute myocardial infarction, congestive heart failure, diabetes mellitus, and age older than 80 years as having diminished perioperative and long-term survival rates after carotid endarterectomy. Recurrent

carotid stenosis has also been felt to indicate a higher risk of complication from endarterectomy. Meyer et al reported a perioperative morbidity and mortality rate of 10.8% in their series of 82 patients undergoing carotid endarterectomy for recurrent stenosis; that was 5 times the risk of a routine endarterectomy at their institution (51). Cranial and cervical nerve injuries may occur in 21% of patients, although there are few permanent injuries (52).

Radiation-induced carotid stenosis is more difficult to treat surgically because of long lesion length, periarterial scarring with ill-defined planes of resection, and a higher rate of wound complications (53–55).

These categories of high risk for carotid endarterectomy are not uniformly accepted. In a recent study, age older than 80 was found not to be a significant risk (56). Hill et al and O'Hara et al found no increased morbidity or mortality for re-operation for carotid stenosis compared with primary carotid endarterectomy (57,58). Combined carotid endarterectomy and coronary artery bypass grafting has a high risk of stroke, but this risk may come almost completely from the coronary artery surgery rather than from the carotid procedure (59). Gasparis et al stratified endarterectomy patients into low- versus high-risk based on age older than 80 years, New York Heart Association class III/IV angina, Ca-

Table 2
Sundt's Definition of Medical, Neurological, and Angiographic Risk for Carotid Artery Surgery

Risk	Definition (49)
Medical	Coronary artery disease (angina, myocardial infarction <6 mo, congestive heart failure), hypertension (>180/110 mm Hg), severe peripheral vascular disease, chronic obstructive pulmonary disease, age older than 70 years, severely obese
Neurological	Neurological deficit within 24 h, general cerebral ischemia, recent cerebrovascular accident (<7 d), frequent transient ischemic attacks
Angiographic	Contralateral internal carotid artery occlusion, siphon stenosis, plaque >3 cm distally in internal carotid artery or >5 cm proximal in common carotid artery, bifurcation at C2 vertebra, short thick neck, and soft thrombus extending from an ulcerative lesion

nadian class III/IV heart failure, myocardial infarct within 6 months, steroid- or oxygen-dependent pulmonary disease, creatinine level of ≥ 3 , contralateral carotid occlusion, high carotid bifurcation, re-operation, or neck irradiation (60). The risk of perioperative stroke or death was 1.3% in the high-risk group and 1.1% in the low-risk group (not significant).

Carotid Endarterectomy.—In summary, these trials have demonstrated that surgical carotid endarterectomy confers a significant benefit over best current medical management in patients with symptomatic carotid stenosis $\geq 70\%$ with lesser, albeit significant, degrees of benefit in symptomatic lesions of 50% to 69% and asymptomatic lesions of $\geq 60\%$. However, important caveats apply. Patient selection criteria should be strictly adhered to (61). A recent, prospective, city-wide audit of 184 consecutive patients undergoing carotid endarterectomy reported that only 49% of these procedures were for appropriate indications (62). The surgeon should have a perioperative complication rate low enough to ensure the full (or any) benefit from the procedure. Some authors have even suggested that surgical teams provide data on their rates of stroke or death within 30 days of surgery, adjusted for the severity of carotid disease and coexisting conditions, to referring physicians and patients (63). Finally, there is ongoing debate as to the cost-effectiveness of surgery for asymptomatic carotid stenosis which,

according to some authors, is not proven (37).

ENDOVASCULAR TREATMENT OF CAROTID OCCLUSIVE DISEASE

Endovascular treatment (angioplasty and stenting) of carotid occlusive disease may offer the following advantages over endarterectomy: general anesthesia is usually not required, thus allowing the patient's clinical status during the procedure to be monitored; increased patient comfort and significant cost savings because of shorter recuperation period; no cervical incision is made, thus eliminating the risk of cranial nerve palsies, wound infections, or neck hematomas; procedures can be performed simultaneously on carotid, vertebral, and coronary arteries; morbidity and mortality rates may be reduced in patients considered to be at higher risk for surgery (who have significant comorbidities, contralateral carotid occlusion, postendarterectomy restenosis, radiation-induced stenosis, previous radical neck dissection); and it provides an option for treatment of carotid stenosis in patients who are not suitable candidates for CEA (ie, patients with surgically inaccessible lesions).

Carotid Balloon Angioplasty

Percutaneous transluminal balloon angioplasty for carotid artery stenosis was first reported by Kerber et al in 1980 (64). In 1987, Theron et al published the first large series of internal

carotid angioplasty in 48 patients with de novo atherosclerosis or postsurgical restenosis. Technical success was achieved in 94% of cases, with a 4.1% rate of serious morbidity (65). In Kachel's review of the literature through 1995, 523 carotid angioplasty procedures had subsequently been reported (66). The overall technical success rate was 96.2%, with a 2.1% rate of morbidity, 6.3% rate of transient minor complications, and no deaths. In one of the largest single-institution series, Gil-Peralta et al (1996) performed 85 balloon angioplasties in 82 patients with symptomatic carotid stenoses of $>70\%$ over a 4-year period (67). They reported a technical success rate of 92% (residual stenosis $<50\%$), with 30-day mortality of 0% and a major morbidity rate of 4.9%, which compares very favorably to the ECST and NASCET results. The rate of recurrent stenosis (all of which were asymptomatic) was 6.7% at a mean follow-up of 18.7 months, with almost all of these occurring between months 3 and 6. Rates of restenosis (<2 years) reported in other large angioplasty series are between 0% and 16% (66,68–71); in carotid endarterectomy series, rate of restenosis was $\approx 10\%$ in the first year (51,72–74).

Despite these favorable results, balloon angioplasty has a number of potential limitations, including vessel wall recoil, angiographically evident intimal dissection, and plaque dislodgement with particulate embolization. Angioplasty of atherosclerotic lesions has been reported to generate emboli composed of atheroma, cholesterol crystals, thrombus, and platelet aggregates (75–78). Embolization of microparticles has also been demonstrated during and after carotid endarterectomy and has been shown to correlate with complex plaque morphology (79) and with clinical postoperative cerebral ischemia (80–83). However, studies examining the frequency of emboli during carotid balloon angioplasty using transcranial Doppler (TCD) have failed to show a clear-cut correlation between embolism frequency and neurological sequelae (76–78). Crawley et al, in an analysis of 14 patients undergoing carotid balloon angioplasty versus 14 endarterectomy patients with shunt placement, reported an average of 202 embolic signals during carotid balloon

angioplasty compared with 52 during carotid endarterectomy. However, during the recovery period of 20 minutes, the average number of embolic signals was 5 for balloon angioplasty versus 19 for endarterectomy. There was no correlation between the number of TCD-detected emboli and the periprocedural stroke rate (77).

The risk of cerebral damage is thought to depend on the size and composition of the embolic material as well as the extent and location of brain involvement. Because it is difficult to accurately distinguish between air and particulate emboli using TCD (84), the lack of correlation between emboli and clinical sequelae has led to the suggestion that the majority of emboli detected during balloon angioplasty are either gaseous or small platelet aggregates <200 μm in diameter, both of which correlate with a more benign outcome (75–77). This underscores the importance of premedication with antiplatelet agents to prevent larger platelet aggregates (85).

Endovascular revascularization of carotid occlusive disease may result in cerebral hypoperfusion from luminal compromise by catheters and guidewires crossing the stenotic lesion and/or during balloon inflation. This is of even greater relevance in the presence of contralateral carotid artery occlusion or stenosis. Eckert et al monitored 22 patients undergoing carotid balloon angioplasty using TCD, noting that a >50% reduction of middle cerebral artery mean blood flow velocity compared with baseline values represented a critical threshold for the development of ischemic symptoms in conscious patients even with short occlusion times of 10 to 40 seconds (86). However, Crawley et al reported hemodynamic ischemia was significantly greater with endarterectomy than balloon angioplasty and was not predictive of adverse neurological outcome (77). It is recommended to keep balloon inflation and occlusion times <30 seconds to avoid potential cerebral ischemia. If there is attendant compromise of the contralateral carotid artery, then establishing the adequacy of the cerebral collateral circulation becomes even more important and the procedure should be performed with as little sedation as possible to facilitate neurological monitoring. Tsurutani et al described the

successful use of a continuous-perfusion dilatation catheter for high-risk patients with poor collateral circulation (87).

Carotid Stenting

The impetus for carotid stenting has arisen principally from trials of stenting with balloon angioplasty versus simple balloon angioplasty in the coronary arteries, which have consistently demonstrated a persistent benefit in event-free survival at 1 year and a lower rate of repeat angioplasty (88–90). The purported advantages of stent placement over simple angioplasty include avoiding plaque dislodgment, intimal dissection, elastic vessel recoil, and late restenosis. Despite the fact that it is unknown whether these benefits apply to the carotid circulation, endovascular carotid revascularization is now most commonly performed with stents.

Since 1996, there have been 11 large carotid stent series published in which the total number of patients is 1311 (71,91–101) (Table 3). Comparative analysis of these reports is made difficult by inconsistencies in the sample populations, lesion characteristics, endovascular techniques, and outcome data. However, the overall reported rate of technical success is >95%; procedure-related mortality rates (including cardiac deaths) are 0.6% to 4.5%; major stroke rates are 0% to 4.5%; minor stroke rates are 0% to 6.5%; and a 6-month restenosis rate is <5%. This excludes the other studies that represented very-high-risk cohorts (98,99,102–105). Similar favorable results were reported by Al-Mubarak et al, who reported on 51 consecutive patients undergoing simultaneous or staged carotid artery stenting and percutaneous coronary intervention. Technical success was achieved in all carotid arteries, with a minor stroke rate of 4% and no major strokes, myocardial infarctions, or deaths (106). In the NASCET, the perioperative stroke and death rate was 5.8%, with 0.6% mortality rate mostly caused by myocardial infarction (23).

Vitek et al presented their experience in treating 404 patients with carotid angioplasty and stenting (107). They report a technical success rate of 98%, 30-day morbidity/mortality rate of 1.9%, major stroke rate of 0.7%, minor stroke rate of 5.8%, and a 5% rate

of restenosis (>50% narrowing). The authors report a lower complication rate in the last 122 patients (with increased procedure-related clinical experience): minor stroke rate of 2.5% with no major strokes or deaths. Wholey et al have published the results of a worldwide stent survey in which 3047 endovascular cervical carotid artery stent procedures are reported from 24 centers in North America, Europe, Asia, and South America (108). They reported a 30-day procedure-related mortality rate of 0.98%, major stroke rate of 1.35%, minor stroke rate of 2.53%, and a restenosis rate at 6 and 12 months of 2.23% and 2.48%, respectively. Centers having worked with <50 cases had a 6.4% rate of major stroke and death compared with 2.3% for centers having worked with between 50 and 100 cases. The authors thus suggest a 50-case learning curve for carotid stenting.

Many of these case series also analyzed outcomes for patients considered at higher risk for surgery (ie, NASCET-ineligible). In the NASCET, the perioperative stroke and death rate was 5.8%, with 0.6% mortality rate mostly caused by myocardial infarction (23). NASCET criteria were applied to the patient cohorts in 5 of these carotid stenting series, demonstrating that 79% of these 574 patients would have failed eligibility because of comorbidities (91,95,96,99). Despite this, morbidity rates of 2.0% to 7.9% and mortality rates of 0.6% to 2.0% for these early carotid stenting reports compare favorably to those in the NASCET and the ECST. However, 41% (n=233) of these patients had asymptomatic carotid stenosis for which lower endarterectomy morbidity and mortality rates would be expected. Similarly, Yadav et al reported on 22 patients with angioplasty and stenting for postendarterectomy carotid stenosis with no major and only 1 minor stroke (4.5%) (109). Lanzino et al also reported favorable results in 18 patients undergoing angioplasty and stenting for recurrent carotid stenosis after endarterectomy, with no periprocedural strokes and 1 transient ischemic attack (110). Mericle et al also reported on 23 patients with high-grade carotid stenosis and a contralateral carotid occlusion undergoing elective carotid stenting (111). The 30-day peri-

Table 3
Carotid Stent Series Data

Reference	Patient Data			Complications					Restenosis Rate (%)		Remarks
	N of Patients	N of Stents	Asymptomatic Stenosis (%)	Technical Success Rates (%)	30-Day Morbidity/ Mortality (%)	No. of Deaths/ Mortality Rate (%)	Major Stroke Rate (%)	Minor Stroke Rate (%)	6-Month (%)	12-Month (%)	
Roubin (101)	528	604	48	98	7.4	8 (1.6)	1.0	4.8	16 (3.0)		
Theron (71)	69	69	NS	100	NS	2 embolic complications (3) no deaths	2	4.5	4 (time not specified)		1 Death, cardiac-related
Diethrich (92)	110	129	72	99.1	7.3	2 (1.8)	2	4.5	NS/ID		
Yadav (95)	107	189	36	100	7.9	1 (0.9)	1.9	6.5	4.9	NS	
Vozzi (94)	22	19	55	96	NS	1 (4.5)	4.5	4.5	NS/ID		
Criado (93)	33	NS	27	100	NS	0	0	0	3 (mean 8-month follow-up)		
Wholey (96)	108	NS	44	95	NS	2 (1.9)	1.8	1.8	1 (mean 6-month follow-up)		1 Death, cardiac-related, day 20
Henry (144)	163	178	35	99.4	NS	0	1.8	1.2	2.3%	ID	Distal cerebral protection used in 32 cases
Teitelbaum (98)	22	31	32	96.2	27.3	1* (4.5)	18.2	13.6	14.3%	NS	High-risk cohort
Waigand (99)	50	56	72	100	2	1 (2)	2	2	8.7% (mean 8-month follow-up)		High-risk cohort
Bergeron (100)	99	99	42	97	7.1	0	0	1	4.2% (mean 13-month follow-up)		

NS indicates not specified; ID, insufficient data.
* Cardiac-related death.

operative stroke and death rate was 0%. This is in contrast to the NASCET, which reported a perioperative stroke/death rate for contralateral occlusions of 14.3% (23).

