



## Short Term Outcomes of Endarterectomy to Asymptomatic Extracranial Carotid Artery Disease

### Ekstrakranial Karotis Arter Hastalığına Uygulanan Endarterektomi Kısa Dönem Sonuçları


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#### ABSTRACT

**Aim:** Recently published papers regarding the treatment of carotid artery stenosis are in contradiction with previous trials. Some experts have argued that this evidence supports a conservative approach to carotid revascularization (carotid endarterectomy or carotid stenting) in asymptomatic patients. The objective of this study is to evaluate outcomes of carotid endarterectomy based on preoperative symptom status.

**Material and Methods:** This retrospective study included patients underwent carotid endarterectomy to internal carotid artery between August 2008 and August 2015. Patients were divided into two groups according to preoperative symptoms. Asymptomatic group consisted of 41 patients with no preoperative neurological symptoms, and symptomatic group of 62 patients with preoperative neurological symptoms (vertigo, amaurosis fugax, transient ischemic attack and ischemic stroke). Postoperatively, all patients received standard therapy in line with the recommendation of the guidelines.

**Results:** One hundred and three patients were enrolled in this study. The mean age of patients was 68.20±9.79 (range, 41-86) years, and 27 (26.2%) of them were female. There were no statistically significant difference in terms of demographic characteristics between the groups except risk groups; asymptomatic group had more high risk grouped patients (p=0.001). Asymptomatic group was associated with statistically significantly more postoperative mortality compared with symptomatic group (p=0.028). None of the preoperative variables were related to postoperative stroke. In symptomatic group, postoperative stroke was seen in the patients who had preoperative transient ischemic attack and major stroke.

**Conclusion:** Time of surgical treatment in asymptomatic carotid artery disease should be planned according to patients' cardiac risk factors.

**Keywords:** Carotid artery stenosis; endarterectomy; stroke.

#### ÖZ

**Amaç:** Yakın zamanda yayınlanan karotis arter darlığı tedavisindeki çalışmalar eski sonuçlarla çelişmektedir. Bazı uzmanlar, bu bulguların asemptomatik hastalarda karotis revaskülarizasyona (karotis endarterektomi veya karotis stentleme) konservatif yaklaşımı desteklediğini ifade etmektedir. Bu çalışmanın amacı karotis endarterektomi sonuçlarının preoperatif semptom durumuna dayalı olarak incelenmesidir.

**Gereç ve Yöntemler:** Bu retrospektif çalışmaya Ağustos 2008 ve Ağustos 2015 tarihleri arasında internal karotis arter darlığına karotis endarterektomi uygulanan hastalar dahil edilmiştir. Hastalar preoperatif semptomlarına göre iki gruba ayrıldı. Asemptomatik grup preoperatif nörolojik semptomu bulunmayan 41 hasta içermekte ve semptomatik grup preoperatif nörolojik semptomu (vertigo, amorozis fugax, geçici iskemik atak ve iskemik inme) olan 62 hasta içermekte idi. Postoperatif dönemde tüm hastalara kılavuzların önerisine uygun olarak standart tedavi uygulandı.

**Bulgular:** Bu çalışmaya 103 hasta dahil edildi. Hastaların ortalama yaşı 68,20±9,79 (aralık, 41-86) yıl ve 27 (%26,2)'si kadın idi. Gruplar arasında, risk grubu dışında demografik özellikler açısından istatistiksel anlamlı farklılık yoktu; asemptomatik grupta yüksek riskli olarak gruplanan hasta daha fazlaydı (p=0,001). Asemptomatik grupta, semptomatik grup ile karşılaştırıldığında postoperatif mortalite istatistiksel olarak anlamlı şekilde daha fazla görüldü (p=0,028). Preoperatif değişkenlerinin hiç biri postoperatif inme ile ilişkili değildi. Semptomatik grupta, postoperatif inme preoperatif geçici iskemik atak ve majör inme olan hastalarda görüldü.

**Sonuç:** Asemptomatik karotis arter hastalığında cerrahi tedavinin zamanlaması hastanın kardiyak risk faktörlerine göre yapılmalıdır.

