

# Carotid endarterectomy in Durban — the first 10 years

A. M. KADWA, J. V. ROBBS

**Abstract** This study was a prospective evaluation of the Durban experience with carotid endarterectomy over the past decade. Since 1981, 478 carotid endarterectomies have been performed in 411 patients. The majority of these patients were white men, with an average age of 60,6 years. The indication for surgery was a lateralising transient ischaemic attack or amaurosis fugax in 65,5%, lateralising stroke (< 1 year before surgery) in 14,4%, non-lateralising global cerebral ischaemia in 9,4% and asymptomatic carotid stenosis in 10,7%. Carotid endarterectomy was performed under general anaesthesia and with invasive monitoring; 25% of patients underwent selective shunting. After open carotid bifurcation endarterectomy, all but 6 underwent primary closure (99,4%).

The combined major stroke/mortality rate was 6%. This audit identified a group of patients who presented with a history of stroke within the year preceding surgery and who had a significantly higher postoperative stroke/mortality rate of 20,2%. Long-term follow-up, ranging from 1 month to 96 months, showed 80,7% to be stroke-free after 8 years.

This audit demonstrates a postoperative stroke/mortality rate comparable to that of other series and additionally confirmed the durability of carotid endarterectomy in the long term.

*S Afr Med J* 1993; 83: 248-252.

The success of carotid endarterectomy (CE) is entirely dependent on the achievement of long-term stroke-free survival without peri-operative stroke or mortality. Furthermore, such success should be superior to the best non-operative or medical therapy. The results of numerous studies from recognised vascular units continue to be published, attesting to the success of CE. Unfortunately, not all studies exemplify this success.

The continued performance of CE in any unit therefore requires ongoing evaluation to attest to success. With this in mind, the Durban experience of the past decade was evaluated.

## Patients and methods

All patients who underwent CE for atherosclerotic disease of the carotid bifurcation at the Metropolitan Vascular Service (University of Natal Hospitals, Durban) were included in this evaluation. Their clinical case records, including investigations, operation records, outcome and follow-up, were prospectively documented onto a protocol sheet. The database formed was then analysed.

## Pre-operative assessment

After a careful history and thorough physical examination, all patients underwent a duplex scan of the carotid bifurcation (ATL Mark 600). In patients with significant appropriate disease, intra-arterial digital subtraction angiography was performed routinely to outline the aortic arch and branches; selective carotid views were not done. In addition, all patients underwent computed tomographic scanning of the head (CT scan) to document infarcts and exclude other lesions.

Initial evaluation of cardiac risk status was performed by means of the modified Goldman Risk Index. High cardiac risk patients were further stratified by means of stress electrocardiography, echocardiography, radio-isotope scanning and/or coronary angiography. Other routine tests performed included a haematological and lipid profile, pulmonary function tests and measurement of the creatinine clearance rate.

The following patients in this series were referred for CE: (i) asymptomatic patients with a severe carotid stenosis (> 70%); (ii) patients with lateralising cerebral ischaemic symptoms who demonstrated a severe stenosis or evidence of ulcerated plaque at the appropriate carotid bifurcation — this group included patients who had had transient ischaemic attacks (TIA), amaurosis fugax (AF) or strokes followed by good functional recovery; and (iii) patients with non-lateralising (global) cerebral ischaemia and multiple vessel disease who were shown to have stenoses in the carotid arteries.

## Operative management

All operations were performed under a balanced light general anaesthetic (nitrous oxide, oxygen and isoflurane) combined with a superficial cervical plexus local anaesthetic block. Invasive monitoring was routinely employed and included arterial and central venous pressure monitoring, pulse oximetry, standard electrocardiography, capnography and urine output recordings. A pulmonary flow catheter was selectively employed in high cardiac risk patients.

Department of Surgery, University of Natal, Durban

A. M. KADWA, F.R.C.S.

J. V. ROBBS, CH. M., F.R.C.S.

Accepted 13 Apr 1992.