Mathur et al retrospectively analyzed the risk factors for stroke in 231 patients undergoing elective stenting of the extracranial carotid arteries; 14% of which were NASCET-eligible (112). The overall 30-day stroke rate was 6.9%; however, by stratifying for the NASCET-eligible group, the stroke rate decreased to 2.7%. Advanced age (older than 80 years) and long or multiple stenoses were found to be independent predictors of periprocedural strokes. However, contralateral carotid occlusion, previous carotid endarterectomy, and combined carotid and coronary procedures, all of which are associated with a higher incidence of complications in carotid endarterectomy, were not found to have an increased risk of adverse outcome in stented patients (51,112–115). Increasing age was also identified as a predictor of increased risk for carotid stenting procedures by Chastain et al. The authors stratified 182 patients undergoing elective carotid artery stenting into 3 age groups: older than 80 years, 75 to 79 years, 74 years or younger. The overall rate of major stroke and death (0.5%) was 1.6%, with a 0.5% rate of myocardial infarction. Neurological complications (mostly minor strokes) were significantly more frequent in patients older than age 80 years than for those 74 years or younger (25% versus 8.6%, respectively) (116).

There are few published studies directly comparing carotid endarterectomy with carotid stenting. Jordan et al retrospectively compared 107 endarterectomy patients with 166 prospectively followed-up patients undergoing carotid stenting and reported a higher early minor stroke rate in the stent group (6.6% versus 0.6%) but a higher rate of major stroke/death in the surgical cohort (4.2% versus 2.8%) (117). Jordan also analyzed outcomes from a subset of 109 patients undergoing endarterectomy under regional anesthesia and compared these results to 268 patients undergoing carotid stenting in the same institution. The total early stroke and death rates for stent versus endarterectomy were 9.7% versus 0.9%. Most of these strokes were

minor; the major stroke rates for stent versus endarterectomy were 1.5% versus 0%. There is one report of an early prospective randomized study in 17 patients treated for symptomatic stenoses of >70% (118). The authors reported no complications in 10 patients undergoing endarterectomy; however, 5 of 7 stent patients had strokes, 3 of which were disabling at 30 days. This prompted early stoppage of the trial in favor of endarterectomy. However, this trial had methodological problems that may explain these poor results.

In reviewing the current literature on carotid artery stenting, the technical success rate, procedure-related morbidity and mortality rates, and restenosis rates seem to compare favorably to carotid endarterectomy (119–121). However, inconsistencies in the trial design, reporting criteria, and follow-up render comparison of endarterectomy with endovascular revascularization most challenging (Table 4). The validity of comparisons between such disparate clinical data is unsound. In the case of carotid endarterectomy, there exists class I evidence of efficacy, whereas the bulk of the endovascular data are derived from non-randomized uncontrolled studies, usually from single institutions (122, 123). Class I evidence is that which is proven by a prospective randomized trial with a small chance of false-negative or false-positive values. Therefore, 5 prospective, randomized, multicenter trials comparing carotid endarterectomy to carotid angioplasty or stenting have been undertaken, the results of which are included in Table 4.

The Carotid and Vertebral Transluminal Angioplasty Study (CAVATAS), a large, prospective, randomized, multicenter trial comparing carotid endarterectomy to carotid angioplasty was recently completed. In the CAVATAS, patients with symptomatic stenoses (at least 30% luminal diameter reduction) suitable for surgery were randomized to either angioplasty or surgery (124). Patients unsuitable for endarterectomy were randomized to percutaneous transluminal techniques or medical treatment alone. The CAVATAS randomized 504 patients to surgery and angioplasty over 5 years. There was no significant difference in the risk of stroke or death

related to the procedure between carotid endarterectomy and angioplasty. The rate of any stroke lasting >7 days or death within 30 days of first treatment was $\approx 10\%$ in the surgery or angioplasty groups. The rate of disabling stroke or death within 30 days of first treatment was 6% in both groups. Preliminary analysis of long-term survival showed no difference in the rate of ipsilateral stroke or any disabling stroke in patients up to 3 years after randomization. The rates of stroke or death within 30 days in CAVATAS in both groups are higher than those of many previous reports but not significantly different to the ECST rate of 7%. Cranial nerve injury and myocardial ischemia were only reported at the time of treatment in the surgical group. Long-term follow-up is not yet available (125).

The Wallstent Trial was an industry-supported, prospective, randomized trial comparing endarterectomy and carotid stenting for symptomatic stenosis $\geq 60\%$ (126). The results have been published in abstract (127). In this study, 219 patients with symptomatic carotid stenosis of 60% to 90% diameter were randomized to endarterectomy or stenting. The risk of any perioperative stroke or death was 4.5% for surgery and 12.1% for stenting. At 1 year, the risk of a major stroke was 0.9% for surgery versus 3.7% for stenting. This trial was stopped early because of poor results from stenting.

A single-center community hospital study randomized 104 symptomatic patients to either carotid endarterectomy or stenting without distal protection (128). Perioperative stroke or death rate was 2% for surgery and 0% for stenting. Other complications for the surgery group totaled 16% and included hematoma (requiring treatment), cranial/cervical nerve injury, and hypotension (requiring treatment). Other complications for the stent group totaled 45% and included transient cerebral ischemia, leg amputation, retroperitoneal hemorrhage, bradycardia (requiring temporary pacing), and hypotension (requiring treatment).

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial randomized 307 high-risk patients to endarterectomy or carotid stenting using a

distal protection device. Perioperative (30-day) results have been presented in abstract (129). High risk was defined as congestive heart failure (class III/IV) or ejection fraction <30%, open heart surgery needed within 6 weeks, recent myocardial infarction (24 hours to 4 weeks), or unstable angina (CCS class III/IV). Perioperative stroke and death rates were 7.3% for surgery versus 4.4% for stenting. Rates of myocardial infarction were 7.3% for surgery versus 2.6% for stenting.

The Carotid Revascularization Endarterectomy versus Stent Trial (CREST), a North American, multicenter, randomized, controlled trial comparing the efficacy of surgical endarterectomy with carotid stenting, is currently in progress (130,131). In the CREST, patients with symptomatic extracranial carotid stenosis of $\geq 50\%$ are randomized between stent-supported angioplasty and endarterectomy. To demonstrate a clinically significant difference between the 2 treatments, CREST will require at least 2500 patients, excluding comparison between various clinical subgroups (eg, recurrent stenosis), for which an even greater number will be required.

Adjuncts to Stenting

Potential areas of innovation include methods of providing cerebral protection using intravascular filters or balloons; smaller-diameter, more flexible, and hence less traumatic delivery systems; lowering rates of restenosis secondary to intimal hyperplasia by using local catheter brachytherapy; radiation-emitting stents (132–134); or biologically active coatings (135) and improved adjuvant pharmacological regimes using antiplatelet agents such as the glycoprotein IIb/IIIa inhibitors, which could potentially reduce the incidence of acute thromboembolism and improve long-term patency (136). This genuine potential for future improvement has prompted some authors to suggest a direct comparison with carotid endarterectomy may be premature (46,137–139).

It remains unclear whether carotid artery stent placement helps reduce the number of particulate emboli by trapping them beneath the metallic meshwork. Current stent designs may trap larger fragments but not efficiently prevent microemboli because

Table 4
Carotid Stent Series Data

Study	Stenosis, %	Symptomatic	N Patients (CEA)	High-Risk Excluded	Minor Stroke, %	Perioperative				Annual			
						Major Stroke	MI	Death	Ipsilateral Stroke, %	Ipsilateral Disabling Stroke, %	Any Stroke, %	Death, %	Duration
NASCET (23,25,26)	>70	Yes, <120 days	328	Yes	3.7 ^c	1.5	0.9	0.6	4.5	1.3	6.3	1.6	2
NASCET (23,25,26)	50-70	Yes, <180 days	430	Yes	4.7	0.8	NA	1.2	3.1	0.6	4.8	1.9	5
NASCET (23,25,26)	<50	Yes, <180 days	678	Yes	Combined	Combined	NA	Combined	3	0.9	5.1	2.1	5
ECST (37)	All	Yes, <180 days	1745	No	3.5 ^d	3.2 ^h	NA	1	2.3	1.6	3.2	2.9	3
VA-CSP-309 (36)	>50	Yes, <120 days	91	Yes	2.2 ^e	1.1 ⁱ	NA	3.3	3	NA	NA	NA	3
ACE (47,48)	>70 ^a	Yes, <180 days	1292	No	6.4 ^j	2.1 ^k	NA	0.2 ⁿ	2.2 ^o	1.2 ^l	3.5	3.9	5
ACAS (34)	>60	No	825	Yes	2.8 ^e	2.1 ^k	1.9 ^m	1.9	1.2 ^p	NA	2	8.2	4
VA-CSP-167 (36)	>50	No	211	Yes	0.9 ^f	4.6 ^l	NA	NA	4.1	2	NA	2.7 ^s	3
ACE (47,48)	>70 (most)	No	1512	No	4 ^g	4	NA	2	3.2	1.1	NA	3.7	3
CAVATAS (125)	>30 ^b	90	253 CEA 251 Stent	Yes	4	4	NA	2	4.5 ^t	0.9 ^q	3.6	3.6	1
Wallstent (127)	>60	Yes	112 CEA 107 Stent	NA	12.1	12.1	NA	NA	3.7	3.7	12.1 ^r	12.1 ^r	1
Brooks et al (128)	>70	Yes	51 CEA 53 Stent	No	0	2	1	1	2	2	NA	NA	1
SAPPHIRE (129)	≥50% ^t	Yes, >48 h	151 CEA 156 Stent	No	3.3	2.0	7.3	2	0	0	NA	NA	1

Notes on unique definitions and exceptions used by the various studies:

- ^a Most lesions >70% stenosis.
- ^b Minimum stenosis not specified.
- ^c Defined as modified Rankin Scale <3 at 90 days after treatment.
- ^d Nondisabling stroke >7 days after procedure.
- ^e Type of stroke not defined.
- ^f Transient neurological deficit, ie, TIA.
- ^g Defined as modified Rankin Scale <3 at 30 days.
- ^h Defined as fatal or disabling stroke.
- ⁱ Defined as stroke before endarterectomy.
- ^j Defined as any stroke or death, reported as 2.2% disabling stroke or death in CAVATAS commentary.
- ^k Major stroke of 1.2% after endarterectomy, 0.6% after angiography, and 0.2% before angiography.
- ^l Defined as any stroke or death.
- ^m Excluded fatal myocardial infarction.
- ⁿ 0.1% death from endarterectomy.
- ^o Includes any perioperative stroke or death.
- ^p Includes 1.2% transient neurological deficits.
- ^q Includes any major stroke.
- ^r Includes any major stroke, vascular death, or procedural death.
- ^s Estimated from figures presented for death and disabling stroke.
- ^t ≥50% symptomatic stenosis, ≥80% asymptomatic stenosis.

the interstices size is too large (140). A recent prospective study, in which patients undergoing carotid artery stenting were examined preprocedurally and postprocedurally with MRI, failed to show evidence of brain signal abnormality referable to emboli. However, a similar prospective study examining 17 patients with diffusion-weighted MRI showed new (clinically silent) lesions in 3 cases (141,142).

The problem of distal embolization during balloon angioplasty and carotid stenting has increased interest in providing methods of cerebral protection. A triple-coaxial catheter system, designed to provide cerebral protection, has been described by Theron et al (143). Theron et al reported distal embolic complications in 3 of 38 patients (8%) undergoing internal carotid artery balloon angioplasty without distal protection versus 0 of 43 patients (0%) undergoing the same procedure using distal balloon protection (71,140). Henry et al used Theron's distal occlusion balloon technique in 32 of 163 carotid stenting cases (144). However, 2 of the 3 major strokes that occurred in this series were in conjunction with this device. The authors cited prolonged procedure time and increased embolism risk when traversing ulcerated lesions as potential problems associated with its use.

A number of commercial devices aimed at reducing the microembolic burden associated with carotid angioplasty and/or stenting, using filters or guide wire attached balloons, are currently undergoing development. These include a low-profile embolic filter deployed and retrieved on a 0.014-inch or 0.018-inch shaft that serves as the guidewire for balloon and stent delivery catheters. Studies in ex vivo models have shown >90% capture of particles >200 μm and 100% capture of particles >500 μm (145). Alternatively, a 0.014-inch guidewire with a protection balloon incorporated into the tip has been used. After angioplasty and stenting with the protection balloon inflated, an over-the-wire aspiration catheter is passed through the dilated area to clear debris (146). This balloon-protection method has the disadvantage of temporary occlusion of carotid flow, whereas filter devices allow constant cerebral perfusion.

SUMMARY: CAROTID STENTING

The results of carotid angioplasty and stenting vary. Case series show results comparable to endarterectomy, particularly in NASCET-ineligible patients. However, 2 large, prospective, randomized trials have given discordant results, with CAVATAS showing carotid angioplasty and/or stenting to have comparable outcomes to surgery and the WALLSTENT trial showing carotid stenting to have significantly inferior outcomes compared with surgery. Given these discordant results and inconsistencies in patient selection and in definitions used to report outcomes, uniform reporting standards are needed, along with guidance for study design. This will allow creation of reliable trials to study the safety and effectiveness of carotid endovascular revascularization using current and future technology.

Patient Selection

Discussion.—Patients can be selected according to multiple factors such as degree of stenosis, presence of symptoms, and presence of factors that place the patient at high risk for endarterectomy. Degree of stenosis is first measured with noninvasive studies such as carotid duplex sonography, MRA, or CTA. Various endarterectomy and stent trials (Tables 3, 4) have defined symptomatic patients as those with symptoms within 90 to 180 days of trial entry. For purposes of consistency, it is recommended that symptomatic patients be defined as those with neurological symptoms or neurological changes within 6 months (180 days) of treatment, consistent with NASCET entry criteria. Symptoms may be before stroke or transient neurologic event. Transient events may be hemispheric or retinal (amaurosis). The patient population can be classified as either “low-risk cohort” or “high-risk cohort” of patients with respect to endarterectomy. It is unknown if such patients are also at higher risk if treated with carotid stenting. Although it is generally accepted that some patients can be categorized as high risk, as noted earlier this is not uniformly accepted (60). The low-risk cohort is those patients with similar risk factors who

were enrolled into the NASCET and ACAS study. The definition of the high-risk cohort is more controversial. Suggestions for categorizing high-risk patients are listed in Table 5, based on criteria used in previous stent trials and from the criteria of Sundt (Table 2). The high-risk cohort can be defined as having ≥ 1 anatomical risk factors or ≥ 2 group A comorbidity risk factors or ≥ 1 group B comorbidity risk factors as defined in Table 5.

