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Original Article / Özgün Makale

Does severe contralateral carotid artery stenosis affect the outcomes of carotid endarterectomy?

Ciddi kontralateral karotis arter darlığı karotis endarterektomi sonuçlarını etkiler mi?

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ABSTRACT

Background: This study aims to evaluate the effect of contralateral internal carotid artery stenosis on postoperative stroke and mortality rate and blood pressure alterations following carotid artery endarterectomy.

Methods: Between January 2009 and April 2017, a total of 152 carotid artery endarterectomy operations in 141 consecutive patients (30 females, 111 males; mean age 70.0±10.2 years; range, 48 to 92 years) with internal carotid artery stenosis were retrospectively analyzed. The patients were divided into two groups as those with contralateral internal carotid artery stenosis <70% (n=95) and contralateral internal carotid artery stenosis ≥70% (n=26). Stroke and mortality rates in the early postoperative period (within the first 30 days), postoperative blood pressure alterations at six and 24 hours, non-neurological outcomes, and baseline demographic characteristics were analyzed and compared between the groups.

Results: Both groups showed similar results in terms of the demographic characteristics. There was no statistically significant difference in the postoperative blood pressure alterations at six (p=0.917) and 24 hours (p=0.6), stroke rate (7.6% vs. 3.1%, p=0.282), mortality rate (3.8% vs. 2.1%, p=0.519), non-neurological complications (15.3% vs. 11.4%, p=0.736), and length of hospital stay (p>0.05) between the groups. The patients with contralateral severe internal carotid artery stenosis were younger (p=0.005).

Conclusion: The present study shows that the presence of a contralateral severe internal carotid artery stenosis does not increase the risk of postoperative stroke and mortality rates and blood pressure alterations. Therefore, carotid artery endarterectomy can be performed with acceptable complication rates in patients with contralateral severe internal carotid artery stenosis with strict perioperative hemodynamic monitoring.

Keywords: Blood pressure; carotid endarterectomy; contralateral carotid artery stenosis; stroke.

ÖZ

Amaç: Bu çalışmada, karotis arter endarterektomi sonrasında kontralateral internal karotis arter darlığının ameliyat sonrası inme ve ölüm oranı ve kan basıncı değişiklikleri üzerindeki etkisi değerlendirildi.

Çalışma planı: Ocak 2009 - Nisan 2017 tarihleri arasında, internal karotis arter darlığı olan 141 ardışık hastada (30 kadın, 111 erkek; ort. yaş 70.0±10.2 yıl; dağılım 48-92 yıl) toplam 152 karotis arter endarterektomi ameliyatı retrospektif olarak incelendi. Hastalar kontralateral internal karotis arter darlığı <%70 (n=95) ve kontralateral internal karotis arter darlığı ≥%70 (n=26) olanlar olmak üzere iki gruba ayrıldı. Ameliyat sonrası erken dönemde (ilk 30 gün içinde) inme ve mortalite oranları, ameliyat sonrası altı ve 24. saatte kan basıncı değişiklikleri, nörolojik olmayan sonuçlar ve başlangıç demografik özellikleri incelendi ve gruplar arasında karşılaştırıldı.

Bulgular: Her iki grup da demografik özellikler açısından benzer sonuçlar gösterdi. Gruplar arasında ameliyat sonrası altıncı saat (p=0.917) ve 24. saat (p=0.6) kan basıncı değişikliği, inme oranı (%7.6 ile %3.1, p=0.282), ölüm oranı (%3.8 ile %2.1, p=0.519), nörolojik olmayan komplikasyonlar (%15.3 ile %11.4, p=0.736) ve hastanede kalış süresi açısından istatistiksel olarak anlamlı fark yok idi (p>0.05). Kontralateral ciddi internal karotis arter darlığı olan hastalar daha genç idi (p=0.005).

