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Relationship between carotid artery stenosis percentage and complications in patients treated with carotid stenting

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Abstract. – OBJECTIVE: To determine whether there is a relationship between carotid artery stenosis percentage and complications.

PATIENTS AND METHODS: The study included 109 patients treated with carotid artery stenting in our center. The indication for stenting was accepted as carotid artery stenosis above 50% in symptomatic patients and over 70% in asymptomatic patients. Complications were compared between groups with <90% and ≥90% stenosis.

RESULTS: There was no procedure-related mortality in any of the patients. Minor complications developed in 22 patients (20.2%). Prolonged hypotension/bradycardia occurred in 17 patients (77.3%), and a transient ischemic attack in five (22.7%). Inguinal access complications were detected in three patients (2.7%). Major complications developed in 11 patients (10%), of whom five (45.4%) had hyperperfusion syndrome, five (45.4%) had microinfarcts, and one (9%) had acute stent thrombosis. No significant difference was observed in age, gender, major and minor complications, or inguinal access site complications between the patients with <90% and ≥90% stenosis. There was also no statistically significant difference in complications according to the open or closed cell morphology of the selected stent.

CONCLUSIONS: The most important result of our study is that there was no significant difference in complications between the patients who underwent carotid stenting due to <90% and ≥90% stenosis.

Key Words:
Carotid stenosis, Carotid stenting, Stroke.

Introduction

Acute ischemic stroke is currently one of the primary causes of mortality. Since it can cause long-term or permanent disability, it is important to identify and prevent the causes of stroke. Extracranial carotid artery disease is one of the leading causes of stroke[1], responsible for 8-15% of ischemic stroke cases. Although carotid endarterectomy is still considered the primary treatment method, carotid artery stenting is frequently used, and a low complication rate is the reason for preference[2]. Complication rates of carotid artery stenting (CAS) have considerably decreased with the introduction of distal embolic protection filters[2].

Current guidelines[3] state that medical therapy is sufficient for the treatment of carotid artery stenosis below 50%. However, if stenosis is over 50% in symptomatic patients and over 70% in asymptomatic patients, surgical or endovascular methods are recommended[4].

The most common complications[4] of carotid stenting are embolic infarcts, prolonged hypotension/bradycardia, and hyperperfusion syndrome. Cerebral hyperperfusion syndrome[5] is defined as an increase in cerebral blood flow over 100% compared to baseline with a new onset of headache ipsilateral to the carotid revascularization, with or without focal neurological deficits and seizures.

Carotid artery stenosis over 90% sometimes causes concern among clinicians who will perform the procedure in terms of complication development. In the current study, we aimed to determine whether there was a relationship between stenosis percentage and complications in patients treated with CAS in our center.

Patients and Methods

The study included 109 patients who did not accept surgical treatment or were treated with carotid artery stenting in our center between January 2020 and June 2021, considering the high risk of surgical treatment due to comorbidities. The indication for stenting was accepted as carotid artery stenosis above 50% in symptomatic patients and over 70% in asymptomatic patients. Patients who had a history of a

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permanent or transient ischemic attack within six months before the procedure were considered symptomatic. However, patients with concomitant intracranial stenosis or those who could not receive dual antiaggregant therapy were excluded from the study. Patient data and follow-up results were obtained from the hospital's electronic system.

The Ethics Committee of the Sakarya University Faculty of Medicine approved the study. Informed consent was obtained from all patients before the procedure.

Clopidogrel (75 mg, 1x1) and aspirin (100 mg, 1x1) were initiated in all patients at least five days before the procedure. The patients were also evaluated for possible clopidogrel resistance, and those with clopidogrel resistance were excluded from the study. It was recommended that the patients continue dual antiaggregant therapy for at least six months after stenting.

A 6F vascular sheath was placed in the right femoral artery under local anesthesia. 70 U/kg heparin was administered intraarterially. Then, the common carotid artery to be operated on was reached using a guiding catheter. Acquisition of three-dimensional digital subtraction angiography (3D-DSA) was performed on a flat panel detector angiographic system (Artis zee; Siemens Healthineers AG, Erlangen, Germany). Afterwards, 3D images of the stenosis in the carotid artery were obtained. These images were processed on the workstation and the percentage of stenosis in the carotid artery was automatically calculated.