Exposure of the carotid bifurcation was obtained via an oblique incision along the anterior border of the sternocleidomastoid muscle. Open carotid bifurcation endarterectomy was performed after systemic heparinisation (5 000 U). Selective shunting based on a mean carotid stump pressure of < 50 mmHg was employed — a silicone shunt with a side-arm to measure shunt pressure continuously was used for this purpose. Tacking sutures of the distal intima were rarely necessary as a good end-point was meticulously attained. Primary closure of the arteriotomy with a fine monofilament non-absorbable vascular suture (6,0) was routinely performed except in small-calibre internal carotid arteries which required patch closure. Post-completion intra-operative angiography was not performed. In the latter part of the series, a continuous-wave 10 MHz ultrasound probe was used to assess the audible Doppler signal at the endarterectomy site and distally. Reversal of heparinisation at the completion of the operative procedure was not routinely performed except in patients with prolonged suture-line bleeding.

At the conclusion of the operation, smooth reversal of the anaesthetic combined with gentle extubation minimised swings in blood pressure. All patients were transferred to the intensive care unit where monitoring of vital signs was continued over the ensuing 24 hours.

Postoperative complications including wound haematoma or infection, temporary neurological or cranial nerve deficit, stroke and death were recorded. Patients with an uneventful postoperative course were discharged on the 3rd postoperative day. Patients who developed a postoperative stroke underwent a CT scan of the head and a duplex scan of the endarterectomy site whenever possible.

### Follow-up

All patients were followed up at the end of the first month and thereafter at 6-monthly intervals. Follow-up documentation included the recording of significant events such as death, recurrence of cerebral ischaemic events and restenosis. Duplex scanning was performed selectively in patients with recurrence of symptoms or where there was clinical suspicion of restenosis, e.g. in cases where a bruit developed.

The follow-up data were used to draw up a life-table by the actuarial method. Ipsilateral ischaemic stroke appropriate to the area of the endarterectomised artery was accepted as the only 'hard' end-point for life-table analysis. A stroke-free curve was plotted with the life-table data.

### Results

Since 1981, 478 carotid endarterectomies were performed in 411 patients — bilateral staged operations were performed in 67. Fig. 1 indicates the number of operations performed per year. The 1991 figure represents the number performed up to the end of September that year.

There were 294 white, 85 Asiatic, 23 coloured and 9 black patients. Of these, 256 were men and 155 women. The average age was 60,6 years (range 35 - 82 years) and 90% were more than 50 years old. The incidence of risk factors is outlined in Table I. Hypertension (53,8%) and smoking (50,9%) were encountered most frequently.

The clinical presentation of the patients is detailed in Table II: 10,7% were asymptomatic, 65,5% had had a TIA or AF, 14,4% had had a completed stroke within 1 year of presentation with good functional recovery, and 9,4% had symptoms of global cerebral ischaemia such as dizziness, light-headedness, syncope, loss of memory and tinnitus.

TABLE I.  
Risk factors

	No. of patients	%
Hypertension	221	53,8
Smoking	209	50,9
Ischaemic heart disease	115	27,9
Diabetes	95	23,1
Peripheral vascular disease	44	10,7
Old stroke (>1 year)	27	6,6
Coronary artery bypass	16	3,9
Chronic obstructive airways disease	11	2,7

TABLE II.  
Clinical presentation

	Total operations	%
Asymptomatic	51	10,7
TIA (including amaurosis fugax)	313	65,5
Stroke < 1 year	69	14,4
Global cerebral ischaemia	45	9,4

### Operative findings

Table III summarises the degree of stenosis as judged intra-operatively. The majority of operations (62,7%) were performed for stenosis exceeding 50%, while 34,6% of the operations were performed for lesser degrees of stenosis. The latter were usually associated with ulcerated plaque, which was present in a total of 62,7% of patients. Plaque haemorrhage was uncommon (14,8%).