Sonuç: Bu çalışma, ciddi kontralateral internal karotis arter darlığı varlığının ameliyat sonrası inme ve ölüm oranı ve kan basıncı değişikliği riskini artırmadığını göstermektedir. Bu nedenle, karotis endarterektomi kontralateral ciddi internal karotis arter darlığı olan hastalarda titiz perioperatif hemodinamik takip altında kabul edilebilir komplikasyon oranları ile uygulanabilir.

Anahtar sözcükler: Kan basıncı; karotis endarterektomi; kontralateral karotis arter darlığı; inme.

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Carotid endarterectomy (CEA) is a safe and an effective surgical technique which prevents stroke in symptomatic and asymptomatic patients with severe internal carotid artery (ICA) stenosis.[1] During CEA, the transaction of the carotid sinus baroreceptors may lead to increase in the blood pressure, heart rate, and stroke.[2,3] In addition, contralateral severe ICA stenosis is considered another potential factor for blood pressure alterations. Thus, management of patients with contralateral severe ICA stenosis or occlusion still remains controversial during CEA.[4-6] Contralateral ICA stenosis and occlusion are seen in 12.04% and 2.3-25% of patients undergoing CEA, respectively.[6-8] Additionally, contralateral severe ICA occlusion has been proposed to increase the perioperative death[1] and associated with a 5 to 10% stroke rate;[9] however, no correlation was found in the Asymptomatic Carotid Atherosclerosis Study.[6,10] On the other hand, contralateral severe ICA stenosis was not found to have a significant effect on the perioperative stroke and death rate.[1,11]

In the present study, we aimed to evaluate the effect of contralateral severe ICA stenosis on postoperative stroke and mortality rates and blood pressure alterations following CEA.

PATIENTS AND METHODS

Between January 2009 and April 2017, a total of 152 CEAs in 141 consecutive patients (30 females, 111 males; mean age 70.0±10.2 years; range, 48 to 92 years) who were diagnosed with symptomatic and asymptomatic ICA stenosis and admitted to our clinic were retrospectively analyzed. Of the patients, 25 patients (20.6%) were aged >80 years. The mean age was 64.9±10.6 (range, 48 to 89) years in patients with contralateral severe ICA stenosis, whereas it was 71.2±10.0 (range, 48 to 92) years in patients without severe ICA stenosis (p=0.005). Bilateral staged CEA was performed in 11 patients. Of those, 10 patients had contralateral severe ICA stenosis and one symptomatic patient did not have contralateral severe ICA stenosis. In addition, 13 patients were excluded due to insufficient computed tomography angiography (CTA) data and five patients were excluded due to simultaneous coronary artery bypass grafting (CABG). Contralateral ICA occlusion was present in only two patients (1.6%); therefore, we did not include them in this study. The patients were divided into two groups as those with contralateral ICA stenosis <70% and contralateral ICA stenosis ≥70%. Of those, contralateral ICA <70% was present in 95 patients (78.5%), while contralateral severe (≥70%) ICA stenosis was present in 26 patients (21.5%).

Physical and laboratory examination findings, demographic characteristics, medical history, risk factors, and medications used were recorded. The demographic characteristics of the groups are shown in Table 1. We considered hemiparesis, hemiplegia, amaurosis fugax, peripheral facial paralysis, and transient ischemic attack as preoperative neurological symptoms. Of note, asymptomatic patients were coincidentally diagnosed by other clinics or diagnosed during investigations of patients with the peripheral arterial disease, aortoiliac disease, abdominal aortic aneurysm, and coronary artery disease. Also, we routinely performed bilateral carotid artery Doppler ultrasound (DUS) to those group of patients, except for patients with coronary artery disease younger than 65 years. If more than 70% of the ICA stenosis was diagnosed, stenosis was confirmed by CTA. The treatment indication was ≥50% of the ICA stenosis for symptomatic patients and ≥70% of the ICA stenosis for asymptomatic patients in line with the The North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria and European Society for Vascular Surgery (ESVS) 2017 guideline.[12,13]

