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N. A. Syed

*Aga Khan University*

A. Zakaria

*Aga Khan University*

B. A. Khealani

*Aga Khan University*

M. Wasay

*Aga Khan University*

S. M. Baig

*Aga Khan University*

*See next page for additional authors*

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**Authors**

N. A. Syed, A. Zakaria, B. A. Khealani, M. Wasay, S. M. Baig, and Z. Sophie

# Should Carotid Endarterectomy be performed for Symptomatic Carotid Stenosis Pakistan?

N. A. Syed, A. Zakaria, B. A. Khealani, M. Wasay, S. M. Baig, Z. Sophie\*  
Neurology Section, Departments of Medicine and Surgery\*, The Aga Khan University, Karachi.

## Abstract

**Objective:** The risk of stroke and death associated with carotid endarterectomy is operator dependant. Data regarding risks of this procedure are not available in Pakistan and therefore it is difficult to make accurate risk benefit analysis for individual patients. Our objective was to determine safety of carotid endarterectomy at an academic tertiary care center in Pakistan.

**Methods:** Patients who underwent carotid endarterectomy (CEA) at our hospital during a ten-year period were identified through ICD-9 coding system of the hospital medical records. Demographic features, associated medical problems and immediate postoperative complications were recorded and analyzed.

**Results:** Sixty-three carotid endarterectomies were performed on 59 patients. Ages range from 43 to 80 (mean  $61 \pm 8$ ) years; 53 were male and 10 were female. Common associated diseases among these patients were hypertension; 38 (64.4%), ischemic heart disease; 26 (44%), diabetes mellitus; 24 (40.7%); dyslipidemia; 19 (32.2%) and renal insufficiency; 13 (22%). Most common complication was neuropraxia (transient neuropathy) 5 (7.9%), followed by pneumonia and stroke; each in 3 (4.8%) patients. None of the strokes related to the surgical procedure were disabling. Two of the patients who had stroke, recovered fully within 17 weeks and one recovered partly but was independent in all daily activities of living (ADLs). One patient died following simultaneous coronary artery bypass graft (CABG) and CEA. The risk of stroke or death for patients undergoing CEA was high with simultaneous CABG (3/11, 27%) and low for patients undergoing CEA alone (1/52, 2%).

**Conclusion:** Carotid endarterectomy is a safe procedure in patients with symptomatic carotid stenosis at our hospital and should be performed, when indicated. (JPMA 53:589;2003).

## Introduction

Stroke is a major cause of death and disability worldwide. In the last 20 years there has been a tremendous growth in stroke research in an attempt to find ways to prevent and treat patients with this devastating disease. Advances in our understanding of the pathophysiology of ischemic stroke have helped bring in new and innovative therapies in the prevention and treatment of ischemic strokes. Thrombosis in the cerebral blood vessels is a complication of atherosclerosis. Atherosclerosis involving the bifurcation of the carotid arteries has been recognized as an important cause of stroke for over 50 years.<sup>1, 2</sup>

Symptomatic atherosclerotic plaques in the carotid artery involve primarily the carotid bulb and are characterized by increased cellular proliferation, lipid accumulation, calcification, ulceration, hemorrhage, and thrombosis.<sup>3</sup> The risk of an ischemic stroke following carotid artery stenosis is not uniform. Factors increasing the risk of stroke include plaque morphology (ulcerated versus smooth morphology) and the degree of stenosis. The NASCET trial showed that patients with an ulcerated plaque and greater than 70% stenosis had an approximately twofold increase in stroke risk compared with patients with smooth stenosis.<sup>4</sup>

