SVS
SOCIETY for VASCULAR SURGERY
SPECIAL COMMUNICATION

Management of atherosclerotic carotid artery disease: Clinical practice guidelines of the Society for Vascular Surgery

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The Society for Vascular Surgery (SVS) appointed a committee of experts to formulate evidence-based clinical guidelines for the management of carotid stenosis. In formulating clinical practice recommendations, the committee used systematic reviews to summarize the best available evidence and the GRADE scheme to grade the strength of recommendations (GRADE 1 for strong recommendations; GRADE 2 for weak recommendations) and rate the quality of evidence (high, moderate, low, and very low quality). In symptomatic and asymptomatic patients with low-grade carotid stenosis (<50% in symptomatic and <60% in asymptomatic patients), we recommend optimal medical therapy rather than revascularization (GRADE 1 recommendation, high quality evidence). In symptomatic patients with moderate to severe carotid stenosis (more than 50%), we recommend carotid endarterectomy plus optimal medical therapy (GRADE 1 recommendation, high quality evidence). In symptomatic patients with moderate to severe carotid stenosis (≥50%) and high perioperative risk, we suggest carotid artery stenting as a potential alternative to carotid endarterectomy (GRADE 2 recommendation, low quality evidence). In asymptomatic patients with moderate to severe carotid stenosis (≥60%), we recommend carotid endarterectomy plus medical management as long as the perioperative risk is low (GRADE 1 recommendation, high quality evidence). We recommend against carotid artery stenting for asymptomatic patients with moderate to severe (≥60%) carotid artery stenosis (GRADE 1 recommendation, low quality evidence). A possible exception includes patients with ≥80% carotid artery stenosis and high anatomic risk for carotid endarterectomy. (J Vasc Surg 2008;48:480-6.)

The Society for Vascular Surgery (SVS) undertook the task of developing clinical practice guidelines to aid over 2500 of its member surgeons and their patients in the process of decision-making. Realizing that some areas in vascular surgery are controversial either because of lack of evidence or because of the presence of inconsistent and imprecise evidence, the SVS designated selected topics as high priority areas in need of clinical practice guidelines. The SVS appointed committees with expertise in the questions at hand and drew on systematic reviews of the available evidence to inform its key recommendations. Results from systematic reviews and their quantitative pooling of evidence, eg, meta-analysis, offer higher precision and apply to a wider range of patients than individual trials.[1] These committees commissioned the Knowledge and Encounter Unit, Mayo Clinic, Rochester, Minnesota, to search for relevant existing reviews and to conduct new systematic reviews to answer specific questions.

One of the topics chosen by the SVS is the management of carotid artery stenosis. Carotid endarterectomy has long been considered the best surgical treatment for carotid disease with a proven track record in reducing mortality and morbidity.[2,3] However, carotid stenting has emerged as an alternative, effective and less invasive approach that may be more attractive to patients at higher perioperative risk and patients who prefer to avoid open procedures and their associated morbidities. Several randomized controlled trials (RCTs) were conducted to compare the two procedures with some showing stenting to be noninferior to endarterectomy[4,5] and some showing inferiority.[6] When a meta-analysis pooled these studies, the pooled risk estimates were imprecise with very wide confidence intervals[7] making inference from these trials challenging. Knowing that new RCTs were recently published, the carotid committee of

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the SVS requested an update of previous reviews to determine the current status of the research evidence about the treatment of carotid artery stenosis in the two clinical scenarios of symptomatic and asymptomatic patients.

In issuing clinical practice guidelines, the SVS has adopted the GRADE system because it separates the quality of evidence from the strength of recommendations.[8] This separation allows guideline users (clinicians, patients, and policymakers) to recognize factors other than evidence, such as patient values and preferences that guideline committees considered when making these recommendations. Hence, despite lower quality evidence, the committee may issue a strong recommendation if the values and preferences that guideline developers bring to bear are such that when considering even low quality evidence, they are confident that the benefits of an intervention outweigh its undesirable outcomes (or vice versa).[9]

The GRADE system depicts recommendations as either strong (GRADE 1) denoted by the phrase "we recommend" or weak (GRADE 2) denoted by the phrase "we suggest". Aside from the strength of recommendations, the quality of evidence is rated as high quality (typically derived from well conducted large and consistent randomized trials), moderate quality (typically derived from less rigorous or inconsistent randomized trials or some observational studies), and low or very low quality (derived from observational studies, case series, and unsystematic clinical observations).

