

Guidelines for the use of carotid endarterectomy: current recommendations from the Canadian Neurosurgical Society



Evidence

Études

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Abstract

Objective: To develop guidelines on the suitability of patients for carotid endarterectomy (CEA).

Options: For atherosclerotic carotid stenosis that has resulted in retinal or cerebral ischemia: antiplatelet drugs or CEA. For asymptomatic carotid stenosis: CEA or no surgery.

Outcomes: Risk of stroke and death.

Evidence: Trials comparing CEA with nonsurgical management of carotid stenosis.

Values: Greatest weight was given to findings that were highly significant both statistically and clinically.

Benefits, harms and costs: Benefit: reduction in the risk of stroke. Major harms: iatrogenic stroke, cardiac complications and death secondary to surgical manipulations of the artery or the systemic stress of surgery. Costs were not considered.

Recommendations: CEA is clearly recommended for patients with surgically accessible internal carotid artery (ICA) stenoses equal to or greater than 70% of the more distal, normal ICA lumen diameter, providing: (1) the stenosis is symptomatic, causing transient ischemic attacks or nondisabling stroke (including retinal infarction); (2) there is no worse distal, ipsilateral, carotid distribution arterial disease; (3) the patient is in stable medical condition; and (4) the rates of major surgical complications (stroke and death) among patients of the treating surgeon are less than 6%. Surgery is not recommended for asymptomatic stenoses of less than 60%. Symptomatic stenoses of less than 70% and asymptomatic stenoses of greater than 60% are uncertain indications. For these indications, consideration should be given to (1) patient presentation, age and medical condition; (2) plaque characteristics such as degree of narrowing, the presence of ulceration and any documented worsening of the plaque over time; (3) other cerebral arterial stenoses or occlusions, or cerebral infarcts identified through neuroimaging; and (4) surgical complication rates at the institution. CEA should not be considered for asymptomatic stenoses unless the combined stroke and death rate among patients of the surgeon is less than 3%.

Validation: These guidelines generally agree with position statements prepared by other organizations in recent years, and with a January 1995 consensus statement by a group of experts assembled by the American Heart Association.

Sponsor: Canadian Neurosurgical Society.

Résumé

Objectif : Élaborer des lignes directrices au sujet des patients aptes à subir une endartérectomie de la carotide.

Options : Dans les cas de sténose de la carotide avec athérosclérose qui a entraîné une ischémie rétinienne ou cérébrale : médicaments antiplaquettaires ou endartérectomie de la carotide. Dans les cas de sténose de la carotide sans symptôme : endartérectomie de la carotide ou aucune intervention chirurgicale.

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‡ See related article page 693



Résultats : Risque d'attaque et de mort.

Preuves : Études comparant l'endartérectomie de la carotide au traitement non chirurgical de la sténose de la carotide.

Valeurs : On a accordé le poids le plus important aux résultats très significatifs sur les plans à la fois statistique et clinique.

Avantages, préjudices et coûts : Avantage : réduction du risque d'attaque. Principaux préjudices : attaque iatrogène, complications cardiaques et décès découlant de manipulations chirurgicales de l'artère ou du stress systémique imposé par l'intervention chirurgicale. On n'a pas tenu compte des coûts.