**Anahtar kelimeler:** Karotis arter darlığı; endarterektomi; inme.

## INTRODUCTION

Recently published papers regarding the treatment of carotid artery stenosis are in contradiction with previous trials. Transient ischemic attacks (TIA) occurred in nearly 70 percent of patients as the qualifying event for entry in the NASCET trial cohort, and observational data suggest that ischemic stroke due to extracranial carotid disease is preceded by TIA in 50 to 75 percent of patients (1-4). However, these data may be subject to selection bias as large disabling or lethal strokes were systematically excluded from NASCET and most studies assessing prestroke symptoms due to the inability to obtain a direct patient history. Some experts have argued that this evidence supports a conservative approach to carotid revascularization (carotid endarterectomy, CEA or carotid stenting) in asymptomatic patients (5,6). The objective of this study is to evaluate the outcomes of CEA based on preoperative symptom status.

## MATERIAL AND METHODS

The institutional local ethics committee approved the study (Konya Education and Research Hospital, dated 14.01.2016 and approval number: 04-21). This retrospective study included the patients who had surgically treated internal carotid artery (ICA), in the period from August 2008 to August 2015 in Konya Education and Research Hospital. The end points of study were postoperative stroke and mortality. Given the involvement of ICA stenosis, patients were divided into two groups. Asymptomatic group of patients consisted of 41 patients with no preoperative neurological symptoms, and symptomatic group of 62 patients with preoperative neurological symptoms (vertigo, amaurosis fugax, TIA and ischemic stroke). Patients had either deep or superficial cervical plexus block anesthesia which was decided by anesthesiology, none needed to switch general anesthesia. Bupivacaine and lidocaine were used as the anesthetic agent. Shunt used in the absence of sufficient back flow to the internal carotid artery, or contralateral carotid artery with severe stenosis or in patients with neurologic deficits observed after clamping during the operation. Carotid arteriotomy closed either primary or by way of a patch. Postoperatively all patients had standard medication dictated by guidelines such as antithrombotic, antiplatelet, statin, antihypertensive- if needed-, and antibiotic. Cardiac risk groups were categorized as high risk group (myocardial infarction, MI in 6 weeks, USAP and/or CCS III-IV angina, congestive heart failure, valvular heart disease (intervention needed) and left ventricular ejection fraction lower than 30%), moderate risk group (MI in more than 6 weeks, stable angina pectoris and/or CCS I-II angina, medication required arrhythmia and left ventricular ejection fraction 30-50%) and low risk group (diabetes mellitus, hypertension, chronic obstructive pulmonary disease, obesity, chronic renal insufficiency, peripheral arterial disease, dyslipidemia and left ventricular ejection fraction more than 50%). Stenosis detected with Doppler ultrasound and confirmed by MRI, CT or conventional angiography.

### Statistical Analysis

Distribution of the numerical data was examined using Shapiro-Wilk and Kolmogorov-Smirnov tests. Continuous variables were displayed by the mean and

standard deviation if normally distributed and by the median, interquartile range and range if there was no normal distribution. Categorical variables were displayed as counts and percentages. Continuous variables were analyzed with Independent samples t test or Mann-Whitney U test according to the normality assumption. Group comparison was done using the Pearson chi-square and Fisher exact tests, where appropriate. All tests were two-sided, and a p-value of 0.05 or lower was considered statistically significant. All statistical analyses were performed using IBM SPSS v.21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

## RESULTS

Totally 103 patients were enrolled in this study. The mean age of patients was 68.20±9.79 (range, 41-86) years, and 27 (26.2%) of them were female. Table 1 depicts baseline patient characteristics and there were no significant difference among groups except risk groups (Asymptomatic group had more high risk grouped patients, p<0.001).

Asymptomatic patients' group was associated with significantly more postoperative mortality compared with symptomatic patients' group (p=0.028, Table 2).

High-risk cardiac grouped patients were found to be associated with postoperative MI. Hospital mortality was seen in 9 patients. Two patients on the postoperative 3<sup>rd</sup> day had CABGx3 and 2 had CABGx3+AVR. One patient was waiting for CABG, and all five died due to MI. Two patients had additional morbidity (chronic obstructive pulmonary disease), and two patients died due to postoperative major stroke.

