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Original Article

Early results of carotid endarterectomy and risk factors for in-hospital stroke

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Abstract

Aim: Carotid endarterectomy (CEA), which is performed to prevent the development of cerebrovascular events (CVE) due to carotid artery disease (CAD), is currently the most effective treatment. Perioperative adverse clinical conditions may develop due to patient factors, technique or other reasons. Perioperative stroke is the cause of mortality and morbidity that can develop within 30 days postoperatively. The aim of this study is to present the early results of patients who underwent CEA and investigate the factors affecting the development of early stroke.
Material and Methods: Patients who underwent CEA between 2013-2020 were retrospectively analyzed. 529 patients were evaluated. A total of 550 endarterectomy procedures were performed in 529 patients. Demographic data, presence of symptoms, contralateral carotid artery stenosis, anesthetic method, operation technique, postoperative stroke, mortality were recorded from the hospital database.
Results: The analyses were based on the results of 550 endarterectomy. The mean age of the patients was 67.0±8.4 years. While 164 (29.8%) of the patients were symptomatic, concomitant contralateral carotid artery stenosis was detected in 138 (25.1%) patients. Considering early postoperative adverse effects, there was no cranial nerve damage, while reoperation for bleeding was necessary in 27 (4.9%) patients. Postoperative ischemic stroke occurred in 20 (3.6%) patients. Mortality occurred in eight (1.5%) patients. Gender, rate of DM, HL, CRF or current CAD did not differ in patients with and without postoperative stroke. The patients with postoperative stroke tended to more frequently have contralateral ICA stenosis but the groups did not differ significantly (p=0.117). In early stroke development after CEA, the presence of pre-procedural symptoms was a significant factor (p<0.001). According to the multivariate analysis preoperative presence of symptoms increased risk by 6.41 (95% CI: 2.22-18.54, p=0.001).
Conclusion: Carotid artery revascularization is a safe and effective treatment modality for the prevention of ischemic CVE with low mortality and morbidity rate. Being symptomatic is a significant risk factor for the development of stroke in the early period. It may be useful to group the symptoms and evaluate the extent to which each symptom affects the development of stroke in prospective randomized studies.

Keywords: Carotid endarterectomy, stroke, symptomatic

INTRODUCTION

Carotid endarterectomy (CEA), which is performed to prevent the development of cerebrovascular events (CVE) due to carotid artery disease is currently the most effective treatment method in symptomatic (1) and asymptomatic (2) severe carotid artery stenosis. Although CEA is an effective surgery, perioperative adverse clinical conditions may develop due to patient factors, technique or other reasons. Perioperative stroke, which is among these undesirable clinical conditions, is the cause of mortality and morbidity that can develop within 30 days postoperatively. The risk of stroke and death in symptomatic patients is 3.2% and in asymptomatic patients in 1.4% (3).

Risk factors for stroke after CEA include contralateral carotid artery stenosis and the presence of uncontrolled HT before or after surgery (4). The development of cerebral hypoperfusion during the ischemic period after cross-clamp placement in CEA

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is one of the determinants of peroperative stroke (5). Cerebral monitoring during this period is of importance. When CEA is performed using a shunt, there is a risk of embolism due to shunt placement and prolonged operation time. The association of cerebrovascular risk factors such as age, sex, diabetes, and coronary artery disease (CAD) with the development of early neurological deficits after CEA is still not clear (6).

Many studies have reported the effect of surgical technique on perioperative carotid artery thrombosis and stroke. Although anesthetic method, cerebral ischemia prevention, use of a shunt, arteriotomy closure methods, the choice of eversion or conventional endarterectomy have been investigated, a superiority in any approach has not been demonstrated.

The aim of this study is to present the early results of patients who underwent CEA in our center and investigate the factors affecting the development of early stroke.

MATERIAL AND METHODS

Patients who underwent CEA at Dr. Siyami Ersek Research and Training Hospital between 2013 and 2020 were retrospectively included. The study approval was obtained from the hospital scientific committee and Haydarpaşa Numune Hospital Ethics Committee with the registration number HNEAH-KAEK 2022/181-3920. 569 patients underwent CEA. 40 patients who underwent concomitant open-heart surgery were excluded from the study. The remaining 529 patients were evaluated. A total of 550 endarterectomy procedures were performed in 529 patients.

