

Two-year results of carotid artery stenting

Karotis arter stentleme işleminin iki yıllık sonuçları

Şakir Arslan, M.D., Erkan Köklü, M.D., İsa Öner Yüksel, M.D., Göksel Çağırıcı, M.D.,
Nermin Bayar, M.D., Akar Yılmaz, M.D., Görkem Kuş, M.D., Nurgül Yılmaz, M.D.,#
Yasemin Biçer Gömceli, M.D.,# Bekir Erol, M.D.*

Department of Cardiology, Antalya Training and Research Hospital, Antalya;

#Department of Neurology, Antalya Training and Research Hospital, Antalya;

*Department of Radiology, Antalya Training and Research Hospital, Antalya

ABSTRACT

Objectives: The effectiveness of carotid artery stenting (CAS) for primary and secondary prevention of ischemic stroke has been demonstrated. The aim of our study was the clinical and radiological evaluation of the reliability of the CAS procedure over a two-year follow-up period.

Study design: This study included 120 patients (mean age, 68 (48-86) years) admitted to our hospital between December 2010 and March 2013 for whom CAS was decided in the neurology, cardiovascular surgery and cardiology council. Symptomatic cases with more than 50% stenosis by angiography and asymptomatic patients with stenosis of more than 70% were included in the study. 80% of the asymptomatic patients were those detected during the screening before the coronary bypass surgery.

Results: The success rate of the procedure was found as 97.5%. No mortality or myocardial infarction was observed in any of the patients in whom CAS was applied successfully. In 1 symptomatic patient (0.8%), ischemic cerebrovascular event with sequelae was observed 24 hours after the procedure. In total, transient ischemic attack was observed in 2 patients (1.7%) 6 and 11 months after the procedure. Asymptomatic restenosis was detected in 3 patients (2.5% of the total, with 2 in the asymptomatic and 1 in the symptomatic group). Symptomatic restenosis was not observed. None of the patients experienced hyperperfusion syndrome.

Conclusion: We believe the CAS procedure can be performed safely in symptomatic and asymptomatic patients with low complication and high success rates.

ÖZET

Amaç: İskemik inmeden primer ve sekonder korunmada karotis artere stent yerleştirilmesinin (KASY) etkinliği gösterilmiştir. Bizim bu çalışmadaki amacımız, KASY işleminin güvenilirliği ve iki yıllık sonuçlarını klinik ve radyolojik olarak değerlendirmektir.

Çalışma planı: Aralık 2010 ile Mart 2013 tarihleri arasında hastanemize başvuran, nöroloji, kalp damar cerrahisi, kardiyoloji konseyinde KASY kararı verilmiş 120 hasta (ortalama yaş 68 [48-86]) çalışmaya alındı. Çalışmaya semptomlu olup karotis arterde anjiyografik olarak %50'nin üzerinde darlık olanlarla, semptomsuz olup karotis arterde %70'in üzerinde darlık olan hastalar alındı. Semptomsuz hastaların %80'ini koroner baypas cerrahisi öncesi taramada tespit edilen hastalar oluşturuyordu.

Bulgular: İşlem başarısı %97.5 bulundu. Başarılı şekilde KASY işlemi uyguladığımız hastalardan hiçbirinde ölüm, miyokart enfarktüsü görülmedi. Bir hastada (%0.8) işlemden 24 saat sonra sekelli iskemik serebrovasküler olay gelişti. Toplam iki hastada (%1.7) işlemden altı ve 11 ay sonra geçici iskemik atak (GİA) gözlemlendi. Toplam üç (%2.5) hastada (iki hasta semptomsuz, bir hasta semptomlu grupta idi) semptomsuz restenoz görüldü. Semptomlu restenoz saptanmadı. Hiçbir hastada hiperperfüzyon sendromu yaşanmadı.

Sonuç: Karotis artere stent yerleştirilmesi işleminin semptomlu veya semptomsuz hastalarda düşük komplikasyon ve yüksek başarı oranları ile güvenli bir şekilde yapılabileceği kanaatindeyiz.

Received: November 25, 2013 Accepted: March 14, 2014

Correspondence: Dr. Erkan Köklü. Yenigün Mahallesi, 1067 Sokak, 6b/13 Muratpaşa, Antalya.

Tel: +90 242 - 249 44 00 e-mail: drerkankoklu@gmail.com

© 2014 Turkish Society of Cardiology



Ischemic cerebrovascular events are cited as the most common cause among patients confined to bed, and are the third leading cause of mortality. [1] Atherosclerosis is responsible for about one-third of all strokes and 90% of cerebral thromboembolic events. Ninety percent of atherosclerotic events within the carotid artery system are observed in the 2 cm segment including the beginning of the internal carotid artery (ICA). Carotid artery stenting (CAS) is an alternative to carotid endarterectomy (CEA). [2] The effectiveness of CAS for primary and secondary prevention of ischemic stroke has been demonstrated. [2,3]

The aim of our study was the clinical and radiological evaluation of the reliability of the CAS procedure during a two-year follow-up.

PATIENTS AND METHODS

One hundred and twenty patients, aged 48-86 years (mean, 68 years), who were admitted to our hospital between December 2010 and March 2013 and approved by the neurology, cardiovascular surgery and cardiology council for CAS procedure, were included in the study. Symptomatic cases with more than 50% stenosis by angiography and asymptomatic patients with more than 70% stenosis were included in the study. CAS was calculated according to the NASCET criteria. Symptomatic patients were defined as those who had experienced a cerebrovascular event within the last six months with or without sequelae, transient ischemic attack (TIA), and a history of amaurosis fugax. Eighty percent of the asymptomatic patients were those detected during the screening before the coronary bypass surgery.