Baseline blood pressures were measured noninvasively on the day of admission until discharge and invasively measured during the perioperative period. More than 140 mmHg systolic blood pressure or more than 40% increase of baseline systolic blood pressure was considered postoperative alteration.[3]

Transthoracic echocardiographic imaging was performed to all patients and the decision of preoperative coronary angiography was made according to the ejection fraction and motion disorder of the left ventricle wall or additional treadmill test result. The preoperative neurological symptoms and postoperative neurological event were evaluated by neurologists. We performed CEA (eversion endarterectomy or conventional endarterectomy + patch plasty) under general anesthesia with pharmacological support for blood pressure control. CEA + patch plasty (polytetrafluoroethylene, Dacron graft or autologous vein) was performed in 71 (58.6%) of patients and eversion endarterectomy was performed in 50 patients (41.4%). The surgical technique was based on preoperative clinical and angiographic examination and with the choice of the attending cardiovascular surgeon. A clamping test for one minute was performed to measure the mean stump blood pressure (Vmean) change after CCA and ECA clamping before arteriotomy to patients who underwent conventional CEA and the relative changes

in the regional cerebral oxygen saturation (rSO_2) in the frontal lobe using the near-infrared spectroscopy (NIRS). We administered protamine according to the activated coagulation time at the end of the surgery, when needed. All patients underwent surgery under single anticoagulant (acetic salicylic acid 100 mg/day or clopidogrel 75 mg/day) and continued with single or dual antiplatelet and statin therapy throughout the life and low-molecular-weight heparin was administered for three days after surgery. Postoperative stroke rate, death rate, blood pressure alteration, bleeding, cranial nerve injury, and myocardial infarction were analyzed. We routinely performed cranial and cervical CTA and diffusion MRI to all patients who had postoperative major neurological complications and consulted with the Neurology Physicians. During the postoperative period, hypertension was treated with either intravenous (esmolol, nitroglycerin) or oral vasodilators as metoprolol succinate, angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARBs), or calcium channel blockers. Postoperative DUS evaluation was performed at one and six months and every six months or once a year thereafter.

Table 1. Baseline data of patients with and without contralateral severe internal carotid artery stenosis

	Contralateral severe ICA stenosis (n=26)			Without contralateral severe ICA stenosis (n=95)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Distribution	21.5			78.5			
Age (year)			64.9±10.6			71.2±10.0	0.005
Gender Female	5	19.2		18	18.9		0.871
Right ICA stenosis (%)			86.7±8.0			75.4±16.6	0.02
Left ICA stenosis (%)			84.0±9			79.0±14.4	0.108
Operation side (right)	9	34.6		51	53.6		1
Operation side (left)	7	26.9		43	45.2		1
Operation side (bilateral)	10	38.5		1	1.2		0.001
Preoperative neurologic symptoms	18	69.2		71	74.7		0.573
Diabetes mellitus	13	54.2		64	68.8		0.177
Hypertension	15	57.6		35	63.7		0.07
Coronary artery disease	14	58.3		43	36.8		0.035
Chronic obstructive pulmonary disease	4	15.3		20	21		0.781
Peripheral arterial disease	2	7.7		7	7.3		0.956
Smoking	5	19.2		27	28.4		0.454
Hemoglobin (g/dL)			12.1±1.8			13±1.8	0.035
Hematocrit (%)			37.4±5.2			39.0±5.0	0.159
Creatinin			1.4±1.7			1.1±0.4	0.059
Total cholesterol			170±40.9			174.5±49.2	0.74
Triglyceride			155.5±60.2			147.5±82.6	0.65
High density lipoprotein			46.9±20.9			41.8±14.9	0.17
Low density lipoprotein			95.2±39.8			106.4±4	0.224
Ft3			2.8±0.4			2.8±1.0	0.848
Ft4			1.3±0.3			1.3±25	0.592
Thyroid-stimulating hormone			1.9±3.0			1.5±1.3	0.478

ICA: internal carotid artery; SD: Standard deviation; Ft3: FreeT3; Ft4: FreeT4.