Recommandations : L'endartérectomie de la carotide est clairement recommandée pour les patients dont la sténose de l'artère carotide interne (ACI) est accessible chirurgicalement et atteint ou dépasse 70 % du diamètre normal de la lumière de l'ACI plus distale, aux conditions suivantes : (1) la sténose doit être symptomatique et causer des accès ischémiques transitoires ou des attaques qui n'entraînent pas d'incapacité (y compris infarctus de la rétine); (2) il n'y doit pas y avoir de maladie artérielle plus grave de distribution de la carotide ipsilatérale distale; (3) l'état du patient doit être stable; (4) les taux de complications chirurgicales majeures (attaque et décès) chez les patients du chirurgien traitant doivent être inférieurs à 6 %. L'intervention chirurgicale n'est pas recommandée dans le cas des sténoses asymptomatiques de moins de 60 %. Les indications sont incertaines dans le cas des sténoses symptomatiques de moins de 70 % et des sténoses asymptomatiques de plus de 60 %. Dans le cas de ces indications, il faut tenir compte des facteurs suivants : (1) présentation, âge et état médical du patient; (2) caractéristiques de la plaque comme le degré de rétrécissement, la présence d'ulcération et toute aggravation documentée de la plaque avec le temps; (3) autres sténoses ou occlusions artérielles cérébrales ou infarctus cérébraux définis par neuro-imagerie; (4) taux de complications chirurgicales de l'établissement. Il ne faut pas envisager une endartérectomie de la carotide dans le cas des sténoses symptomatiques si le taux combiné d'attaques et de décès chez les patients du chirurgien n'est pas inférieur à 3 %.

Validation : Ces lignes directrices correspondent en général aux énoncés de position préparés par d'autres organisations ces dernières années et à l'énoncé consensuel de janvier 1995 publié par un groupe d'experts réunis par l'American Heart Association.

Commanditaire : Société canadienne de neurochirurgie.

Carotid endarterectomy (CEA) is the surgical procedure to remove occlusive atherosclerotic plaque from the origin of the internal carotid artery. Only a decade ago, the use of CEA to prevent thromboembolic stroke was seriously questioned, in part because of reports of high rates of surgical complications, and in part because the indications for CEA were unproved at that time.^{1,2} In response to these concerns, a number of multicentre randomized controlled trials were launched; these validated the use of CEA under certain circumstances.³⁻⁸ Because the results of these studies have led to a resurgence in the popularity of CEA in Canada, the Canadian Neurosurgical Society decided to prepare guidelines to assist clinicians in determining the suitability of patients for this procedure. Technical issues in the performance of CEA will not be addressed in these guidelines. This report was prepared by a special cerebrovascular committee of the society.

Methods

We carried out a MEDLINE search of all controlled trials of carotid endarterectomy published in English since 1966 with the use of key words "endarterectomy" and "carotid" and MeSH headings "clinical trials (phase I, II, and III)," "controlled clinical trials" and "randomized clinical trials."

Experimental and animal studies were excluded. The studies selected for detailed analysis were 6 widely known randomized controlled trials published since 1991.³⁻⁸ Other relevant studies, including separate reports from the randomized trials as well as reports from nonrandomized studies, were also considered. The data from each of these trials were summarized and assigned a level of evidence according to the levels established by the Canadian Task Force on the Periodic Health Examination.⁹ All summaries of trial data and recommendations for treat-



ment were reviewed and agreed upon by the writing group of the Canadian Neurosurgical Society.

Findings

Trials involving symptomatic stenoses

For patients with symptomatic high-grade carotid stenoses, CEA was shown to have a beneficial effect in the North American Symptomatic Carotid Endarterectomy Trial (NASCET).³ The first report from NASCET showed that, for patients with either transient ischemic attacks (TIAs) or nondisabling stroke within 120 days before entry into the trial and a stenosis of between 70% and 99% of normal lumen diameter on cerebral angiography, CEA was clearly superior to drug therapy in preventing stroke, lowering the 2-year risk of ipsilateral stroke from 26% to 9% ($p < 0.001$). The risk of stroke in patients treated with drugs increased with higher degrees of carotid stenosis; correspondingly, the benefit from surgery was greater for patients with more severe stenoses. The rate of perioperative stroke and death was 5.8% (within 30 days of surgery) in the surgical group, which totalled 328 patients. According to the trial results, only 6 patients with severe stenoses needed to undergo CEA to prevent 1 ipsilateral stroke in 2 years.¹⁰ There were a number of inclusion and exclusion criteria for patients enrolled in NASCET; the following are among the more important. Patients were excluded from the study if they: (1) had an intracranial lesion that was more severe than the surgically accessible lesion; (2) had a cerebral infarction that deprived them of all useful function in the affected territory; and (3) were 80 years of age or older. Patients were temporarily ineligible if they: (1) had uncontrolled hypertension, diabetes mellitus or unstable angina; (2) had had a myocardial infarction within the previous 6 months; or (3) had signs of progressive neurologic dysfunction. The degree of angiographic stenosis was calculated by comparing the maximal luminal diameter stenosis with the diameter of the normal internal carotid artery past the bulb (hereafter referred to as the "NASCET method").

