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ORIGINAL ARTICLE

Clinical Outcomes and Midterm Mortality After Carotid Endarterectomy: A Single Center Study

Karotis Endarterektomi Sonrası Klinik Sonuçlar ve Orta Dönem Mortalite: Tek Merkez Çalışması

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ABSTRACT

Objective: This single-centre study aimed to investigate the clinical outcomes and midterm mortality in patients who underwent carotid endarterectomy (CEA) for various indications.
Methods: The study included 109 patients who underwent CEA at our institution. Demographic characteristics, indications for surgery, operative techniques, and early postoperative complications were recorded. Follow-up data were obtained for a mean period of 23.3 ± 17.2 months, and mortality causes, and neurological outcomes were analysed.
Results: The mean age of the patients (73 men and 36 women) was 66.53 ± 8.00 years. Indications for CEA included transient ischemic attack (TIA) in 21.1% and a history of ischemic stroke in 26.6% of patients. Overall, 86.2% had unilateral carotid stenosis of 70% or more. Most patients (89.9%) were operated under general anaesthesia, and the conventional carotid endarterectomy technique was employed most (78.0%). The most frequent reconstruction method for the longitudinal carotid arteriotomy was Dacron patch plasty (56.0%). Early follow-up revealed low hospital mortality (0.9%) and limited postoperative complications (3.7% TIA, 1.8% major neurological complications, and 1.8% minor neurological complications). During the follow-up period, absolute survival was 87.0%.
Conclusion: Our study demonstrates favourable early outcomes and acceptable long-term mortality rates following CEA. However, larger and multicentre studies are warranted to further confirm these results and enhance our understanding of CEA's long-term benefits.

Keywords: Carotid artery stenosis, endarterectomy, mortality, stroke

ÖZ

Amaç: Bu tek merkezli çalışma, çeşitli endikasyonlar için karotis endarterektomi (CEA) uygulanan hastalarda klinik sonuçları ve orta dönem mortaliteyi araştırmayı amaçlamıştır.
Gereç ve Yöntemler: Çalışma, kurumumuzda CEA uygulanan 109 hastayı içermektedir. Demografik özellikler, cerrahi endikasyonlar, operasyon teknikleri ve erken postoperatif komplikasyonlar kaydedilmiştir. Ortalama 23.3 ± 17.2 aylık takip verileri elde edilmiş ve mortalite nedenleri ve nörolojik sonuçlar analiz edilmiştir.
Bulgular: Hastaların ortalama yaşı 66.53 ± 8.00 yıldır ve 73 erkek ile 36 kadın bulunmaktadır. CEA endikasyonları, hastaların %21.1'inde geçici iskemik atak (TIA) ve %26.6'sında iskemik inme öyküsüdür. Genel olarak, hastaların %86.2'sinde unilateral karotis darlığı %70 veya daha fazladır. Hastaların çoğuna (%89.9) genel anestezi altında ameliyat uygulanmış olup, en yaygın kullanılan cerrahi teknik geleneksel karotis endarterektomidir (%78.0). Longitudinal karotis arteriyotomisinin en sık kullanılan rekonstrüksiyon yöntemi Dacron yama plastisidir (%56.0). Erken takip döneminde düşük hastane mortalitesi (%0.9) ve sınırlı postoperatif komplikasyonlar tespit edilmiştir (%3.7 TIA, %1.8 büyük nörolojik komplikasyonlar ve %1.8 küçük nörolojik komplikasyonlar). Takip döneminde, mutlak sağkalım oranı %87.0 olarak belirlenmiştir.
Sonuç: Çalışmamız, CEA sonrası olumlu erken sonuçları ve kabul edilebilir uzun dönem mortalite oranlarını göstermektedir. Ancak, bu sonuçları desteklemek ve CEA'nın uzun dönem faydalarını daha iyi anlamak için daha büyük ve çok merkezli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Karotis arter hastalıkları, endarterektomi, mortalite, inme

Introduction

Stroke is the second cause of mortality worldwide after ischemic heart disease; remaining as a silent menace that poses a significant burden on global health (1). As the aging population continues to grow it is anticipated that the burden of stroke will increase significantly in the coming years. In Turkey the incidence of stroke is estimated to be around 141.7-158 per 100,000 people which is higher than the global average. Stroke mortality increased by 56% between 2002 and 2017 in Turkey, making it vital to explore effective interventions for stroke prevention and treatment (2). Of all strokes, ischemic strokes are the most common type, accounting for up to 80% of cases. Carotid artery disease, specifically atherosclerosis of the carotid arteries, is a leading cause of ischemic stroke. Large vessel ischemic strokes constitute approximately 16.6% of all stroke cases, with 8% of all ischemic strokes attributed to extracranial internal carotid artery stenosis. Moreover, extracranial internal carotid artery occlusion accounts for about 3.5% of all ischemic strokes.(3) The importance of carotid artery stenosis diagnosis and management has been extensively recognized and highlighted in numerous reviews and guidelines. The recent 2023 ESVS guidelines offer three treatment

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modalities for extracranial carotid artery stenosis: best medical therapy, carotid artery stenting, and carotid endarterectomy (4).