TABLE III.  
Degree of stenosis

Category	Degree of stenosis (%)	Total operations	%
A	0 - 4	16	3,3
B	5 - 15	60	12,5
C	16 - 49	90	18,8
D	50 - 99	300	62,9
E	100	12	2,5

Four hundred and sixty-six patients underwent open carotid bifurcation endarterectomy. Of these, 460 had primary closure, 3 had vein-patch closure and 3 had interposition-reversed saphenous vein grafts inserted. Twelve additional patients with occluded internal carotid arteries underwent CE with external carotid angioplasty. Twenty-five per cent had a shunt inserted selectively as a mean carotid stump pressure of less than 50 mmHg was measured intra-operatively.

### Postoperative complications

The postoperative complications are summarised in Table IV.

TABLE IV.  
Postoperative complications (< 1 month)

	No. of operations	%
Local		
Wound haematoma	33	6,9
Wound infection	7	1,4
Transient cranial nerve deficit	19	3,9
Central neurological deficit		
Transient neurological deficit	9	1,8
Stroke	23	4,8
Death	17	3,5

### Local

Thirty-three (6,9%) procedures were complicated by wound haematoma. Eleven patients developed an expanding haematoma with airway obstruction which required emergency decompression with evacuation of the haematoma; 2 of these patients required tracheostomy and 5 (15%) eventually died.

Wound infection was rare and occurred in 7 patients (1,4%). Two of these patients developed a false aneurysm approximately 1 month after surgery and both underwent repeat surgery with primary repair in one and a vein-patch angioplasty in the other; *Staphylococcus aureus* was cultured in both instances.

Nineteen patients (1,8%) developed cranial nerve palsies following surgery. The majority of these involved the mandibular branch of the facial nerve, and were presumably the result of neuropraxias caused by retraction injuries. Two patients had evidence of a hypoglossal nerve palsy. Most of these cranial nerve palsies resolved spontaneously within 3 months of surgery.

### Central neurological deficit

Nine patients (1,8%) developed a transient central neurological deficit evident on recovery from anaesthesia. Four manifested with monoparesis, and hemiparesis occurred in 5 patients. All of these resolved spontaneously within 24 hours and all occurred in the neighbourhood of the CE.

Twenty-three patients (4,8%) developed a stroke during the postoperative period (<1 month). Five (1,1%) of these strokes were classified as minor and manifested with an ipsilateral monoplegia on the CE side; all recovered with minimal disability. Eighteen strokes were classified as major (3,7%) with a dense ipsilateral hemiplegia in 17 and a contralateral hemiplegia in the other. Six of these major strokes were fatal (26%). Of the 11 survivors, 2 were permanently institu-

tionalised and required continuous nursing care, while the remaining 9 eventually recovered sufficiently to achieve functional independence and almost complete mobility.

Seven strokes occurred intra-operatively and the rest postoperatively, between the 1st and the 14th day after surgery. CT scan of the head was performed in 18 patients: 14 had an ipsilateral infarct in the area of the CE, 1 had multiple infarcts, 1 had an infarct contralateral to the CE side and 1 had intracerebral haemorrhage on the operated side. A duplex scan was performed in 16 patients and confirmed a patent endarterectomy site in 15 and occlusion in 1.

### Mortality

Seventeen patients (3,5%) died in the early postoperative period (< 1 month). Seven of these deaths were cardiac-related, with acute myocardial infarction the cause in 6 patients. There were 6 fatal strokes. Three patients died of respiratory failure: aspiration pneumonia occurred in 1, aspiration pneumonia after emergency tracheostomy for an expanding wound haematoma in another, and acute respiratory obstruction caused by laryngeal oedema in the 3rd. One other patient died of acute renal failure.

### Stroke mortality

Table V shows the postoperative stroke/mortality rate in relation to the pre-operative clinical presentation. Patients who presented with stroke within the year preceding CE had a higher postoperative stroke rate (14,5%), mortality rate (11,5%) and combined stroke/mortality rate (20,2%) than those who presented with an asymptomatic stenosis, TIA or global cerebral ischaemia. This was statistically significant ( $P < 0,001$ ). The combined stroke/mortality rate for all operations was 7,2%.