Demographic data (age, gender, hypertension, hyperlipidemia, presence of diabetes mellitus, presence of additional CAD, chronic renal failure), presence of symptoms, contralateral carotid artery stenosis, anesthetic method, operation technique (endarterectomy, eversion, patch use, primary closure, shunt use), reoperation for bleeding, intra-hospital postoperative stroke, mortality were recorded from the hospital database. In patients who underwent bilateral endarterectomy, each endarterectomy was evaluated as a separate surgical procedure.

Definitions

Patients were considered symptomatic in the presence of transient ischemic attack (TIA), amorosis fugax or stroke within the previous 6 months. Surgical treatment was performed for ≥50% internal carotid artery (ICA)stenosis in these patients. Surgical treatment was performed for ≥70% ICA stenosis in asymptomatic patients. For patients with bilateral carotid stenosis, the symptomatic side or the side of higher-grade carotid stenosis was treated first.

Carotid artery stenosis was diagnosed using doppler ultrasonography (DUSG), digital substruction angiography (DSA), or computed tomography (CT) examinations. CT was performed to determine the exact anatomical localization before the surgical procedure in patients with carotid artery stenosis detected by DUSG. DSA was performed in patients with suspected carotid artery total occlusion who could not undergo lumen imaging on CT due to ICA intensive calcification.

Hypertension (HT) was defined as systolic blood pressure of >140mmHg or diastolic blood pressure of >90 mmHg or being on antihypertensive drugs. Hyperlipidemia (HL) was defined as total cholesterol >200mg/dL, low-density lipoprotein cholesterol (LDL) >120mg/dL, high-density lipoprotein (HDL) cholesterol level <40mg/dl, triglyceride level >150mg/dL, or the use of lipid-lowering drugs. Patients taking antidiabetic drugs (oral hypoglycemic agents or insulin) and patients with plasma high fasting glucose levels, or HbA1c ≥6,5 were considered diabetes mellitus (DM) (7). CAD was defined as patients with CAD detected in preoperative coronary angiography or coronary computed tomography, patients with aortic coronary bypass history, and patients who underwent coronary artery percutaneous stent procedure. Chronic renal failure (CRF) denoted patients on a hemodialysis program or whose glomerular filtration rate (GFR) was <60mL/min/1.73 m² (8).

Surgical Procedure Monitorization and Anesthesia

Peripheral iv catheter, radial artery catheterization and systolic-diastolic-mean blood pressure measurement, electrocardiography (ECG), peripheral oxygen saturation (sPO2), and Near Infrared Spectroscopy (NIRS) (Covidien Invos Oximeter, Mansfield, MA USA) monitoring were initiated during the anesthesia phase of the surgery.

In patients operated under general anesthesia, anesthesia induction was achieved with Propofol, Fentanyl, and Rocuronium. Sevofluran was used as a maintenance anesthetic agent. For patients operated with regional anesthesia, 0.03 mg/kg of midazolam was administered for sedation before applying Bupivacaine at C2, C3, C4 levels for cervical block.

Local anesthesia (cervical plexus block) was preferred because it allows close evaluation of cerebral function by awake testing and hemodynamic stability during carotid artery cross- clamping. General anesthesia was preferred in patients with severe anxiety who did not prefer local anesthesia, and in patients whose local anesthesia depth was not sufficient. Patients underwent systemic heparinization and antibiotic prophylaxis.

Surgery

In all patients, a longitudinal incision was made along the anterior edge of the sternocleidomastoid muscle (SCM). Conventional carotid endarterectomy (CCEA) was performed with a longitudinal incision to the ICA. In the eversion carotid endarterectomy (ECEA) method, ICA was transected from the common carotid artery (CCA) at the carotid sinus level and reimplanted with a primary suture, known as the Etheredge technique (9).