Carotid endarterectomy is one of the most studied surgical procedures in the literature. However, there are still ongoing research efforts to further optimize its indications, refine techniques, and explore mid and long-term outcomes to enhance its effectiveness and safety. In this study, researchers aimed to analyze the midterm follow-up results of carotid endarterectomy, specifically focusing on mortality, in order to gain insights into the procedure's effectiveness and safety over an extended period.

Material and Methods

Patients who underwent carotid endarterectomy between January 2017 and December 2021 were included in this retrospective study. Exclusion criteria comprised patients diagnosed with carotid stenosis during preoperative cardiac surgery evaluation, as well as patients with a history of ipsilateral carotid surgery or carotid stenting. After applying these exclusion criteria, a total of 109 patients were deemed appropriate for inclusion in the study. The primary endpoint of the study was late mortality. Additionally, the study assessed preoperative demographic characteristics of the patients, details of the surgical technique and any modifications made, as well as the occurrence of early and late complications.

Definitions and Follow Up:

In this retrospective study, various clinical definitions were employed to investigate the outcomes of CEA in patients with carotid artery disease. Preoperative TIA was characterized as a completely reversible neurologic attack lasting less than 24 hours, while preoperative ischemic stroke was defined as an irreversible neurologic attack of ischemic origin. Asymptomatic patients were identified as those undergoing stroke-sparing surgery without any preoperative history of TIA or ischemic stroke. Coronary artery disease was defined based on angiographic evidence of stenosis of 50% or more in at least one coronary artery, a positive cardiovascular stress test along with scintigraphic evidence of cardiac ischemia or receiving medical or surgical treatment for coronary artery disease. Renal impairment was classified according to the KDIGO classification as G2 and above (5). Residual stenosis was determined as the presence of at least 30% stenosis of the operated carotid artery based on postoperative duplex ultrasound.

Regarding postoperative events, in-hospital mortality was defined as mortality occurring before discharge or within 30 days postoperatively. Postoperative early TIA referred to a fully reversible neurological attack lasting less than 24 hours that manifested within the first 30 days following CEA. Postoperative early major neurological complications were classified as cerebral infarction, intracranial haemorrhage, or seizures that occurred within the initial 30 days post-CEA. Minor neurological complications were defined as complications attributed to cranial nerve damage or injury resulting from the CEA procedure. Late myocardial infarction and congestive heart failure were defined as a history of hospitalization or coronary intervention for coronary artery disease and a history of hospitalization for congestive heart failure, respectively. Peripheral vascular intervention was defined as patients who underwent open surgery or percutaneous intervention for limb revascularization. The need for carotid reintervention was defined as re-carotid surgery or carotid stent placement on the ipsilateral carotid artery.

In this retrospective study, demographic, operative and early postoperative data were collected from the patient files and hospital electronic data system after hospital's local ethics committee approval. Mid and long-term data were obtained through phone interviews with the patients or their relatives.

Surgical Procedure

All CEAs were performed by five different senior surgeons. All patients were operated after the decision of carotid endarterectomy in the council formed by cardiovascular surgeons, neurologists, and cardiologists. The choice of anaesthesia, either local or general, was based on the surgeon's operative plan. Additionally, the surgical approach was selected based on the senior surgeon's preference, with two options available: conventional CEA, involving a longitudinal arteriotomy with patch or primary closure, or eversion CEA. During the surgical procedure, a near-infrared spectroscopy (NIRS) probe was placed on the forehead of all patients. In cases where patients had neurologic symptoms under local anaesthesia, or when the NIRS value decreased by 20% compared to the preoperative value, a selective carotid shunt (Pruitt-Inahara; LeMaitre Vascular Inc, Burlington, MA – USA) was utilized. Following the CEA, all patients were admitted to the intensive care unit (ICU) for postoperative monitoring. Invasive arterial blood pressure monitoring was implemented during this period. Additionally, carotid duplex ultrasonography was performed on all patients in the early postoperative stage.

Statistical Analysis

Statistical analyses were performed using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive demographic characteristics and postoperative outcomes were presented as numbers and percentages for categorical variables, while continuous variables were expressed as mean ± standard deviation. To compare freedom from the selected outcome variable, namely late mortality, Kaplan-Meier curves were utilized.