The stenosis in the internal carotid artery (ICA) was passed with a 0.014-inch microwire, and an embolic protection device (EPD) was placed distal to the stenosis. In cases where the EPD or stent could not be delivered after the stenosis due to pre-occlusive stenosis, pre-dilatation angioplasty was performed with a 3-mm balloon catheter. The EPD was then positioned distal to the stenosis. A self-expandable stent was placed at a size and diameter suitable for the stenosis length and vessel structure. In cases where full patency could not be achieved after stenting, in-stent angioplasty was performed with a 5-mm or 6-mm balloon catheter. Before balloon angioplasty, 1 mg of atropine was intravenously administered to reduce the possibility of bradycardia development. After confirming full patency, the filter was removed. Control cerebral angiography images were taken to detect possible embolisms, and the procedure was terminated.

Statistical Analysis

MedCalc (ver. 12, Ostend, Belgium) was used for statistical analyses. Descriptive statistics were given as median (minimum-maximum) and mean±standard deviation. Categorical variables were expressed as frequencies and percentages. Pearson's Chi-squared and Yates's corrected version of Pearson's Chi-squared tests were used to compare categorical variables. The independent-sample *t*-test was used to compare continuous variables with a normal distribution. The Mann-Whitney U test was used for the data that did not conform to the normal distribution according to the Kolmogorov-Smirnov test. A p-value<0.05 was accepted as statistically significant.

Results

A total of 109 patients were included in the study. The mean age of the patients was 68±9.2 years. Seventy-one patients (65.1%) were males, and 38 (34.9%) were females. Concerning comorbidities, 71% had hypertension, 31% had diabetes mellitus, 38% had hyperlipidemia, and 61% had coronary artery disease. In addition, 42% of the patients had a smoking history of more than 20 years.

The procedure was performed on the right ICA in 53 patients (48.6%) and the left ICA in 56 (51.4%). The stent diameter was 7 mm in 44 patients (40.4%), 8 mm in five (4.6%), and 9 mm in 60 (55%). WALLSTENT™ stents (Boston Scientific Corp. Marlborough, MA, USA) were used in 79 patients (72.5%), and Protégé™ (Stanford, CA, USA) stents (ev3 Inc.) in 30 (27.5%). Contralateral ICA was totally occluded in six patients (6%). While 47 patients (43.1%) had more than 90% stenosis, 62 patients (57.9%) had stenosis below 90%. Pre-dilatation angioplasty was required in seven patients (7.3%) since the stent could not be advanced to the distal stenosis, and all these patients had 90% or higher stenosis.

Minor complications were determined to be ICA vasospasm, resistant hypotension/bradycardia, and transient ischemic attack, while embolic stroke, intracranial hemorrhage, hyperperfusion syndrome, and acute stent thrombosis were accepted as major complications[3]. There was no procedure-related mortality among any of the patients. Minor complications developed in 22 patients (20.2%). There was prolonged hypotension/bradycardia in 17 patients (77.3%) and a transient ischemic attack in five (22.7%). These complications were resolved over time with conservati-

ve treatments. In addition, complications of the inguinal access site were detected in three patients (2.7%). Two inguinal hematomas were resolved with conservative treatment. A pseudoaneurysm was treated with percutaneous thrombin injection without sequelae. Major complications developed in 11 patients (10%), including hyperperfusion syndrome in five (45.4%), microinfarcts in five (45.4%), and acute stent thrombosis in one (9%).

In statistical analyses, no significant difference was found between the patients with stenosis below and above 90% in terms of age, gender, major and minor complications, or inguinal access complications (Table I). In addition, complications did not statistically significantly differ according to the open or closed cell morphology of the selected stent (p=0.236).

Discussion

The most important result of our study is that there was no significant difference in complications between the patients who underwent carotid stenting due to <90% and ≥90% stenosis.

Carotid artery stenosis is one of the preventable causes of ischemic stroke. The most common cause of carotid artery stenosis is atherosclerotic[6] stenosis. Diabetes mellitus, hypertension, smoking, and hyperlipidemia are primary etiological[7] factors. Embolic and ischemic strokes resulting from these atherosclerotic strictures can cause mortality and morbidity. It is recommended to treat[8] stenosis at over 50% in symptomatic patients and over 70% in asymptomatic patients.

For many years, carotid endarterectomy was considered the primary method in the treatment of carotid artery stenosis. However, with technological developments, widespread use of embolic protection filters, and increasing stenting experience, CAS[9] has become a strong alternative to endarterectomy. As suggested by Burgazli et al[2], carotid artery stenting may be recommended as a first-line or alternative treatment in patients with symptomatic stenosis who are at high risk for open surgery. In a study by Cole et al[10] the rate of perioperative stroke was reported to be higher in carotid artery endarterectomy than in stenting, especially in symptomatic patients.