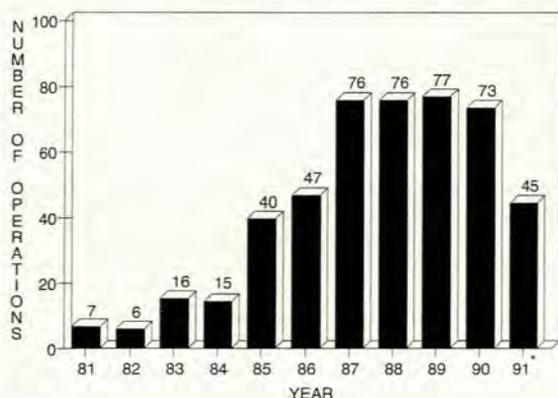


FIG. 1. Number of operations (\*up to September 1991).

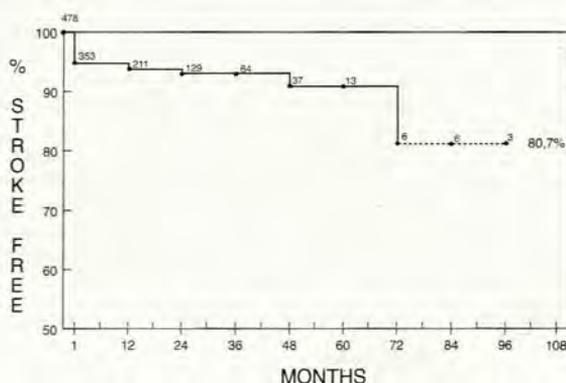


FIG. 2. Ipsilateral ischaemic stroke-free curve.

TABLE V. Postoperative stroke and mortality (< 1 month)

Presentation	No. of patients	Stroke		Death		S/M	
		No.	%	No.	%	No.	%
No stroke	409	13	3,1	9	2,2	20	4,8
Asymptomatic stenosis	51	2	3,9	2	3,9	3	5,8
TIA	313	10	3,1	5	1,5	14	4,4
Global symptoms	45	1	2,2	2	4,4	3	6,6
Stroke	69	10	14,5*	8	11,5*	14	20,2*
Total	427	21	4,9	17	3,5	31	7,2

\*  $\chi$ -test =  $P < 0,001$ .

S/M = combined stroke/mortality rate.

**TABLE VI.**  
**Life-table stroke-free rates**

Interval (mo.)	No. in interval	No. of strokes	No. of deaths	No. lost	No. withdrawn	No. at risk	Interval	Stroke-free (%)	
								Cumulative	SE
0 - 1	478	23	18	57	5	438	94,8	94,8	0
1 - 6	383	1	5	49	5	353	99,8	94,7	1,1
6 - 12	323	1	3	30	50	281	99,7	94,4	1,3
12 - 18	293	1	5	16	35	211	99,6	94,0	1,5
18 - 24	182	0	2	14	13	167	100,0	94,0	1,7
24 - 30	153	1	2	24	21	129	99,4	93,4	2,1
30 - 36	105	0	1	7	24	89	100,0	93,4	2,5
36 - 42	73	0	0	7	20	64	100,0	93,4	2,9
42 - 48	56	0	0	5	11	48	100,0	93,4	3,4
48 - 54	40	1	0	4	9	37	97,3	90,8	4,5
54 - 60	26	0	0	1	9	21	100,0	90,8	6,0
60 - 66	16	0	0	1	4	13	100,0	90,8	7,6
66 - 72	11	1	0	1	2	9	88,9	80,7	11,8
72 - 78	7	0	0	0	1	6	100,0	80,7	14,4
78 - 84	6	0	0	0	0	6	100,0	80,7	14,4
84 - 90	6	0	0	0	0	6	100,0	80,7	14,4
90 - 96	6	0	0	0	6	3	100,0	80,7	20,5

**Long-term follow-up**

The follow-up period ranged from 1 to 96 months. Table VI displays the life-table analysis and Fig. 2 illustrates the stroke-free curve for the entire cohort of patients. After successful CE, 6 patients (1,32%) developed an ipsilateral ischaemic stroke on the side of the CE; this gives an ipsilateral ischaemic stroke event rate of 0,16% per annum.