Further analysis of these NASCET results for patients with severe (greater than 70%) stenoses showed that plaque ulceration shown by angiography¹¹ or a contralateral internal carotid artery occlusion (but not stenosis)¹² significantly increased the risk of stroke without CEA. When these risk factors were present, the surgical risk was higher, but the benefit from surgery was also greater.

NASCET is continuing. The trial is now comparing the results of surgical and drug management for stenoses of less than 70%. Randomization for this arm of NASCET was completed in late 1996, and follow-up will continue for approximately 1 more year before results

concerning the best treatment for moderate and mild stenoses (less than 70%) will be issued.

The same year that NASCET published its findings concerning severe stenoses, the first results of a parallel trial (the European Carotid Surgery Trial, ECST) were released.⁴ The results were similar to those of NASCET, indicating a striking clinical benefit of surgery compared with drug therapy for stenoses greater than 70%. The total 3-year risk for all strokes and death was 12.3% for patients who underwent CEA and 21.9% for control patients (difference 9.6%, standard deviation 3.3%, $p < 0.01$), and the perioperative stroke and death rate (within 30 days) was 7.5%. However, the method of stenosis measurement in ECST differed significantly from that in NASCET; as a result, a stenosis of 70% according to ECST was roughly equivalent to a stenosis of 40% according to NASCET.¹³ The first results from ECST also suggested that surgery was not indicated for stenoses of less than 30% by the ECST method (very mild stenoses), since the small risk of stroke without surgery was outweighed by the risks of surgery. A favourable trend in stroke reductions from surgery for severe stenoses was also found in a small US Veterans Administration trial, which was stopped because of the clear results from both NASCET and ECST.⁵ The second stage of ECST, comparing surgery with drug treatment for more moderate stenoses (30%–69% by the ECST method), has recently been published.⁶ For patients who had stenoses of 30% to 69%, CEA was of no benefit and even had an adverse effect on stroke-free survival for the first several years of follow-up. However, the risk of major stroke or death among patients in this study was 7.9% (within 30 days). It must also be remembered that, owing to the method of angiographic interpretation used in this trial, many of the patients studied had stenoses of less than 40% according to the NASCET method.

Trials involving asymptomatic stenoses

The efficacy of CEA for treatment of asymptomatic carotid stenosis was tested in a randomized trial involving 444 men in 11 US Veterans Administration hospitals.⁷ To be eligible for this study, patients had to have carotid stenosis of 50% or greater according to the NASCET method. The outcome in this trial was rate of ipsilateral neurologic events (TIA and stroke). At almost 4 years' follow-up, the surgical group did significantly better than the controls (event rate 8.0% in the surgical group and 20.6% in the control group, $p < 0.001$). However, when just stroke or stroke and death combined were examined, there were no significant differences between treatment groups. There was a trend in favour of surgical treatment when stroke alone was the outcome (rate of stroke of

4.7% in the surgical group and 9.4% in the control group at 4 years' follow-up, $p < 0.06$). The rate of stroke and death within 30 days of surgery in this study was 4.3%. The major problem with this study was that TIAs were grouped with stroke as a primary outcome, even though CEA is intended to prevent death or lasting disability due to stroke, not TIAs.¹⁴

