Eur J Vasc Endovasc Surg **32,** 229–235 (2006)
doi:10.1016/j.ejvs.2006.03.016, available online at http://www.sciencedirect.com on SCIENCE DIRECT®

Early Carotid Endarterectomy after Ischemic Stroke: The Results of a Prospective Multicenter Italian Study

E. Sbarigia,[1*] D. Toni,[2] F. Speziale,[1] M.C. Acconcia[3] and P. Fiorani[1,a]

[1]*I Cattedra di Chirurgia Vascolare,* [2]*Dipartimento di Scienze Neurologiche, and* [3]*Malattie del Cuore e Grossi vasi – Attilio Reale, Università di Roma La Sapienza, viale del Policlinico, 00161 Rome, Italy*

Objectives. *To evaluate safety of early carotid endarterectomy (CEA) in patients with acute brain ischemia presenting to the emergency department stroke units (EDSU).*
Methods. *The neurologists, neuroradiologists and vascular surgeons on duty in emergency departments enrolled 96 patients who underwent very early CEA according to a predefined protocol within two years. The protocol included evaluation of neurological status by National Institute of Health Stroke Scale (NIHSS), neuroimaging assessment, ultrasound of the carotid arteries and Transcranial Doppler. Patients with NIHSS > 22 or whose neuroimaging showed brain infarct >2/3 of the middle cerebral artery territory were excluded. All eligible patients underwent CEA as soon as possible. Primary end points of the study were mortality, neurological morbidity by NIHSS and postoperative hemorrhagic conversion on neuroimaging. Statistical analysis was performed by univariate analysis.*
Results. *The mean time elapsing between the onset of stroke and endarterectomy was 1.5 days (±2 days). The overall 30-day morbidity mortality rate was 7.3% (7/96). No neurological mortality occurred. On hospital discharge, three patients (3%) experienced worsening of the neurological deficit (NIHSS score 1 to 2, 1 to 3 and 9 to 10 respectively). Postoperative CT demonstrated there were no new cerebral infarcts nor hemorrhagic transformation. At hospital discharge 9/96 patients (9%) had no improvement in NHISS scores, 37 were asymptomatic and 45 showed a median decrease of 4.5 NIHSS points (range 1–18). By univariate analysis none of the considered variables influenced the clinical outcome.*
Conclusion. *Our protocol selected patients who can safely undergo very early (<1.5 days) surgery after acute brain ischemia. Large randomized multicenter prospective trials are warranted to compare very early CEA versus best medical therapy.*

Keywords: Acute ishemic stroke; Extracranial internal carotid artery stenosis; Early carotid endarterectomy; Prospective not randomised study.

Introduction

Even though some studies report that early carotid endarterectomy (CEA) has a favorable outcome[1–13] most neurologists and vascular surgeons are reluctant to undertake CEA immediately after the onset of stroke for fear that hemorrhagic transformation of the cerebral infarct will occur. Reports describing conversion of an infarction into a hemorrhagic infarction after early reperfusion came mainly from the early series of patients operated on without preoperative computed tomographic (CT) scan so that appropriate candidates could not be selected for surgery.[14,15]

Recently, trials of pharmacological reperfusion with intravenous or intra-arterial thrombolysis on strictly selected cohorts of patients have given satisfactory results in terms of reducing the severity of neurological sequelae proving that in such patients reperfusion of the ischemic territory of the brain can be done with acceptable risks.[16–20] As thrombolysis of intracranial artery thrombosis can be performed only within the first hours from stroke, the Emergency departments organized stroke units to permit a very fast work up. Sometime the patients with acute stroke screened for thrombolysis have an appropriate internal carotid artery stenosis responsible for cerebral embolisation. In these cases, neurologists and vascular surgeons were obliged to reconsider the indications for urgent or early CEA.

In a meta-analysis report including the major trials on carotid endarterectomy (NASCET and ECST) Bond *et al.*[21] concluded that patients with a stabilized deficit operated upon within 4 to 6 weeks after stroke seemed not to be at higher surgical risk. However, the characteristics that identify a patient as suitable

*Corresponding author. Enrico Sbarigia, MD, Università di Roma La Sapienza, I Cattedra di Chirurgia Vascolare, viale del Policlinico, 00161 Rome, Italy.
E-mail address: enrico.sbarigia@fastwebnet.it
[a] The Participating Centers are found in Appendix A.