Six patients developed symptomatic restenosis of the endarterectomy site (1,2%). All underwent repeat surgery with patch angioplasty. Neo-intimal hyperplasia was the cause of restenosis confirmed both at operation and on histological examination. There was no post-operative stroke or mortality following these procedures.

**Discussion**

After an almost threefold increase in the number of CEs performed in this unit since 1985, approximately 75 such operations are now performed annually. This increase is not only the result of improvements in diagnostic accuracy, especially with the advent of duplex scanning, but also that of greater awareness among physicians of the efficacy of CE for stroke prophylaxis.

Although the Durban metropolitan area comprises a cosmopolitan population, black patients make up only 2,2% of the entire series. This is almost certainly a direct reflection of the rarity of extracranial cerebrovascular disease among blacks.<sup>1,2</sup> The epidemiological data for the rest of the patients are in fact, no different from those of other Western series.

The majority of patients underwent CE for symptomatic carotid artery disease (89,3%); lateralising TIA and AF were the commonest modes of presentation. In comparison with other series,<sup>3,4</sup> asymptomatic carotid artery disease was present in a much smaller proportion (10,7%) of patients submitted for CE. This probably reflects the reluctance of physicians to refer such patients for operative treatment.

CE was performed in 9,4% of patients with symptoms of non-lateralising or global cerebral ischaemia caused by multiple vessel disease. The aim of CE in this group was to improve inflow into the anterior cerebral circulation and subsequently into the posterior cerebral circulation, via collaterals, thereby relieving symptoms. A previous study from this unit in these patients found surgery to be safe and rewarding, with good relief of symptoms in the medium term.<sup>3</sup>

Approximately one-third of the operations (34,6%) in this series were performed for stenosis of less than 50%; many of these operations were, in fact, performed for suspected concomitant plaque ulceration. It is now well established that plaque ulceration is the predominant cause of lateralising cerebral ischaemic events.<sup>6-8</sup> No studies to date have prospectively randomised symptomatic patients with minimally stenotic ulcerated plaques between CE and medical therapy. The prime reason for lack of such studies relates to difficulties in establishing an accurate pre-operative diagnosis of plaque ulceration as both duplex scan and angiography are equally inaccurate in this respect.<sup>9</sup> Future refinements and advances in duplex scan technology will undoubtedly greatly facilitate the accurate characterisation of plaque morphology. In the absence of controlled studies, most vascular surgeons believe the symptomatic, minimally stenotic ulcerated plaque to be a harbinger of future stroke and would therefore recommend prophylactic CE.

All patients in this series underwent CE under general anaesthesia as a matter of routine for two reasons: (i) it ensures adequate stable cerebral blood flow and oxygen consumption as a result of accurate control of blood pressure, ventilation and depth of anaesthesia; and (ii) the 'sleeping' patient can comfortably undergo whatever exacting procedure is required without disturbing the surgeons. A recently randomised prospective study comparing local with general anaesthesia revealed no significant difference regarding peri-operative complications.<sup>10</sup>

Carotid stump pressure measurement was employed in this series as a method of determining cerebral tolerance to temporary carotid occlusion. A shunt was necessary in 25% of cases for cerebral protection during CE. The frequency with which a shunt is used, among 'selective shunters' in other series, varies between 10% and 50%.<sup>11</sup> Although shunt use may be unnecessary in more than 90% of patients, a small number (1 - 2%) may sustain irreversible neurological damage if it is not used.