Results

The study population had a mean age of 66.53 ± 8.00 years, consisting of 73 men and 36 women. CEA was indicated for TIA in 23 (21.1%) patients and for a history of ischemic stroke in 29 (26.6%) patients. Stroke-sparing

CEA was performed in 57 (52.3%) asymptomatic patients with severe internal carotid artery (ICA) stenosis. Among the patients, 94 (86.2%) had ipsilateral carotid stenosis of 70% or more, 15 (13.8%) had ipsilateral carotid stenosis ranging from 50-69%, and 15 (13.8%) had contralateral carotid stenosis of 70% or more (Table 1).

Table 1: Demographics and clinical characteristics of patients

	N=109
Patients Characteristics	n (%) / mean ±SD
Demographic feature	
Age (years)	66.53 ± 8.00
Male	73 (67.0)
Transient ischemic attack (< 6 months)	23 (21.1)
Ischemic stroke (>6 months)	29 (26.6)
Asymptomatic	57 (52.3)
Diabetes mellitus	66 (60.6)
Arterial hypertension	76 (69.7)
Coronary artery disease	62 (56.9)
Renal impairment	21 (19.2)
Preoperative dual antiplatelet	10 (9.2)
İpsilateral >70	94 (86.2)
İpsilateral >50-69	15 (13.8)
Contralateral >70	15 (13.8)

CEA was performed under local anaesthesia in 11 (10.1%) cases and under general anaesthesia in 98 (89.9%) cases. Eversion carotid endarterectomy was performed in 24 (22.0%) patients, while 85 (78.0%) underwent conventional carotid endarterectomy. The longitudinal carotid arteriotomy was reconstructed using primary closure in 17 (15.6%) patients, Dacron patch plasty in 61 (56.0%), and saphenous vein patch plasty in seven (6.4%) patients. Carotid shunt was employed in 19 (17.4%) patients (Table 2).

Table 2: Operational data of the patients

	N=109
Operational data	n (%) / mean ±SD
General anesthesia	98 (89.9)
Local anesthesia	11 (10.1)
Primary closure	17 (15.6)
Saphenous vein patch plasty	7 (6.4)
Dacron patch plasty	61 (56.0)
Eversion carotid endarterectomy	24 (22.0)
Shunt use	19 (17.4)

In the early follow-up, hospital mortality occurred in one patient (0.9%), four patients experienced postoperative early TIA (3.7%), two patients had major neurological complications (1.8%) (one ischemic and one haemorrhagic), and two patients had minor neurological complications (1.8%). The patient with intracerebral haemorrhage was operated by a neurosurgery team after diagnosis. In this patient, hospital mortality occurred in second postoperative day of CEA. One of the minor neurological complications was vagus nerve injury and the other was hypoglossal nerve injury.

During the mean follow-up time of 23.3 ± 17.2 months, absolute survival was 87.0%. The Kaplan-Meier curve for mortality is given in Figure 1. Mortality causes included lung cancer (three patients), heart failure (two patients), cerebral infarction (two patients), intracranial haemorrhage (two patients), myocardial infarction (four patients), and abdominal aortic rupture (one patient). Major neurological complications occurred in 11 patients during follow-up, with six being ipsilateral strokes and five being contralateral strokes. Additionally, carotid stents were placed in two patients with ipsilateral residual carotid stenosis during the follow-up period (Table 3).

Table 3: Mid-term follow-up of carotid endarterectomy patients

	N=108
	n (%) / mean ±SD
Mortality	14 (13.0)
Major neurologic complication	11(10.1)
Transient ischemic attack	9 (8.3)
Myocardial infarction	8 (7.4)
Congestive heart failure	10 (9.3)
Peripheral vascular intervention	9 (8.3)
Need for carotid re-intervention	2 (1.9)

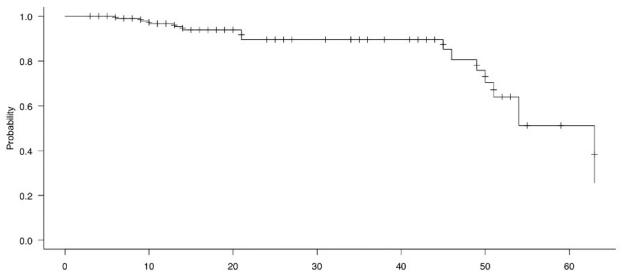

Figure 1: Kaplan-Meier curve for mortality (in months)

Discussion

Carotid artery stenosis has been extensively studied and recognized as a significant risk factor for ischemic stroke. It can be accompanied by a range of symptoms, including transient ischemic attacks (TIAs), minor strokes, or major strokes, necessitating a comprehensive understanding of the disease's progression and tailored management strategies.

