Carotid Endarterectomy for the Prevention of Strokes in Patients with Symptomatic Carotid Stenosis

Claudio S. Cinà, MSc, FRCSC, Associate Clinical Professor, Department of Surgery, Division of Vascular Surgery, McMaster University, Hamilton, ON.

Catherine M. Clase, MSc, FRCPC, Associate Professor, Department of Medicine, Division of Nephrology, McMaster University, Hamilton, ON.

Carotid endarterectomy is effective in preventing strokes in patients with symptomatic carotid stenosis greater than 50%. The magnitude of the benefit is greater with increasing degree of stenosis, male sex, greater number of risk factors for strokes, strokes or hemispheric transient ischemic attacks rather than amaurosis fugax, recurrent events, plaque ulceration, contralateral carotid occlusion and tandem (intracranial and extracranial) stenosis. The effectiveness of carotid endarterectomy, however, is very sensitive to the rate of perioperative events, and centres providing care for these patients need to prospectively monitor their complication rates.

Key words: carotid stenosis, carotid endarterectomy, stroke, transient ischemic attacks.

Introduction

Stroke is the most important cause of long-term disability,[1] and second only to ischemic heart disease as a cause of death.[2] Carotid endarterectomy (CE) was introduced in the 1950s for the prophylaxis of strokes. Since the early 1990s, a number of randomised trials have addressed the effectiveness of this intervention. The indications and benefit of this intervention depend on a number of factors, including the presence or absence of symptoms, type of symptoms, degree of stenosis, anatomic features of the plaque, sex and coexistent risk factors.

Since there are substantial differences between the management of symptomatic and asymptomatic patients, we will discuss only the management of patients with symptomatic carotid disease.

Neurologic Symptoms

Traditionally, transient ischemic attacks (TIAs) are defined as brief episodes of focal loss of brain function lasting less than 24 hours.[3] Symptoms may include hemiparesis, dysarthria, dysphasia, diplopia and monocular blindness (amaurosis fugax). A new definition for TIAs has recently been proposed based on the presence or absence of associated brain infarct as diagnosed by computerised tomography or magnetic resonance imaging.[4] A similar episode of focal neurological dysfunction, without evidence of trauma or hemorrhage, is designated an ischemic stroke if it lasts more than 24 hours or causes death.[3] If the patient has a history of any symptoms in the ipsilateral eye or brain, the carotid stenosis would be regarded neurologically symptomatic, and the relevant question is whether the patient may be a candidate for CE.

The Trials

The effectiveness of CE for symptomatic patients with greater than 50% ipsilateral symptomatic carotid artery stenosis has been demonstrated in two randomised controlled trials: the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[5-16] and the European Carotid Surgery Trial (ECST).[17-20] Overall, 6,078 patients have been randomised (3,777 to surgery, 2,301 to medical treatment). Angiography was used to assess the severity of carotid stenosis in all patients, but the method of calculation of percentage of stenosis differed between studies (Figure), and must be taken into consideration when assessing the results (Table 1). In this article, all references to degrees of stenosis are according to the formula used in NASCET.

Although there are caveats in the application of the results of subgroup analysis to clinical practice, the ECST and NASCET trials provided analyses which suggest factors other than degree of stenosis that can be taken into account when considering indications for CE. Consistency of clinically and statistically significant results across studies, presence of a gradient effect and biologic plausibility suggest which observations may be applied to clinical practice.

Table 1

Conversion Between Different Methods of Measurements of Carotid Stenosis

	Severity of Disease					
	Minimal	Moderate		Severe		Occlusion
ECST	24%	58%	70%	82%	99%	100%
NASCET	0%	30%	50%	70%	99%	100%

Conversion from ECST to NASCET was done using the formula: ECST % stenosis=0.6(NASCET % stenosis) + 40[38]

Main Results and Degree of Stenosis

Surgery is harmful in patients with stenosis < 50%, while the benefits are most evident in those with high-grade stenosis.[13,18] A meta-analysis of the results of the ECST and NASCET trials[21,22] showed that in patients with a 70–99% carotid stenosis, CE is associated with a 48% relative risk reduction (RRR) in the number of disabling or fatal strokes or death, and a 6.7% absolute risk reduction (ARR), corresponding to a number needed to treat (NNT) of 15 (i.e., 15 surgeries need to be done to prevent one fatal stroke or death over the subsequent three-year period). Surgery is beneficial in patients with 50–69% stenosis, but the RRR was 27% and the ARR was 4.7% with a corresponding NNT of 21 (Table 2).[21,22] Increasing degrees of stenosis (70–79%, 80–89%, 90–99%) are associated with increasing benefit from surgery (Table 3).[5] A similar gradient effect was observed in ECST,[18] which also showed that surgery for patients with carotid stenosis less that 50% was harmful.[19,23]

In conclusion, symptomatic patients with > 50% carotid stenosis benefit from CE and this benefit increases with the severity of disease, from an NNT of 21 in patients with 50–69% stenosis to an NNT of four in those with 90–99% stenosis.