Patch angioplasty closure after CE was rarely performed in this series (0,6%) and its role remains controversial. Two published randomised prospective studies showed that primary closure was more frequently associated with carotid stenosis or occlusion in the short term (< 1 year).<sup>12,13</sup> There was, however, no significant difference in postoperative stroke incidence among the primary closure and patch closure groups, but both studies contained small subgroups which reduced the

statistical validity of their results. Until large, multicentre, prospective randomised studies are undertaken, the controversy will remain.

Post-completion assessment of the CE was performed subjectively by means of either digital palpation of pulses or interpretation of audible signals with a continuous-wave Doppler probe. Intra-operative angiography may reveal technical defects such as intimal flaps or stenosis. It is, however, not favoured because it is time-consuming and potentially dangerous. In addition, angiogram pictures are difficult to interpret immediately after endarterectomy and false-positives may result in unnecessary re-exploration. Furthermore, they provide no assessment of flow. Intra-operative duplex scanning is currently the best method of objectively assessing the endarterectomised site.

The combined postoperative major stroke and mortality rate in this series was 6%. If one excludes non-ischaemic stroke or stroke contralateral to the territory of endarterectomy, the figure decreases to 5,6%. Although not strictly comparable, this figure is similar to those in two recently reported series: 7,5% in the MRC European Carotid Study Trial (ECST)<sup>14</sup> and 8% in the North American Symptomatic Carotid Endarterectomy Trial (NASCET).<sup>14</sup> The combined postoperative stroke/mortality rate in the group who had presented for treatment after a stroke which had occurred within the preceding year was significantly higher at 20,2%. This figure seems to be unacceptably high at first glance. However, if cognisance is taken of their poor natural history (20 - 40% die in the 1st month after the stroke, approximately 15% of survivors die each subsequent year and 10% of survivors suffer a recurrent stroke each year<sup>15-17</sup>), these patients still probably benefit from CE in the longer term.

The long-term follow-up data in the life-table and the stroke-free curve clearly show the durability of CE as a stroke-prevention operation. The ipsilateral stroke event rate was 0,16% per year and 80,7% of patients were still stroke-free after 8 years. Both the ECST and NASCET studies confirmed similar stroke prevention efficacy in the short to medium term.<sup>14,18</sup>

It is now abundantly clear in the light of the findings of ECST and NASCET<sup>14,18</sup> that CE is superior to medical therapy in the symptomatic patient with severe stenosis (>70) in the medium term (3 years). The ECST study, in addition, showed CE to be of little benefit in the symptomatic patient with minimal stenosis (0 - 29%). Both the above studies have continued to recruit symptomatic patients with moderate stenosis (30 - 69%) and it is hoped on completion of these studies to determine the optimal management of this latter group.

At the present time, no prospective randomised studies have been made of the asymptomatic patient with significant carotid stenosis. However, published data from several comparative studies have shown a 60 - 100% reduction in stroke rate following CE compared with medical therapy in the medium term.<sup>19</sup> Three prospective randomised trials are currently in progress which, it is hoped, will address the correct management of asymptomatic carotid stenosis, viz. the Mayo Asymptomatic Carotid Endarterectomy Study Group,<sup>20</sup> the Asymptomatic Carotid Atherosclerosis Study Group<sup>21</sup> and the Cooperative Veterans Administration Asymptomatic Carotid Stenosis Study.<sup>22</sup> The first phase

report of the latter study was published recently and demonstrates a postoperative stroke/mortality rate of 4,3%.<sup>23</sup> It is anticipated that in the course of the next few years the short- to medium-term follow-up will be completed in all the abovementioned trials, thereby finally resolving the controversy.

In conclusion this evaluation of a decade's experience with CE has shown results that compare favourably to Western series and therefore justify its continued performance. The evaluation has, in addition, identified a group who presented with a history of stroke within the year preceding surgery who had a higher combined postoperative stroke/mortality rate. CE is still prudent in this group in the light of their documented unfavourable natural history.