In this article, the carotid committee of the SVS presents five key recommendations encompassing several permutations and clinical scenarios to clarify the roles of carotid endarterectomy, carotid stenting, and best medical care, in the management of symptomatic and asymptomatic patients with low, moderate, and severe degrees of stenosis. Recommendations are followed by the corresponding evidence: values and preferences, which are factors other than evidence that the committee considered when issuing recommendations; and if needed, technical remarks, describing the committee's consensus regarding best practices in medical management, carotid endarterectomy, and carotids stenting.

RECOMMENDATION

In symptomatic and asymptomatic patients with low grade carotid stenosis (stenosis <50% in symptomatic patients and <60% in asymptomatic patients); we recommend optimal medical therapy rather than revascularization (GRADE 1 recommendation, high quality evidence).

Evidence

A systematic review and meta-analysis of randomized trials that compared carotid endarterectomy with medical management in patients with ipsilateral symptomatic carotid stenosis[3] pooled results from two large multicenter RCTs that included a total of 5950 patients, the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[10,11] and the European Carotid Surgery Trial (ECST).[12] Patients with low grade stenosis (NASCET <50%, ECST <70%) were in fact, harmed by surgery to the extent that endarterectomy increased the risk of disabling stroke or death by 20% (95% confidence interval [CI] 0%-44%) and the number of patients needed to be operated on to cause one disabling stroke or death was 45 (95% CI 22 - infinity). Despite the inadequate blinding of outcome assessors in NASCET and ECST (unblinded assessors presented data to a blinded outcome review board); both trials were well executed, used the intention-to-treat analysis, and had adequate allocation concealment.

Values statement

In formulating this recommendation, the committee placed a relatively higher value on preventing harms associated with carotid endarterectomy, particularly stroke, death and myocardial infarction, and a relatively lower value on the cost and side effects of medical management (eg, gastrointestinal bleeding with aspirin, myopathy with statins, and so on).

Medical therapy

The best medical management for stroke prevention was highlighted in clinical practice guidelines issued jointly in 2006 by the American Heart Association and the American Stroke Association, and cosponsored by the Council on Cardiovascular Radiology and Intervention and the American Academy of Neurology.[13] Lowering blood pressure to a target below 120/80 mm Hg by life style interventions and antihypertensive treatment is recommended in persons who have had an ischemic stroke or transient ischemic attack (TIA) and are beyond the hyperacute period. Angiotensin-converting enzymes and angiotensin receptor blockers are recommended as first-choice medications for patients with diabetes. Glucose control to near-normoglycemic levels (target hemoglobin A1C ≤7%) is recommended among diabetics to reduce microvascular complications and, with lesser certainty, macrovascular complications. Patients with elevated cholesterol, comorbid coronary artery disease, or evidence of an atherosclerotic origin should be managed according to NCEP III guidelines, which include lifestyle modification and/or medications. Statin agents are recommended targeting low density lipoprotein cholesterol (LDL-C) of <100 mg/dL for those with coronary heart disease (CHD) or symptomatic atherosclerotic disease and LDL-C of <70 mg/dL for very high-risk persons with multiple risk factors. Patients who have smoked in the last year should be counseled to quit. Counseling and smoking cessation medications have been found to be effective in helping smokers to quit. Lower quality evidence suggested possible benefits of avoiding environmental tobacco smoke, reduction of alcohol consumption by heavy drinkers, weight reduction for obese patients, and increasing physical activity. Antiplatelet agents are recommended for patients with noncardioembolic ischemic stroke or TIA. Aspirin (50 to 325 mg/d), the combination of aspirin and extended-release dipyridamole, and clopidogrel are all acceptable options for initial therapy.[13]

RECOMMENDATION

In symptomatic patients with moderate to severe carotid stenosis (≥50%) we recommend carotid endarterectomy plus optimal medical therapy (GRADE 1 recommendation, high quality evidence).