Table 3a depicts demographics of only postoperative stroke observed patients and as seen none of the preoperative variables were related with postoperative stroke (Table 3a). On the other hand, among symptomatic patients, preoperative TIA, and major stroke were associated with higher postoperative stroke rates (Table 3b). Comparison of postoperative stroke observed patients according to preoperative symptom revealed relationship (Table 3c).

**Table 1.** Demographics of study groups

	Asymptomatic (n=41)	Symptomatic (n=62)	P
<b>Sex</b>			
Male	30 (73.2%)	46 (74.2%)	0.908
Female	11 (26.8%)	16 (25.8%)	
<b>Age, years</b>	68.66±9.42	67.90±10.09	0.704
<b>CEA side</b>			
Right	20 (48.8%)	39 (62.9%)	0.156
Left	21 (51.2%)	23 (37.1%)	
<b>Carotid lesion</b>			
Right	60 (60) [10-100]	70 (60) [10-100]	0.851
Left	60 (50) [10-100]	50 (55) [10-100]	0.374
<b>Risk group</b>			
High	15 (36.6%)	4 (6.5%)	<0.001
Moderate	6 (14.6%)	9 (14.5%)	
Low	20 (48.8%)	49 (79.0%)	
<b>Primary closure</b>	13 (31.7%)	18 (29.0%)	0.772

CEA: Carotid endarterectomy

**Table 2.** Postoperative outcomes of study groups

Outcome	Asymptomatic (n=41)	Symptomatic (n=62)	P
CVE	1 (2.4%)	4 (6.5%)	0.646
MI	4 (9.8%)	1 (1.6%)	0.080
Bleeding	2 (4.9%)	1 (1.6%)	0.562
Mortality	7 (17.1%)	2 (3.2%)	<b>0.028</b>

CVE: Cerebrovascular event, MI: Myocardial infarction

**Table 3a.** Demographics of postoperative stroke (cerebrovascular event) observed patients

	Non-CVE (n=98)	CVE (n=5)	P
<b>Symptomatic</b>	58 (59.2%)	4 (80.0%)	0.646
<b>Sex</b>			
Male	72 (73.5%)	4 (80.0%)	0.999
Female	26 (26.5%)	1 (20.0%)	
<b>Age, years</b>	68.09±9.93	70.40±6.80	0.610
<b>CEA side</b>			
Right	54 (55.1%)	5 (100%)	0.070
Left	44 (44.9%)	0 (0.0%)	
<b>Carotid lesion</b>			
Right	85 (20) [10-100]	80 (20) [70-90]	0.680
Contralateral	30 (40) [10-99]	50 (30) [30-60]	0.232
Left	70 (25) [10-100]	---	---
Contralateral	30 (40) [10-100]	---	---
<b>Risk group</b>			
High	18 (18.4%)	1 (20.0%)	0.194
Moderate	13 (13.3%)	2 (40.0%)	
Low	67 (68.4%)	2 (40.0%)	
<b>Primary closure</b>	29 (29.6%)	2 (40.0%)	0.636

CVE: Cerebrovascular event, CEA: Carotid endarterectomy

**Table 3b.** Comparison of postoperative stroke observed patients according to the complaints at admission

	Non-CVE (n=98)	CVE (n=5)	P
<b>Asymptomatic</b>	40 (40.8%)	1 (20.0%)	
<b>Symptomatic</b>			
Dizziness	17 (17.3%)	0 (0.0%)	0.100
Left-sided hemiparesis	6 (6.1%)	0 (0.0%)	
Right-sided hemiparesis	11 (11.2%)	0 (0.0%)	
TIA	2 (2.1%)	2 (40.0%)	
Uneventful CVE	1 (1.0%)	0 (0.0%)	
Syncope	2 (2.1%)	0 (0.0%)	
Amaurosis fugax	1 (1.0%)	0 (0.0%)	
Numbness in the arm	2 (2.1%)	0 (0.0%)	
Major stroke	16 (16.3%)	2 (40.0%)	