According to the latest guidelines released by European Society of Vascular Surgery (ESVS) in 2023 and the European Stroke Organization (ESO) in 2021, CEA is recommended as a beneficial intervention for asymptomatic patients with carotid artery stenosis exceeding 60% and symptomatic patients with carotid

artery stenosis exceeding 50% (4,6). With reported one-year recurrence rates ranging from 5% to 17%, recurrent stroke is associated with high mortality rates, with a five-year mortality risk ranging from 5% to 15% (7,8). Additionally, the ten-year recurrence rate is strikingly high, reaching up to 51%, highlighting the significant long-term risk faced by individuals who have experienced a stroke (9). In symptomatic patients it is currently believed that early intervention within 14 days of symptom onset is associated with improved outcomes and reduced risks of recurrent stroke. Also, recent research has revealed that early recurrent strokes following transient ischemic attacks may be higher than previously estimated.

In our study, general anesthesia emerged as the preferred anesthesia type in 89.1% of patients. The GALA trial, the largest randomized controlled trial (RCT) comparing anesthesia types, reported no significant difference in perioperative death, stroke, or myocardial infarction between general anesthesia and local anesthesia (10). Mracek et al. (11) demonstrated that general anesthesia was associated with higher patient satisfaction and future preference for this type of anesthesia. These results highlight the complexity of anesthesia choices and the need for individualized approaches in optimizing patient outcomes and experiences.

The Cochrane review conducted by Chonkgrutsut et al. (12) indicated that there was no significant difference between routine shunting and no shunting in terms of stroke and mortality outcomes. Similarly, Wiske et al.'s study (13), after adjusting for patient risk factors, found no discernible difference between patients who underwent never shunting and those who underwent selective shunting. These findings suggest that the use of shunting may not offer substantial benefits in terms of stroke and mortality rates. In our study, shunting was employed in 17.4% of patients, and the decision to use shunting was left to the discretion of the operating surgeon.

In our study, Dacron patching emerged as the preferred method for operative technique, accounting for 56% of patients, followed by eversion carotid endarterectomy at 22%. Primary closure and vein patch were employed in 15.6% and 6.4% of patients, respectively. Moreover, a recent meta-analysis of 23 randomized controlled trials (RCTs) demonstrated that eversion endarterectomy and patching with bovine pericardium or PTFE were associated with a lower incidence of short and late negative outcomes (14). Additionally, a review conducted by Rerkasem et al. (15) revealed that patching was effective in reducing the risk of both perioperative and later stroke during long-term follow-up. Furthermore, Paraskevas et al. (16) argued that eversion carotid endarterectomy demonstrated superiority over conventional carotid endarterectomy in terms of perioperative outcomes and late restenosis. However, it exhibited similar results to patched carotid endarterectomy concerning both early and late outcomes.

The all-cause mortality rate in the present study was 13%, with myocardial infarction identified as the primary cause of mortality, followed by malignancy as the second leading cause. In a recent study by Waden et al. (17), a 5-year all-cause mortality rate of 11.7% was reported, with symptomatic patients experiencing a slightly higher rate of 12.4%. Notably, their study also identified cardiac events as the primary cause of mortality and malignancy as the secondary cause, which aligns with our findings. Additionally, Mannheim et al. (18), in a prospective randomized study, found a 5-year all-cause mortality rate of 19.6%. On the other hand, Batolla et al., reported a mortality rate of 7% with a mean follow up time of 34 months. Indeed, the varying mid and long-term mortality rates reported in the literature may be attributed to heterogeneous patient groups and potential bias in patient selection. Differences in patient characteristics, comorbidities, risk factors, and treatment approaches across different studies can significantly influence mortality outcomes. Moreover, varying methodologies and study designs, including retrospective versus prospective approaches, may introduce bias in patient selection, potentially impacting the reported mortality rates.

Several limitations should be considered when interpreting the findings of this study. Firstly, the retrospective nature of the study design may introduce inherent biases, such as selection bias and incomplete data collection. Additionally, the study's single-center nature may limit the external validity, as the results might not be representative of practices in other healthcare settings or regions. Variability in surgical techniques and expertise among different surgeons may also have influenced the outcomes. Finally, the duration of follow-up might not be sufficient to capture all potential late complications or assess the long-term effectiveness of CEA.

In conclusion, this study evaluated the outcomes of CEA in a population of patients with carotid artery disease. The results indicate that CEA is an effective procedure for managing carotid stenosis, with low early postoperative mortality and complication rates. Also, the study demonstrates that carotid endarterectomy (CEA) has shown acceptable mortality and morbidity rates, making it an effective and safe procedure for managing carotid artery disease. The findings underscore the importance of careful patient selection, appropriate surgical techniques, and continued vigilance in the management of carotid artery disease. Further prospective studies may help validate these conclusions and provide additional insights into the long-term efficacy and safety of CEA.

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Author's contributions to the article

E.Y. constructed the main idea and hypothesis of the study. M.B developed the theory and arranged/ edited the material and method section. E.Y and

M.B have evaluated the data in the Results section. Discussion section of the article written by M.B. E.Y and M.B. reviewed, corrected, and approved. In addition, all authors discussed the entire study and approved the final version.

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