Evidence

Moderate stenosis. Among symptomatic NASCET patients with stenosis of 50% to 69%, the 5-year rate of any ipsilateral stroke was 15.7% in patients treated surgically compared with 22.2% in those treated medically. To prevent one ipsilateral stroke during the 5-year follow up period, 15 patients would have to undergo carotid endarterectomy.[11]

High-grade stenosis. Symptomatic NASCET patients with stenosis of 70% to 99% who underwent endarterectomy had a cumulative risk of any ipsilateral stroke at 2 years of 9% compared with 26%for those who were treated medically. To prevent one ipsilateral stroke, six patients would have to undergo carotid endarterectomy. For a major or fatal ipsilateral stroke, the corresponding estimates were 2.5% and 13.1%. To prevent one major or fatal ipsilateral stroke, nine patients would have to undergo carotid endarterectomy.[10]

Results from ECST were similarly supportive of endarterectomy in symptomatic patients with 70% to 99% stenosis. The 3-year risk of ipsilateral stroke was 2.8% in patients randomized to endarterectomy and16.8% in those randomized to medical therapy alone. The 3-year risk of disabling or fatal stroke, or surgical death was 6.0% for the surgical group and 11.0% for the medically treated patients. Therefore, to prevent an ipsilateral stroke or the composite outcome of disabling or fatal stroke or surgical death, 7 and 20 patients had to undergo endarterectomy, respectively.[12]

Carotid endarterectomy for nonhemispheric symptoms, vertebrobasilar symptoms, acute stroke, or for stroke or TIA with internal carotid occlusion is not supported by high quality evidence but rather by very low quality evidence (case series and unsystematic observations).[14-17] In these settings, and faced with paucity of evidence, surgeon's complication rate and patient's values and preferences play a major role in decision making.

The exclusion criteria for NASCET withheld endarterectomy from patients with life expectancy of less than 5 years and patients with significant comorbid conditions (massive stroke, liver, kidney or respiratory failure, or cancer). They also excluded patients over the age of 79, those who had a prior ipsilateral carotid endarterectomy, and those in which angiographic visualization of both carotid arteries and intracranial branches was not possible. The risk benefit balance in these populations is, therefore, unclear and our recommendation requires judicious and selective application. In fact, some observational studies support the safety and efficacy of carotid endarterectomy in some of these excluded groups.[18,19] Case by case decision-making, involvement of patients' values and preferences, as well as surgeons experience and surgical center outcomes should be considered.

There are no data to suggest that carotid endarterectomy is less effective than medical management in any cohort of patients with symptomatic high-grade (≥50%) carotid stenosis. In addition, no data exist to support or refute the value of endarterectomy for the management of symptomatic patients with nonstenotic but severely ulcerated plaques. While there could be a subset of symptomatic patients with less than 50% stenosis that might benefit from CEA, current published data do not permit identification of such a cohort.

Values statement

In recommending endarterectomy for symptomatic patients with moderate to severe (≥50%) carotid stenosis, the committee placed a relatively higher value on preventing the outcome of stroke with the associated disability and morbidity and a relatively lower value on avoiding the downsides of endarterectomy (cost, perioperative complications such as death, and myocardial infarction).

Carotid endarterectomy

Through a longitudinal or transverse incision, after systemic heparin administration the internal, common and external carotid arteries are sequentially occluded with atraumatic vascular clamps. A longitudinal incision is made anteriorly in the common carotid artery proximal to the obviously diseased segment, and extended distally along the anterior surface of the internal carotid artery beyond the offending plaque. If a shunt is elected it is inserted at this time. Dividing the digastric muscle distally or the omohyoid muscle proximally may increase exposure.