The results of a much larger randomized trial examining CEA for asymptomatic stenoses, the Asymptomatic Carotid Atherosclerosis Study (ACAS), were published in 1995.⁸ A total of 1662 patients were enrolled if carotid Doppler or angiography indicated stenosis greater than or equal to 60% (according to the NASCET method). All patients randomly assigned to receive surgery underwent angiography first, but patients randomly assigned to the control group did not require angiography. At a median follow-up of 2.7 years, Kaplan-Meier estimates of 5-year risks were calculated, and the results showed a benefit for the group that had received surgery. The 5-year rate of ipsilateral stroke and death, combined with any postoperative stroke and death among the patients who had undergone CEA, was calculated to be 5.1% for the treated patients and 11.0% for the controls. However, the risk of any major stroke or of death did not differ significantly between groups, and women did not appear to benefit from surgery. The reason for this sex difference is uncertain, but it may be partly explained by a higher perioperative complication rate among women (3.6%) than among men (1.7%). To prevent 1 stroke in a patient with asymptomatic stenosis in a 2-year period, an estimated 67 patients would have to undergo CEA.¹⁰ To accomplish this objective, the risk of perioperative stroke and death would have to be only 1.5%, the very low figure obtained by the ACAS surgeons after exclusion of all angiography-related strokes.

Two other randomized trials of CEA for asymptomatic stenosis have been conducted. The Carotid Artery Stenosis with Asymptomatic Narrowing: Operation Versus Aspirin (CASANOVA) study involved 400 patients and showed no benefit from surgery. Unfortunately, however, this study excluded patients with stenoses of 90% or greater, limiting the usefulness of this information.¹⁵ The second study, the Mayo Asymptomatic Carotid Endarterectomy (MACE) trial was stopped after the random assignment of only 71 patients because an unexplained excess of patients in the treatment group suffered myocardial infarctions.¹⁶ We judged that these 2 trials provided too little information to contribute significantly to these guidelines.

Recommendations

Measurement of carotid artery stenosis

At present we recommend that decisions concerning a

patient's suitability for CEA be based on catheter cerebral angiography and that the stenosis be measured according to the NASCET method. In this method, stenosis is expressed as a percentage from the angiographic view showing the greatest stenosis. The narrowest diameter of the residual lumen (N) is compared with the luminal diameter of the internal carotid artery well beyond the bulb (D), and the percentage of stenosis is calculated as $(1-N/D) \times 100$ (Fig. 1) (level I evidence, grade A recommendation).¹⁷ We hope that less invasive investigations such as magnetic resonance angiography (MRA)¹⁸ or 3-dimensional computed