1078–5884/000229 + 07 $35.00/0

for early endarterectomy after stroke have not been clearly identified.

The aim of this prospective multicenter study was to evaluate the safety of CEA undertaken as soon as possible after stroke, according to a predefined protocol for selecting patients.

Methods

The Surgical Treatment of Acute Cerebral Ischemia (STACI), a neurologically controlled observational multicenter Italian study, approved by local ethical committees, was conducted from September 2001 to September 2003. During the study, 13 Italian hospitals enrolled 96 consecutive patients.

All participating centers were experienced in carotid surgery and in the diagnosis and treatment of acute cerebral ischemia. In each center the participating team included neurologists, neuro-radiologists and vascular surgeons on duty in the emergency department (ED). After the neurologist and the vascular surgeon on duty in Stroke Unit of the ED observed an eligible patient the neurological status was assessed according to The National Institutes of Health Stroke Scale (NIHSS)[22] immediately before carotid endarterectomy (CEA) (Table 1). All the preoperative work up was done in the ED and comprised contrast cerebral CT scan or magnetic resonance imaging (MRI), echo color Doppler (ECD) ultrasonography of the supra-aortic vessels to assess the degree of stenosis in the extra-cranial carotid arteries and transcranial Doppler (TCD) to verify the patency of the intracranial arteries (especially the M1 and M2 portions of the middle cerebral artery). None of the patients underwent angiography. Inclusion and exclusion criteria for patients enrollment are listed in Table 2.

Eligible consenting patients underwent operation as soon as possible. Anesthetic and operative technique, monitoring and intraoperative control procedures, were performed at the surgeons discretion. Immediately after the operation and at discharge from the hospital neurologists assessed the patient again with the NIHSS scale to evaluate the outcome of revascularization. The primary endpoints of STACI were overall mortality, perioperative stroke rate at 30 days, and the incidence of perioperative cerebral hemorrhage.

Statistical analysis

Categorical data were presented as absolute frequencies and percent values. Quantitative measurements were expressed as mean ± SD. In the univariate

Table 1. Simplified NIH Stroke Scale (NIHSS)

1a Level of consciousness
- 0 = Alert
- 1 = Not alert
- 2 = Ottunded
- 3 = Coma

1b LOC questions
- 0 = Answers both questions correctly
- 1 = Answers one question correctly
- 2 = Answers neither questions

1c LOC commands
- 0 = Performs both tasks correctly
- 1 = Performs one task correctly
- 2 = Performs neither tasks correctly

2 Best Gaze
- 0 = Normal
- 1 = Partial gaze palsy
- 2 = Forced deviation

3 Visual
- 0 = No visual loss
- 1 = Partial hemianopia
- 2 = Bilateral hemianopia (blind including cortical lesion)

4 Facial Palsy
- 0 = Normal: symmetrical movements
- 1 = Minor paralysis
- 2 = Partial paralysis
- 3 = Complete paralysis

5 Motor Arm
- 0 = No drift
- 1 = Drift
- 2 = Some effort against gravity
- 3 = No effort against gravity
- UN = Amputation or joint fusion
  - 5a Left Arm
  - 5b Right Arm

6 Motor Leg
- 0 = No drift
- 1 = Drift
- 2 = Some effort against gravity
- 3 = No effort against gravity
- UN = Amputation or joint fusion
  - 5a Left Leg
  - 5b Right Leg

7 Limb Ataxia
- 0 = Absent
- 1 = Present in one limb
- 2 = Present in two limbs
- UN = Amputation or joint fusion

8 Sensory
- 0 = Normal
- 1 = Mild to moderate
- 2 = Severe to total

9 Best Language
- 0 = Normal
- 1 = Mild to moderate aphasia
- 2 = Severe aphasia
- 3 = Mute, global aphasia

10 Dysarthria
- 0 = Normal
- 1 = Mild to moderate dysarthria
- 2 = Severe dysarthria
- UN = intubated or other physical barrier