The endarterectomy is begun by carefully developing a subadvential plane with a freer dissector in the common carotid artery, completed circumferentially, feathered to a good end-point proximally and continued distally, everting the plaque out of the external carotid artery and then completed in the internal carotid artery where the plaque transitions into normal intima. Today, most evidence strongly supports arteriotomy closure with an autogenous vein, Dacron, or polytetrafluoroethylene patch using a running 6-0 polypropylene suture.

Alternatively, eversion endarterectomy is performed by obliquely amputating the internal carotid artery at the common carotid bifurcation and rolling back the adventitial layer until normal intima is recognized distally at the distal endpoint. Residual plaque in the common and external carotid arteries is endarterectomized at this time. After completion of the endarterectomy, the internal carotid artery is re-anastomosed to the common carotid artery with a running 6-0 polypropylene suture.

RECOMMENDATION

In symptomatic patients with moderate to severe carotid stenosis (≥50%) and high perioperative risk, we suggest carotid artery stenting as a potential alternative treatment to carotid endarterectomy. (GRADE 2 Recommendation, low quality evidence). High anatomic risk defined as: (1) previous CEA with recurrent stenosis; (2) prior ipsilateral radiation therapy to neck with permanent skin changes; (3) previous

Table. Summary of evidence (carotid endarterectomy vs stenting)

		Quality assessment				
No of studies	*Design*	*Limitations*	*Consistency*	*Directness*	*Imprecision*	*Quality*
Death at 30 days						
5	RCTs	Serious[a]	No important inconsistency	No uncertainty about directness	None	⊕⊕⊕O Moderate
Any stroke at 30 days						
5	RCTs	Serious[a]	No important inconsistency	No uncertainty about directness	Sparse or imprecise data[b]	⊕⊕OO Low
Non fatal myocardial infarction at 30 days						
3	RCTs	Serious[a]	No important inconsistency	No uncertainty about directness	None	⊕⊕⊕O Moderate

[a]Allocation concealment was not conducted in four trials, and seven trials did not blind data collectors or outcome assessors.
[b]Imprecision is based on risk difference which has wide confidence interval.

ablative neck surgery (eg, radical neck dissection, laryngectomy); (4) common carotid artery stenosis below the clavicle; (5) contralateral vocal cord paralysis; and (6) presence of a tracheostomy stoma.

The authors could not define "high medical risk" with equal precision. Dialysis dependent renal failure, extremely low left ventricular ejection fraction, and oxygen or steroid dependent chronic lung disease are examples of potentially useful high medical risk criteria. Data on the influence of such medical factors on carotid endarterectomy outcomes are inconsistent and generally of poor quality.

Evidence

Upon the request of the carotid committee of the SVS, a meta-analysis of randomized trials that compared carotid angioplasty and carotid endarterectomy was updated to include recent trials.[20] This review pooled results from ten RCTs that included a total of 3182 patients with carotid stenosis over 50%. The majority of patients were symptomatic and in one of the trials they were designated as being at high risk for carotid endarterectomy.[5] Allocation concealment and blinding of outcome assessors were adequate in 6/10 and 2/10 trials, respectively. At 30 days and compared with endarterectomy, carotid angioplasty was associated with nonsignificant reduction in the risk of death (risk ratio [RR] 0.61 [0.27-1.37]; 95% CI 0.43, 1.66; $I^2 = 0\%$); nonsignificant reduction in the risk of non-fatal myocardial infarction (RR 0.43 [0.17-1.11]; CI 0.16, 0.96; $I^2 = 0\%$); and nonsignificant increase in the risk of any stroke (RR 1.29 [0.37-2.26]; CI 0.82, 2.31; $I^2 = 40\%$). Considering that these procedures are performed to prevent stroke, the statistically nonsignificant increase in strokes associated with stenting is perhaps clinically significant. In terms of comparing stenting with medical management, only two trials are available.[21,22] Pooled estimate of odds ratio of the outcome of death or any stroke was imprecise and associated with high heterogeneity (OR 0.28; 95% CI 0.02-3.23; I =70%).[23] Hence, the evidence for stenting appears to be derived solely from comparisons with endarterectomy. The Table summarizes the evidence comparing endarterectomy and stenting using relative and absolute risk measures.