In local anesthesia, the 3-minute awake test was performed after ICA cross clamping. Endarterectomy was continued in patients who did not develop neurological deficits during the test or who did not have a 10% reduction in NIRS monitoring. In patients with neurological dysfunction or reduced NIRS by more than 10%, the cross-clamp was removed, and a shunt was placed. The shunt

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was used in conjunction with NIRS monitoring under general anesthesia. Any hypotension or HT during the procedure was managed with intravenous agents. The Arteriotomy was closed with a primary suture or using a synthetic patch material. ECEA was preferred in patients with elongated ICA and with an ICA diameter <4mm. Arteriotomy was closed primarily in patients with sufficient lumen diameter. After removal of the cross-clamp, protamine sulfate was given in patients with widespread bleeding at the surgical site with ACT >200. Neutralization of heparin was not performed in other patients. In each patient, a drain was placed at the surgical site to prevent hematoma.

Postoperative adverse effects

Adverse events included CVE, cranial nerve damage, reoperation for bleeding, and postoperative myocardial infarction (MI). Symptomatic chest pain in the perioperative or early postoperative period accompanied by ECG change (collapse or elevation of new ST segments or elevation of two or more adjacent leads >1 mm elevation) or elevated cardiac enzymes was considered MI.

Reoperation for bleeding revision was defined as hematoma causing respiratory distress requiring reexploration in the neck region in the early period and bleeding over 100 cc per hour. Stroke was defined as new onset clinical neurological dysfunction lasting more than 24 hours. Hemorrhagic or ischemic stroke was diagnosed via cranial CT. Neurological dysfunction was confirmed by a neurologist. Mortality was defined as mortality due to cerebrovascular event or MI in the peroperative period or in the intensive care unit.

Intensive care unit follow-up

Since prevention of hemodynamic instability, neurological dysfunction, hypoxia, or cardiac dysfunction is critical in the early postoperative period, all patients were followed up in the intensive care unit on the day of the surgery. Dual antiplatelet and statin therapy were given as standard postoperative medical treatment.

Statistical Analysis

Statistical analysis was carried out using SPSS v25.0 (IBM, Armonk, USA). Categorical variables are given as numbers and percentages while continuous parameters are given as mean and standard deviation. Categorical variables were compared using the Chi squared test and continuous variables using the Student's t test. Significance was set as $p<0.05$. Factors significant in univariate analysis were carried on to logistic regression analysis.

RESULTS

During the study period, 569 patients underwent CEA. 40 patients who underwent concomitant open-heart surgery were excluded from the study. The remaining 529 patients were evaluated. A total of 550 endarterectomy procedures were performed in 529 patients. The analyses were based on the results of 550 endarterectomy (Figure 1).

The mean age of the patients was 67.0±8.4 years. 150 (28.4%) of the patients were female and 379 (71.6%) were male. DM was present in 399 (72.5%) patients, HL in 326 (59.3%), HT in 331 (60.2%), CRF in 57 (10.4%), and concomitant CAD in 264 (49%). While 164 (29.8%) of the patients were symptomatic, concomitant contralateral carotid artery stenosis was detected in 138 (25.1%) patients (Table 1).

Table 1. Demographic data of study patients

Patients	n=529
Age	67.0±8.4
Diabetes Mellitus	399(72.5%)
Hyperlipidemia	326(59.3%)
Hypertension	331(60.2%)
Chronic Renal Failure	57(10.4%)
Coronary Artery Disease	264(49.0%)
Symptomatic Patients	164(29.8%)
Contralateral Carotid Artery Stenosis	138(25.1%)