To avoid confounding the effects of other procedures with the effect of elective carotid revascularization, the selected patients should not undergo any interventional carotid, coronary, or peripheral treatment within 30 days before enrollment or after procedure unless this is part of the study protocol.

Recommendation for Reporting.—Inclusion and exclusion criteria must be reported. These include age, categorization of patients as symptomatic or asymptomatic, type of symptoms, degree of stenosis, technique for measuring the degree of stenosis, and presence and type of high-risk comorbidities.

Define Outcome of Therapy

Discussion.—The primary objective of any study involving the carotid artery should be to evaluate the safety and long-term efficacy of the stenting device versus either surgical or medical control population or historical controls for atherosclerosis in preventing ipsilateral stroke and/or death. As noted in Table 4, various studies have used perioperative (within 30 days) events of minor stroke, major stroke, myocardial infarction, and death as outcomes. Long-term events used as outcomes include ipsilateral stroke, ipsilateral disabling stroke, any stroke, and death. These long-term events can be measured as a 1-year risk or an annualized risk over longer time periods. To assess long-term efficacy, patients should continue to be followed up annually for at least 2 to 5 years.

Recommendations for Reporting.—It is recommended that the primary endpoint for any study should be the occurrence of major adverse events, defined as death or ipsilateral stroke at 6 months and 1 year after proce-

Table 5
Definition of Risk Factors for Carotid Endarterectomy

Anatomical Risk Factors (≥ 1)	Comorbidity Risk Factors Group A (≥ 2)	Comorbidity Risk Factors Group B (≥ 1)
Previous carotid endarterectomy	Patients older than age 80 years	NYHA (New York Heart Association) class III or IV heart failure
Contralateral carotid artery occlusion	Myocardial infarction within previous 6 mo	COPD (chronic obstructive pulmonary disease) with FEV1 (forced expiratory ventilation) $< 30\%$ predicted
Previous radical neck dissection or radiation therapy to neck region	Unstable angina (defined as resting pain with ECG changes)	History of liver failure with elevated prothrombin time
Target lesion above C2 (level of jaw)	Requires concurrent CABG (coronary artery bypass grafting), AAA (abdominal aortic aneurysm) repair or peripheral vascular surgery	
Low cervical carotid lesions		
Dissection		
Inability to extend neck (ie, cervical osteoarthritis, mobility limitations)		
Tandem lesions $\geq 70\%$ stenosis, intracranial stenosis, or occlusion		
Contralateral laryngeal palsy		
At risk for wound infection		
Tracheostomy		

ture or myocardial infarction (Q-wave and non-Q-wave) 30 days after procedure.

The secondary safety endpoint should be freedom from any stroke, myocardial infarction (Q-wave and non-Q-wave) or death at 30 days and freedom from target lesion revascularization at 1 year. The secondary efficacy endpoint is acute success defined by lesion, device (stent delivery system and distal protection device), and procedural success.

Pretreatment Evaluation

Discussion and Recommendations for Reporting.—Pretreatment evaluation should include assessment of degree of stenosis using noninvasive imaging, neurological assessment (NIH stroke scale, Barthel index, and Rankin scale) performed by a neurologist, preprocedural laboratory results such as hematocrit, hemoglobin, platelet count, white blood cell count with differential, serum creatinine, pregnancy test (for women of child-bearing potential), CK, CK-MB, or troponin-I, prothrombin time, and activated partial thromboplastin time. These laboratory results should be obtained within 72 hours of the procedure. A 12-lead ECG should be performed and documented for all patients before the procedure. A baseline brain CT or MRI scan should be obtained to document any preexistent infarction and exclude nonvascular neuropathology such as

tumor that may mimic transient ischemic attacks. Evaluation of severity of underlying chronic obstructive lung disease may require pulmonary function tests. Evaluation of cardiac function may require measurement of cardiac output or severity of underlying coronary artery disease. Not all of this information needs to be reported in the published data, but it should be collected for patient stratification and assessment of outcomes and complications. The tests used for pretreatment evaluation should be reported. Training of the person performing the neurological assessment (ie, neurologist or non-neurologist) should be reported.

Treatment Description

The results of carotid revascularization will vary depending on operator and institutional experience (43,56, 147–151). Previous operator experience should, therefore, be reported.

Medical therapy may need to be adjusted for arteriography. Patients using long-term anticoagulation may need to have their treatment converted to heparin. Patients with preexisting renal disease may be admitted 1 day early for intravenous hydration or monitored vasodilator therapy (152). Oral enteric-coated aspirin and clopidogrel (Plavix) have been recommended at least 3 days before the procedure to reduce periprocedural platelet emboli. Experimental data suggest that aspirin and clopidogrel

have a synergistic effect on platelet anti-aggregation, antithrombotic activity and in preventing myointimal proliferation (restenosis) (153,154). After the procedure, oral antiplatelet agents are usually continued.

The procedure may be performed under general anesthesia but is more commonly performed under local anesthesia at the puncture site along with conscious sedation, which allows continuous monitoring of the patient's neurological status (155). Although patients may have been included in the study based on previous noninvasive imaging or arteriography, the final determination of stenosis severity is made from the arteriogram at the time of intervention (**Figure**). Because the carotid stenosis may be eccentric, the optimal projection to demonstrate the stenosis should be found, which may require multiple projections or rotational angiography (156). In the case of presumed ICA occlusion, prolonged filming is necessary, because otherwise delayed, faint, antegrade opacification of the cervical ICA may be missed ("string sign" of critical ICA stenosis) (157). Standard AP and lateral intracranial views should be obtained in all cases to establish the adequacy of the intracranial collateral circulation via the external carotid and anterior communicating arteries and also to document any intracranial stenotic lesions. Many experienced operators also advocate routine vertebral angiography to assess collateral flow via the posterior communicating arter-

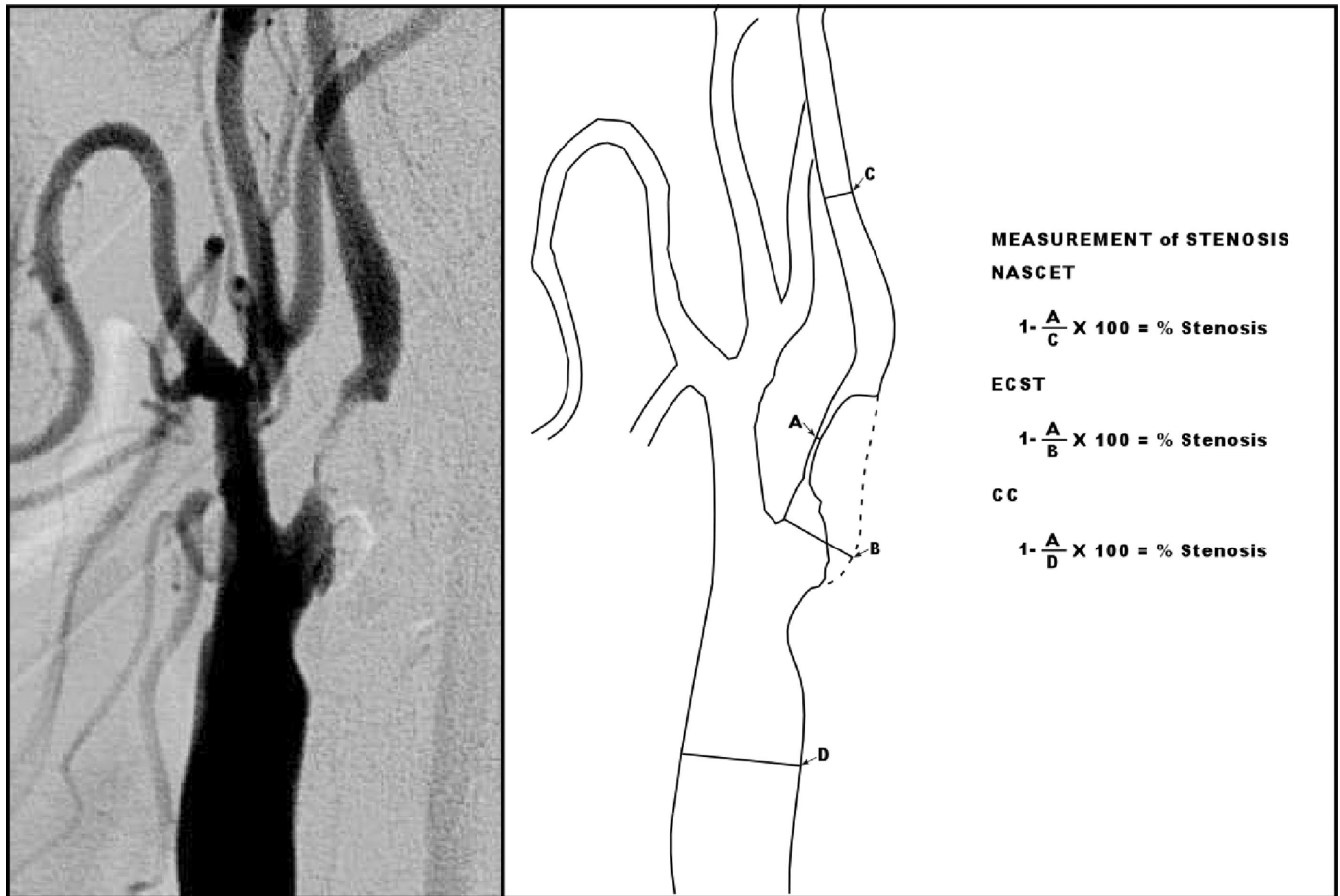


Figure. Measurement of carotid stenosis using North American Symptomatic Carotid Endarterectomy Trial (NASCET), European Carotid Surgery Trial (ECST), and Common Carotid (CC) methods. All 3 methods demonstrate a high degree of reproducibility overall. The NASCET method used most frequently in the United States is reliable but tends to underestimate the degree of stenosis. The NASCET ratio should not be applied if there is near-occlusion with reduction in the diameter of the cervical internal carotid artery beyond the stenosis. Such a reduction in the diameter of the internal carotid artery beyond the site of stenosis would consequently underestimate the severity of stenosis. CC and ECST methods grade the stenosis similarly and generally are in agreement. For atherosclerotic disease that narrows the carotid bulb, the percentage difference between NASCET and ECST increases. Carotid stenosis measured at ultrasound tends to correlate better with ECST and CC methods (23,26,29,186–188).

ies and document any extracranial or intracranial vertebrobasilar stenoses. Certainly, in cases of contralateral carotid occlusion, bilateral severe stenosis, or deficient anterior collateral pathways, evaluation of the adequacy of collateral flow via the posterior circulation becomes even more important.

The use of systemic heparin is standard. Glycoprotein IIb/IIIa inhibitors such as abciximab have been shown to decrease mortality and morbidity in a number of coronary stent studies and also potentially improve long-term patency rates, but their role remains undefined in carotid artery stenting (158–160). These agents may have a potential role in the uncommon event of acute stent thrombosis because

platelet aggregation (white thrombus) represents the primary mechanism (161).

The decision to predilate the lesion using balloon angioplasty depends on the type and size of stent being used, the narrowest lumen diameter, and the morphological configuration of the stenotic segment. Many operators perform routine predilatation to ≈ 4.0 mm diameter. However, others suggest that the risk of embolism is high during this part of the procedure, and if atraumatic crossing of the lesion with the stent-delivery catheter is possible without predilatation, then it may be attempted.

The currently used stents are either balloon-expandable or self-expand-

able, with the self-expandable stents made of either stainless steel or Nitinol. Early reports of carotid stenting mainly used balloon-expandable stents such as the Palmaz stent (Johnson & Johnson Interventional Systems), which can usually be positioned with greater precision than self-expandable types (91–94,96,162). However, reports of a 2% to 16% rate of Palmaz stent collapse on follow-up imaging has led to increased use of self-expandable types (91,108,163). Mathur et al reported Palmaz stent collapse in 11 of 70 patients (16%) at 6-month angiographic follow-up, attributing this to probable external compression. Furthermore, carotid Doppler ultrasound performed retro-

spectively in 7 patients with stent compression was only 29% sensitive (163). Compression of balloon-expandable stents has been found to be a significant cause of restenosis in the superficial femoral arteries and hemodialysis grafts (164). The 1999 global survey of 3047 carotid stenting procedures by Wholey et al reported 3033 endovascular carotid stents placed. Balloon-expandable Palmaz stents were used in 47% of cases; self-expandable Wall stents in 46%; and other stents including Strecker (Medi-tech), Integra (Medi-tech), Symphony (Medi-tech), and SMART stents (Cordis) in the remaining 7% of cases (108). In this series, 28 stent deformations occurred exclusively with the Palmaz stent (2%). However, Bergeron et al reported no instances of compression at a mean 13-month follow-up among 96 patients with carotid stenosis, all treated with Palmaz stents (100). Nevertheless, the balloon-expandable stent may not be an ideal choice for superficially exposed arteries such as the internal carotid. However in non-exposed locations such as the vertebral artery or great vessel origins, the superior positional accuracy of deployment may be advantageous. Self-expanding Nitinol stents offer the purported advantage of crush recoverability or "spring-like" behavior. If an external force compresses or deforms a Nitinol stent, then it will reassume its expanded shape on removal of the external stress.

In terms of stent sizing, based on current techniques, the stent margins should optimally extend 1 cm beyond the proximal and distal margins of the stenotic plaque. This may necessitate crossing the external carotid artery origin, which does not usually result in significant clinical sequelae. The stent diameter should be 1 to 2 mm larger than the largest vessel diameter that the stent will need to appose. Stent oversizing leads to a greater metallic coverage of the lesion per unit area, which is theoretically advantageous in preventing distal embolism, reducing tissue prolapse, and is not necessarily associated with a higher rate of restenosis (165,166).

Postdeployment angioplasty using a high-pressure (12- to 20-atm), semi-compliant balloon may then be performed to closely appose the stent and intima and, moreover, expand regions

of residual stent narrowing. This may require the use of varying diameter balloons, particularly if the stent extends into the common carotid artery. Obvious gaps between the stent circumference and endoluminal surface potentially increases the risk of acute or delayed thromboembolism (140). Angioplasty beyond the stent margins is not recommended because it may result in acute vessel dissection, symptomatic vasospasm, or subsequent restenosis. Some operators do not advocate routine postdeployment angioplasty of the stent other than for obvious gaps between the stent and vessel wall and regions of residual stenosis, suggesting that this reduces the risk of embolic complications and improves restenosis rates because of reduced intimal injury.