Values statement

Patients who place high value on avoiding surgical scar or perioperative morbidity and mortality may opt for stenting, whereas stroke-averse patients may opt for carotid endarterectomy. Guideline developers placed a relatively higher value on avoiding the outcome of stroke and a relatively lower value on statistically significant but perhaps clinically trivial increases in perioperative complications.

Carotid artery stenting

Carotid artery stenting is performed under local anesthesia with mild or no sedation. Patients are placed on clopidogrel and aspirin. Arterial access is achieved through a retrograde femoral artery approach. Brachial, radial, or direct CCA approaches have been used in some instances. Noninvasive or angiographic arch assessment assists in guiding the optimal approach to the CCA. Patients are heparinized to an activated clotting time (ACT) of 250-300 seconds. The CCA is selectively cannulated with a 5F directional catheter over a 0.035-inch guidewire. Currently available stents are deployed through a 6F sheath or an 8F guiding catheter placed in the CCA within a few centimeters of the lesion. The use of one of several embolic protection devices (EPD) is recommended. It seems unlikely that a randomized trial will be performed to determine their neurologic efficacy. Distal filters or occlusive balloons have been most commonly used and are approved in the United States (US). Angioplasty is performed with a 3 to 4 mm balloon to ensure safe passage of the stent. Atropine may be given prior to angioplasty or selectively, to prevent vasovagal complications. Current rapid-exchange stent platforms work over the 0.014-inch wires of the EPDs. Self-expanding nitinol stents are preferred; open and closed cell designs, as well as tubular and tapered shapes have been approved for use in the US. Reliable comparative studies are still required to guide selection of one stent design over the other.

Post-stenting angioplasty is performed with a balloon undersized by 20% to 40% of CA diameter and the stent length. A moderate residual stenosis (20% to 30%) is generally acceptable since continued expansion of nitinol stents

Table. Continued.

Relative risk (95% CI)	*Summary of findings (per 1000 patients)*	
	Endarterectomy median event rate	*Stenting calculated event rate*
RR 0.61 (0.27 to 1.37)	13.7	8.4
RR 1.29 (0.37 to 2.26)	27.0	34.8
RR 0.43 (0.17 to 1.11)	9.8	4.2

may show additional luminal recruitment over time. Finally, the EPD is removed over a retrieval catheter. The completion angiogram must visualize the extra- and intracranial circulation in two or more views. The sheath is removed when the ACT is ≤150 seconds; arterial closure devices can be used to obviate the need for normalization of the ACT. Patients are placed on clopidogrel for at least 4 weeks and on aspirin indefinitely.

RECOMMENDATION

In asymptomatic patients with moderate to severe carotid stenosis (≥60%), we recommend carotid endarterectomy plus medical management as long as perioperative risk is low. (GRADE 1 recommendation, high quality evidence).

Evidence

The efficacy of carotid endarterectomy in asymptomatic patients was evaluated in a systematic review and meta-analysis that pooled results from three RCTs.[2] These trials included 5223 patients with asymptomatic moderate to severe carotid stenosis. The degree of stenosis was ≥50% in the Veteran Affairs Cooperative Study[24] and ≥60% in the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST).[25,26] All three trials had high methodological quality including allocation concealment, blinded outcome assessment and applied intention-to-treat analysis. The incidence of 30-day perioperative stroke or death was 2.8%. Patients who underwent carotid endarterectomy fared better than those treated medically. The relative risk of perioperative stroke, death or any subsequent stroke was 0.69 (0.57 to 0.83) and the relative risk of perioperative stroke, death, or subsequent ipsilateral stroke was 0.71 (0.55 to 0.90), both favoring endarterectomy. There was no important inconsistency in results across trials ($I^2 = 0$). For the outcome of any stroke or death, there was a nonsignificant trend towards fewer events in the surgical group (RR 0.92, 95% CI 0.83 to 1.02).