Similarly patients with greater degree of stenosis appear to be at greater risk of ischemic stroke; patients with a 75% stenosis have a two-year risk of ipsilateral stroke (after hemispheric TIA) of 37.4%, whereas patients with a 95%

stenosis have a 2 years risk of 96.3%.<sup>5</sup>

Treatment of carotid stenosis comprises of measures to stabilize the progression of the plaque and its complications and procedures to eliminate or reduce the plaque. Common measures to stabilize the progression of the plaque, and its complications include risk factor modification and medications. The target modifiable risk factors include hypertension, diabetes, smoking, dyslipidemia and obesity. The medications used to stabilize and reduce complications and progression of the plaque include anti-platelet agents, statins, and angiotensin converting enzyme inhibitors. The most common procedure to eliminate or reduce the plaque is carotid endarterectomy. By removing the thrombotic plaque and the stenosis, carotid endarterectomy decreases the risk for ischemic stroke. However, the risk reduction conferred by the procedure varies greatly amongst different patient populations. The possible benefit of carotid endarterectomy is dependant on the perioperative risk of the surgical intervention, which differs from center to center and surgeon to surgeon. The most feared complication of carotid endarterectomy is major stroke and death. It has been recommended that the surgical complication rate of stroke/death is in the range of not more than 5-7% for symptomatic patients, to provide significant benefit to the patient.<sup>4, 8, 11</sup>

The complications of carotid endarterectomy include ischemic stroke, intracerebral hemorrhage and hyperperfusion

syndrome. Local complications include wound infection, wound hematoma, false aneurysm formation, carotid suture line rupture, cervical nerve injury and cranial nerve injury.<sup>16,17</sup>

Cranial nerve injury occurs frequently and has been reported in 12.5% to 27% of patients undergoing carotid endarterectomy, most of these are temporary.<sup>16,17</sup>

A number of studies have addressed the predisposing factors leading to stroke or death following carotid endarterectomy. Interestingly, a review of 1160 patients at 12 medical centers found no significant association between the complication rate and the different techniques of carotid endarterectomy.

Among asymptomatic patients, the ACAS trial associated perioperative stroke with diabetes mellitus, postoperative hypertension and contralateral carotid stenosis.<sup>18</sup> Other studies suggest preoperative hypertension, ischemic heart disease, diabetes mellitus, combination with coronary artery bypass surgery, and an age over 75 years as predisposing factors for increased perioperative complications.<sup>13,19</sup>

The data concerning morbidity and mortality of carotid endarterectomy for symptomatic stenosis at academic medical centers in Pakistan is very limited. Physicians are often forced to make recommendations and decisions regarding carotid endarterectomy without the benefit of preexisting unambiguous data on outcome of carotid endarterectomy. This has led to a need for assessment of risk of Carotid endarterectomy in our local environment. In order to address this question, we analyzed patient characteristics and the outcome of carotid endarterectomy at the Aga Khan University Hospital for 59 consecutive patients undergoing the procedure for symptomatic carotid artery disease. To our knowledge, this is the first systematic review of the complications of symptomatic carotid endarterectomy in Pakistan.

## Methods

A retrospective analysis was performed to assess the incidence of perioperative complications in patients undergoing carotid endarterectomy for symptomatic carotid artery disease, between January 1991 and December 2000 at the Aga Khan University Hospital, Karachi.

Data was extracted from patient medical records using a pretested questionnaire. The degree of stenosis was determined by the radiologist performing cerebral angiography and recorded as a percentage value. Information regarding demographics, and risk factors for atherosclerosis (including presence or absence of diabetes, hypertension and tobacco use) were analyzed. All post-operative complications were documented. Any neurologic deficit occurring during or following surgery was classified as originating from the

peripheral nervous system (for example, traction injury of the hypoglossal nerve or compression injury to the ulnar nerve) or the central nervous system (stroke) based on physical examination and results of ancillary studies. Neurologic deficit resulting from a new central nervous system lesion was considered to be a stroke occurring as an adverse complication of carotid endarterectomy. Stroke was considered disabling if the patient had a Rankin score of 3 or more at 90 days.<sup>20</sup> Data was analyzed using EPI Info 6.0 and SPSS version 10.0.