11 Extinction and inattention
- 0 = No abnormality
- 1 = Visual tactile, auditory or personal inattention or extinction
- 2 = Profound hemi inattention or extinction (does not recognize own hand or orients only to one side of the space)

Table 2. Inclusion − exclusion criteria of the study

The inclusion criteria for patients enrollment:
- Clear time of onset of symptoms;
- NIHSS less than 22;
- Absence or evidence of recent ischemic infarct in the appropriate hemisphere <1/3 of the middle cerebral artery territory irrespective of blood brain barrier disruption at CT Scan or MRI,
- Internal carotid artery stenosis at ECD >70% or ulcerated plaque <70%, appropriate to cerebral ischemia;
- Patent middle cerebral artery appropriate to symptoms in the detectable portion M1 and M2.

The exclusion criteria for patients enrolment:

A. By clinical presentation at admission:
- Uncertain time onset of symptoms;
- Severe neurological deficit (NIHSS > 22);
- Cerebral ischemia onset with epileptic crisis;
- Previous ischemic or hemorrhagic stroke with relevant residual deficit (ranking stroke scale ≥ 2)
- History of cerebral haematomas;
- Other central nervous system disease with residual permanent deficit.

B. By CT Scan at admission:
- Recent cerebral infarct extending <1/3 of the middle cerebral artery territory;
- Presence of cerebral hemorrhage;
- Cerebral neoplasia;
- Cerebral AV malformation;
- Cerebral aneurysm;

analysis performed, the patient population was divided into the clinically improved (decrease of NIHSS ≥ 4) and those not improved (decrease of NIHSS < 4), and compared by Fisher exact probability test for categorical variables and Mann−Whitney test for quantitative variables. A p value ≤0.05 was considered statistically significant.

Results

Of the 96 patients enrolled in the 13 centers, 81 were men. The mean age was 70.8 years (range 51−85 y). Seventy four (77%) patients had hypertension, 59 (61%) were smokers, 34 (35%) were diabetic and 27 (28%) had dyslipidemia. The mean NIHSS score at operation was 5.7 ± 4 (SD) points, median 4 (range 1−20). Preoperative cerebral CT or MRI detected acute cerebral infarct in 58 of the 96 cases (60%); in three cases scans showed contrast enhancement. The results of Echo-color Doppler assessment before operation are reported in Table 3. The mean time elapsing between the onset of stroke and CEA was 1.5 days (±2 days) (range 8 h−11.5 days) (Table 4).

Of the 96 patients enrolled, 53 (55%) were operated on within 24 hours after the onset of stroke; and 94 (98%) within the first week. Only two were operated on during the second week after stroke onset. Reasons for delay were clinical instability ($n = 1$) and consent uncertainty ($n = 2$).

Data on the type of anesthesia, reconstructive procedure and intraoperative monitoring and protection are reported in Table 5.

The overall 30-day morbidity-mortality rate was 7.3% (7/96). Two patients died, one from cardiac failure and the other from aspiration pneumonia (2.1%). No neurological deaths occurred. Three patients (3.1%) experienced a slight worsening of the neurological deficit at hospital discharge. In one patients the

Table 3. Echo-color Doppler assessment before operation

Symptomatic side	*n*	%
% stenosis		
60−69	15	15.6%
70−89	49	51.0%
90−99	31	32.3%
Fresh thrombosis	1	1.1%
Total	96	
Contralateral artery % stenosis		
0−50	65	68%
51−70	20	21%
71−90	4	4%
91−99	1	1%
100	6	6%

Table 4. Interval between the onset of stroke and carotid endarterectomy (CEA)

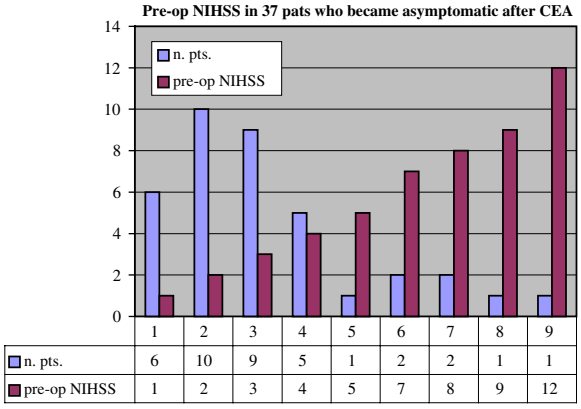
Day	1	53
	2	20
	3	6
	4	5
	5	5
	6	5
	8	1
	12	1
Total		96

{Mean time from onset of stroke and endarterectomy: 1.5 days ± 2 (SD) (range: 8 h−11.5 days)}.