In our study, minor complications developed in 22 (20.1%) patients, of whom 17 (77.3%) had prolonged hypotension/bradycardia and five (22.7%) had a transient ischemic attack. Following appropriate medical treatment, all these patients were discharged without sequelae. Hematoma at the inguinal access site, dissection in the common femoral artery, and a pseudoaneurysm in the common femoral artery occurred in one patient each. The pseudoaneurysm was treated with a percutaneous thrombin injection under ultrasound guidance. The dissection in the common femoral artery was successfully treated with balloon angioplasty.

In our study, hyperperfusion syndrome developed in five patients. Hyperperfusion syndrome[11] was diagnosed based on the presence of a severe headache, confusion, visual disturbances, epileptic seizures, or focal neurologic deficits after excluding the possibility of stroke with diffusion magnetic resonance[12] imaging (MRI). The patients with hyperperfusion syndrome were admitted to the intensive care unit to keep their blood pressure under control and for close monitoring. All patients were transferred to inpatient wards after 24-72 hours without any sequelae. When the angiography images were examined, it was determined that all these patients had 90% or higher stenosis. It was also noted that in four (80%) of these patients, the anterior and posterior communicating arteries were not sufficiently developed, and the collateral circulation was weak. This high rate shows that the circle of Willis should be examined in detail in order to predict hyperperfusion syndrome before carotid stenting.

In five patients (45%), following the development of neurological deficits, millimetric microinfarct foci were observed in the diffusion MRI examination. Two of these patients had

Table I. Comparison of patients with stenosis below and above 90%.

	Stenosis ≥90% (n=47)	Stenosis <90% (n=62)	*p*-value
Age (mean)	67	68	0.526
Gender (male/female)	30/17	41/21	0.457
Major complication	5 (10.6%)	6 (9.6%)	0.935
Minor complication	9 (19.1%)	13 (21%)	0.889
Inguinal access site complication	1 (2.1%)	2 (3.2%)	0.062

loss of strength in the upper extremities, and the remaining three had disorientation and speech disorders. The stenosis was over 90% in three of these patients and less than 90% in two. There was no statistically significant relationship between stenosis percentage and the risk of infarction.

Şahin et al[13] showed in their study that balloon predilation is an effective method with acceptable complication rates. In our study, there was no significant difference in the risk of infarction and complications when patients who underwent predilatation angioplasty were compared with patients who did not require this procedure. These patients were followed up in the intensive care unit in consultation with a neurologist. Following clinical improvement, they were transferred to inpatient wards and discharged later. No sequelae were observed in the six-month follow-up of these patients.

Due to the development of sleepiness and non-sensical responses to verbal stimuli in one patient, six to eight hours after the procedure, a control ultrasound examination was performed, revealing that the stent had been thrombosed. The patient was rapidly processed, and the thrombosis in the stent lumen was treated with aspiration and balloon angioplasty. Although the clopidogrel aggregation test was normal before the procedure, clopidogrel was discontinued due to the possible resistance risk, and ticagrelor (90 mg, 2x1) was started. The patient was recommended to continue aspirin (100 mg, 1x1). In the third and sixth months of follow-up, the stent was confirmed to be patent, and the patient had no major neurological deficits.

There are also studies in the literature[14] investigating whether the stent cell design has an effect on the risk of embolism and complications in patients undergoing carotid stenting. Timaran et al[15] showed that there was no significant difference between open-cell and closed-cell stents in terms of embolism risk. Similarly, in our study, it was observed that whether the stent selected in the treatment was open-cell or closed-cell did not make any significant difference in terms of complications.

Our study had certain limitations, the first concerning the retrospective and single-center design. Second, the number of patients was low. Further comprehensive, prospective, and multi-center studies are needed on this subject. Finally, the long-term patency of the patients could not be evaluated within the scope of this study; therefore, this can be the subject of future studies.

Conclusions

Carotid artery stenting is a very effective method with low complications and high success rates. In our study, there was no significant difference between carotid artery stenosis percentage and major or minor complications that occurred after stenting in patients who underwent carotid artery stenting. The limitations of our study include the single-centered design and the non-homogeneous sample.

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Ethics Approval
The study was approved by the Ethics Committee of the Sakarya University Faculty of Medicine (Date: 07.04.2023, decision No.: 236388-34) and performed following the principles of the Helsinki Declaration.

Conflict of Interest
The authors declare that they have no conflict of interest.

Informed Consent
Informed consent was obtained from all patients before the procedure.

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Data Availability
The datasets generated during and/or analyzed during the current study may be made available by the corresponding author on request.

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