There is insufficient information to define technical success scientifically. For extremity and renal angioplasty, technical success requires <30% diameter residual stenosis by angiography and may require improvement in trans-stenotic pressure gradient (167, 168). In the coronary literature, technical success for balloon angioplasty and stenting had originally been defined as at least 20% relative improvement with a decrease in stenosis to <50% but has recently been revised to a decrease in stenosis to <20% diameter (169,170). However, unlike extremity, renal, or coronary stenoses, carotid stenoses are very rarely symptomatic because of hemodynamic compromise. Rather, symptoms arise because of thromboembolism formation on the carotid plaque. It is unknown what degree of correction of carotid stenosis is necessary to reduce the risk of embolization, but removal of the embolic source is fundamental. It is possible that in the attempt to more completely eliminate residual stenosis by full balloon dilation, additional emboli may be produced during the procedure that could cause a higher risk of procedural complications. Alternatively, leaving a higher degree of residual stenosis may lead to a higher rate of late restenosis, which at this time is of uncertain clinical significance. Some carotid stenting trials have defined technical success as residual stenosis <30% (171). Others have used a definition of residual stenosis <50% (172). In the absence of definitive scientific evidence, technical success in this doc-

ument is arbitrarily defined as stent placement resulting in improvement of the stenosis by >20%, with a final residual stenosis <50% using NASCET measurement criteria. Some practices may prefer to use a lesser degree of residual stenosis as their desired endpoint for technical success.

Iatrogenic vasospasm may occur during the procedure but usually resolves soon after removal of the guidewire from the internal carotid artery. Some investigators describe the use of injectable nimodipine (200 μ g diluted in 10 mL injected slowly as a 2 mL to 3 mL bolus) (140) or nitroglycerin (100 μ g) (96) into the carotid artery to treat mechanically induced vasospasm. Re-calcitrant iatrogenic vasospasm usually responds well to low-pressure balloon angioplasty (<3 atm).

AP and lateral cerebral angiograms are obtained after stenting to exclude any embolic branch occlusion and to document new patterns of flow. Heparinization is generally allowed to taper physiologically rather than reverse using protamine sulfate. Alternatively, the femoral sheath may be removed immediately after the procedure without the need for heparin reversal using percutaneous closure devices. The patient is usually monitored in the intensive care unit for 12 to 24 hours after treatment. Antiplatelet agents are frequently administered after procedure, such as Clopidogrel for 4 to 6 weeks and enteric-coated aspirin indefinitely.

The patient should be carefully examined neurologically after the procedure. Neurological deficits may be caused by intracranial embolism, hemorrhage, or reperfusion injury (173, 174). After successful revascularization, lowering of the mean arterial pressure to 10% to 20% below baseline may be desirable to prevent cerebral reperfusion injury. Intravenous diltiazem may be used postprocedurally to control elevated blood pressure, particularly if associated with headache or neurological sequelae, because it has minimal cerebral vasodilatory effects (175).

Postprocedural prolonged bradycardia or hypotension, or both may occur as a result of carotid sinus dysfunction, necessitating the use of intravenous vasopressors or inotropic agents (176).

Recommendations for Reporting.—Previous operator and institutional experience should be described. This includes the number of previous carotid revascularization procedures, preferably with at least 30-day outcomes for technical success and 30-day periprocedural complications of stroke, myocardial infarction, or death. The procedure should be described in sufficient detail that it could be reproduced accurately by others. Reporting requirements include use of adjunct antiplatelet agents before and during the procedure, use of anticoagulation during the procedure, type of anesthesia (general or conscious sedation), and techniques of neurological and physiological monitoring during the procedure. The technique of cerebral angiography should be reported (ie, AP and lateral cerebral views, other vessels evaluated such as vertebral and contralateral carotid to look for collateral vessels). Final determination of the severity of the carotid stenosis to be treated and a description of the stenotic plaque (ie, ulceration, overhanging margins, circumferential narrowing) is made from the angiogram at the time of the intervention. The technique of carotid stenting must be reported, including use of guide catheter, technique of crossing the lesion, use of predilation and diameter of predilation before stenting, type of stent used, stent diameter and length selection, and poststent deployment balloon dilation. Post-treatment degree of residual stenosis should be reported. Use of medications to prevent bradycardia, treat vasospasm, and control blood pressure should be reported. The use of postprocedural antiplatelet or anticoagulant medications should be reported.

Evaluation

Discussion.—Posttreatment evaluation should include the information necessary to evaluate for study endpoints: stroke, death, myocardial infarction, restenosis, and complications. The major morbidity of carotid revascularization, whether from stenting or endarterectomy, is perioperative (within the first 30 days). Therefore, patients must be evaluated in this time period for major and mi-

nor strokes using the NIHSS and myocardial infarction using ECG and cardiac enzymes. Stroke definitions listed should be used.

Carotid revascularization is intended to reduce the long-term risk of stroke from the carotid stenosis; therefore, long-term evaluation of treated patients for 2 to 5 years is necessary to determine the incidence of ipsilateral stroke that can be attributed to the treated vessel. Neurologic assessment including the NIH Stroke Scale, Barthel index, and modified Rankin scale for all subjects should be performed by a neurologist at 6 months and 12 months after procedure and yearly thereafter for 2 to 5 years. The NIH Stroke Scale is a somatically oriented measure of neurological function. Its limitations are relatively reduced weighting of neuropsychological measures. For instance, a patient with global aphasia receives 2 points on the NIH Stroke Scale, the same number of points received by a patient with hemianopsia but with significantly different implications for functional recovery. The Barthel Index is a measure of functional dependency that has implications for rehabilitative needs and long-term cost of chronic care for the neurologically disabled. The modified Rankin Scale is a rather crude measure of social recovery that has not been validated in patient care before 3 months. Consequently, the modified Rankin Scale should be recorded but has clinical significance only at 90 days and beyond.

Assessment of long-term mortality is also important, but will be markedly affected by patient selection—high-risk patients with multiple medical comorbidities are likely to die sooner regardless of carotid revascularization—and is best assessed in randomized trials.

Posttreatment evaluation should also include evaluation for recurrent carotid stenosis. Recurrent carotid stenosis after endarterectomy is usually asymptomatic, but repeat revascularization is necessary in $\approx 5\%$ of patients who receive endarterectomy (58,177). Similarly, repeat endovascular revascularization for restenosis has been reported in 8% of patients undergoing carotid stenting (178), although the rate may be higher in patients in whom the original carotid

stent was placed to treat a recurrent stenosis caused by endarterectomy (179). Follow-up evaluation is easily performed with carotid duplex ultrasound and should be obtained at least 2 to 4 weeks after procedure, 10 to 12 months after procedure, and if ischemic symptoms recur. More frequent surveillance intervals may be desirable (177).

Recommendations for Reporting.—In the perioperative (30-day) period, patients should be evaluated for stroke, myocardial infarction, and death. Stroke is defined as per this document. Beyond the perioperative period, patients should be evaluated for stroke, death, and restenosis. Degree and length of residual stenosis or restenosis should be reported at least once during the 30 days after treatment, preferably before discharge, at 10 to 12 months after procedure, and if ischemic symptoms recur.

COMPLICATIONS

Discussion.—Stroke is a complication of carotid revascularization and an outcome measure of the effectiveness of the revascularization. The stroke may be ipsilateral or contralateral to the treated vessel. Neurological deficits as a complication of the procedure may be caused by intracranial embolism, hemorrhage, or reperfusion injury (174). The phenomenon of reperfusion hemorrhage after surgical endarterectomy is well described. Ouriel et al in a review of 1471 patients undergoing surgical endarterectomy reported a 0.75% incidence of intracerebral hemorrhage. Hemorrhage occurred at a median of 3 days postoperatively and accounted for 35% of the total perioperative neurological events. Death from massive hemorrhage and herniation occurred in 36% of cases. Factors correlating with an increased hemorrhage risk were hypertension, high-grade ipsilateral stenosis, high-grade contralateral stenosis or occlusion, and younger age (180). This complication has also been reported with carotid angioplasty. Schoser et al reported 2 patients with reperfusion hemorrhage, 1 intraparenchymal hemorrhage and 1 subarachnoid hemorrhage after balloon angioplasty for carotid and vertebral artery stenosis (174).

Table 6
Classification of Complications

Complication	Class
Abscess	Infectious/Inflammatory
Angina/coronary ischemia	Cardiac
Idiosyncratic reaction	Medication-related
Allergic/anaphylactoid reaction	Contrast-related
Arterial occlusion/thrombosis, puncture site	Vascular
Arterial occlusion/thrombosis, remote from puncture site	Vascular
Arteriovenous fistula	Vascular
Congestive heart failure	Cardiac
Device malfunction with adverse effect	Device-related
Death related to procedure	Death
Death unrelated to procedure (30-day mortality)	Death
Embolization, arterial	Vascular
Fluid/electrolyte imbalance	General nonvascular
Hematoma bleed, remote site	Vascular
Hematoma bleed at needle, device path: nonvascular procedure	Vascular
Hematoma bleed, puncture site: vascular procedure	Vascular
Incorrect drug	Medication-related
Incorrect dosage	Medication-related
Intimal injury/dissection	Vascular
Ischemia/infarction of tissue/organ	Vascular
Incorrect site of administration	Medication-related
Local infection	Infectious/inflammatory
Liver failure	General nonvascular
Migration	Device-related
Myocardial infarction	Cardiac
Malposition	Device-related
Nausea/vomiting	General nonvascular
Other (cardiac)	Cardiac
Other (contrast-related)	Contrast-related
Other (CNS complication)	Neurologic
Other dose-dependent complication	Contrast-related
Other (device related)	Device-related
Other (gastrointestinal)	General nonvascular
Other (general nonvascular)	General nonvascular
Other (hematologic)	General nonvascular
Other (infectious/inflammatory)	Infectious/inflammatory
Other (medication related)	Medication-related
Other (neurologic)	Neurologic
Other (respiratory/pulmonary)	Respiratory/pulmonary
Other (vascular)	Vascular
Pancreatitis	Infectious/inflammatory
Pulmonary embolism	Respiratory/pulmonary
Pulmonary embolism	Vascular
Peritonitis	Infectious/inflammatory
Hypotension	Cardiac
Hypoxia	Respiratory/pulmonary
Pulmonary edema	Respiratory/pulmonary
Peripheral nervous system complication	Neurologic
Pneumothorax	Respiratory/pulmonary
Pseudoaneurysm	Vascular
Respiratory arrest	Respiratory/pulmonary
Renal failure	Contrast-related
Arrhythmia	Cardiac
Septicemia/bacteremia	Infectious/inflammatory
Seizure	Neurologic
Septic shock	Infectious/inflammatory
Stroke	Neurologic
Tissue extravasation	Contrast-related
Transient ischemic attack	Neurologic
Unintended perforation of hollow viscus	General nonvascular
Vascular perforation or rupture	Vascular
Vagal reaction	Cardiac
Vasospasm	Vascular
Venous occlusion/thrombosis, puncture site	Vascular
Venous occlusion/thrombosis, remote from puncture site	Vascular

Minor, major, and disabling stroke have not been uniformly defined in previous studies of endarterectomy or carotid stenting (Table 4). The authors of this document have attempted to provide a uniform set of definitions for neurological events and a means of classification for these events by category (Table 6). It is felt that these definitions will allow a more specific and relevant categorization of stroke incidence and severity to be consistently described. These definitions are listed.

Other major complications include myocardial infarction and death, which, in combination with stroke, are the major adverse events used to compare carotid stenting and endarterectomy. Some complications are unique to endovascular as compared with surgical revascularization. Carotid stenting may cause severe bradycardia and hypotension as a result of carotid sinus dysfunction requiring cardiac pacing, although the need for this has diminished with use of intravenous vasopressors or inotropic agents (176). Endovascular revascularization may also produce vascular injuries such as dissection, perforation, hematoma, pseudoaneurysm, and groin infection. Surgical revascularization may produce cranial nerve injuries and local wound hematomas and infections.

Recommendations for Reporting.—Complications within 30 days of the procedure are considered perioperative and procedure related. Neurological deficits are reported using the definitions listed. A stroke may be described as reversible and minor versus major or permanent and minor versus major.

A stroke is any sudden development of neurological deficits attributable to cerebral ischemia and infarction.

Neurological complication—neurological deterioration evidenced by an increase in the NIHSS of ≥ 1 point.

Transient deficit—a neurological complication having complete resolution within 24 hours.

Reversible stroke—a neurological complication having a duration of >24 hours and ≤ 30 days.

Permanent stroke—a neurologi-

Table 7
Definitions of Complications

Minor complications
No therapy, no consequence
Nominal therapy, no consequence; includes overnight admission for observation only
Major complications
Require therapy, minor hospitalization (<48 h)
Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 h)
Permanent adverse sequelae
Death

cal complication having a duration of >30 days.

Minor deficit—neurological deterioration evidenced by an increase of the NIHSS of <4 points without the presence of aphasia or hemianopsia.

Major deficit—neurological deterioration evidenced by an increase of the NIHSS of ≥ 4 points or the presence of aphasia or hemianopsia.

Neurological deficits should be listed as ipsilateral or contralateral. Because deaths are frequently secondary to stroke or myocardial infarction, it is misleading to sum the individual totals of stroke, myocardial infarctions, and death. Rather, a combined rate of nonfatal stroke, nonfatal myocardial infarction, and death should also be reported, with cause of death described. Other complications should be listed and graded according to previously defined SIR categories of type and severity (Tables 6, 7).

COMPARISON BETWEEN TREATMENT GROUPS/ANALYSIS

Randomization and Blinding.—Case series may be useful in demonstrating safety and effectiveness of a technique but are unreliable in comparing different therapies. The major advantage of a trial over an observational study is the ability to demonstrate causality. In particular, randomly assigning the intervention can eliminate the influence of confounding variables, and blinding can eliminate the possibility that the observed

effects of the intervention are caused by other treatments or by biased ascertainment (96). Because the success and complications of carotid revascularization are so heavily dependent on patient selection, comparisons of revascularization techniques should be made in randomized trials rather than by comparison with historical controls.