Table 5. Intraoperative management of the 96 patients

Anesthetic technique	Cases	%	
General Anesthesia	61	63.5	
Local Anesthesia	35	36.5	
Operative technique		Patch	Direct suture
Standard CEA	72	47	25
Eversion CEA	21	−	−
Bypass	3	−	−
I.O. Monitoring in General Anesthesia			
SSEPs	25		
TCD	15		
EEG	5		
N.S.°	8		
Shunt	31*		

*In 8 patients routine shunt in general anesthesia.
°N.S. not stated.



	1	2	3	4	5	6	7	8	9
n. pts.	6	10	9	5	1	2	2	1	1
pre-op NIHSS	1	2	3	4	5	7	8	9	12

Fig. 1. Pre-operative NIHSS score in 37 patients who were asymptomatic at discharge from hospital.

NIHSS score progressed from 1 to 2 points, in one case from 1 to 3 and in the other from 8 to 11. Two more patients (2.1%), one operated on at 40 and the other at 60 hours after the onset of the neurological deficit had a worsening of their deficit in the first 24 hours after operation. This worsening was transient (lasting 36 hours) and associated with postoperative headache. Serial postoperative CT scans showed no new cerebral infarct or conversion to hemorrhage and the NIHSS was improved by 2 and 10 points by discharge respectively.

The postoperative NIHSS score at hospital discharge showed that in 9.3% (9/96) patients the neurologic deficit remained unchanged; in 37/96 (38.5%) patients the stroke resolved (Fig. 1); and in 45/96 (47%) the NIHSS score markedly improved (median 4.5 points; range 1−18) (Fig. 2). Postoperative CT scans detected no hemorrhagic transformation of cerebral infarcts, even in the three patients whose preoperative cerebral scan showed contrast enhancement.

Table 6 shows the results of the univariate analysis. None of the considered variables (age > 75), sex, smoking, hypertension, hyperlipemia, diabetes, cardiac disease, time of operation (>24), intraoperative shunt, visible cerebral infarct on preoperative CT Scan, influenced the clinical outcome.

Discussion

The results of our multicenter study show that patients whose neuroimaging studies document in the early hours after stroke a recent, limited cerebral infarction can safely undergo very early CEA (1.5 days after stroke). Our study underlines that if patients to undergo early CEA after an acute stroke are strictly selected, early surgery incurs similar risks to elective surgery. We attribute the low risk rate for early revascularization in our study chiefly to our decision to recruit in the various centers a series of patients who were homogeneous from the standpoint of anatomical cerebral damage. In contrast, we made no attempt to limit recruitment by clinical criteria, we included patients who had moderate or even severe, stable neurological deficits because similar neurological presentations can correspond to cerebral infarctions that differ notably according to their localization. When we reviewed the literature we found only three prospective studies concerning early CEA in patients with acute stroke. None of the three are comparable because the inclusion and exclusion criteria differ. The study conducted by Hubner *et al.*,[23] for example, included all patients with acute stroke, even those with an unstable neurologic deficit, who are at notoriously high risk for early revascularization. The studies conducted by Eckstein[24] and Ricco[25] included also a number patients who were asymptomatic when they underwent surgery. The only feature in common is that none of the three used selection criteria restricting the surgical indications according to the extension of the acute cerebral infarction.