Table 2. Preoperative symptoms of patients with and without contralateral severe internal carotid artery stenosis

	Contralateral severe ICA stenosis (n=26)		Without contralateral severe ICA stenosis (n=95)		Total		
	n	%	n	%	n	%	*p*
Symptomatic	18	69.2	71	74.7	89	73.5	0.572
Hemiparesis	11	42.3	44	46.3	55	45.4	0.132
Hemiplegia	1	3.8	3	3.1	4	3.3	1
Amaurosis fugax	2	7.6	3	3.1	5	4.1	0.292
Transient ischemic attacks	1	3.8	7	7.3	8	8.4	1
Facial paralysis	1	3.8	8	8.4	9	9.4	0.682
Speech disturbances	2	7.6	6	6.3	8	8.4	0.680

ICA: internal carotid artery; SD: Standard deviation.

A written informed consent was obtained from each patient. The study protocol was approved by the Ondokuz Mayıs University Ethics Committee (OMU KAEK 2017/357). The study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows version 21.0 software (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean and standard deviation (SD) or interquartile range (IQR) or median (min-max) values, while categorical data were expressed in number and percentage. Independent sample t-test was used to compare continuous data between the groups including ≥70% contralateral ICA stenosis and <70% contralateral ICA stenosis for parametric variables. The chi-square and Fisher's exact tests were used for categorical variables. The Mann-Whitney U test was used for non-parametric variables, when the independent sample t-test was not met. A *p* value of <0.05 was considered statistically significant.

RESULTS

A significant difference was found in the age of the patients (p=0.005), while there was no significant difference in preoperative symptoms, demographic characteristics, and baseline systolic blood pressure values between the groups. The gender distribution was similar in patients with and without contralateral severe ICA stenosis (female, 19.2% vs. 18.9%, respectively, p=0.871). The mean ICA stenosis ipsilateral to the surgical site was 82.4±12.6% (range, 45 to 99%). The mean right ICA stenosis was 86.7±8.0% in patients with severe contralateral stenosis and was 75.4±16.6% in patients without (p=0.02). The mean left ICA stenosis was 84.0±9% in patients with severe contralateral stenosis and was 79.0±14.4% (p=0.108) in patients without. There was no statistically significant difference in the right and left ICAs stenosis (p=0.67). Intraluminal shunt was used in 12 patients (three patients with contralateral severe ICA stenosis, nine patients without 11.5% vs. 9.5%, p=0.755). Both groups showed similar results in terms of the type of surgery. No difference was found in terms of the mean operative time in patients with contralateral severe ICA stenosis and patients without contralateral severe ICA stenosis (84±12.3 min vs. 85.4±17.4 min, p=0.701). A total of 32 patients (26.4%) were asymptomatic, of those eight patients (30%) had severe contralateral ICA stenosis (Table 2). While 89 patients (73.5%) were symptomatic, of those 18 (20.2%) had severe contralateral ICA stenosis (p=0.572). In the present study, a total of five (3.5%) postoperative strokes occurred (two patients with contralateral severe ICA stenosis (7.6%, 3.1%, p=0.282) (Table 3). The early postoperative (within the first 30 days) mortality rate was 2.47% (three patients, one patient with contralateral severe ICA stenosis, 3.8% vs. 2.1%, p=0.519). The most common reason for perioperative stroke was comprising thromboembolic event (p=0.519). Permanent neurological sequelae were reported in one patient (0.82%) with contralateral severe ICA stenosis (p=0.214). Six patients (4.9%) developed cranial nerve damage (the marginal mandibular branch of the facial nerve and hypoglossal nerve) (p=0.608) and seven patients (5.7%) developed hematoma during the postoperative period (p=0.642), 10 patients (8.2%) received postoperative revision due to bleeding (p=0.446). In total, postoperative non-neurological complications (including bleeding and