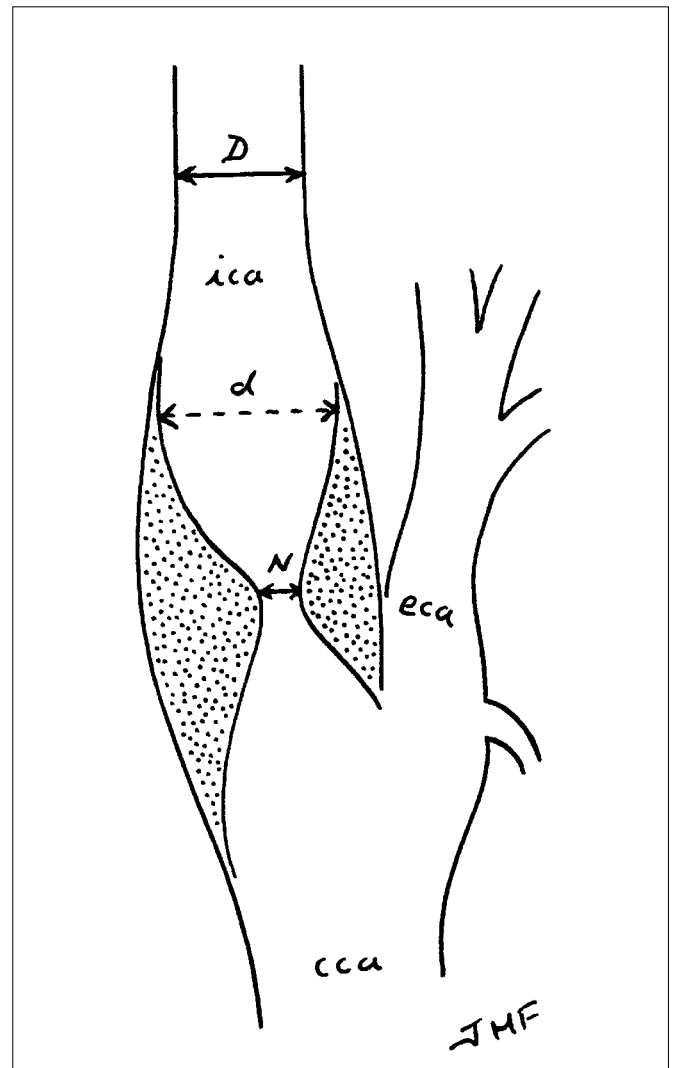


Fig. 1: Recommended method of measuring carotid stenosis. The residual lumen diameter (N) is measured at the point of greatest narrowing on the angiographic projection that shows the stenosis at its maximum. This diameter is compared with the lumen diameter of the distal internal carotid artery at a point where the arterial walls become parallel (D), not at a point of poststenotic dilatation distal to the obstruction (d). The percentage stenosis is calculated as $(1-N/D) \times 100$. cca = common carotid artery, eca = external carotid artery, ica = internal carotid artery.



tomography (CT-angiography)¹⁹ will be developed and be as accurate as catheter angiography, which they could then replace. Until then, whenever possible, patient management decisions should be based on the accurate and certain measurements obtained from cerebral angiography; in particular, ultrasonographic examinations alone should not form the basis of an important management decision.²⁰ In patients with severe peripheral vascular disease that precludes safe cerebral angiography, and patients who refuse angiography, it may be reasonable to formulate treatment on the basis of the combined results of carotid ultrasonographic investigation and MRA (level III evidence).

Surgery guidelines

Patients should be considered appropriate candidates

for CEA if they have symptomatic stenoses: ipsilateral, surgically accessible, 70% to 99% internal carotid artery stenoses that have resulted in TIAs or nonprogressing, nondisabling stroke (level I evidence, grade A recommendation) (Fig. 2). Surgeons offering CEA for these indications should have a combined rate of stroke and death among their patients of less than 6%, or should be able to achieve a rate lower than this after accumulating reasonable experience after surgical training.

Symptomatic stenoses of less than 70% and asymptomatic stenoses of greater than 60% are uncertain indications for CEA, and clear recommendations cannot be made at this time. NASCET results are expected to clarify the indications for surgery for symptomatic stenoses of less than 70% within the next several years. With regard to asymptomatic carotid stenoses of greater than 60%,