CVE: Cerebrovascular event, TIA: Transient ischemic attack

**Table 3c.** Comparison of postoperative stroke observed patients according to the preoperative symptom

	Non-CVE (n=58)	CVE (n=4)	P
Dizziness	17 (29.3%)	0 (0.0%)	0.144
Left-sided hemiparesis	6 (10.3%)	0 (0.0%)	
Right-sided hemiparesis	11 (19.0%)	0 (0.0%)	
TIA	2 (3.4%)	2 (50.0%)	
Uneventful CVE	1 (1.7%)	0 (0.0%)	
Syncope	2 (3.4%)	0 (0.0%)	
Amaurosis fugax	1 (1.7%)	0 (0.0%)	
Numbness in the arm	2 (3.4%)	0 (0.0%)	
Major stroke	16 (27.6%)	2 (50.0%)	

CVE: Cerebrovascular event, TIA: Transient ischemic attack

**DISCUSSION**

Carotid artery stenosis is a common presentation of atherosclerotic disease. A total of 9% to 12% of patients with the known atherosclerotic disease has high-grade carotid artery stenosis (7). CEA is a widely accepted method of treating patients with significant carotid artery stenosis.

In our study, we detected higher mortality rate (8.7%) comparing to the literature. In larger trials and reviews, mortality rate reported ranging from 1% to 6.7% (1,8). Medical complications following CEA were associated with myocardial infarction history or angina and hypertension (9). During NASCET trial patients with recent myocardial infarction or unstable angina pectoris or heart failure were excluded and thus causing low peri-procedural medical complication rate. On the other hand, trials concluding high risk grouped patients had worse outcome parallel to our findings (10,11). Kumamaru et al. (12) and O'Neill L et al. (13) had showed that surgeon reported case-volume and 30-day mortality are inversely proportional and our results support this two reports.

Interestingly Galyfos et al. (14) reported that low to moderate risk grouped patients had increased cardiac troponin I levels associated with myocardial ischemia comparing to high risk grouped patients. Asymptomatic carotid atherosclerosis is also a marker of increased risk for myocardial infarction and vascular death (11,15,16). Thus, asymptomatic carotid atherosclerosis is considered a risk equivalent for cardiovascular disease. In our study, groups had statistically significant difference according to cardiac risk groups, and mortality observed patients were mostly in high cardiac risk group.

Dodick et al. (5) and Shanik et al. (6) argued that large trials may have selection bias due to as large disabling or lethal strokes were systematically excluded. Natural history studies advocate majority of strokes caused by carotid artery disease are preceded by TIA, and the incidence of unprotected stroke is low (5). There are papers advocating best medical treatment alone for asymptomatic carotid artery disease patients (15-19). On the other hand major trials as VA, ACAS, and ACST I-II encourage intervention for asymptomatic carotid artery disease (20-23).

The NASCET described five baseline variables for increased risk factor: hemispheric TIA as qualifying event, contralateral carotid occlusion, ipsilateral ischemic lesion on CT scan and irregular or ulcerated ipsilateral plaque. Also, ECST confirmed findings of NASCET and added age and sex as predictive risk factors (24). In our study we observed increased postoperative stroke in preoperatively symptomatic patients (TIA and CVE) parallel to the literature.

Interestingly we have observed postoperative stroke in patients with right-sided procedure applied in contrast to NASCET's finding.

This study had some limitations. Because this study was retrospective and randomization between groups was not performed, it is conceivable that there are differences in patient characteristics among the groups and that a selection bias. Furthermore, this study enrolled in a multi-surgeon center which also may contribute to selection bias. Additionally, the study was limited by the number of patients with CEA. Finally, our long-term follow-up was limited to 30 days.

**CONCLUSION**

Asymptomatic carotid artery disease patients' surgery time should be planned according to their cardiac risk factors.