It may be impossible for observers to be blinded with respect to therapy (ie, surgery versus endovascular). However, neurological and functional assessments performed at defined time points after treatment should ideally be performed by examiners blinded to the subject's treatment. In addition, a core laboratory should assess the results of the follow-up imaging studies in a manner blinded to treatment assignment and clinical outcome.

Intention to Treat.—Randomized surgical trials of carotid endarterectomy have been reported based on intention to treat. Because of this, some events such as stroke, death, or myocardial infarction may be attributed to the treatment, even if the event occurs before revascularization. Case series will underreport these events, because events are usually reported only in those patients actually treated. The longer the delay between randomization and treatment, the greater the discrepancy between randomized trials and case series. The determination for the study entrance start time should be defined as the randomization contact date/time. Therefore, analyses in randomized trials should be performed for 3 subject populations: randomized subjects (intent to treat), subjects treated as randomized, and evaluable subjects. Randomized subjects should be defined as all subjects randomized to treatment or control. The population of subjects treated as randomized should include all subjects randomized to treatment who were revascularized and all subjects randomized to control who were not revascularized, if a nonrevascularization arm is included in the study. More likely, studies will include patients treated with different methods of revascularization. The evaluable subject population should be defined as all subjects who did not have certain protocol deviations as specified by the

project team. Analysis of this subpopulation is helpful to distinguish treatment effect in the intended population from the effect of treating unintended patients included as protocol violations. A complete analysis for each of the 3 populations may be necessary, depending on study design.

Analysis.—Demographics should be summarized, including age, gender, and presence of symptoms. Outcomes should be stratified according to presence of symptoms, degree of stenosis, and risk of endarterectomy, including medical and anatomic comorbidities, as described in Table 5. Patients treated with combined carotid revascularization and coronary artery bypass grafting, if included in the study, should be stratified separately, because it is not possible to identify which of the 2 procedures is responsible for the complication. Groups should be compared for perioperative (30 days) and long-term (6 months and preferably up to 2 to 3 years) events. Perioperative group comparison should include mortality, any stroke (ischemic versus hemorrhagic), ipsilateral stroke, major versus minor stroke (as defined previously), cardiac events (myocardial infarction, increased congestive heart failure), and medical and procedural complications. If the comparison group includes carotid endarterectomy, then procedural complications should include cranial nerve injuries and neck hematomas. Combined outcomes of stroke plus death, and stroke plus death plus myocardial infarction, should also be compared, because there will be some patients with multiple events.

Because the major stroke morbidity is in the perioperative period, providing annual risk of stroke over time can be misleading. For example, if a procedure has a 10% risk of perioperative stroke but a 0% risk of stroke subsequently, over 5 years the annual risk of stroke is 2%. The same long-term risk is calculated from a procedure with a 0% risk of perioperative stroke but a 2% risk of stroke over each of the next 5 years. Furthermore, the European Carotid Stroke Trial found that the risk of stroke from an untreated carotid stenosis decreases to the risk of a revas-

cularized carotid after ≈ 3 years. If long-term data are acquired for 10 years, then the clinical benefit in the initial years will be masked. The long-term benefit is more accurately perceived if the long-term risk is reported excluding the perioperative period ("subsequent annual event rate"). This is not consistent with the reporting used in previous surgical trials; therefore, it is recommended that long-term annual risk of stroke be reported including and excluding the perioperative period. The analysis of long-term data should include Kaplan-Meier or life-table curves indicating freedom from stroke (ipsilateral or any stroke), death, stroke plus death, and restenosis.

Recommendations for Reporting.—Randomized trials should be reported based on intention to treat. Other analyses (patients treated as randomized, assessable patients) may be helpful. Results are presented using life-table or Kaplan-Meier analyses. Results should be stratified according to symptoms, degree of stenosis, and risk factors. Results are reported for stroke (stratified as described), cardiac events, mortality, and restenosis. Annualized event rates should be reported including and excluding the perioperative events.

COSTS

Retrospective studies examining the cost of endarterectomy versus stenting have indicated lower costs for their respective procedures (181–183). Surgical procedures will include the costs of anesthesia and operating room time, whereas endovascular procedures will include the costs of catheters and stents and angiographic room time. Cost-effectiveness analysis includes costs with respect to outcomes and may favor endarterectomy if stenting has a higher mortality and major stroke rate than endarterectomy (184). Recommendations for reporting standards for cost-analysis of carotid revascularization are beyond the scope of this document. However, it is useful to report information on length of hospitalization and number of ICU days.

CONCLUSION

Carotid stenting offers the potential of nonsurgical treatment of carotid bifurcation stenoses with possibly lower morbidity than surgery in those patients in high surgical risk categories. Reliable evaluation of the outcomes of carotid stenting is limited at this time because the outcomes have been reported in multiple case series with few randomized trials, and the outcomes are heavily affected by patient selection. In addition, the long-term durability of carotid stents in preventing stroke and the long-term patency rates of carotid stents are not yet established. Comparisons with surgical outcomes will require uniform reporting and more randomized trials using the most promising techniques, such as cerebral protection devices. The goal of this document is to provide the definitions necessary for uniform reporting of these trials (Table 8).

GLOSSARY OF TERMS:

Abrupt closure—defined as the occurrence of a new and severe reduced flow within the target vessel that has persisted and requires rescue by a nonassigned treatment strategy (including emergency surgery) or results in stroke, myocardial infarction, or death. Abrupt closure requires proven association with a mechanical dissection of the treatment site or instrumented vessel, thrombus, or severe spasm. Abrupt closure does not connote "no reflow" (caused by microvascular flow limitation), in which the carotid artery is patent but had reduced flow. Abrupt closure also does not connote transient closure with reduced flow in which the *index* treatment application does reverse the closure.

Subabrupt closure—defined as abrupt closure that occurred after the *index* procedure is completed (and the subject has left the angiography suite) and before the 12-month follow-up endpoint.

Acute gain—defined as the immediate dimensional change in minimal luminal diameter (in mm) that has occurred after the final postdilatation as compared with the minimal luminal diameter at baseline and measured by angiography from the average of 2 orthogonal views.

Death—death may be divided into 2 categories: (1) neurological death, defined as death caused by stroke, death related to complication of the procedure, including bleeding, vascular repair, or surgery, and any death in which a neurological cause cannot be excluded; and (2) nonneurological death, which is defined as death not caused by neurological causes listed here.

Dissection—graded according to National Heart Lung and Blood Institute (NHLBI) criteria (185):

- Type A Luminal haziness
- Type B Linear dissection
- Type C Extraluminal contrast (ie, "cap dissection")
- Type D Spiral dissection
- Type E Dissection with reduced flow
- Type F Dissection with total occlusion

Emergent carotid endarterectomy (CEA)—defined as CEA performed on an urgent or emergent basis for severe vessel dissection or treatment failure resulting in vessel occlusion.

In-lesion measurement—defined as the measurements either within the stented segment or within 5 mm proximal or distal to the stent edges.

In-stent measurement—defined as the measurements within the stented segment.

Major adverse events—include death, myocardial infarction (Q-wave and non-Q-wave), and stroke.

Minimal luminal diameter (MLD)—defined as the mean minimum lumen diameter derived from the angiographic view that allows optimal visualization of the target lesion.

Myocardial infarction—a positive diagnosis of myocardial infarction is made when one of the following criteria is met: (1) Q-wave MI will be defined as a new Q-wave in ≥ 2 leads and in the presence of elevated CK or CK-MB; (2) non-Q-wave MI will be defined as a CK elevation > 2 -times upper limit of normal in the presence of elevated CK-MB.

Perforation—extravasation of contrast material outside the arterial lumen that is localized (confined to the tissue immediately surrounding the artery) or nonlocalized (not confined to the tissue immediately surrounding the artery).

Procedural success—attainment of adequate restoration of cerebral blood

Table 8
Recommendations for Reporting Standards

	Required	Highly Recommended	Recommended
Preprocedural Data			
Patient population	X		
Age, race	X		
Neurological history	X		
Primary symptom necessitating treatment	X		
Risk factors		X	
Comorbidities	X		
Study Design			
Inclusion criteria	X		
Exclusion criteria	X		
Primary endpoint(s)	X		
Secondary endpoint(s)		X	
Degree of stenosis	X		
Lesion location	X		
Lesion N	X		
Previous medical therapy		X	
Previous surgical therapy	X		
Procedure Data			
Level of experience			X
Description of revascularization procedure	X		
Postprocedure stenosis	X		
Pharmacologic adjuncts		X	
Complications	X		
Hospital days		X	
ICU days		X	
Postprocedural Data			
Stratification by symptoms, high-risk categories	X		
Stroke			
Reversible vs permanent	X		
Major vs minor	X		
Ipsilateral vs total	X		
Ischemic vs hemorrhagic at 30 days and 6 and 12 months	X		
Annualized rate of stroke	X		
Subsequent annualized rate of stroke			X
Myocardial infarction at 30 days	X		
Mortality at 30 days and 6 and 12 months	X		
Recurrent stenosis at 12 months	X		
Target lesion revascularization	X		

flow through the target lesion and the absence of in-hospital major adverse events. In general, improvement of stenosis by >20% with final residual stenosis <50% is the recommended standard.

Restenosis—defined as >50% in-stent diameter stenosis after previous

balloon angioplasty or stent-supported angioplasty.

Reference vessel diameter (RVD)—defined as the cephalad portion of the internal carotid artery deemed healthy and representative of reference.

Angiographic protocol for determining RVD is as follows: once image

calibration has been obtained, normal and diseased arterial segments obtained in 2 orthogonal previously unforeshortened projections without vessel overlap and demonstrating the 2 most severe views of the stenosis (“worst views”) will be selected for analysis. A computer-assisted edge detection algorithm may be applied to obtain quantitative carotid dimensions. Operator discretion must be applied to determine if the automated system obtained appropriate measurements. Side branches, the position of the balloon catheter during inflation, and other anatomic landmarks may be used to select identical segments of the normal vessel in serial projections. The minimal lumen diameter and a 5 to 7 mm segment of the distal parallel-tract cervical internal carotid artery may be used for determination of relative percent diameter stenosis. The mean diameter of the proximal common carotid artery and an estimate of normal reference diameter at the site of maximum stenosis should also be provided.

Stent thrombosis—demonstration of intraluminal thrombus or subacute closure within the stented vessel by duplex ultrasound, CT, MR or catheter angiography. Such studies may be initiated as part of the work-up for post-procedural cerebral ischemia (TIA or stroke).

Stroke—any sudden development of neurological deficits attributable to cerebral ischemia or infarction.

Neurological complication—neurological deterioration evidenced by an increase in the NIHSS of ≥ 1 point.

Transient deficit—neurological complication having complete resolution within 24 hours.

Reversible stroke—neurological complication having a duration of ≥ 24 hours and ≤ 30 days.

Permanent stroke—neurological complication having a duration of >30 days.

Minor deficit—neurological deterioration evidenced by an increase of the NIHSS of <4 points without the presence of aphasia or hemianopsia.

Major deficit—neurological deterioration evidenced by an increase of the NIHSS of ≥ 4 points or the presence of aphasia or hemianopsia.

Target lesion revascularization (TLR)—any repeat percutaneous inter-

vention on the target lesion or CEA of the target vessel.

Clinically-driven revascularizations are those in which the patient had recurrent neurological symptoms (TIA, stroke, amaurosis fugax, central retinal artery occlusion) or in-lesion diameter stenosis $\geq 70\%$ by angiography with or without ischemic signs or symptoms.

Nonclinically driven repeat target lesion revascularizations are those in which the patient underwent a non-emergent revascularization for a diameter stenosis $< 50\%$ (by angiography). Nonemergent repeat target lesion revascularization for a diameter stenosis $< 70\%$ by angiography, in patients without either a positive carotid duplex scan or neurological symptoms are also considered nonclinically driven.

Target vessel failure (TVF)—target vessel revascularization, stroke, or death that cannot be clearly attributed to a vessel other than the target vessel.

Technical success

Lesion success—attainment of adequate restoration of cerebral blood flow through the target lesion using any percutaneous method. Self-expanding stents with elastic or super-elastic properties may result in progressive dilatation of residual stenosis after the conclusion of the procedure. In addition, balloon dilatation after stent placement risks additional thromboembolism. Residual stenosis may be tolerated if the operator believes there is no threat of abrupt stent thrombosis or thromboembolic phenomena. In general, improvement of stenosis by $> 20\%$ with final residual stenosis $< 50\%$ is the recommended standard.

Device success—attainment of adequate restoration of cerebral blood flow through the target lesion using only the assigned device. In general, improvement of stenosis by $> 20\%$ with final residual stenosis $< 50\%$ is the recommended standard.

Procedure success—attainment of adequate restoration of cerebral blood flow through the target lesion and no in-hospital major adverse events. In general, improvement of stenosis by $> 20\%$ with final residual stenosis $< 50\%$ is the recommended standard.

Transient ischemic attack (TIA)—focal neurologic abnormalities of sud-

den onset and brief duration (ie, lasting < 24 hours) that reflect dysfunction in the distribution of the affected artery. TIAs include transient monocular blindness (eg, amaurosis fugax defined as a transient episode of ipsilateral blindness, or partial blindness, lasting ≤ 10 minutes) and transient hemispheric attacks.

Unanticipated adverse device effect (UADE)—any serious adverse effect on health or safety or any life-threatening problem or death that is caused by or associated with an investigational device. The effect must not have been previously identified in nature, severity, or degree of incidence in the investigational plan. Other serious problems associated with the device that affect the rights or welfare of study subjects may also be considered UADEs.

Vascular complication—the occurrence of any of the following: (1) hematoma at access site > 5 cm; (2) false aneurysm; (3) AV fistula; (4) retroperitoneal bleed; (5) peripheral ischemia/nerve injury; (6) procedure related transfusion; and/or (7) vascular surgical repair.