Other Outcomes

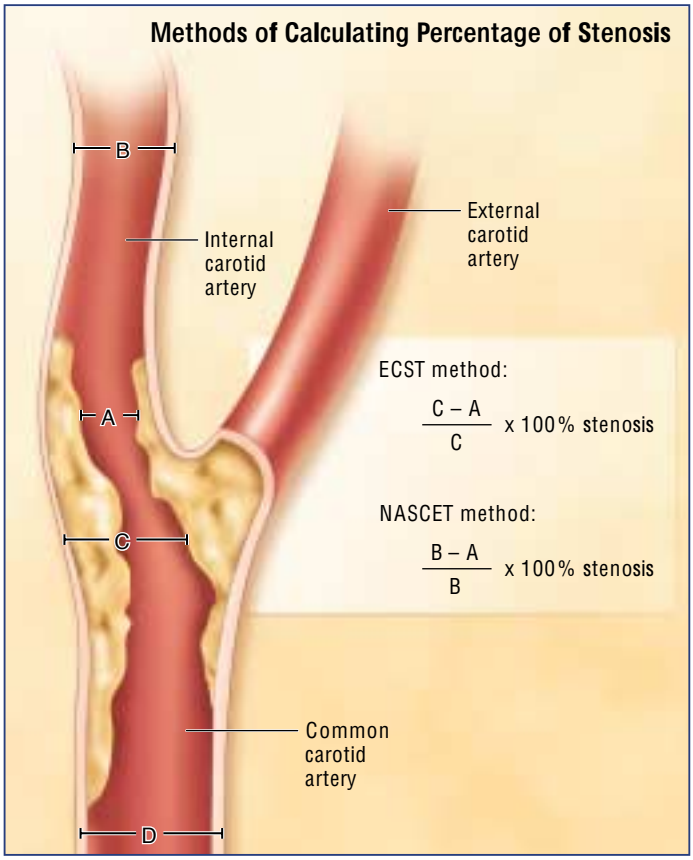
Perioperative Complications

Serious complications during CE other than strokes are rare: 1–2% myocardial infarction, 3% postoperative wound infections, 5% hematoma, and reversible nerve injury in 5–7%.[5,24,25] In the NASCET trial, the incidence of stroke or death was 6.7%, and that of nonfatal disabling stroke was 1.6%. The presence of a contralateral carotid occlusion, surgery for the left carotid, female sex, diabetes mellitus, hemispheric infarct on CT or MRI and diastolic blood pressure > 90 mmHg each are associated with an increase in the risk of perioperative events.[5]

Functional Status Outcomes

NASCET provided an analysis of the functional status in patients undergoing CE with 70–99% stenosis compared with medical treatment.[9] A functional status score capturing the domains of vision, language comprehension, speech fluency, swallowing, upper and lower limb function and the integrated functions of ability to go shopping and to make visits outside one's home, was used to evaluate patients at baseline and over time. The mean scores diverged over time, with a statistically significant difference in favour of the surgical group. The NNT to prevent one previously non-disabled person from suffering major disability at three years was 11 patients.

In conclusion, in patients with high-grade stenosis, CE not only reduces the number of strokes compared with medical treatment but also results in improved functional outcome over time.



Age and Sex

Older age and male sex are associated with greater benefit of surgery.[13,18] Surgery appears to provide the largest benefit in surgically-fit patients older than 75 years: the ARR is 29% (NNT 3) for stenosis > 70%, and 17% (NNT 6) for stenosis of 50–69%.[26]

Women have a lower risk of stroke compared with men for any degree of stenosis. Accordingly, the benefit of surgery is less evident: in patients with a moderate degree of stenosis (50–60%), the NNT to prevent one disabling stroke is 16 for men and 125 for women.[5]

Surgically-fit elderly patients therefore benefit greatly from CE. Surgery should be considered for symptomatic men and women with > 70% stenosis, may be indicated in symptomatic men with 50–70% stenosis, but is generally not indicated for women with stenosis in this range.