## Carotid endarterectomy procedure

All patients undergoing carotid endarterectomy had symptomatic carotid stenosis diagnosed on carotid duplex ultrasound and confirmed with cerebral angiography. Carotid endarterectomy was performed under general anesthesia. Patients on warfarin were required to stop warfarin prior to surgery and demonstrate an INR of <1.5. Aspirin was stopped one day prior to surgery. During endarterectomy, intra-arterial hemodynamic monitoring was used to follow changes in blood pressure. 5000 units of heparin; were administered intravenously immediately prior to clamping of the carotid artery. This was not reversed at the end of the procedure. Exposure was obtained using a standard incision along the anterior border of the sternocleidomastoid muscle. A David shunt was used in all patients. Primary closure of the vessels were achieved. No patch closures were performed. Closed suction drainage was used routinely in wound closures. Postoperative care was administered in the recovery room. Patients were kept in high dependency unit or the recovery room overnight to allow close monitoring of cardiopulmonary and neurologic status. Patients were generally ambulated the day following surgery and antiplatelet therapy was restarted on the first post operative day. Mean hospital stay was 6 ± 3.4 days.

## Results

Fifty nine consecutive patients who underwent carotid endarterectomy for symptomatic carotid disease were identified. A total of 63 carotid endarterectomy procedures were performed on 59 patients. Simultaneous coronary artery bypass grafting was performed on 11 patients. Mean age for all patients was 60 years with a range of 43 to 80 years. The age and sex demographic factors are summarized in Table 1.

The most common concurrent disease in our patient population was hypertension, followed by ischemic heart disease, diabetes mellitus and dyslipidemia (Table 1). Thirty three (52%) patients were smokers at the time of surgical intervention. Mean hospital stay was 6 ± 3.4 days.

The complications were classified as General surgical complications (e.g. deep venous thrombosis, pneumonia) and complications specific to carotid endarterectomy (mainly

Table No. 1. Base line characteristics\*.

Age	
Mean age (in years)	61 f8yrs
Age range (in years)	37 (43-80yrs)
Gender	
Males	49(83%)
Females	10(17%)
Male:Female	4.9 : 1
Associated diagnosis	
Hypertension	38(64.4%)
Ischemic heart disease	26(44%)
Diabetes mellitus	24(40.7%)
Dyslipidemia	19(32.2%)
Renal insufficiency	13(22%)

\*Percentages in parenthesis

stroke and local nerve injury due to retraction).

The general surgical complications (Table 2) were frequent and resolved without any sequelae. Pneumonia was the most common general surgical complication (4.8%).

Table No. 2. General surgical complications of carotid endarterectomy.\*

Complications	
Pneumonia	3 (4,8%)
Deep venous thrombosis	2(3.2%)
Electrolyte Imbalance	2 (3,2%)
Congestive cardiac failure	2(3.2%)
Ulnar nerve compression	1
Myocardial infarction	1 (1.6%)

\*Percentages in parenthesis

The complication specific to carotid endarterectomy comprised of stroke and local nerve injury due to stretching/retraction. Neuropraxia is nerve injury characterized by functional impairment due to failure of intact nerve fibers to conduct nerve impulses. Neuropraxia is most commonly due to temporary stretching or pressure on a nerve. Neuropraxia was the more common peripheral nerve complication (7.9%), followed by stroke (4.8%) (Table 3).

One patient died. He underwent simultaneous carotid endarterectomy and CABG and sustained cardiac arrest during the surgery. Neuropraxia occurred in 4 patients, Two patients suffered a hypoglossal nerve injury, one patient suffered palsy of the marginal branch of the facial nerve, and one patient had a combined lesion of the hypoglossal nerve and the marginal branch of the facial nerve and one patient

Table No. 3. Complications due to carotid endarterectomy.

Complications	
Neuropraxia of cranial nerves*	(7,9%)
Stroke	3(4.8%)
Death	1 (1.6%)

\*12th cranial nerve: 2 patients, marginal branch of facial: 1 patient. both: 1 patient and unclear: 1 patient.