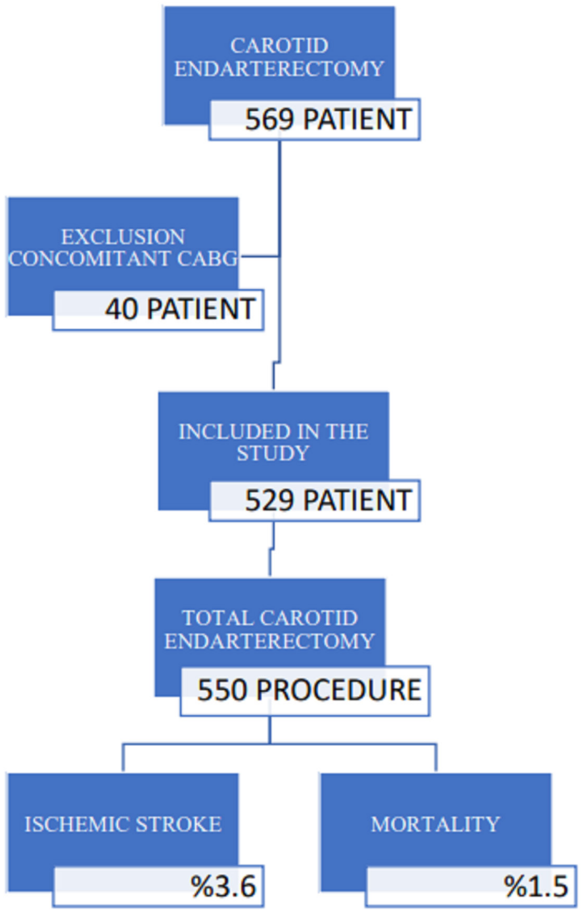

Figure 1. Flow chart of patient enrollment

When we examine the surgical data 256 (48.4%) patients underwent left, 252 (47.6%) patients underwent right, and 21 (4.0%) patients underwent bilateral endarterectomy. CCEA was performed in 523 (95.1%) patients and ECEA in 27 (4.9%)

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patients. While patch closure was performed in 108 (19.6%) patients, a shunt was required in 14 (2.5%) patients. Local anesthesia was performed in 368 (66.9%) patients and general anesthesia in 182 (33.1%) patients (Table 2).

Table 2. Surgical findings of carotid endarterectomy

Surgical Procedure	n=550 (%)
Side	
Left	256 (48.4%)
Right	252 (47.6%)
Bilateral	21 (4.0%)
Surgical Method	
CCEA	523 (95.1%)
ECEA	27 (4.9%)
Patch Closure	108 (19.6%)
Shunting	14 (2.5%)
Anesthesia	
Local	368 (66.9%)
General	182 (33.1%)

CCEA: Conventional carotid endarterectomy ,ECEA: eversion carotid endarterectomy

Considering early postoperative adverse effects, there was no cranial nerve damage, while reoperation for bleeding was necessary in 27 (4.9%) patients. Postoperative ischemic stroke occurred in 20 (3.6%) patients. Permanent plegia developed in 9 patients, temporary paralysis in 2 patients, acute cranial infarct, and loss of consciousness after stroke in 9 patients. Eight (1.5%) patients died. (Table 3) 3 of the 8 patients died due to MI, 3 patients died due to hemorrhagic transformation and intracranial shift development after stroke, and 2 patients died due to widespread cranial infarction after stroke.

Table 3. Early adverse effects after carotid endarterectomy

	n= 529(%)
Stroke	20 (3.6%)
Bleeding Revision	27 (4.9%)
Mortality	8 (1.5%)

Patients with and without early postoperative stroke were compared. Gender, rate of DM, HL, CRF or current CAD did not differ in patients with and without postoperative stroke. Patients with postoperative stroke were older (70.7 vs 66.9, p=0.046) The patients with postoperative stroke tended to more frequently have contralateral ICA stenosis but the groups did not differ significantly (p=0.117). The application of CCEA or ECEA surgical techniques was not found to affect stroke development (p=0.985). Similarly, performing the surgery under local or general anesthesia was not found to affect stroke development. Arteriotomy closure with primary or patchplasty was also not found to have an effect on stroke development. The use of a shunt was necessary in one patient who developed stroke, while the use of shunts did not differ significantly between the groups. In early stroke development after CEA, the presence of pre-procedural symptoms was a significant factor (p<0.001) (Table 4).

Table 4. Analysis of factors affecting stoke development.