Medical Risk Factors

Data from the NASCET study show that for symptomatic patients with > 70% carotid stenosis, a greater number of identifiable clinical risk factors (Table 4) was associated with a higher annual risk of stroke (0 to three risk factors, 7%; four to five, 9%; six or more, 16%), and with an increased benefit from CE as demonstrated by increased ARR and reduced NNT (Table 5).[13]

However, patients in NASCET and ECST were excluded if they had coexisting medical disease likely to produce significant mortality and morbidity (e.g., cardiac valvular or

Table 2

Effectiveness of Surgery by Degree of Stenosis[21,22]

% Stenosis	% (95% CI)	% (95% CI)	Number (95% CI)
70–99	RRR 48 (27–63)	ARR 6.7 (3.2–10)	NNT 15 (10–31)
50–69	RRR 27 (5–44)	ARR 4.7 (0.8–8.7)	NNT 21 (11–125)
< 49	RRI 20 (0–44)	ARI 2.2 (0–4.4)	NNH 45 (22–∞)

RRR, relative risk reduction; RRI, relative risk increase; ARR, absolute risk reduction; ARI, absolute risk increase; NNT, number needed to treat; NNH, number needed to harm.

rhythm disorders, uncontrolled hypertension or diabetes, unstable angina pectoris or myocardial infarction in the previous four months).[13] Results of these trials, therefore, are not generalizable to patients who have these conditions. Further evidence for the impact of operative risk on outcomes is provided by a retrospective review of 562 patients undergoing CE for symptomatic and asymptomatic disease in a large community hospital.[27] In patients rated as Goldmann class I and II,[28] overall incidence of mortality and non-fatal myocardial infarction was 2%, while 21% of patients in class III and IV experienced one of these complications.

When considering patients' preoperative vascular risk profiles, a balance must therefore be maintained between exclusion of those whose surgical risks are most profound, but inclusion of those whose concomitant vascular risk factors increase their ability to benefit from the intervention.

Table 3

Absolute Risk Reduction Associated with Surgery for Ipsilateral Stroke at Two Years, and NNTs, According to Percentage of Ipsilateral Stenosis[5]

% Stenosis	ARR %	NNT
70–79	12	8
80–89	18	6
90–99	27	4

ARR, absolute risk reduction; NNT, number needed to treat.

Outcomes by Neurologic Symptom

Retinal transient ischemic attacks have a better prognosis compared with hemispheric TIAs: the risk of stroke at three years for > 50% stenosis is 10% and 20%, respectively.[29] Surgery is, accordingly, less beneficial in patients with amaurosis fugax: for example, the NNT to prevent one stroke at three years is 77 when the most recent neurologic event is amaurosis fugax, and 11 when it is a hemispheric TIA.[29] Similarly, the benefit of CE is greater in patients who have had a hemispheric stroke compared to those with TIAs: for example, in patients with 50–69% stenosis, the NNT to prevent one disabling stroke is 13 for patients with a recent stroke compared to 59 in patients with TIA.[5]

Among patients whose most recent neurologic event is amaurosis fugax, a number of risk factors have been identified that increase the risk of stroke and the benefit of surgery. These include age greater than 75 years, male sex, previous history of hemispheric TIA or stroke, history of intermittent claudication, high grade stenosis (80–99%) and the absence of cerebrovascular collateral circulation assessed by angiography. The risk of stroke at three years is 2% in those with one or fewer risk factors, 12% in those with two, and 24% in patients with three or more risk factors.[29]

In conclusion, patients with amaurosis fugax have a better prognosis than those with hemispheric TIAs. Patients at low risk for stroke (one or no risk factors) are better treated medically (NNH 45; i.e., 45 CEs need to be done to harm one patient). Patients with two or more risk factors benefit from CE (NNT 20 and NNT 7, respectively).

Recurrent Events

In NASCET and ECST, an inclusion criterion was a recent neurologic event, called the qualifying event. In patients with no events prior to their qualifying event or whose neurologic events all occurred in the six months immediately preceding the qualifying event, CE is associated with an ARR for stroke of 11% (NNT 9), while in patients with long-standing recurrent events over a period of 12 months prior to the qualifying event the ARR is 30% (NNT 3).[14]

Thus, patients with longer histories of recurrent ischemic events appear to have greater ability to benefit from surgery than those whose ischemic events are more recent in onset.