The exclusion criteria for ACAS and ACST were similar to those for NASCET, and participating surgeons in both studies were preselected for good surgical results. The application of our recommendation to excluded groups, including trial-eligible patients cared for in centers with not as good surgical outcomes, requires judgment that considers the potential benefits and harms of the alternative courses of action as well as the values and preferences of the patient and their clinical circumstances; if applying our recommendations to these contexts, clinicians should consider these as suggestions (GRADE 2). Similarly, newer medical therapies (statins, more potent antiplatelet agents, and improved management for diabetes and hypertension) might favorably alter the outcome of medical management sufficiently to diminish the strength of this recommendation. Newer therapies were included in ACST and their use in that study did not result in a diminution of the benefit of endarterectomy from that seen in ACAS.

Values statement

The committee placed a relatively higher value on preventing the outcome of stroke with the associated disability and morbidity and a relatively lower value on avoiding the downsides of endarterectomy (cost, perioperative complications such as death and myocardial infarction).

RECOMMENDATION

We recommend against carotid artery stenting for asymptomatic patients with carotid artery stenosis. (GRADE 1, low quality evidence).

Evidence

Paucity of evidence hampers the evaluation of carotid artery stenting in the management of patients with asymptomatic carotid disease. No RCTs have been published comparing carotid stenting with medical management in asymptomatic patients. In terms of comparing stenting with endarterectomy in asymptomatic patients, the systematic review by Murad et al[20] included two trials that reported this comparison.[5,27] There were insufficient data to evaluate the effect of therapy on individual outcomes. The effect of therapy on the composite outcome of death, stroke, and nonfatal myocardial infarction was very imprecise (RR0.52; 95% CI 0.20 to 1.33) due to the small number of patients (323) and events (18). All the events were in the SAPHIRE trial whereas Brooks et al did not

contribute to the pooled estimate because it was a zero-event trial, ie, none of the patients in either study arm had a death, stroke, or myocardial infarction. Hence, the committee is unable to determine whether stenting is noninferior to endarterectomy or best medical management. One possible exception to this recommendation is the asymptomatic patient with low medical risk, compelling carotid disease, and high-risk anatomy (as defined above). For these patients the committee suggests that practitioners consider carotid artery stenting as a potential alternative to medical management or carotid endarterectomy if the carotid artery stenosis is ≥80%.

Values statement

In making this recommendation, guideline developers placed a relatively high value on avoiding the potential downsides of an invasive procedure in the clinical context of low risk patients with unclear risk-to-benefit ratio. In these patients, medical therapy may provide sufficient reduction in the risk of events at a favorable risk-to-benefit ratio. Furthermore, in medically high-risk patients it seems likely that in the absence of symptoms, medical therapy will be safer than either surgical or endovascular treatments.

SUMMARY AND CONCLUSIONS

Using the best available evidence, we have made recommendations for the management of commonly encountered carotid disease patients. We have applied the GRADE system to these recommendations in order to indicate the strength of the data supporting our guidelines and the strength of our convictions in offering these guidelines. Factors other than data (eg, experience, values, surgeon, or patient preferences) often play a role in decision making, especially when supporting data are imperfect. The strength of a recommendation may not be solely a function of the strength of the supporting data. To summarize our recommendations in order of their strength and the quality of supporting data, we offer the following:

Strong Recommendations + High Quality Evidence:

a) We recommend optimal medical therapy without revascularization in symptomatic patients with <50% stenosis.
b) We recommend optimal medical therapy without revascularization in asymptomatic patients with <60% stenosis.
c) We recommend carotid endarterectomy plus optimal medical therapy in symptomatic patients with ≥50% carotid stenosis.
d) We recommend carotid endarterectomy plus optimal medical management in asymptomatic patients with ≥60% stenosis and low perioperative risk.