\*Percentages in parenthesis

Table No. 4. Comparison of complications in patients with and without simultaneous CABG.^\*

S. No.	Complication	Simultaneous CABG	CEA only	p value
1	Any complication	11/11 (100)	19/52 (37)	<0.001
2	Stroke alone	2/11 (18)	11/52(2)	0.051
3	Death	1/11 (9)	0/52	0.059
4	Stroke and death Combined	3/11 (27)	11/52 f,2)	0.008
5	Pneumonia	3/ 11 (27)	(1)/52	(0)01
6	Cranial Neuropraxia	2/11 (27)	3/52 (6)	0.21

^CABG= coronary artery bypass grafting

\*Percentages in parenthesis

suffered an unspecified nerve injury. All patients with neuropraxia underwent detailed neurological examinations, and all patients recovered from their nerve injury without any sequelae.

Stroke occurred in 3 (4,8%) patients. None of the patients suffered a disabling stroke. Two had complete recovery while one had subtle residual hemiparesis. The patient with residual hemiparesis was fully functional and independent in activities of daily life (ADLs). The stroke in all the patients was detected clinically in the postoperative period. Two patients who suffered stroke had evidence of arterial ischemia referable to the distribution of the operated carotid artery. One patient had an ischemic stroke in the contralateral hemisphere, which could not be directly accounted for by the carotid endarterectomy. However this patient was included in the morbidity for the carotid endarterectomy, as all new central nervous system lesions were considered, for the purposes of this study, to be a complication of surgery.

Of the three patients acquiring a stroke, the first had a mild right hemiparesis, which resolved within 4 months. The second patient suffered mild right upper extremity

monoparesis, which resolved within three months, and one patient developed a left hemiparesis with mild residual weakness at 17 months, without any functional impairment.

## Discussion

Stroke is a common clinical problem in Pakistan, accounting for 6.4% of all hospital admissions in two major hospitals in Karachi.<sup>1-3</sup> Many of these strokes have carotid artery stenosis as underlying etiology. A hospital based review revealed the rate of moderate to severe carotid stenosis to be 13.4% in the Karachi population, although this study was limited by sample size.<sup>23</sup>

These findings indicate a fairly high volume of carotid artery disease in Pakistan. On the other hand, the total number of patients that underwent carotid endarterectomy at our hospital is relatively small. This could be related to reluctance on the part of the physicians to refer patients for carotid endarterectomy in the absence of clear data establishing its safety in Pakistan. Additionally, the low volume of carotid endarterectomy at our institution could also be due to high Cost of such a procedure. Cultural issues such as a general reluctance to undergo surgery in our population may also deter many patients from carotid endarterectomy.

The gender bias towards males in our study is another interesting finding; 83% patients in our study were male. This again could reflect referral patterns, economic issues and cultural bias that would result in males undergoing carotid endarterectomy more frequently than females. Further studies of patient and physician perception and attitudes would be helpful to address these questions.

The role of carotid endarterectomy is well established in the literature. There have been 3 recent major trials evaluating the role of carotid endarterectomy in symptomatic carotid stenosis: North American Symptomatic Carotid Endarterectomy Trial (NASCET)<sup>7,8</sup> European Carotid Surgery Trial (ECST)<sup>9,10</sup> and the VA Cooperative Symptomatic Carotid Stenosis Trial (VACS).<sup>11</sup> The results of these trials indicated that carotid endarterectomy reduces the risk of stroke and disability in patients with symptomatic high-grade carotid stenosis. It is important to note that these studies addressed the question of carotid endarterectomy in symptomatic patients. By symptomatic, it is implied that these patients had a history of minor strokes, or TIA's referable to the distribution of the stenosed carotid artery. Symptomatic carotid disease has a relatively higher risk of subsequent strokes: In the NASCET trial for patient with symptomatic carotid stenosis, the 2-year risk of stroke in patients who received medical therapy but did not undergo surgery was 26%. This was reduced to 9% in patients that underwent carotid endarterectomy.