Table 3. Postoperative outcomes of patients with and without contralateral severe internal carotid artery stenosis

	Contralateral severe ICA stenosis (n=26)			Without contralateral severe ICA stenosis (n=95)			Total		
	n	%	Mean±SD	n	%	Mean±SD	n	%	*p*
Total complication	9	34.6		19	20		28	23.1	
Neurologic complication									
Postoperative stroke	2	7.6		3	3.1		5	4.1	0.282
Thromboembolic	1	3.8		2	2.1		3	2.4	0.519
Cerebral hyperperfusion syndrome	1	3.8		1	1		2	1.6	0.385
Permanent neurological sequelae	1	3.8		0	0		1	0.8	0.214
Cranial nerve damage	2	7.6		4	4.2		6	4.9	0.608
Facial nerve paralysis	1	3.8		2	2.1		3	2.4	0.519
Hypoglossal nerve paralysis	1	3.8		2	2.1		3	2.4	0.519
Non-neurologic complications	5	19.2		12	12.6		17	14	0.523
Bleeding	3	11.5		7	7.3		10	8.2	0.446
Hematoma	2	7.6		5	5.2				0.642
Myocardial infarction	0	0		0	0				
Renal insufficiency	0	0		0	0				
Gastrointestinal system complication	0	0		0	0				
Heart failure	0	0		0	0				
Postoperative death	1	3.8		2	2.1		3	2.4	0.519
Postoperative systolic blood pressure alterations									
Postoperative sixth hour systolic BP			137.1±24.5			136.7±14.8			0.917
Postoperative first day systolic BP			127.6±10.1			126.5±9.3			0.6

ICA: internal carotid artery; SD: Standard deviation; BP: Blood pressure.

minor hematomas) were not significantly different in patients with and without contralateral severe ICA stenosis (p=0.523).

Both blood pressure difference at the postoperative sixth and 24th hours were not significantly different between the groups (p=0.917, p=0.6, respectively). In addition, there was no significant difference in the in-hospital stay (p>0.05). No perioperative myocardial infarction was observed.

DISCUSSION

Although there are several studies on contralateral ICA occlusion in the literature, there are few articles for contralateral severe ICA stenosis. Therefore, we addressed into these important issues. Ricotta et al.[14] showed that <70% contralateral ICA stenosis was present in 77.3% of cases, >70% was present in 12.9% of cases, and contralateral ICA occlusion was present in 9.8% of cases. Our results are also consistent with these findings and we found that <70% contralateral carotid stenosis was present in 78.5% of the patients and stenosis >70% was present in 21.5% of the patients. Patients with contralateral severe ICA stenosis were younger, had lower hemoglobin levels, and a higher rate of right ICA stenosis. These findings suggested that the grade of atherosclerosis was more advanced in patients with contralateral severe ICA stenosis and presumably initiated in younger ages, particularly in the right ICA (p=0.02 vs. p=0.108); however, preoperative symptoms were not significantly different in terms of contralateral severe ICA stenosis (p=0.573). Only one symptomatic patient underwent bilateral CEA without contralateral severe ICA stenosis. Although it was statistically significant, it did not reach clinical significance. In addition, using intraluminal shunt during surgery did not affect the results in terms of contralateral severe ICA stenosis (p=0.755). The rate of postoperative stroke (p=0.282) and early death rate within 30 days (p=0.519) did not significantly differ. In addition, Halm et al.[15] found that >50% contralateral stenosis was an independent risk factor for stroke in symptomatic patients and the effect of contralateral ICA occlusion was also found to be similar to the >70% contralateral carotid stenosis.