Despite these differences, a detailed analysis of the complications reported in all three studies shows that the rate of complications directly related to

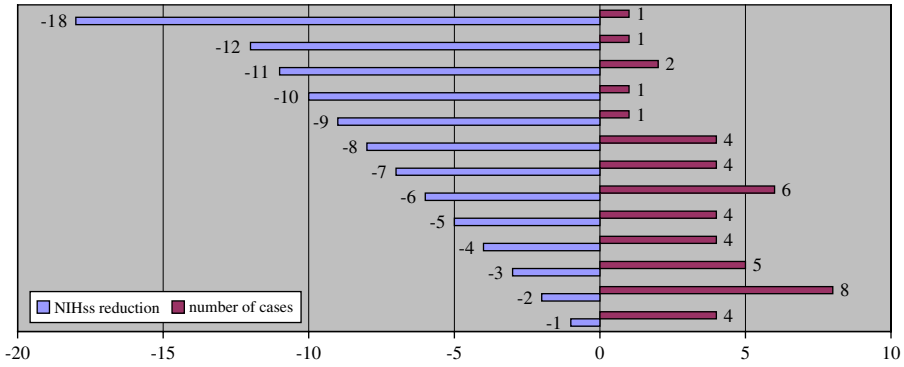


Fig. 2. Reduction in National Institute of Health Stroke Scale (NIHSS) at discharge in the 45 patients with residual neurological deficit.

Table 6. Results of Univariate analysis for neurological outcome by 4 points of NIHSS to evaluate clinical improvement by usual neurological examination

Variables	Neurological outcome by 4 points NIHSS				p^*
	Not improved ($n = 59$)		Improved ($n = 37$)		
	mean ± SD		mean ± SD		
	n	%	*n*	%	
Age	70.7 ± 8.5		70.9 ± 9.3		NS
Age					NS
- <75 y	33	55.9	20	54.1	
- ≥75 y	26	44.1	17	45.9	
Sex					NS
- F	9	15.3	6	16.2	
- M	50	84.7	31	83.8	
Smoking					NS
- No	24	40.7	13	35.1	
- Yes	35	59.3	24	64.9	
Hypertension					NS
- No	14	23.7	8	21.6	
- Yes	45	76.3	29	78.4	
Hyperlipemia					NS
- No	40	67.8	29	78.4	
- Yes	19	32.2	8	21.6	
Diabetes					NS
- No	37	62.7	25	67.6	
- Yes	22	37.3	12	32.4	
Coronary Disease					NS
- No	40	67.8	29	78.4	
- Yes	19	32.2	8	21.6	
Timing of operation					NS
- <24 h	30	50.8	23	62.2	
- ≥25 h	29	49.2	14	37.8	
Timing of operation (hours)	36.2 ± 32.9		46.7 ± 61.8		NS
Shunt					NS
- No	39	66.1	25	67.6	
- Yes	20	33.9	12	32.4	
CT Scan (acute infarct)					NS
- No	32	54.2	22	59.5	
- Yes	27	45.8	15	40.5	
NIH-T0	3.5 ± 2.4		9.0 ± 3.7		**<0.0001**
NIH-T0					**<0.0001**
- <5	46	78.0	5	13.5	
- ≥5	13	22.0	32	86.5	
NIH-T1	2.0 ± 2.8		1.9 ± 2.0		NS
NIH_Δ(T1-T0)	−1.5 ± 1.3		−7.0 ± 3.2		**<0.0001**
NIH_precent variation	−0.5 ± 0.5		−0.8 ± 0.2		NS

*Quantitative variables: Mann−Whitney test; qualitative variables: Fisher's exact.

revascularization of the cerebral infarct is minimal given that most complications (1.8% in the study conducted by Eckstein,[24] and 1.5% in that of Hubner *et al.*[23]) were related to technical factors (intraoperative embolisms or preoperative thrombosis, or both events) that have little bearing on the risk of early revascularization after an acute ischemic stroke. Hence technical complications apart, the results of these studies also confirm that the risk of early revascularization after acute stroke is not high if patients are appropriately selected.

Another important reason why our findings differ from those of published studies is the time elapsing after the onset of stroke symptoms and revascularization by CEA. The mean time lapse of 1.5 days is the shortest so far reported. This is a noteworthy finding considering that 5−12% of patients are reported risk to suffer a recurrent stroke early after the primary event.

Early reperfusion may also assist the relatively ischaemic cerebral tissue (ischemic penumbra). Only 3/96 (3%) patients had a slight worsening of their clinical conditions after CEA. We observed a rapid improvement in our patients' immediate postoperative neurologic conditions. At discharge, approximately 40% of patients had a normal neurological examination and a half had NIHSS scores indicating an improved neurologic deficit.