Lacunar Strokes

Pathologic studies have suggested[30] that the underlying process in lacunar strokes may not be artery-to-artery embolism. If this was the case, patients with a lacunar event might be expected to benefit less from CE than others, perhaps having a response more in keeping with asymptomatic carotid stenosis. A subgroup analysis from NASCET in patients with 50–99% stenosis showed that patients with non-lacunar and lacunar strokes benefit from CE, but the benefit is, as anticipated, greater in those with non-lacunar strokes (NNT=7 and NNT=11, respectively).[31]

Delay to Surgery in Patients with Stroke

One of the clinical questions in patients with a recent stroke and ipsilateral carotid stenosis is the timing of CE. The concern is that operating immediately might carry a risk of hemorrhagic transformation of the ischemic stroke, while delay exposes the patient to a further period at risk of recurrent artery-to-artery embolism and stroke. A subgroup analy-

Table 4

Risk Factors Modifying the Effectiveness of Surgery[13]

Demographic factors	Stroke risk factors	Vascular morbidity	Anatomic factors
Age > 70	Smoking	Prior stroke	Stenosis > 80%
Male sex	Diabetes	Cardiovascular accident within 31 days	Plaque ulceration
	Hyperlipidemia		
	Hypertension	Myocardial infarction	
	SBP > 160mmHg	Congestive heart failure	
	DBP > 90mmHg	Intermittent claudication	

sis from NASCET found no difference between patients who suffered a stroke and underwent CE within or after 30 days from the event.[8] Similar results were obtained when the 14- or 21-day intervals were analysed.

These data offer no support for either those who advocate urgent surgery for patients with stroke and carotid stenosis or those who have cautioned that complications of CE are higher with early surgery. The only conclusion that can be drawn is that early surgery after hemispheric stroke is not associated with very high risk in carefully selected cases.

Plaque Ulceration

In symptomatic patients with 70–99% stenosis, patients with angiographic evidence of plaque ulceration experience a higher risk of stroke compared to those without ulceration,[6] and greater benefit from surgery (Table 6). However, sensitivity and specificity for detecting ulcerated plaques by angiogram was 46% and 74%, respectively, with a positive predictive value of 72%.[32] Plaque ulceration likely increases the benefit of surgery and may be helpful in making the final decision of whether to offer CE.

Near Occlusion of the Carotid Artery

It has been hypothesized that patients with near occlusion of the symptomatic carotid artery (i.e., very severe stenosis, delayed flow of angiographic material and reduced distal arterial calibre) have a different prognosis and greater risk from surgery than patients with lesser degrees of stenosis. A subgroup analysis from NASCET found no statistically significant differences across categories for either perioperative events or one-year risk of ipsilateral stroke.

Within the limitation of this subgroup analysis, with its small number of patients and events,[10] patients with near occlusion of the carotid artery can be considered similar in risk to other patients with high-grade stenosis.

Contralateral Carotid Disease

The risk of perioperative complications (stroke or death) in patients with contralateral occlusion is higher (15%) than in those whose contralateral artery is stenosed but patent (6%).[7] In spite of this increased risk, however, the benefit of surgery in terms of the outcome "any stroke or death" at two years is greater in the group with contralateral occlusion (ARR 45%, NNT 2) than in the group with contralateral high-grade stenosis (ARR 20%, NNT 5). Interestingly, the group with an occluded contralateral carotid had a higher incidence (52%) of ipsilateral plaque ulceration than the group with contralateral high-grade stenosis and the group without contralateral stenosis (34% and 35%, respectively). If these effects of plaque ulceration on the ability to benefit from CE were real, then plaque ulceration might be an important confounder in this analysis of the effect of contralateral carotid occlusion.

In conclusion, a contralateral carotid occlusion does not represent a contraindication for surgery, but patients should be warned of a higher perioperative risk.

Tandem Extracranial and Intracranial Carotid Stenosis

The presence of intracranial carotid (ICC) stenosis detected by contrast or magnetic resonance angiography is an independent risk factor for stroke,[33] and ICC stenosis of some degree is found in 20–50% of patients who have internal carotid artery (ICA) stenosis.[34-37]

Table 5

Number of Medical Risk Factors and Two-year Risk for Ipsilateral Stroke[13]

No. of risk factors	ARR (%)	NNT
0–5	8	13
6	14	7
≥ 7	30	3

ARR, absolute risk reduction; NNT, number needed to treat.