Weise et al.[16] compared the outcomes of males and females in terms of contralateral severe ICA stenosis and occlusion and concluded that postoperative stroke rate, restenosis and myocardial infarction were significantly higher in females. Interestingly, in our study cohort, we found no difference between the patients with contralateral ICA occlusion and patients with contralateral severe ICA stenosis or without severe ICA stenosis. Our findings are consistent with previous studies,[15,17,18] suggesting no significant difference in the postoperative stroke rate and blood pressure alterations in patients with and without severe ICA stenosis.

Carotid endarterectomy prevents stroke and can be performed with a low perioperative stroke and death risk. Cerebral ischemia, hemorrhage, thrombosis or embolism are the main causes of postoperative stroke in patients undergoing CEA.[1,19] Thus, a careful evaluation before surgery is essential for CEA, including the evaluation of the status of the contralateral ICA and vertebrobasilar and intracerebral collateral circulation. In addition, cerebral protection by monitoring with the NIRS, blood pressure control, and selective shunting may reduce the postoperative stroke rate.[19] The development of vertebrobasilar circulation to provide adequate circulation of the circle of Willis is the most accepted hypothesis for contralateral ICA occlusion.[20,21] Some authors concluded that contralateral ICA occlusion increases the stroke risk, TIA risk, and short term all-cause mortality in patients undergoing CEA;[1,19-23] however, no correlation was found for postoperative outcomes in several studies.[4,14,18] Furthermore, no correlation was found between the ICA cross-clamping time and postoperative stroke rate between general and local anesthesia.[5,24-26] Ricotta et al.[14] concluded that contralateral ICA occlusion did not increase the postoperative stroke risk, while it increased the risk of cardiovascular burden. In addition, contralateral severe ICA stenosis and occlusion was found to be associated with prolonged length of in-hospital stay.[22] However, we found no significant difference in terms of the length of in-hospital stay.

In their study, Akyuz et al.[3] compared patients with contralateral ICA stenosis (50 to 99%) or occlusion (100%) and patients without stenosis. They reduced the cut-off value for ICA stenosis to 50% and added patients with contralateral ICA occlusion to severe ICA stenosis group. They concluded that patients with contralateral carotid artery stenosis or occlusion had significantly higher systolic, diastolic, and mean arterial blood pressures. Although the overall diabetes mellitus (DM) rate was high (68.5%), no significant difference was found between the groups (p=0.18).

The low postoperative cardiac complications can be attributed to the high preoperative coronary angiography rates and strict perioperative hemodynamic monitoring. The reason for the relatively long operative time was the use of a rigorous surgical procedure. Preoperative respiratory function test and respiratory

physiotherapy were routinely applied in patients with chronic obstructive pulmonary disease. This routine application was thought to reduce the postoperative length of in-hospital stay, even if the preoperative stay of the patient prolonged to four to five days. The proportion of patients with chronic renal failure was low, although most of the patients had DM.

Nonetheless, this study has some limitations. First, the number of patients in our study may seem relatively small, compared to previous studies. Second, data were non-randomized and retrospectively collected. Third, the power of some outcomes may have been reduced due to a single-center study. Fourth, the rate of contralateral occlusion was very low in our study, compared to previous studies and this might have affected the outcomes of our study, since several studies proposed that the difference in the postoperative blood pressure was particularly significant in patients with contralateral severe ICA occlusion.[3] Finally, we were unable to evaluate the baroreceptor sensitivity during the postoperative period.

In conclusion, our results suggest that the presence of a contralateral severe ICA stenosis does not increase the risk of postoperative stroke and mortality rates and blood pressure alterations and non-neurological complications, showing similar neurological complication rates between the groups. Thus, CEA can be performed with acceptable complication rates in patients with contralateral severe ICA stenosis. In addition, the present study highlights the importance of preoperative evaluation of contralateral ICA, strict perioperative blood pressure control, and intraoperative cerebral circulation monitoring. However, further large-scale, prospective, randomized studies are needed to shed light into the related factors for proper management of contralateral severe ICA stenosis.

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