#### REFERENCES

1. Robbs JV. Atherosclerotic peripheral arterial disease in blacks: an established problem. *S Afr Med J* 1985; **67**: 797-801.
2. Robbs JV, Human RR, Rajarathnam P. Extracranial arterial reconstruction for chronic cerebral ischaemia: an audit experience in the Durban teaching hospitals. *S Afr Med J* 1986; **70**: 653-657.
3. Hertzner NR, Arison R. Cumulative stroke and survival ten years after carotid endarterectomy. *J Vasc Surg* 1985; **2**: 661-668.
4. Callow AD, Mackey WC. Long-term follow-up of surgically managed carotid bifurcation atherosclerosis. *Ann Surg* 1989; **210**: 308-316.
5. Kadwa AM, Robbs JV. Non-lateralising cerebral ischaemic syndromes — is surgery worthwhile? *S Afr J Surg* 1989; **27**: 37.
6. Moore WS, Hall AD. Ulcerated atheroma of the carotid artery: a cause of transient cerebral ischemia. *Am J Surg* 1968; **116**: 237.
7. Blaisdell FW, Glockman M, Trunkey DD. Ulcerated atheroma of the carotid artery. *Arch Surg* 1974; **108**: 491-496.
8. Bartynski WS, Darbouze P, Nemir P. Significance of ulcerated plaque in transient cerebral ischemia. *Am J Surg* 1981; **141**: 353-357.
9. Kadwa AM, Robbs JV, Ray R. Carotid plaque morphology and neurological symptoms: a correlation between angiography, duplex scan and intra-operative findings. *S Afr J Surg* 1989; **27**: 194.
10. Forsell C, Takolander R, Bergqvist D, Johansson A, Persson NH. Local versus general anaesthesia in carotid surgery: a prospective randomised study. *Eur J Vasc Surg* 1989; **3**: 503-509.
11. Archie JP. Technique and clinical results of carotid stump back-pressure to determine selective shunting during carotid endarterectomy. *J Vasc Surg* 1991; **13**: 319-327.
12. Eikelboom BC, Ludwig JW, Vermeulen FEE. Benefits of carotid patching: a randomised study. *J Vasc Surg* 1988; **7**: 240-247.
13. Lord RSA, Raj TB, Stary DL, Peter A, Goh KH. Comparison of saphenous vein patch, polytetrafluoroethylene patch, and direct arteriotomy closure after carotid endarterectomy: Part I. Perioperative results. *J Vasc Surg* 1989; **9**: 521-529.
14. European Carotid Study Trialists' Collaborative Group. MRC European carotid surgery trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. *Lancet* 1991; **337**: 1235-1243.
15. Matsumoto N, Whisnant JP, Kurland LT. Natural history of stroke in Rochester, Minnesota, 1955 through 1969: an extension of a previous study, 1945 through 1954. *Stroke* 1973; **4**: 20.
16. Baker RN, Schwartz WS, Ramseyer JC. Prognosis among survivors of ischemic stroke. *Neurology* 1968; **18**: 933.
17. Wallace DC. A study of the natural history of cerebral vascular disease. *Med J Aust* 1967; **1**: 90.
18. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991; **325**: 445-453.
19. Thompson JE. Carotid endarterectomy for asymptomatic carotid stenosis: an update. *J Vasc Surg* 1991; **13**: 669-676.
20. Mayo Asymptomatic Carotid Endarterectomy Study Group. Effectiveness of carotid endarterectomy for asymptomatic carotid stenosis: design of a clinical trial. *Mayo Clin Proc* 1989; **64**: 897-904.
21. The Asymptomatic Carotid Atherosclerosis Study Group. Study design for randomised prospective trial of carotid endarterectomy for asymptomatic atherosclerosis. *Stroke* 1989; **20**: 844-849.
22. Veterans Administration Cooperative Study. Role of carotid endarterectomy in asymptomatic carotid stenosis. *Stroke* 1986; **17**: 534-548.
23. Towne JB, Weiss DG, Hobson W. First phase report of Cooperative Veterans Administration Asymptomatic Carotid Stenosis Study — operative morbidity and mortality. *J Vasc Surg* 1990; **11**: 252-259.