In a study on 8 patients submitted to CEA within 2 days of stroke, compared to 8 patients treated with heparin, Hubner *et al*.[23] demonstrated, through pre- and post-operative diffusion-weighted (DW) and perfusion-weighted (PW) MR, a reduction of the cerebral ischemic lesion in the patients operated on. Speculatively, these data might suggest a role of surgical reperfusion in rapidly improving the clinical course even 24 to 48 hours after stroke onset, as we observed in our patients. Obviously, this speculation would need to be tested in large number of patients studied with DW and PW MR.

Finally, even though 60% of the patients had CT-documentable evidence of recent brain infarct before CEA, the postoperative CT scans disclosed no conversion into hemorrhagic transformation.

Our study has two limitations: the small number of patients enrolled and the disadvantage that none of the participating centers had access to the mentioned highly sensitive diagnostic imaging techniques, that would have allowed us to increase the safety levels of the surgical indications and probably to include a larger number of patients.

In conclusion, this prospective multicenter study suggests that the protocol we applied may help in identifying the right candidates for very early (<1.5 days) surgery after acute stroke. These encouraging results warrant confirmation in a larger randomized multicenter prospective study, selecting patients with the most sensitive neuroimaging techniques presently available, and designed to compare early versus late surgery and/or medical therapy.

Appendix A. Participating centers

1. I Cattedra di Chirurgia Vascolare Università di Roma La Sapienza. − Paolo Fiorani
2. Cattedra Chirurgia Vascolare Università di Roma Tor Vergata. − Giuseppe Raimondo Pistolese
3. Azienda ospedaliera Monaldi, Napoli. − Basilio Crescenzi
4. U.O. Chirurgia Vascolare ad angiologia Ospedale Aosta. − Flavio Peinetti
5. Cattedra Chirurgia Vascolare Università di Firenze. − Carlo Pratesi
6. Chirurgia Vascolare Policlinico Monteluce, Perugia. − Piergiorgio Cao
7. Cattedra Chirurgia Vascolare Università di Siena. − Carlo Setacci
8. Cattedra di Chirurgia Vascolare, Università degli studi di Milano, Istituto E. Malan, Policlinico San Donato Milanese. − Domenico Tealdi
9. Chirurgia Vascolare Ospedale San Raffaele Milano. − Roberto Chiesa
10. Cattedra di Chirurgia Vascolare Università degli studi di Milano Ospedale San Carlo. Carlo Settembrini
11. Chirurgia Vascolare Ospedale Pellegrini Napoli. − Gianfranco Pane
12. Chirurgia Vascolare Ospedale Mauriziano Di Torino. − Domenico Palombo
13. Clinica Chirurgica Università di Trieste. − Roberto Adovasio

References

1 Gasecki AP, Ferguson GG, Eliasziw M, Clagett GP, Fox AJ, Hachinski V *et al*. Early endarterectomy for severe carotid artery stenosis after a non-disabling stroke: results from the North American Symptomatic Carotid Endarterectomy Trial. *J Vasc Surg* 1994;**20**:288−295.

2 Sacco RL, Foulkes MA, Mohr JP, Wolf PA, Hier DB, Price TR. Determinants of early recurrence of cerebral infarction. The Stroke DataBank. *Stroke* 1989;**20**:983−989.

3 Dosick SM, Whalen RC, Gale SS, Brown OW. Carotid endarterectomy in the stroke patient: computerized axial tomography to determine timing. *J Vasc Surg* 1985;**2**:214−219.

4 Meyer FB, Sundt Jr TM, Piepgras DG, Sandok BA, Forbes G. Emergency carotid endarterectomy for patients with acute carotid occlusion and profound neurological deficits. *Ann Surg* 1986;**203**:82−89.

5 Pritz MB. Timing of carotid endarterectomy after stroke. *Stroke* 1997;**28**:2563−2567.

6 Gertler JP, Blankensteijn JD, Brewster DC, Moncure AC, Cambria RP, LaMuraglia GM *et al*. Carotid endarterectomy for unstable and compelling neurologic conditions: do results justify an aggressive approach? *J Vasc Surg* 1994;**19**:32−40.