Acknowledgments: Drs Randall Higashida and Philip Meyers authored the first draft of this document and served as topic leaders during the subsequent revisions of the draft. Dr David Sacks is former chair of the SIR Technology Assessment Committee and is the current SIR Standards Division Councilor. All other authors are listed alphabetically. Other members of the Technology Assessment Committees who participated in the development of this clinical practice guideline are (listed alphabetically): Gary J. Becker, MD; John J. Borsa, MD; John Cardella, MD; Patricia E. Cole, PhD, MD; William B. Crenshaw, MD; Michael D. Dake, MD; Chieh-Min Fan, MD; Scott C. Goodwin, MD; Richard J. Gray, MD; Ziv Haskal, MD; John A. Kaufman, MD; Thomas B. Kinney, MD; Sanjoy Kundu, MD; Lindsay Machan, MD; Louis G. Martin, MD; Albert A. Nemcek, Jr, MD; Reed Ali Omary, MD; Nilesh H. Patel, MD; David A. Phillips, MD; John H. Rundback, MD; James E. Silberzweig, MD; Michael C. Soulen, MD.

REFERENCES

1. The National Advisory Neurological Disorders and Stroke Council. *Stroke and cerebrovascular disease*. National Institutes of Health Report: Bethesda, Md; 1992:26–27.
2. Bonita R, Beaglehole R. Stroke: populations, cohorts, and clinical trials. In: Whisnant JP, ed. *Stroke Mortality*. Oxford, England: Butterworth-Heinemann, Ltd; 1993:59–79.
3. 1999 Heart and Stroke Statistical Update. Dallas, Tex: American Heart Association; 1998:13–15.
4. Matchar D, Duncan P. *Cost of Stroke* Clinical Updates. 1994:9–12.
5. Dyken M. *Stroke Risk Factors in Prevention of Stroke* In: Norris JW, Hachinski VC, eds. New York: Springer-Verlag; 1991:83–102.
6. Ricci S, Flamini FO, Marini M, Antonini D, Bartolini S, Celani MG, Ballatori E, De Angelis V. The prevalence of stenosis of the internal carotid in subjects over 49: a population study. *Epidemiol Prev* 1991; 13:173–176.
7. Prati P, Vanuzzo D, Casaroli M, Di Chiara A, De Biasi F, Feruglio GA, Touboul PJ. Prevalence and determinants of carotid atherosclerosis in a general population. *Stroke* 1992; 23:1705–1711.
8. O'Leary DH, Polak JF, Kronmal RA, Kittner SJ, Bond MG, Wolfson SK Jr, Bommer W, Price TR, Gardin JM, Savage PJ. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. *Stroke* 1992; 23:1752–1760.
9. Zarins CK. Carotid endarterectomy: the gold standard. *J Endovasc Surg* 1996; 3:10–15.
10. Baker JD, Rutherford RB, Bernstein EF, Coubier R, Ernst CB, Kempczinski RF, Riles TS, Zarins CK. Suggested standards for reports dealing with cerebrovascular disease. Subcommittee on Reporting Standards for Cerebrovascular Disease, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery/North Am Chapter, International Society for Cardiovascular Surgery. *J Vasc Surg* 1988; 8:721–729.
11. DeBakey ME. Carotid endarterectomy revisited. *J Endovasc Surg* 1996; 3:4.
12. Eastcott HH, Pickering GW, Rob CG. Reconstruction of internal carotid artery in a patient with intermittent attacks of hemiplegia. *Lancet* 1954; 267:994–996.
13. Eastcott HH. Late thoughts and reflections on carotid reconstruction for the prevention of ischemic stroke. *J Endovasc Surg* 1996; 3:5–6.
14. Barnett H. Symptomatic carotid endarterectomy trials. *Stroke* 1991; 21:III/2–III/5.
15. Barnett H. Evaluating methods for prevention in stroke. *Ann R Coll Physicians Surg Can* 1991; 24:33–42.
16. Shaw DA, Venables GS, Cartledge NE, Bates D, Dickinson PH. Carotid end-

- arterectomy in patients with transient cerebral ischaemia. *J Neurol Sci* 1984; 64:45–53.
17. Muuronen A. Outcome of surgical treatment of 110 patients with transient ischemic attack. *Stroke* 1984; 15: 959–964.
 18. Slavish LG, Nicholas GG, Gee W. Review of a community hospital experience with carotid endarterectomy. *Stroke* 1984; 15:956–959.
 19. Brott T, Thalinger K. The practice of carotid endarterectomy in a large metropolitan area. *Stroke* 1984; 15: 950–955.
 20. Warlow C. Carotid endarterectomy: does it work? *Stroke* 1984; 15:1068–1076.
 21. Barnett HJ, Plum F, Walton JN. Carotid endarterectomy—an expression of concern. *Stroke* 1984; 15:941–943.
 22. Winslow CM, Solomon DH, Chassin MR, Koscoff J, Merrick NJ, Brook RH. The appropriateness of carotid endarterectomy. *N Engl J Med* 1988; 318:721–727.
 23. The North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991; 325:445–453.
 24. Tu JV, Hannan EL, Anderson GM, Iron K, Wu K, Vranizan K, Popp AJ, Grumbach K. The fall and rise of carotid endarterectomy in the United States and Canada. *N Engl J Med* 1998; 339:1441–1447.
 25. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, Rankin RN, Clagett GP, Hachinski VC, Sackett DL, Thorpe KC, Meldrum HE. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North Am Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 1998; 339:1415–1425.
 26. North Am Symptomatic Carotid Endarterectomy Trial. Methods, patient characteristics, and progress. *Stroke* 1991; 22:711–720.
 27. Ferguson GG, Eliasziw M, Barr HW, Clagett GP, Barnes RW, Wallace RW, Taylor DW, Haynes RB, Finan JW, Hachinski VC, Barnett HJ. The North Am Symptomatic Carotid Endarterectomy Trial: surgical results in 1415 patients. *Stroke* 1999; 30:1751–1758.
 28. Paciaroni M, Eliasziw M, Kappelle LJ, Finan JW, Ferguson GG, Barnett HJ. Medical complications associated with carotid endarterectomy. North Am Symptomatic Carotid Endarterectomy Trial (NASCET). *Stroke* 1999; 30: 1759–1763.
 29. The European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. *Lancet* 1991; 337: 1235–1243.
 30. The European Carotid Surgery Trialists' Collaborative Group. Endarterectomy for moderate symptomatic carotid stenosis: interim results from the MRC European Carotid Surgery Trial. *Lancet* 1996; 347:1591–1593.
 31. The European Carotid Surgery Trialists' Collaborative Group. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998; 351:1379–1387.
 32. Donnan GA, Davis SM, Chambers BR, Gates PC. Surgery for prevention of stroke. *Lancet* 1998; 351:1372–1373.
 33. Mayberg MR, Wilson SE, Yatsu F, Weiss DG, Messina L, Hershey LA, Colling C, Eskridge J, Deykin D, Winn HR. Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. Veterans Affairs Cooperative Studies Program 309 Trialist Group. *JAMA* 1991; 266: 3289–3294.
 34. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for Asymptomatic Carotid Artery Stenosis. *JAMA* 1995; 273:1421–1461.
 35. Connors JJ and Wojak JC. General considerations for endovascular therapy of the extracranial internal carotid artery at the bifurcation. *Interventional Neuroradiology. Strategies and Practical Techniques*. In: Philadelphia: WB Saunders; 1999: 442–456.
 36. Hobson RW, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med* 1993; 328:221–227.
 37. Warlow C. Endarterectomy for asymptomatic carotid stenosis? *Lancet* 1995; 345:1254–1255.
 38. Halliday AW, Thomas D, Mansfield A. The Asymptomatic Carotid Surgery Trial (ACST). Rationale and design. Steering Committee. *Eur J Vasc Surg* 1994; 8:703–10.
 39. Results of a randomized controlled trial of carotid endarterectomy for asymptomatic carotid stenosis. Mayo Asymptomatic Carotid Endarterectomy Study Group. *Mayo Clin Proc* 1992; 67:513–518.
 40. Rothwell PM, Slattery J, Warlow CP. A systematic review of the risks of stroke and death due to endarterectomy for symptomatic carotid stenosis. *Stroke* 1996; 27:260–265.
 41. Rothwell P, Warlow C. Is self-audit reliable? *Lancet* 1995; 346:1623.
 42. Rothwell PM, Slattery J, Warlow CP. A systematic comparison of the risks of stroke and death due to carotid endarterectomy for symptomatic and asymptomatic stenosis. *Stroke* 1996; 27:266–269.
 43. Wennberg DE, Lucas FL, Birkmeyer JD, Bredenberg CE, Fisher ES. Variation in carotid endarterectomy mortality in the Medicare population: trial hospitals, volume, and patient characteristics. *JAMA* 1998; 279:1278–1281.
 44. Lepore MR Jr, Sternbergh WC III, Salartash K, Tonnessen B, Money SR. Influence of NASCET/ACAS trial eligibility on outcome after carotid endarterectomy. *J Vasc Surg* 2001; 34:581–586.
 45. Estes J, Guadagnoli E, Wolf R, LoGerfo F, Whittemore A. The impact of cardiac comorbidity after carotid endarterectomy. *J Vasc Surg* 1998; 28: 577–584.
 46. Dorros G. Stent-supported carotid angioplasty: should it be done, and, if so, by whom? A 1998 perspective. *Circulation* 1998; 98:927–930.
 47. Taylor DW, Barnett HJ, Haynes RB, Ferguson GG, Sackett DL, Thorpe KE, Simard D, Silver FL, Hachinski V, Clagett GP, Barnes R, Spence JD. Low-dose and high-dose acetylsalicylic acid for patients undergoing carotid endarterectomy: a randomised controlled trial. ASA and Carotid Endarterectomy (ACE) Trial Collaborators. *Lancet* 1999; 353:2179–2184.
 48. Spence D, Eliasziw M. Endarterectomy or angioplasty for treatment of carotid stenosis? *Lancet* 2001; 357:1722–1723.
 49. Sundt TJ, Meyer F, Piepgras D, Fode N, Ebesold M, Marsh W. Risk Factors and Operative Results. Sundt's Occlusive Cerebrovascular Disease. Philadelphia: WB Saunders. 1994: 241–247.
 50. Sundt T, Sandok B, Whisnant J. Carotid endarterectomy. Complications and preoperative assessment of risk. *Mayo Clin Proc* 1975; 50:301–306.
 51. Meyer FB, Piepgras DG, Fode NC. Surgical treatment of recurrent carotid artery stenosis. *J Neurosurg* 1994; 80:781–787.
 52. AbuRahma AF, Choueiri MA. Cranial and cervical nerve injuries after repeat carotid endarterectomy. *J Vasc Surg* 2000; 32:649–654.
 53. Loftus CM, Biller J, Hart MN, Cornell SH, Hiratzka LF. Management of radiation-induced accelerated carotid atherosclerosis. *Arch Neurol* 1987; 44: 711–714.
 54. Murros KE, Toole JF. The effect of radiation on carotid arteries. A review article. *Arch Neurol* 1989; 46:449–455.
 55. Mellièrè D, Becquemin JP, Berrahal D, Desgranges P, Cavillon A. Manage-