Weak Recommendation + Low Quality Evidence:

e) We suggest carotid stenting as a potential alternative treatment to carotid endarterectomy in symptomatic patients with ≥50% stenosis and high operative perioperative risk.
f) We suggest that carotid artery stenting is inappropriate for asymptomatic patients with carotid artery stenosis. Possible exceptions may include patients with acceptable medical risk who present with severe carotid artery stenoses (≥80%) and high anatomic risk for carotid endarterectomy (as defined above) but with compelling anatomy for stenting.

Practice guidelines can be only as robust as their evidence basis. In the absence of high quality, reliable data, clinical decisions must be based on lower quality data and on clinical experience, judgment, values, and preferences. The GRADE system allows us to separate the strength of our recommendations from the quality of our supporting data. The authors of this article recognize that the data from which these guidelines were formulated are imperfect and that our values played a significant role in guideline formulation. Furthermore, the huge variability among patients with cerebrovascular disease, both in their anatomic and physiologic features, makes application of guidelines problematic. Often patients do not mesh cleanly with the criteria established for clinical trial eligibility.

We also recognize that the very criteria used to define patient cohorts are subject to change. For example, we have used degree of stenosis to define various patient cohorts throughout. Symptomatic patients with <50% stenosis are determined to be best served by medical therapy alone, while those with ≥50% stenosis are deemed to require surgery. Asymptomatic patients with ≥60% stenosis are deemed candidates for endarterectomy, while in those with <60% stenosis, medical therapy is preferred. The severity of stenosis may not be the best predictor of plaque behavior, but it is reproducibly quantifiable and currently used as the measure of disease severity in all clinical trials. We recognize that in the future these guidelines will be revised if new methodologies can better predict the clinical behavior of atherosclerotic plaques.

Consensus eluded the authors in several areas. We could not completely agree on the role of carotid stenting in asymptomatic patients. We did agree that data supporting stenting in this setting were of poor quality because of the absence of a medically managed control group. A majority felt that patients with acceptable medical risk, high anatomic risk, and compelling carotid pathology should be considered candidates for stenting. A minority felt that in the absence of trials comparing medical therapy with stenting in this cohort, such a recommendation, even as GRADE 2 was ill advised.

We also failed to reach consensus over many details in the technical performance of endarterectomy and stenting. Originally we had hoped to present technical guidelines using the GRADE system, but we found both that supporting data were inconsistent and generally of low quality and that all recommendations were GRADE 2 (at best). For example, the authors could not reach consensus on whether protamine reversal of heparin after carotid declamping should be recommended or not recommended. Some small scale prospective randomized trials support protamine use and others support its avoidance. Similarly, we could not reach consensus on optimal cerebral monitoring and protection during endarterectomy or on the preferred patch for use in carotid closure. Since each of us has strong, though not necessarily fully evidence-based, opinions on these and other technical

points and since each of us is reputed to be expert in endarterectomy and/or stenting, we felt that we must report our inability to reach consensus and conclude that each surgeon must establish his/her own preferred technique, monitor his/her results carefully, and modify the chosen technique if problems are identified or compelling new data become available.

We are hopeful that these guidelines will be useful to carotid surgeons, will promote a uniform, evidence based, effective and safe approach to carotid disease management, and will serve the best interests of those patients who seek our help.

This article is dedicated to Dr Robert Hobson in recognition of his leading role in bringing scientific discipline to the study of carotid disease management.

AUTHOR CONTRIBUTIONS

Conception and design: RH, WM, EA, MM, KC, AC, VM, ME, DM, RB, BP
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REFERENCES