**REFERENCES**

1. North American Symptomatic Carotid Endarterectomy Trial Collaborators, Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med.* 1991;325(7):445-53.
2. Pessin MS, Duncan GW, Mohr JP, Poskanzer DC. Clinical and angiographic features of carotid transient ischemic attacks. *N Engl J Med.* 1977;296(7):358-62.
3. Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, et al. The Harvard Cooperative Stroke Registry: a prospective registry. *Neurology.* 1978;28(8):754-62.
4. Russo LS Jr. Carotid system transient ischemic attacks: clinical, racial, and angiographic correlations. *Stroke.* 1981;12(4):470-3.
5. Dodick DW, Meissner I, Meyer FB, Cloft HJ. Evaluation and management of asymptomatic carotid artery stenosis. *Mayo Clin Proc.* 2004;79(7):937-44.
6. Shanik GD, Moore DJ, Leahy A, Grouden MC, Colgan MP. Asymptomatic carotid stenosis: a benign lesion? *Eur J Vasc Surg.* 1992;6(1):10-5.
7. Kurvers HAJM, van der Graaf Y, Blankensteijn JD, Visseren FLJ, Eikelboom BC, SMART Study Group. Screening for asymptomatic internal carotid artery stenosis and aneurysm of the abdominal aorta: comparing the yield between patients with manifest atherosclerosis and patients with risk factors for atherosclerosis only. *J Vasc Surg.* 2003;37(6):1226-33.
8. European Carotid Surgery 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(8752):1235-43.
9. Paciaroni M, Eliasziw M, Kappelle LJ, Finan JW, Ferguson GG, Barnett HJ. Medical complications associated with carotid endarterectomy. North American Symptomatic Carotid Endarterectomy Trial (NASCET). *Stroke.* 1999;30(9):1759-63.
10. Thomas DJ. Protected carotid artery stenting versus endarterectomy in high-risk patients reflections from SAPHIRE. *Stroke.* 2005;36(4):912-3.
11. Goessens BMB, Visseren FLJ, Kappelle LJ, Algra A, van der Graaf Y. Asymptomatic carotid artery stenosis and the risk of new vascular events in patients with manifest arterial disease: the SMART study. *Stroke.* 2007;38(5):1470-5.
12. O'Neill L, Lanska DJ, Hartz A. Surgeon characteristics associated with mortality and morbidity following carotid endarterectomy. *Neurology.* 2000;55(6):773-81.
13. Kumamaru H, Jalbert JJ, Nguyen LL, Gerhard-Herman MD, Williams LA, Chen CY, et al. Surgeon case volume and 30-day mortality after carotid endarterectomy among contemporary medicare beneficiaries: before and after national coverage determination for carotid artery stenting. *Stroke.* 2015;46(5):1288-94.
14. Galyfos G, Tsioufis C, Theodorou D, Katsaragakis S, Zografos G, Filis K. Cardiac troponin I after carotid endarterectomy in different cardiac risk patients. *J Stroke Cerebrovasc Dis.* 2015;24(3):711-7.
15. Spence JD. Management of asymptomatic carotid stenosis. *Neurol Clin.* 2015;33(2):443-57.
16. Chimowitz MI, Weiss DG, Cohen SL, Starling MR, Hobson RW 2nd. Cardiac prognosis of patients with carotid stenosis and no history of coronary artery disease. Veterans Affairs Cooperative Study Group 167. *Stroke.* 1994;25(4):759-65.
17. Marquardt L, Geraghty OC, Mehta Z, Rothwell PM. Low risk of ipsilateral stroke in patients with asymptomatic carotid stenosis on best medical treatment: a prospective, population-based study. *Stroke.* 2010;41(1):e11-7.
18. Abbott AL. Medical (nonsurgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. *Stroke.* 2009;40(10):e573-83.
19. Naylor AR, Ricco JB, de Borst GJ, Debus S, de Haro J, Halliday A. Editor's choice - management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg.* 2018;55(1):3-81.
20. Hobson RW 2nd, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med.* 1993;328(4):221-7.
21. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA.* 1995;273(18):1421-8.
22. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet.* 2004;363(9420):1491-502.
23. ACST-2 Collaborative Group, Halliday A, Bulbulia R, Gray W, Naughten A, den Hartog A, Delmestri A, et al. Status update and interim results from the asymptomatic carotid surgery trial-2 (ACST-2). *Eur J Vasc Endovasc Surg.* 2013;46(5):510-8.
24. Ferguson GG, Eliasziw M, Barr HW, Claget GP, Barnes RW, Wallace MC, et al. The North American Symptomatic Carotid Endarterectomy Trial: surgical results in 1415 patients. *Stroke.* 1999;30(9):1751-8.