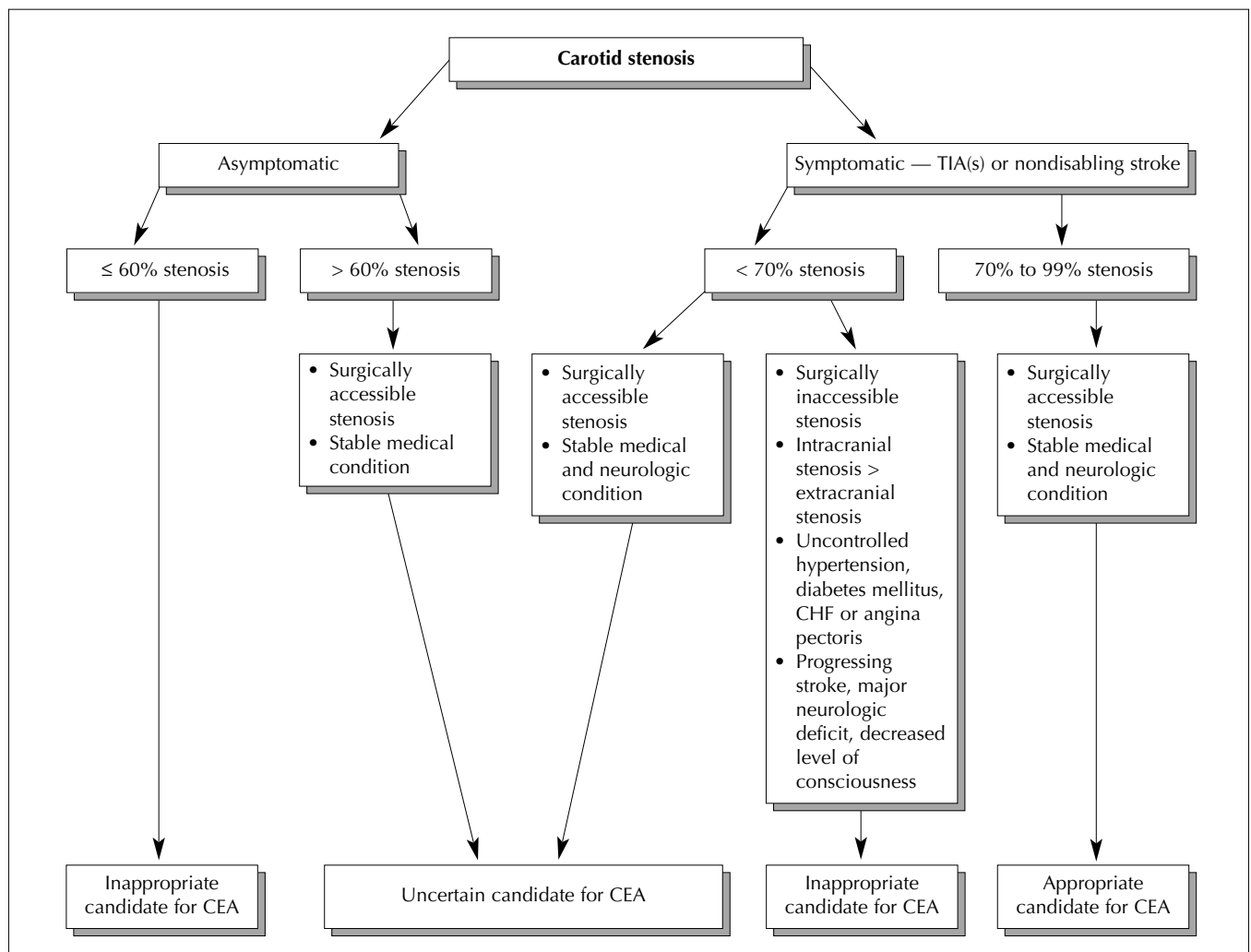


Fig. 2: Algorithm to determine a patient's appropriateness for carotid endarterectomy. The percentage stenosis should be defined by cerebral angiography and the method outlined in Fig. 1. The surgeon's rate of surgical complications (stroke or death) should be less than 6% for CEA in cases of symptomatic stenoses (appropriate or uncertain candidates), and less than 3% in cases of asymptomatic stenoses (uncertain candidates). TIA = transient ischemic attack, CEA = carotid endarterectomy, CHF = congestive heart failure.