- ment of radiation-induced occlusive arterial disease: a reassessment. *J Cardiovasc Surg (Torino)* 1997; 38:261–269.
56. Perler BA, Dardik A, Burleyson GP, Gordon TA, Williams GM. Influence of age and hospital volume on the results of carotid endarterectomy: a statewide analysis of 9918 cases. *J Vasc Surg* 1998; 27:25–33.
 57. Hill BB, Olcott CT, Dalman RL, Harris EJ Jr, Zarins CK. Reoperation for carotid stenosis is as safe as primary carotid endarterectomy. *J Vasc Surg* 1999; 30:26–35.
 58. O'Hara PJ, Hertzner NR, Karafa MT, Mascha EJ, Krajewski LP, Beven EG. Reoperation for recurrent carotid stenosis: early results and late outcome in 199 patients. *J Vasc Surg* 2001; 34:5–12.
 59. Brown KR, Kresowik TF, Chin MH, Kresowik RA, Grund SL, Hendel ME. Multistate population-based outcomes of combined carotid endarterectomy and coronary artery bypass. *J Vasc Surg* 2003; 37:32–39.
 60. Gasparis AP, Ricotta L, Cuadra SA, Char DJ, Purtill WA, Van Bemmelen PS, Hines GL, Giron F, Ricotta JJ. High-risk carotid endarterectomy: fact or fiction. *J Vasc Surg* 2003; 37:40–46.
 61. Marcinczyk MJ, Nicholas GG, Reed JF III, Nastasee SA. Asymptomatic carotid endarterectomy. Patient and surgeon selection. *Stroke* 1997; 28:291–296.
 62. Wong JH, Lubkey TB, Suarez-Almazor ME, Findlay JM. Improving the appropriateness of carotid endarterectomy: results of a prospective city-wide study. *Stroke* 1999; 30:12–15.
 63. Chassin MR. Appropriate use of carotid endarterectomy. *N Engl J Med* 1998; 339:1468–1471.
 64. Kerber CW, Cromwell LD, Loehden OL. Catheter dilatation of proximal carotid stenosis during distal bifurcation endarterectomy. *AJNR Am J Neuroradiol* 1980; 1:348–349.
 65. Theron J, Raymond J, Casasco A, Courtheoux F. Percutaneous angioplasty of atherosclerotic and postsurgical stenosis of carotid arteries. *AJNR Am J Neuroradiol* 1987; 8:495–500.
 66. Kachel R. Results of balloon angioplasty in the carotid arteries. *J Endovasc Surg* 1996; 3:22–30.
 67. Gil-Peralta A, Mayol A, Marcos JR, Gonzalez A, Ruano J, Boza F, Duran F. Percutaneous transluminal angioplasty of the symptomatic atherosclerotic carotid arteries. Results, complications, and follow-up. *Stroke* 1996; 27:2271–2273.
 68. Munari LM, Belloni G, Perretti A, Ghia HF, Moschini L, Porta M. Carotid percutaneous angioplasty. *Neurol Res* 1992; 14:156–158.
 69. Eckert B, Zanella FE, Thie A, Steinmetz J, Zeumer H. Angioplasty of the internal carotid artery: results, complications and follow up in 6 cases. *Cerebrovasc Dis* 1996; 27:2271–2273.
 70. Higashida R, Tsai F, Halbach V, Dowd C, Hieshima G. Transluminal angioplasty, thrombolysis, and stenting for extracranial and intracranial cerebral vascular disease. *J Int Cardiol* 1996; 9:245–255.
 71. Theron JG, Payelle GG, Coskun O, Huet HF, Guimaraens L. Carotid artery stenosis: treatment with protected balloon angioplasty and stent placement. *Radiology* 1996; 201:627–636.
 72. Sundt TM Jr, Whisnant JP, Houser OW, Fode NC. Prospective study of the effectiveness and durability of carotid endarterectomy. *Mayo Clin Proc* 1990; 65:625–635.
 73. Frericks H, Kievit J, van Baalen JM, van Bockel JH. Carotid recurrent stenosis and risk of ipsilateral stroke: a systematic review of the literature. *Stroke* 1998; 29:244–250.
 74. Moore W, Kempczinski R, Nelson J, Toole J. Recurrent carotid stenosis: Results of the asymptomatic carotid atherosclerosis study. *Stroke* 1998; 29:2018–2025.
 75. Bladin CF, Bingham L, Grigg L, Yapanis AG, Gerraty R, Davis SM. Transcranial Doppler detection of microemboli during percutaneous transluminal coronary angioplasty. *Stroke* 1998; 29:2367–2370.
 76. Markus HS, Clifton A, Buckenham T, Brown MM. Carotid angioplasty. Detection of embolic signals during and after the procedure. *Stroke* 1994; 25:2403–2406.
 77. Crawley F, Clifton A, Buckenham T, Loosemore T, Taylor RS, Brown MM. Comparison of hemodynamic cerebral ischemia and microembolic signals detected during carotid endarterectomy and carotid angioplasty. *Stroke* 1997; 28:2460–2464.
 78. McCleary AJ, Nelson M, Dearden NM, Calvey TA, Gough MJ. Cerebral haemodynamics and embolization during carotid angioplasty in high-risk patients. *Br J Surg* 1998; 85:771–774.
 79. Gaunt ME, Brown L, Hartshorne T, Bell PR, Naylor AR. Unstable carotid plaques: preoperative identification and association with intraoperative embolisation detected by transcranial Doppler. *Eur J Vasc Endovasc Surg* 1996; 11:78–82.
 80. Levi CR, O'Malley HM, Fell G, Roberts AK, Hoare MC, Royle JP, Chan A, Beiles BC, Chambers BR, Bladin CR, Donnan GA. Transcranial Doppler detected cerebral microembolism following carotid endarterectomy. High microembolic signal loads predict postoperative cerebral ischaemia. *Brain* 1997; 120:621–629.
 81. Spencer MP. Transcranial Doppler monitoring and causes of stroke from carotid endarterectomy. *Stroke* 1997; 28:685–691.
 82. Gaunt ME, Martin PJ, Smith JL, Rimmer T, Cherryman G, Ratliff DA, Bell PR, Naylor AR. Clinical relevance of intraoperative embolization detected by transcranial Doppler ultrasonography during carotid endarterectomy: a prospective study of 100 patients. *Br J Surg* 1994; 81:1435–1439.
 83. Muller M, Behnke S, Walter P, Omlor G, Schmirgk K. Microembolic signals and intraoperative stroke in carotid endarterectomy. *Acta Neurol Scand* 1998; 97:110–117.
 84. Ringelstein EB, Droste DW, Babikian VL, Evans DH, Grosset DG, Kaps M, Markus HS, Russell D, Siebler M. Consensus on microembolus detection by TCD. International Consensus Group on Microembolus Detection. *Stroke* 1998; 29:725–729.
 85. Goertler M, Baeumer M, Kross R, Blaser T, Lutze G, Jost S, Wallesch CW. Rapid decline of cerebral microemboli of arterial origin after intravenous acetylsalicylic acid. *Stroke* 1999; 30:66–69.
 86. Eckert B, Thie A, Valdueza J, Zanella F, Zeumer H. Transcranial Doppler Sonographic monitoring during percutaneous transluminal angioplasty of the internal carotid artery. *Neuroradiology* 1997; 39:229–234.
 87. Tsurutani T, Orita T, Kitahara T. Percutaneous transluminal angioplasty of the internal carotid artery with a continuous-perfusion dilatation catheter. *AJNR Am J Neuroradiol* 1997; 18:696–698.
 88. Serruys PW, de Jaegere P, Kiemeneij K, Macaya C, Rutsch W, Heyndrickx G, Emanuelsson H, Marco J, Legrand V, Materne P, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group. *N Engl J Med* 1994; 331:489–495.
 89. Macaya C, Serruys PW, Ruygrok P, Suryapranata H, Mast G, Klugmann S, Urban P, den Heijer P, Koch K, Simon R, Morice MC, Crean P, Bonnier H, Wijns W, Danchin N, Bourdennec C, Morel MA. Continued benefit of coronary stenting versus balloon angioplasty: one-year clinical follow-up of Benestent trial. Benestent Study Group. *J Am Coll Cardiol* 1996; 27:255–261.
 90. Serruys PW, van Hout B, Bonnier H, Legrand H, Garcia E, Macaya C, Sousa E, van der Giessen W, Colombo A, Seabra-Gomes R, Kiemeneij F, Ruy-

- grosk P, Ormiston J, Emanuelsson H, Fajadet J, Haude M, Klugmann S, Morel MA. Randomised comparison of implantation of heparin-coated stents with balloon angioplasty in selected patients with coronary artery disease (Benestent II). *Lancet* 1998; 352:673-681.
91. Roubin G, Yadav S, Iyer S, Vitek J. Carotid stent-supported angioplasty: a neurovascular intervention to prevent stroke. *Am J Cardiol* 1996; 78:8-12.
 92. Diethrich EB, Ndiaye M, Reid DB. Stenting in the carotid artery: initial experience in 110 patients. *J Endovasc Surg* 1996; 3:42-62.
 93. Criado FJ, Wellons E, Clark NS. Evolving indications for and early results of carotid artery stenting. *Am J Surg* 1997; 174:111-114.
 94. Vozzi CR, Rodriguez AO, Paolantonio D, Smith JA, Wholey MH. Extracranial carotid angioplasty and stenting. Initial results and short-term follow-up. *Tex Heart Inst J* 1997; 24:67-72.
 95. Yadav JS, Roubin GS, Iyer S, Vitek J, King P, Jordan WD, Fisher WS. Elective stenting of the extracranial carotid arteries. *Circulation* 1997; 95:376-381.
 96. Wholey MH, Jarmolowski CR, Eles G, Levy D, Buechel J. Endovascular stents for carotid artery occlusive disease. *J Endovasc Surg* 1997; 4:326-338.
 97. Henry M, Amor M, Klonaris C, Henry I, Masson I, Chati Z, Leborgne E, Hugel M. Angioplasty and stenting of the extracranial carotid arteries. *Tex Heart Inst J* 2000; 27:150-158.
 98. Teitelbaum GP, Lefkowitz MA, Giannotta SL. Carotid angioplasty and stenting in high-risk patients. *Surg Neurol* 1998; 50:300-312.
 99. Waigand J, Gross CM, Uhlich F, Kramer J, Tamaschke C, Vogel P, Luft FC, Dietz R. Elective stenting of carotid artery stenosis in patients with severe coronary artery disease. *Eur Heart J* 1998; 19:1365-1370.
 100. Bergeron P, Becquemin JP, Jausseran JM, Biasi G, Cardon JM, Castellani L, Martinez R, Fiorani P, Kniemeyer P. Percutaneous stenting of the internal carotid artery: the European CAST I Study. Carotid Artery Stent Trial. *J Endovasc Surg* 1999; 6:155-159.
 101. Roubin GS, New G, Iyer SS, Vitek JJ, Al-Mubarak N, Liu MW, Yadav J, Gomez C, Kuntz RE. Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis: a 5-year prospective analysis. *Circulation* 2001; 103:532-537.
 102. Phatouros CC, Higashida RT, Malek AM, Meyers PM, Lempert TE, Dowd CF, Halbach VV. Clinical use of stents for carotid artery disease. *Neurol Med Chir (Tokyo)* 1999; 39:809-827.
 103. Malek AM, Higashida RT, Phatouros CC, Lempert TE, Meyers PM, Smith WS, Dowd CF, Halbach VV. Stent angioplasty for cervical carotid artery stenosis in high-risk symptomatic NASCET-ineligible patients. *Stroke* 2000; 31:3029-3033.
 104. Malek AM, Higashida RT, Phatouros CC, Lempert TE, Meyers PM, Gress DR, Dowd CF, Halbach VV. Treatment of posterior circulation ischemia with extracranial percutaneous balloon angioplasty and stent placement. *Stroke* 1999; 30:2073-2085.
 105. Malek AM, Higashida RT, Phatouros CC, Lempert TE, Meyers PM, Smith WS, Dowd CF, Halbach VV. Endovascular management of extracranial carotid artery dissection achieved using stent angioplasty. *AJNR Am J Neuroradiol* 2000; 21:1280-1292.
 106. Al-Mubarak N, Roubin GS, Liu MW, Dean LS, Gomez CR, Iyer SS, Vitek JJ. Early results of percutaneous intervention for severe coexisting carotid and coronary artery disease. *Am J Cardiol* 1999; 84:600-602, A9.
 107. Vitek J, Roubin G, Iyer S. Immediate and Late Outcome of Carotid Angioplasty with Stenting. Nashville, Tenn: AANS/CNS/ASITN 1999; 43:41.
 108. Wholey M, Eles G. Clinical experience in cervical carotid artery stent placement. *Carotid Neurovasc Int* 1998; 50:301-306.
 109. Yadav JS, Roubin GS, King P, Iyer S, Vitek J. Angioplasty and stenting for restenosis after carotid endarterectomy. Initial experience. *Stroke* 1996; 27:2075-2079.
 110. Lanzino G, Mericle RA, Lopes DK, Wakhloo AK, Guterman LR, Hopkins LN. Percutaneous transluminal angioplasty and stent placement for recurrent carotid artery stenosis. *J Neurosurg* 1999; 90:688-694.
 111. Mericle RA, Kim SH, Lanzino G, Lopes DK, Wakhloo AK, Guterman LR, Hopkins LN. Carotid artery angioplasty and use of stents in high-risk patients with contralateral occlusions. *J Neurosurg* 1999; 90:1031-1036.
 112. Mathur A, Roubin GS, Iyer SS, Piamsonboon C, Liu MW, Gomez CR, Yadav JS, Chastain HD, Fox LM, Dean LS, Vitek JJ. Predictors of stroke complicating carotid artery stenting. *Circulation* 1998; 97:1239-1245.
 113. Das MB, Hertzner NR, Ratliff NB, O'Hara PJ, Beven EG. Recurrent carotid stenosis. A five-year series of 65 reoperations. *Ann Surg* 1985; 202:28-35.
 114. McCrory DC, Goldstein LB, Samsa GP, Oddone EZ, Landsman PB, Moore WS, Matchar DB. Predicting complications of carotid endarterectomy. *Stroke* 1993; 24:1285-1291.
 115. Vassilidze TV, Cernaianu AC, Gaprindashvili T, Gallucci JG, Cilley JH Jr, DelRossi AJ. Simultaneous coronary artery bypass and carotid endarterectomy. Determinants of outcome. *Tex Heart Inst J* 1994; 21:119-124.
 116. Chastain HD II, Gomez CR, Iyer S, Roubin GS, Vitek JJ, Terry JB, Levine RL. Influence of age upon complications of carotid artery stenting. UAB Neurovascular Angioplasty Team. *J Endovasc Surg* 1999; 6:217-222.
 117. Jordan WD Jr, Schroeder PT, Fisher WS, McDowell HA. A comparison of angioplasty with stenting versus endarterectomy for the treatment of carotid artery stenosis. *Ann Vasc Surg* 1997; 11:2-8.
 118. Naylor AR, Bolia A, Abbott RJ, Pye IF, Smith J, Lennard N, Lloyd AJ, London NJ, Bell PR. Randomized study of carotid angioplasty and stenting versus carotid endarterectomy: a stopped trial. *J Vasc Surg* 1998; 28:326-334.
 119. Higashida RT, Malek AM, Phatouros CC, Lempert TE, Dowd TE, Meyers PM, Halbach VV. Stenting and angioplasty for cerebrovascular disease. Prevention of ischemic stroke. In: Fisher M, Fieschi C, eds. London: Martin Dunitz Publishers; 1999: 231-252.
 120. Phatouros CC, Higashida RT, Lefler JE, Malek AM, Meyers PM, Dowd CF, Halbach VV. Angioplasty and stent placement in the extracranial circulation. Endovascular and percutaneous therapy of the brain and spine. In: Marks MP, Do HM, eds. Philadelphia: Lippincott Williams & Wilkins; 2002: 43-47.
 121. Phatouros CC, Higashida RT, Malek AM, Meyers PM, Lempert TE, Dowd CF, Halbach VV. Carotid artery stent placement for atherosclerotic disease: rationale, technique, and current status. *Radiology* 2000; 217:26-41.
 122. Beebe HG. Scientific evidence demonstrating the safety of carotid angioplasty and stenting: do we have enough to draw conclusions yet? *J Vasc Surg* 1998; 27:788-790.
 123. Hobson RW II. Status of carotid angioplasty and stenting trials. *J Vasc Surg* 1998; 27:791.
 124. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. *Lancet* 2001; 357:1729-1737.
 125. Brown MM. Vascular surgical society of Great Britain and Ireland: results of the carotid and vertebral artery transluminal angioplasty study. *Br J Surg* 1999; 86:710-711.
 126. Alberts MJ, McCann R, Smith TP. A randomized trial of carotid stenting vs endarterectomy in patients with