Table 6

Effects of Plaque Ulceration and Ipsilateral Stenosis on Benefits of Surgery, Expressed as ARR and NNT for the Outcome any Stroke or Death, at Two Years[6]

% Stenosis	Nonulcerated (n=429)		Ulcerated (n=230)	
	ARR	NNT	ARR	NNT
75 (n=270)	12	9	24	4
85 (n=237)	11	9	37	3
95 (n=152)	10	10	56	2

ARR, absolute risk reduction; NNT, number needed to treat.

A subgroup analysis from NASCET showed that symptomatic patients with concomitant ICA and ICC disease have a higher risk of subsequent stroke than patients with isolated ICA stenosis, but CE is not associated with a higher perioperative complication rate or long-term risk of stroke.[33] This means that CE is more effective in these patients because the higher baseline risk of stroke translates into more favourable NNTs: for patients with > 70% ICA stenosis, the NNT at three years is 4 for patients with, and 7 for those without, ICC disease; and for patients with 50–69% stenosis, the NNTs are 12 and 26, respectively.

The presence of tandem intracranial and extracranial carotid disease thus increases the benefit of surgery, and this may be particularly important for decision making in patients whose angiogram shows 50–69% ICA stenosis.

Conclusions

Carotid endarterectomy reduces the risk of death or disabling stroke in surgically fit symptomatic patients with greater than 50% ipsilateral carotid stenosis. Consideration of the degree of stenosis, age, sex, other medical risk factors, stroke (rather than TIA), hemispheric (rather than retinal) events, plaque ulceration and the concomitant existence of ipsilateral intracranial carotid disease may be used to modify the decision as to whether to recommend carotid endarterectomy in addition to continued medical management and risk factor modification.

A final caveat is the low rate of perioperative stroke and death observed in these studies; the overall results are very sensitive to an increase in early postoperative events. It is therefore important that centres providing care for these patients prospectively monitor their complication rates. ◆

No competing financial interests declared.

References

1. Bonita R. Epidemiology of stroke. Lancet 1992;339:342-44.
2. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world. Global Burden of Desease Study. Lancet 1997;349:1269-76.
3. National Institute of Neurological Disorders and Stroke. Special report from the national institute of neurological disorders and stroke. Classification of cerebrovascular diseases III. Stroke 1990;21:637-76.
4. Albers GW, Caplan LR, Easton JD, et al. Transient ischemic attack—Proposal for a new definition. N Engl J Med 2002;347:1713-6.
5. North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET). The benefit of carotid endarterectomy in symptomatic patients with moderate and severe stenosis. N Engl J Med 1998;339:1415-25.
6. Eliasziw M, Streifler JY, Fox AJ, et al. Significance of plaque ulceration in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial. Stroke 1994;25:304-8.
7. Gasecki AP, Eliasziw M, Ferguson GG, et al. Long-term prognosis and effect of endarterectomy in patients with symptomatic severe carotid stenosis and contralateral carotid stenosis or occlusion: results from NASCET. North American Symptomatic Carotid Endarterectomy Trial (NASCET) group. J Neurosurg 1995;83:778-82.
8. Gasecki AP, Ferguson GG, Eliasziw M, et al. Early endarterectomy for severe carotid artery stenosis after a nondisabling stroke: Results from the North American Symptomatic Carotid Endarterectomy Trial. J Vasc Surg 1994;20:288-95.
9. Haynes RB, Taylor DW, Sackett DL, et al. Prevention of functional impairment by endarterectomy for symptomatic high-grade carotid stenosis. JAMA 1994;271:1256-9.
10. Morgenstern LB, Fox AJ, Sharpe BL, et al. The risks and benefits of carotid endarterectomy in patients with near occlusion of the carotid artery. NASCET Group. Neurology 1997;48:911-5.
11. NASCET. Clinical alert: benefit of carotid endarterectomy for patients with high-grade stenosis of the internal carotid artery. National institute of neurological disorders and stroke stroke and trauma division. North American Symptomatic Carotid Endarterectomy Trial (NASCET) investigators. Stroke 1991;22:816-7.
12. North American Symptomatic Carotid Endarterectomy (NASCET) study group. Carotid endarterectomy: three critical evaluations. North American symptomatic carotid endarterectomy study group [editorial]. Stroke 1987;18:987-9.
13. North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET). Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-53.
14. Paddock-Eliasziw LM, Eliasziw M, Barr HWK, et al. Long-term prognosis and the effect of carotid endarterectomy in patients with recurrent ipsilateral ischemic events. NASCET Group. Neurology 1996;47: 1158-62.
15. 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;27:266-9.
16. Streifler JY, Eliasziw M, Benavente OR, et al. The risk of stroke in patients with first-ever retinal vs hemispheric transient ischemic attacks and high-grade carotid stenosis. Arch Neurol 1995;52:246-9.
17. Boiten J, Rothwell PM, Slattery J, et al. Ischaemic lacunar stroke in the European Carotid Surgery Trial. Risk factors, distribution of carotid stenosis, effect of surgery and type of recurrent stroke. Cerebrovascular Diseases 1996;6:281-7.
18. European Carotid Surgery Trialists' Collaborative Group. Randomized trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial. Lancet 1998;351:1379-87.
19. European Carotid Surgery Trialists' Collaborative Group. Endarterectomy for moderate symptomatic carotid stenosis: interim results from the MRC European Carotid Surgery Trial. Lancet 1996;347:1591-3.
20. Moore WS, Barnett HJM, Beebe HG, et al. Guidelines for carotid endarterectomy: A multidisciplinary consensus statement from the Ad Hoc committee, American Heart Association. Circulation 1994;91: 566-79.
21. Cina CS, Clase CM, Haynes RB. Carotid endarterectomy for symptomatic carotid stenosis. The Cochrane Library [4], 2000.
22. Cinà CS, Clase CM, Haynes RB. Refining indications for carotid endarterectomy in patients with symptomatic carotid stenosis: A systematic review. J Vasc Surg 1999;30:606-17.
23. Goldstein LB, Hasselblad V, Matchar DB, et al. Comparison and meta-analysis of randomized trials of endarterectomy for symptomatic carotid artery stenosis. Neurology 1995;45:1965-70.
24. Mayberg MR, Wilson SE, Yatsu F, et al., for the Veterans Affairs Cooperative Studies Program 309 Trialist Group. Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. JAMA 1991;266:3289-94.
25. Rothwell PM. Can overall results of clinical trials be applied to all patients? Lancet 1995;345:1616-9.