Asymptomatic (or silent) carotid stenosis is a relatively benign condition with a rate of ipsilateral stroke of 1-3% per year (for patients with stenosis of greater than 50%)<sup>24, 25</sup>

The benefit of carotid endarterectomy in reducing the risk of stroke in these patients is correspondingly small. Studies have addressed the issue of carotid endarterectomy in patients with asymptomatic stenosis, but the benefit of carotid endarterectomy in these patients is marginal; in the ACAS trial, the absolute reduction of risk for adverse events in surgically treated patients, compared to medically treated patients, was 1%.<sup>12</sup>

The most dreaded complication of endarterectomy is stroke. The risk of stroke must be less than 5-7% for patients to benefit from the procedure. The advantages of Carotid endarterectomy can be offset by a high surgical morbidity/mortality and the perioperative risks need to be assessed. Risks of carotid endarterectomy are dependant on the experience and the expertise of the surgeon and the hospital. The risk of major stroke or death in our population is comparable to the rates in major trials of carotid endarterectomy in symptomatic carotid stenosis. Data from the NASCET trial reveals a rate of perioperative stroke/death of 6.5% and the risk of major stroke/death of 2,1%.<sup>7,8</sup> In the ECST trial, the perioperative morbidity /mortality rate was 7.5%.<sup>9,10</sup> The risk of stroke is much higher in patients with symptomatic carotid stenosis, compared to patients with asymptomatic stenosis. An extensive meta analysis of stroke and death rate following carotid endarterectomy has revealed a perioperative risk of stroke/death of 5.8% for symptomatic carotid stenosis and 3.4% for asymptomatic carotid stenosis.

A meta-analysis reviewed the different randomized trials of endarterectomy for symptomatic carotid artery stenosis and supported the overall benefit of the procedure with an overall 44% decrease in the risk of non-fatal stroke.<sup>4</sup>

Interestingly, the post operative stroke rate appears to be dependant on the physician reporting the data. The rate for postoperative stroke in a large review of 50 studies was 7.7% if data is reported by a neurologist, but only 2.3% if a surgeon reports his own results.<sup>26</sup>

In the current study we analyzed patient characteristics and the outcome of carotid endarterectomy, at the Aga Khan University Hospital for 59 consecutive patients (4 of them underwent surgery twice, once on each side) subjected to this procedure for symptomatic stenosis. The risk of stroke in our population is was 4.8%. There was a single mortality, which occurred in a patient undergoing simultaneous CABG. The combination of carotid endarterectomy and CABG is known to increase the risk of adverse outcome.<sup>27,28</sup>

Table 4 summarizes a subgroup analysis to determine the risk of major complications following CEA alone, compared with combined CEA and CABG. It is interesting to note that the risk of stroke and/or death in our subgroup of patients undergoing CEA alone was 2% (1/52). For the combined CEA and CABG procedure this risk was 27% (3/11). These findings suggest that in our environment, a staged procedure may be safer. Additionally, the risk of 2% for stroke or death following CEA alone suggests CEA is particularly safe in our population if undertaken without a concomitant major surgical procedure.

Cranial nerve injuries that may result from carotid endarterectomy include vocal cord paralysis (2.0-7.6%), hypoglossal injuries (3.3 - 5.5%), facial nerve injury (1.1% - 2.4%), greater auricular nerve (1.1% and injury to the spinal accessory nerve (0.3%).<sup>1-9-32</sup>

None of our patients had permanent nerve injury. The frequency of neuropraxia in our patients was 7.9% (Table 3), which is comparable with internationally reported figures.

Carotid endarterectomy is beneficial for patients with a greater than 70-99% carotid stenosis on angiography. However, accurate knowledge of the perioperative stroke/death rates is necessary in order to make meaningful decisions about the risk/benefit ratio of carotid endarterectomy. The risks of carotid endarterectomy are not well defined in our local environment. Our study reveals a combined risk of debilitating stroke and death of 1.6% in our population. The risk of all stroke and death is 6.4%. The risk of stroke or death in our population is comparable to the established risk of carotid endarterectomy in symptomatic carotid stenosis in the literature. The risk of neuropraxia in our population was 7.9%, which compares favorably with the rate reported in the literature (12.5-27%). We conclude that carotid endarterectomy is a safe and necessary procedure for patients with hemispheric or retinal transient ischemic attacks or non-disabling strokes with underlying high-grade carotid stenosis (70-99%) in the local environment. Local audits are necessary for accurate assessment of the risk/benefit ratio of carotid endarterectomy.

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