- symptomatic carotid stenosis. *J Neurovasc Dis* 1997; 2:228–234.
127. Alberts MJ. Results of a multicenter prospective randomized trial of carotid artery stenting versus carotid endarterectomy. *Stroke* 2001; 32:325–d.
128. Brooks WH, McClure RR, Jones MR, Coleman TC, Breathitt L. Carotid angioplasty and stenting versus carotid endarterectomy: randomized trial in a community hospital. *J Am Coll Cardiol* 2001; 38:1589–1595.
129. Yadav J. Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE). Chicago, Ill: American Heart Association; 2002.
130. Hobson RW II. CREST (Carotid Revascularization Endarterectomy versus Stent Trial): background, design, and current status. *Semin Vasc Surg* 2000; 13:139–143.
131. Hobson RW II, Brott T, Ferguson R, Roubin G, Moore W, Kuntz R, Howard G, Ferguson J. CREST: carotid revascularization endarterectomy versus stent trial. *Cardiovasc Surg* 1997; 5:457–458.
132. Teirstein PS, Massullo V, Jani S, Popma JJ, Mintz GS, Russo RJ, Schatz RA, Guarneri EM, Steuterman S, Morris NB, Leon MB, Tripuraneni P. Catheter-based radiotherapy to inhibit restenosis after coronary stenting. *N Engl J Med* 1997; 336:1697–1703.
133. Fischell TA, Carter AJ, Laird JR. The beta-particle-emitting radioisotope stent (isostent): animal studies and planned clinical trials. *Am J Cardiol* 1996; 78:45–50.
134. Laird JR, Carter AJ, Kufs WM, Hoopes TG, Farb A, Nott SH, Fischell RE, Fischell DR, Virmani R, Fischell TA. Inhibition of neointimal proliferation with low-dose irradiation from a beta-particle-emitting stent. *Circulation* 1996; 93:529–536.
135. Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, Colombo A, Schuler G, Barragan P, Guagliumi G, Molnar F, Falotico R. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002; 346:1773–1780.
136. Oesterle SN, Whitbourn R, Fitzgerald PJ, Yeung AC, Stertzer SH, Dake MD, Yock PG, Virmani R. The stent decade: 1987 to 1997. Stanford Stent Summit faculty. *Am Heart J* 1998; 136:578–599.
137. Hobson RW II, Brott T, Ferguson R, Roubin G, Moore W, Kuntz R, Howard G, Ferguson J. Regarding Statement regarding carotid angioplasty and stenting. *J Vasc Surg* 1997; 25:1117.
138. Heuser RR. Success with carotid stenting; a stroke of good luck or the wave of the future? *Cathet Cardiovasc Diagn* 1998; 44:7–8.
139. Wholey MH. Randomizing carotid endarterectomy to carotid stenting? *J Endovasc Surg* 1999; 6:127–130.
140. Theron J, Guimaraens L, Coskun O, Sola T, Martin J, Rufenacht D. Complications of carotid angioplasty and stenting. *Neurosurg Focus* 1998; 5:1–19.
141. Esselink R, Ernst J, Overtoom T. Neurological transcranial doppler and MRI monitoring in carotid stenting. *Stroke* 1998; 29:2235.
142. Do D, Lovblad K, Knemeyer H. Monitoring of carotid angioplasty and stenting using diffusion-weighted MRI. *J Endovasc Surg* 1999; 6:85.
143. Theron J, Courtheoux P, Alachkar F, Bouvard G, Maiza D. New triple coaxial catheter system for carotid angioplasty with cerebral protection. *AJNR Am J Neuroradiol* 1990; 11:869–877.
144. Henry M, Amor M, Masson I, Henry I, Tzvetanov K, Chati Z, Khanna N. Angioplasty and stenting of the extracranial carotid arteries. *J Endovasc Surg* 1998; 5:293–304.
145. Roubin G, Iyer S, Vitek J. Carotid embolic filter devices: the latest advance in carotid stenting. *J Endovasc Surg* 1999; 6:110.
146. Henry M, Amor M, Tzvetanov K, Chati Z. A new cerebral protection device for carotid angioplasty and stenting. First clinical experience with the Percusurge Guardwire. *J Endovasc Surg* 1999; 6:93.
147. Cebul RD, Snow RJ, Pine R, Hertzner NR, Norris DG. Indications, outcomes, and provider volumes for carotid endarterectomy. *JAMA* 1998; 279:1282–1287.
148. McIvor J, Steiner TJ, Perkin GD, Greenhalgh RM, Rose FC. Neurological morbidity of arch and carotid arteriography in cerebrovascular disease. The influence of contrast medium and radiologist. *Br J Radiol* 1987; 60:117–122.
149. Gabrielsen TO. Commentary: neurological complications of cerebral angiography. *AJNR Am J Neuroradiol* 1986; 15:1408–1411.
150. Wholey MH, Wholey M, Bergeron P, Diethrich EB, Henry M, Laborde JC, Mathias K, Myla S, Roubin GS, Shawl F, Theron JG, Yadav JS, Dorros G, Guimaraens J, Higashida R, Kumar V, Leon M, Lim M, Londero H, Mesa J, Ramee S, Rodriguez A, Rosenfield K, Teitelbaum G, Vozzi C. Current global status of carotid artery stent placement. *Cathet Cardiovasc Diagn* 1998; 44:1–6.
151. Wholey MH, Wholey M, Mathias K, Roubin GS, Diethrich EB, Henry M, Bailey S, Bergeron P, Dorros G, Eles G, Gaines P, Gomez CR, Gray B, Guimaraens J, Higashida R, Ho DS, Katzen B, Kambara A, Kumar V, Laborde JC, Leon M, Lim M, Londero H, Mesa J, Musacchio A, Myla S, Ramee S, Rodriguez A, Rosenfield K, Sakai N, Shawl F, Sievert H, Teitelbaum G, Theron JG, Vaclav P, Vozzi C, Yadav JS, Yoshimura SI. Global experience in cervical carotid artery stent placement. *Catheter Cardiovasc Interv* 2000; 50:160–167.
152. Hunter DW, Chamsuddin A, Bjarnason H, Kowalik K. Preventing contrast-induced nephropathy with fenoldopam. *Tech Vasc Interv Radiol* 2001; 4:53–56.
153. Herbert JM, Dol F, Bernat A, Falotico R, Lale A, Savi P. The antiaggregating and antithrombotic activity of clopidogrel is potentiated by aspirin in several experimental models in the rabbit. *Thromb Haemost* 1998; 80:512–518.
154. Makkar R, Eigler N, Kaul S. Effects of clopidogrel, aspirin and combined therapy in a porcine ex vivo model of high-shear induced stent thrombosis. *Eur Heart J* 1998; 19:1538–1546.
155. Luginbuhl M, Remonda L. Interventional neuroradiology. Recent developments and anaesthesiologic aspects. *Minerva Anesthesiol* 1999; 65:445–454.
156. Elgersma OE, Buijs PC, Wust AF, van der Graaf Y, Eikelboom BC, Mali WP. Maximum internal carotid arterial stenosis: assessment with rotational angiography versus conventional intraarterial digital subtraction angiography. *Radiology* 1999; 213:777–783.
157. Mehigan JT, Olcott CT. The carotid “string” sign. Differential diagnosis and management. *Am J Surg* 1980; 140:137–143.
158. Investigators TE. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. The EPIC-LOG Investigators. *N Engl J Med* 1997; 336:1689–1696.
159. Investigators TC. Randomised placebo-controlled trial of abciximab before and during coronary intervention in refractory unstable angina: the CAPTURE Study. *Lancet* 1997; 349:1429–1435.
160. Chronos N, Vahanian A, Betriu A, Emanuelsson H, Goldberg S, Gulba D, van Hout BA. Use of abciximab in interventional cardiology. *Eur Heart J* 1998; 19:D31–D39.
161. Jeong MH, Owen WG, Staab ME, Srivatsa SS, Sangiorgi G, Stewart M, Holmes DR Jr, Schwartz RS. Porcine model of stent thrombosis: platelets

- are the primary component of acute stent closure. *Cathet Cardiovasc Diagn* 1996; 38:38–43.
162. Bergeron P, Chambran P, Hartung O, Bianca S. Cervical carotid artery stenosis: which technique, balloon angioplasty or surgery? *J Cardiovasc Surg (Torino)* 1996; 37:73–75.
 163. Mathur A, Dorros G, Iyer SS, Vitek JJ, Yadav SS, Roubin GS. Palmaz stent compression in patients following carotid artery stenting. *Cathet Cardiovasc Diagn* 1997; 41:137–140.
 164. Rosenfield K, Schainfeld R, Pieczek A, Haley L, Isner JM. Restenosis of endovascular stents from stent compression. *J Am Coll Cardiol* 1997; 29:328–338.
 165. Piamsomboon C, Roubin GS, Liu MW, Iyer SS, Mathur A, Dean LS, Gomez CR, Vitek JJ, Chattipakorn N, Yates G. Relationship between oversizing of self-expanding stents and late loss index in carotid stenting. *Cathet Cardiovasc Diagn* 1998; 45:139–143.
 166. Izzat MB, Mehta D, Bryan AJ, Reeves B, Newby AC, Angelini GD. Influence of external stent size on early medial and neointimal thickening in a pig model of saphenous vein bypass grafting. *Circulation* 1996; 94:1741–1745.
 167. Sacks D, Marinelli DL, Martin LG, Spies JB. Reporting standards for clinical evaluation of new peripheral arterial revascularization devices. Technology Assessment Committee. *J Vasc Interv Radiol* 1997; 8:137–149.
 168. Martin LG, Rundback JH, Sacks D, Cardella JF, Rees CR, Matsumoto AH, Meranze SG, Schwartzberg MS, Silverstein ML, Lewis CA. Quality improvement guidelines for angiography, angioplasty, and stent placement in the diagnosis and treatment of renal artery stenosis in adults. *J Vasc Interv Radiol* 2002; 13:1069–1083.
 169. Ryan TJ, Bauman WB, Kennedy JW, Kereiakes DJ, King SB III, McCallister BD, Smith, SC Jr, Ullyot DJ. Guidelines for percutaneous transluminal coronary angioplasty. A report of the Am Heart Association/Am College of Cardiology Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Committee on Percutaneous Transluminal Coronary Angioplasty). *Circulation* 1993; 88:2987–3007.
 170. Smith SC Jr, Dove JT, Jacobs AK, Kennedy JW, Kereiakes D, Kern MJ, Kuntz RE, Popma JJ, Schaff HV, Williams DO, Gibbons RJ, Alpert JP, Eagle KA, Faxon DP, Fuster V, Gardner TJ, Gregoratos G, Russell RO. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines)—executive summary. A report of the Am College of Cardiology/Am Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). *J Am Coll Cardiol* 2001; 37:2215–2239.
 171. Yadav J. Stenting and angioplasty with protection in patients at high risk for endarterectomy (The SAPHIRE Study). Chicago, Ill: AHA Scientific Sessions; 2002.
 172. Illig KA, Zhang R, Tanski W, Benesch C, Sternbach Y, Green RM. Is the rationale for carotid angioplasty and stenting in patients excluded from NASCET/ACAS or eligible for AR-CHeR justified? *J Vasc Surg* 2003; 37:575–581.
 173. Meyers PM, Higashida RT, Phatouros CC, Malek AM, Lempert TE, Dowd CF, Halbach VV. Cerebral hyperperfusion syndrome after percutaneous transluminal stenting of the craniocervical arteries. *Neurosurgery* 2000; 47:335–345.
 174. Schoser BG, Heesen C, Eckert B, Thie A. Cerebral hyperperfusion injury after percutaneous transluminal angioplasty of extracranial arteries. *J Neurol* 1997; 244:101–104.
 175. Hirayama T, Katayama Y, Kano T, Tsubokawa T. Control of Systemic Hypertension with Diltiazem, a calcium-antagonist, in patients with a mildly elevated intracranial pressure: a comparative study. *Neurol Res* 1994; 16:97–99.
 176. Qureshi AI, Luft AR, Lopes DK, Lanzino G, Fessler RD, Sharma M, Guterman LR, Hopkins LN. Postoperative hypotension after carotid angioplasty and stenting: report of three cases. *Neurosurgery* 1999; 44:1320–1324.
 177. Hobson RW II, Goldstein JE, Jamil Z, Lee BC, Padberg FT Jr, Hanna AK, Gwertzman GA, Pappas PJ, Silva MB Jr. Carotid restenosis: operative and endovascular management. *J Vasc Surg* 1999; 29:228–238.
 178. Chakhtoura EY, Hobson RW II, Goldstein J, Simonian GT, Lal BK, Haser PB, Silva MB Jr, Padberg FT Jr, Pappas PJ, Jamil Z. In-stent restenosis after carotid angioplasty-stenting: incidence and management. *J Vasc Surg* 2001; 33:220–226.
 179. Leger AR, Neale M, Harris JP. Poor durability of carotid angioplasty and stenting for treatment of recurrent artery stenosis after carotid endarterectomy: an institutional experience. *J Vasc Surg* 2001; 33:1008–1014.
 180. Ouriel K, Shortell CK, Illig KA, Greenberg RK, Green RM. Intracerebral hemorrhage after carotid endarterectomy: incidence, contribution to neurologic morbidity, and predictive factors. *J Vasc Surg* 1999; 29:82–89.
 181. Jordan WD Jr, Roye GD, Fisher WS III, Redden D, McDowell HA. A cost comparison of balloon angioplasty and stenting versus endarterectomy for the treatment of carotid artery stenosis. *J Vasc Surg* 1998; 27:16–24.
 182. Ricotta JJ, Hargadon T, O'Brien-Irr M. Cost management strategies for carotid endarterectomy. *Am J Surg* 1998; 176:188–192.
 183. Fisher WS III, Jordan WD. Carotid angioplasty. *Surg Neurol* 1998; 50:295–299.
 184. Kilaru S, Korn P, Kasirajan K, Lee TY, Beavers FP, Lyon RT, Bush HL, Kent KC. Is carotid angioplasty and stenting more cost effective than carotid endarterectomy? *J Vasc Surg* 2003; 37:331–339.
 185. Shigeyama J, Ito S, Kondo H, Ito O, Matsushita T, Okamoto M, Toyama J, Ban Y, Fukutomi T, Itoh M. Angiographic classification of coronary dissections after plain old balloon angioplasty for prediction of regression at follow-up. *Jpn Heart J* 2001; 42:393–408.
 186. Staikov IN, Arnold M, Mattle HP, Remonda L, Sturzenegger M, Baumgartner RW, Schroth G. Comparison of the ECST, CC, and NASCET grading methods and ultrasound for assessing carotid stenosis. European Carotid Surgery Trial. North Am Symptomatic Carotid Endarterectomy Trial. *J Neurol* 2000; 247:681–686.
 187. Rothwell PM, Gibson RJ, Slattery J, Warlow CP. Prognostic value and reproducibility of measurements of carotid stenosis. A comparison of three methods on 1001 angiograms. European Carotid Surgery Trialists' Collaborative Group. *Stroke* 1994; 25:2440–2444.
 188. Vanninen R, Manninen H, Koivisto K, Tulla H, Partanen K, Puranen M. Carotid stenosis by digital subtraction angiography: reproducibility of the European Carotid Surgery Trial and the North Am Symptomatic Carotid Endarterectomy Trial measurement methods and visual interpretation. *AJNR Am J Neuroradiol* 1994; 15:1635–1641.