	No Stroke n=530(%)	Stroke n=20 (%)	p
Age	66.9±8.4	70.7 ± 6.6	0.046
Sex			0.427
Female	381(71.9%)	16 (80.0%)	
Male	149(28.1%)	4 (20.0%)	
DM	382(72.1%)	17(85.0%)	0.204
HL	319(60.2%)	7(35.0%)	0.023
HT	319(60.2%)	12(60.0%)	0.986
CRF	56(10.6%)	1(5.0%)	0.710
CoAD	260(49.1%)	4(20.0%)	0.011
Contrlateral Carotıd Artery Stenosis	130(24.5%)	8(40.0%)	0.117
Symptom	149(28.1%)	15 (75.0%)	<0.001
Method			0.985
CCEA	504 (95.1%)	19 (95.0%)	
ECEA	26 (4.9%)	1 (5.0%)	
Anestesia			0.481
Local	353 (67.5%)	18 (75.0%)	
General	170 (32.5%)	5 (25.0%)	
Patch Closure	100 (19.2%)	5 (25.0%)	0.563
Shunting	13 (2.5%)	1 (5.0%)	0.408

DM: Diabetes Mellitus, HL: Hyperlipidemia,HT :Hypertension,CRF: Chronic renal failure,CoAD:Coronary artery disease
CCEA: Conventional carotid endarterectomy, ECEA: eversion carotid endarterectomy

Multivariate analysis of risk factors revealed age and preoperative presence of symptoms to be independently associated with postoperative stroke. Age increased the risk of stroke by 1.07 (%95 CI: 1.01 - 1.03, p=0.029) and preoperative presence of symptoms increased risk by 6.41 (%95 CI: 2.22-18.54, p=0.001) (Table 5).

Table 5. Multivariate analysis of risk factors

	O.R(%95CI)	p
Age	1.067 (1.007-1.130)	0.029
Symptom	6.410 (2.216-18.538)	0.001
Hyperlipidemia	0.595 (0.222-1.594)	0.292
Coronary Artery Disease	0.431 (0.136-1.370)	0.146

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DISCUSSION

Approximately 35% of all ischemic strokes are associated with carotid artery stenosis (10). CEA is an effective treatment method in the prevention of ischemic stroke caused by severe carotid disease. Undesirable clinical events may be observed after CEA performed with the intention of stroke prevention, The risk of stroke and death in symptomatic and asymptomatic carotid disease patients is reported at 3.2% and 1.4%, respectively (3). HT, HL, and DM are known risk factors of atherosclerosis. The association of coronary and carotid artery stenosis based on atherosclerosis is also established. The effect of other cerebrovascular risk factors such as age, gender, diabetes, and CAD is controversial in the development of stroke in the early period after CEA (6). In a study on DM patients, major adverse events (MAE) in the early post-CEA period were more frequent in DM patients compared to non-diabetic patients. In the same study, DM is indicated as a risk factor for long-term MAE (11). Our study did not reveal gender, DM, HL, HT, CRF, or CAD to be significant factors in the development of stroke.

Bilateral carotid artery stenosis increases the risk of stroke in the atherosclerotic patient (4). Similarly, contralateral severe carotid stenosis is defined as a risk factor for the development of postoperative stoke due to the lack of adequate collateral circulation (12). Contralateral carotid stenosis was not identified as a risk factor for the development of postoperative stroke in our study (p=0.117). Patients with moderate and severe contralateral carotid artery stenosis were evaluated together and no subgroup evaluation was performed. This may have limited our analysis of contralateral disease and postoperative stroke risk.

The risk of major adverse cardiac events (MACE) are increased in patients undergoing CEA. Inflammatory cytokines, hemodynamic instability, and CAD play a role in increased MACE risk. Go et al. reported a MACE incidence of 1.7%, a perioperative stroke rate of %2 and a 30-day mortality rate of %1. The combined stroke and/or mortality rate was 2.7%, 1.9% for asymptomatic and 4.1% for symptomatic patients (13). Another study also reported a MACE risk of 3.5% and a stroke risk of 4.7% in the first 7 days (14). In our study, early hospital stroke rate was 3.6% and mortality rate was 1.5%, while early mortality rate after MI was 0.56% (3 patients).