1. Oxman A, Guyatt G, Cook D, Montori V. Summarizing the evidence. In: Guyatt G, Rennie D, editors. Users' guides to the medical literature: a manual for evidence-based clinical practice. Chicago: AMA Press; 2002. p. 55-173.
2. Chambers BR, Donnan GA. Carotid endarterectomy for asymptomatic carotid stenosis.[update of Cochrane Database Syst Rev 2000;(2): CD001923; PMID: 10796451]. Cochrane Database of Syst Rev 2005(4):CD001923.
3. Cina CS, Clase CM, Haynes RB. Carotid endarterectomy for symptomatic carotid stenosis. Cochrane Database Syst Rev 2000(2):CD001081.
4. CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomized trial. Lancet 2001;357:1729-37.
5. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493-1501.
6. Space Collaborative Group, Ringleb PA, Allenberg J, Brückmann H, Eckstein HH, Fraedrich G, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomized noninferiority trial. Lancet 2006;368:1239-47.
7. Coward LJ, Featherstone RL, Brown MM. Safety and efficacy of endovascular treatment of carotid artery stenosis compared with carotid endarterectomy: a Cochrane systematic review of the randomized evidence. Stroke 2005;36:905-11.
8. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ 2004;328:1490.
9. Swiglo B, Murad M, Schünemann H, Kunz R, Vigersky RA, Guyatt GH, et al. A case for clarity, consistency, and helpfulness: state-of-the-art clinical practice guidelines in endocrinology using the GRADE system. J Clin Endocrin Metab 2008; Epub (doi:10.1210/jc.2007-1907):PMID: 18171699.
10. 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; 325:445-53.
11. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1998;339:1415-25.
12. 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;337:1235-43.
13. Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: cosponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. Stroke 2006;37:577-617.
14. Ouriel K, May AG, Ricotta JJ, DeWeese JA, Green RM. Carotid endarterectomy for nonhemispheric symptoms: predictors of success. J Vasc Surg 1984;1:339-45.
15. Ricotta JJ, O'Brien MS, DeWeese JA. Carotid endarterectomy for non-hemispheric ischemia: long-term follow-up. Cardiovasc Surg 1994;2:561-6.
16. Illuminati G, Calio FG, Papaspyropoulos V, Montesano G, D'Urso A. Revascularization of the internal carotid artery for isolated, stenotic, and symptomatic kinking. Arch Surg 2003;138:192-7.
17. Paty PSK, Darling RC 3rd, Feustel PJ, Bernardini GL, Mehta M, Ozsvath KJ, et al. Early carotid endarterectomy after acute stroke. J Vasc Surg 2004;39:148-54.
18. Gasparis AP, Ricotta L, Cuadra SA, Char DJ, Purtill WA, Van Bemmelen PS, et al. High-risk carotid endarterectomy: fact or fiction. J Vasc Surg 2003;37:40-6.
19. Reed AB, Gaccione P, Belkin M, Donaldson MC, Mannick JA, Whittemore AD, et al. Preoperative risk factors for carotid endarterectomy: defining the patient at high risk. J Vasc Surg 2003;37:1191-9.
20. Murad MH, Flynn DN, Elamin MB, et al. Endarterectomy vs angioplasty for patients with carotid stenosis. A systematic review and meta-analysis. [in preparation]
21. Ederle J, Featherstone R, Dobson J, Brown M. Endovascular treatment vs medical care in patients with carotid artery stenosis: long-term results from CAVATAS. Cerebrovasc Dis 2007;23(Suppl 2):55.
22. Zhao X, Jia J, Ji X, Peng M, Ling F. A follow-up: stroke in patients with bilateral severe carotid stenosis after intervention treatment. Chin J Clin Rehabil 2003;7:2714-5.
23. Ederle J, Featherstone RL, Brown MM. Percutaneous transluminal angioplasty and stenting for Carotid artery stenosis. Cochrane Database Syst Rev 2007;4.
24. Role of carotid endarterectomy in asymptomatic carotid stenosis. A Veterans Administration Cooperative Study. Stroke 1986;17:534-9.
25. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273:1421-8.
26. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial [erratum appears in Lancet 2004;31:416]. Lancet 2004; 363:1491-1502.
27. Brooks WH, McClure RR, Jones MR, Coleman TL, Breathitt L. Carotid angioplasty and stenting versus carotid endarterectomy for treatment of asymptomatic carotid stenosis: a randomized trial in a community hospital. Neurosurgery 2004;54:318-24; discussion 324-15.

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