26. Alamowitch S, Eliasziw M, Algra A, et al. Risk, causes, and prevention of ischaemic stroke in elderly patients with symptomatic internal-carotid-artery stenosis. Lancet 2001;357:1154-60.
27. Musser DJ, Nicholas GG, Reed JF, III. Death and adverse cardiac events after carotid endarterectomy. J Vasc Surg 1994;19:615-22.
28. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med 1977;297:845-50.
29. Benavente O, Eliasziw M, Streifler JY, et al. Prognosis after transient monocular blindness associated with carotid- artery stenosis. N Engl J Med 2001;345:1084-90.
30. Fisher CM. Capsular infarcts. The underlying vascular lesion. Arch Neurol 1979;36:16-73.
31. Inzitari D, Eliasziw M, Sharpe BL, et al. Risk factors and outcome of patients with carotid artery stenosis presenting with lacunar stroke. North American Symptomatic Carotid Endarterectomy Trial Group. Neurology 2000;54:660-6.
32. Streifler JY, Eliasziw M, Fox AJ, et al. Angiographic detection of carotid plaque ulceration. Comparison with surgical observations in a multicenter study. North American Symptomatic Carotid Endarterectomy Trial. Stroke 1994;25:1130-2.
33. Kappelle LJ, Eliasziw M, Fox AJ, et al. Importance of intracranial atherosclerotic disease in patients with symptomatic stenosis of the internal carotid artery. The North American Symptomatic Carotid Endarterectomy Trail. Stroke 1999;30:282-6.
34. Lord RS, Raj TB, Graham AR. Carotid endarterectomy, siphon stenosis, collateral hemispheric pressure, and perioperative cerebral infarction. J Vasc Surg 1987;6:391-7.
35. Mackey WC, O'Donnell TF, Jr., Callow AD. Carotid endarterectomy in patients with intracranial vascular disease: short-term risk and long-term outcome. J Vasc Surg 1989;10:432-8.
36. Mattos MA, van Bemmelen PS, Hodgson KJ, et al. The influence of carotid siphon stenosis on short- and long-term outcome after carotid endarterectomy. J Vasc Surg 1993;17:902-10.
37. Griffiths PD, Worthy S, Gholkar A. Incidental intracranial vascular pathology in patients investigated for carotid stenosis. Neuroradiology 1996;38:25-30.
38. Rothwell PM, Gibson RJ, Slattery J, et al. Prognostic valve and reproducibility of measurements of carotid stenosis. A comparison of three methods on 1001 angiograms. European Carotid Surgery Trialists' Collaborative Group. Stroke 1994;25:2440-4.