CEA has only a small clinical benefit overall and has reduced the rate of stroke in a randomized trial only when the surgical complication rate for stroke and death combined was less than 2%. We recommend that caution be exercised when considering surgery for asymptomatic stenosis, a condition with a relatively benign natural history.²⁰ Factors such as an increasing severity of plaque stenosis,²⁰⁻²² the presence of plaque ulceration,^{21,23-26} a contralaterally occluded internal carotid artery¹² or documented progression of carotid stenosis over time,²⁷ as well as CT or MRI evidence of asymptomatic cerebral infarction ipsilateral to the stenosis,^{28,29} may all indicate an increased risk of stroke, and they must therefore be considered during the assessment of individual patients.³⁰ Severity of stenosis is likely the most important risk factor for stroke associated with asymptomatic stenosis, although this risk relation was not evident in ACAS (level II evidence).¹⁰

We recommend that surgeons offering CEA for asymptomatic stenosis be able to achieve a combined rate of stroke and death of less than 3%. Asymptomatic stenosis of less than 60% is considered an inappropriate indication for CEA, and surgery under these circumstances is not recommended (level I evidence, grade E recommendation).

Carotid endarterectomy is not recommended for patients with intracranial stenoses more severe than the extracranial stenosis. Surgery is also not recommended for patients with uncontrolled hypertension, diabetes mellitus, congestive heart failure, unstable angina, progressing stroke, a major neurologic deficit or a decreased level of consciousness. Patients with a history of significant cardiac or pulmonary disease should undergo a preoperative medical consultation before a final decision concerning surgery is made (all grade A recommendations).

Timing of carotid endarterectomy after cerebral ischemia

At present there is insufficient information to allow us to formulate unequivocal guidelines concerning the most appropriate timing of carotid endarterectomy after cerebral ischemia. It is unknown, for example, how urgently carotid endarterectomy should be performed after the occurrence or diagnosis of TIAs to provide patients with maximal protection from subsequent cerebral infarctions. Although many surgeons feel that CEA should be postponed to several months after cerebral infarction to avoid the risk of hemorrhage or infarct enlargement, several case studies³¹⁻³³ and recent NASCET data³⁴ have indicated that CEA within 30 days of a minor cerebral infarction is not excessively dangerous. It is not recommended that carotid endarterectomy be deliber-

ately postponed more than 30 days after a hemispheric stroke that does not interfere with daily activities and that is associated with a stenosis of 70% or greater (grade D recommendation).

Major surgery in patients with carotid stenosis

Surgeons are sometimes consulted concerning carotid stenosis in patients scheduled to undergo major surgery, such as coronary artery bypass grafting and major peripheral vascular operations, during which hemodynamic fluctuations are common. When a carotid stenosis is symptomatic and significant, the decision is easier: CEA is indicated for stenosis of 70% or greater and should precede other major procedures whenever possible, although the risk associated with CEA is higher overall in these situations (level II evidence, grade B recommendation).³⁵ When the patient's cardiac condition is too unstable as a result of myocardial ischemia to permit a prior CEA, then a combined coronary artery bypass graft and CEA may be considered (level II evidence, grade B recommendation).³⁶⁻³⁸

Although the management of asymptomatic carotid stenosis found before vascular or coronary surgery is less clear, the risk of stroke in this situation appears to be quite low. There are no risk factors that make prior CEA an absolute requirement in this situation.³⁵

CEA audits

We recommend that institutional audits be performed regularly to determine the results of CEA. Such reviews may identify areas of concern in a specific community with respect to variation in surgical indications or complications (grade A recommendation).³⁹

Future changes to CEA guidelines and use of carotid angioplasty

The guidelines presented here are in accordance with previous recommendations by the American Heart Association,⁴⁰ although more study data were available when we performed our analysis of the literature. These guidelines will require important modifications once the NASCET results concerning stenoses of less than 70% are available. Percutaneous transluminal angioplasty with the use of inflatable balloon-tipped arterial catheters has been performed to dilate carotid stenoses.⁴¹ This procedure has sometimes been accompanied by stent placement.^{42,43} Although these procedures may allow patients to avoid prolonged hospital stays, surgery and anesthesia, the safety and efficacy of the procedures have not yet been established.⁴⁴ Their use for carotid artery stenosis remains experimental.



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