7 Eckstein HH, Schumacher H, Klemm K, Laubach H, Kraus T, Ringleb P *et al*. Emergency carotid endarterectomy. *Cerebrovasc Dis* 1999;**9**:270−281.

8 Whittemore AD, Ruby ST, Couch NP, Mannick JA. Early carotid endarterectomy in patients with small, fixed neurologic deficits. *J Vasc Surg* 1984;**1**:795−799.

9 Khanna HL, Garg AG. 774 carotid endarterectomies for strokes and transient ischaemic attacks: comparison of results of early vs. late surgery. *Acta Neurochir Suppl (Wien)* 1988;**42**:103−106.

10 Rosenthal D, Borrero E, Clark MD, Lamis PA, Daniel WW. Carotid endarterectomy after reversible ischaemic neurologic deficit or stroke: is it of value? *J Vasc Surg* 1988;**8**:527−534.

11 Piotrowski JJ, Bernhard VM, Rubin JR, McIntyre KE, Malone JM, Parent III FN *et al*. Timing of carotid endarterectomy after acute stroke. *J Vasc Surg* 1990;**11**:45−52.

12 Hoffman M, Robbs J. Carotid endarterectomy after recent cerebral infarction. *Eur J Vasc Endovasc Surg* 1999;**18**:6−10.

13 Kahn MB, Patterson HK, Seltzer J, Fitzpatrick M, Smullens S, Bell R *et al*. Early carotid endarterectomy in selected stroke patients. *Ann Vasc Surg* 1999;**13**:463–467.
14 Blaisdell WF, Clauss RH, Gailbraith JG, Smith Jr JA. Joint study of extracranial carotid artery occlusion IV. Review of surgical considerations. *JAMA* 1969;**209**:1889–1895.
15 Wylie EJ, Hein MF, Adams JE. Intracranial hemorrhage following surgical revascularization for treatment of acute strokes. *J Neurosurg* 1964;**21**:212–218.
16 The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischaemic stroke. *N Engl J Med* 1995;**333**:1581–1587.
17 Hacke W, Kaste M, Fieschi C *et al*. for the ECASS-study group. Safety and efficacy of intravenous thrombolysis with a recombinant tissue plasminogen activator in the treatment of acute hemispheric stroke. *JAMA* 1995;**27**:1017–1025.
18 Hacke W, Kaste M, Fieschi C *et al*. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke [ECASS II]. Second European-Australasian Acute Stroke Study Investigators. *Lancet* 1998;**352**:1245–1251.
19 Clark WM, Wissman S, Albers GW, Jhamandas JH, Madden KP, Hamilton S. Recombinant tissue-type plasminogen activator (Alteplase) for ischaemic stroke 3 to 5 hours after symptom onset. The ATLANTIS Study: a randomized controlled trial. Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischaemic Stroke. *JAMA* 1999;**282**: 2019–2026.
20 Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C *et al*. Intra-arterial prourokinase for acute ischaemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism. *JAMA* 1999;**282**: 2003–2011.
21 Bond R, Rerkasem K, Rothwell PM. Systematic review of the risks of carotid endarterectomy in relation to the clinical indication for and timing of surgery. *Stroke* 2003;**34**:2290–2303.
22 Brott T, Adams HP, Olinger CP, Marler JR, Barsan WG, Biller J *et al*. Measurements of acute cerebral infarction: a clinical examination scale. *Stroke* 1989;**20**:8654–8670.
23 Huber R, Muller BT, Seitz RJ, Siebler M, Modder U, Sandmann W. Carotid surgery in acute symptomatic patients. *Eur J Vasc Endovasc Surg* 2003;**25**:60–67.
24 Eckstein HH, Ringleb P, Dorfler A, Klemm K, Muller BT, Zegelman M *et al*. The Carotid Surgery for Ischemic Stroke trial: A prospective observational study on carotid endarterectomy in the early period after ischemic stroke. *J Vasc Surg* 2002;**36**: 997–1004.
25 Ricco JB, Illuminati G, Bouin-Pineau MH, Demarque C, Camiade C, Blecha L *et al*. Early carotid endarterectomy after a nondisabling stroke: a prospective study. *Ann Vasc Surg* 2000; **14**:89–94.

Accepted 18 March 2006
Available online 12 June 2006