Studies on early postoperative stroke have revealed that among symptomatic CEA patients, patients with previous stroke have a higher risk of postoperative stroke compared patients with a history of TIA or ocular TIA (15). Similarly, in this study, the presence of pre-CEA symptoms increased the risk of early ischemic stroke (p<0.001). According to the multivariate analysis preoperative presence of symptoms increased risk by 6.41 (%95 CI: 2.22 - 18.54, p=0.001). The higher risk of stroke in symptomatic patients has been explained by plaque morphology in histopathology studies (16).

The indications and timing of CEA are well defined in guidelines, but there is no consensus on the best anesthesia method. The choice is left to the experience of the surgeon and the anesthesiologists. (17,18) According to the General Anesthesia Versus Local Anesthesia for Carotid Surgery (GALA) trial, no difference existed between general and local anesthesia for perioperative outcomes. The study also recommends a discussion with the patients of the options for anesthesia during the surgery and a decision made together by the anesthesiologist, surgeon and the patient (19). In a prospective randomized trial in which silent ischemic cerebral lesions were detected using MRI imaging, it was concluded that silent cranial ischemia was more common under general anesthesia (20). Our study did not find an association between the anesthetic method and perioperative stroke. It is important to decide on the mode of anesthesia in accordance with the condition of the patient, the severity of accompanying CAD, as well as the experience of the surgeon and anesthesiologist.

CCEA and ECEA techniques have their own advantages and disadvantages. The experience of the surgeon, ICA anatomy and plaque structure can influence the choice of surgical technique. In studies that found ECEA and patch closure superior to the primary closure technique, no difference was reported concerning perioperative stroke (21). In light of current literature, the advantages of each surgical technique over the other is still debatable (22). There was no correlation between CCEA or ECEA techniques and stroke development in the study. For patients undergoing CCEA in Guideline, patch closure is recommended over routine primary closure (23). However, primary closure can be performed in patients with an ICA diameter of sufficient (>6 mm) width (20). There are also studies stating results equivalent to other techniques can be achieved with primary closure (24). Primary closure has advantages such as providing a short cross-clamp time and avoiding patch-related complications. Studies concluding that the type of closure technique has no effect on perioperative and long-term outcomes advocate the noninferiority of primary closure (25). We found no difference between primary closure and patch use in terms of stroke development. When the surgeon finds lumen width to be sufficient, primary closure is the appropriate option. The aim is to ensure a lumen diameter of 6 mm or above (26).

The use of shunts during CEA is a valuable option to prevent cerebral ischemia in cases where it is necessary. While the need for shunt use can be decided after cerebral monitoring or with the awake test, some surgeons prefer its routine use. The reasons why shunt use is not preferred in routine practice are the risk of peripheral embolism during its placement and the technical difficulty during arteriotomy closure. It can also cause damage at the intimal layer, possibly creating a new source for intraoperative or early postoperative thrombosis or postoperative restenosis (27). In the study, it was determined that the use of a shunt was not a associated with perioperative stroke. Only 2.5% of our patients required a shunt during the procedure. In the prevention of early stroke, the awake test, NIRS monitoring, and hemodynamic stabilization are important aspects of perioperative

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management.

LIMITATIONS

This study was a retrospective study. The timing between the onset of patients symptoms and endarterectomy could not be obtained from retrospective data. Cross-clamp durations were not available. The procedures were performed by different surgeons.

CONCLUSION

Carotid artery revascularization is a safe and effective treatment modality for the prevention of ischemic CVE with low mortality and morbidity rate. The surgical strategy, anesthesia technique, atherosclerosis risk determinants are not factors in the development of early stroke. Being symptomatic is a significant risk factor for the development of stroke in the early period. It may be useful to group the symptoms and evaluate the extent to which each symptom affects the development of stroke in prospective randomized studies.

Patient informed consent: Written informed consent of patients was taken preoperatively for each one.

Conflict of Interests: The author declares that there are no conflict of interests.

Financial Disclosure: There are no financial supports.

Ethics committee approval: The study approval was obtained from the hospital scientific committee and Haydarpaşa Numune Hospital Ethics Committee with the registration number HNEAH-KAEK 2022/181-3920.

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