Seventy-five percent of our subjects were symptomatic, 92% were patients with coronary artery disease, 81% were hypertensive, and 44% were diabetic. Eighty-one percent of our study group consisted of male patients, and the smoking rate was 40% (Table 1). The patients were followed for a period ranging from 2 to 21 months (average, 21 months). All patients had carotid Doppler ultrasound examinations before the procedure, and computed tomography (CT) angiography was performed on the patients when necessary.

Following the decision to perform CAS, all patients and their relatives were informed in detail by the neurology and cardiology clinics about the necessity of the process, probable risks and follow-ups af-

ter the procedure, and their consents were obtained. Approval of the study was obtained from the ethics committee of our hospital. All the patients were evaluated in the common committee that included cardiovascular surgery after the evaluation by the neurology clinic.

The patients were included in the process after blood pressure regulation was maintained as less than 135/80 mmHg. The antihypertensive treatments of patients were changed if required.

All patients had been receiving acetylsalicylic acid while under follow-up by a neurology clinic. Clopidogrel 75 mg 1x1 was added to the treatment of those who were approved for CAS. Most patients were given clopidogrel and acetylsalicylic acid 4 to 10 days before the CAS procedure. A small number of patients who did not receive clopidogrel were given 300 mg orally 24 hours before the CAS procedure. Treatment with 100 mg of acetylsalicylic acid was continued in

Abbreviations:

ACT	Activated coagulation time
CAS	Carotid artery stenting
CEA	Carotid endarterectomy
CREST	Carotid Revascularization Endarterectomy and Stent Trial
CT	Computed tomography
EPDs	Embolic protection devices
ICA	Internal carotid artery
PAF	Paroxysmal atrial fibrillation
TIA	Transient ischemic attack
USG	Ultrasound

Table 1. Characteristic of patients

Characteristic feature	%
Mean age (Year)	68 (48-86)
Male gender	81
Symptomatic	75
Asymptomatic	25
Coronary artery disease	92
Hypertension	81
Diabetes	44
Smoking	40
Blood pressures before the procedure (mmHg)	
Systolic	134.2
Diastolic	72.8
Bilateral ICA stenosis (>70%)	15
Opposite side ICA 100% occluded	7
Proximal blockade system	62
Distal embolus prevention	38
Acetyl salicylic acid + clopidogrel	100

ICA: Internal carotid artery.

all patients unless a contraindication was observed. Clopidogrel (75 mg) was continued for one year.

Procedure

The procedures were performed through the transfemoral route with local anesthesia in all patients. Oxygen saturations and arterial blood pressure values of the patients were monitored during the procedure. All the patients were given 75 mg/kg unfractionated heparin as the procedure was initiated. When the duration of the procedure exceeded 30 minutes in some patients, activated coagulation time (ACT) was checked, and additional heparin boluses were given to obtain ACT between 200-250 seconds. The procedures were initiated with arch aortography in order to visualize the initiating points of the extracranial carotid vertebral vascular system. Two-sided cerebral angiography was performed before and after the procedure in order to visualize intracranial segments.

The cerebral protection system selection was decided by looking at the suitability of the cerebral circulation and plaque burden, and stent selection was made by evaluating the features of the plaque causing the stenosis. During the CAS procedure, a proximal blockage system (Mo.Ma[®]) was used for 62% of the patients, and distal embolic protection devices (EPDs, Anjioguard[®] and Emboshield) were used for 38% of the patients. Self-expandable hybrid stent (Cristallo Ideale SE Stent [Invatec]) was used in 85% of the patients and open-cell stent (sinus-Carotid-Conical-RX Stent [OptiMed]) in 15% of patients, and post-dilatation was performed after the stent implantation. In 15% of the patients (18 patients), CAS was bilateral. The opposite carotid arteries of 9 patients (7%) were 100% blocked. In these patients, distal EPD was preferred. Of the patients with asymptomatic bilateral stenosis, interventions in the patients in whom coronary bypass surgery was planned were scheduled at a one-week interval. They then underwent bypass surgery without terminating the anti-thrombocyte treatment. In the other patients, intervention was performed on the symptomatic side or for the asymptomatic more severe stenosis first, and then intervention on the opposite side was performed one month later.

Follow-up

The patients were monitored clinically by the neurology clinic during the hospital stay immediately after the CAS procedure.

All patients were monitored prospectively for an average period of 21 months for restenosis development with carotid Doppler ultrasonography (USG) for major clinic events (mortality, myocardial infarction (MI), stroke, TIA). The patients were evaluated by the neurology and cardiology clinics in the first week, at the end of the first month and then at six-month periods. In the follow-ups, Doppler ultrasound was performed at the 1st and 12th months, and CT angiogram was performed in patients when restenosis was suspected. Restenosis was perceived when the peak flow velocity in the stent was measured to be greater than 224 cm/s on ultrasound and when stenosis of more than 50% was observed.

RESULTS

The procedure could not be performed in four patients in whom CAS was decided. The success rate of the procedure was found to be 97.5%. A guided catheter could not be placed in two patients because of the aortic arch anatomy. In one of the two patients, the guide wire could not be advanced through the lesion due to the highly tortuous lesion. In the other patient, the procedure was unsuccessful through the brachial artery entry since the femoral arteries were occluded. The procedure was terminated without any complication. CEA was performed in these patients. No mortality or MI was observed in any of the CAS patients. In one symptomatic patient (0.8%), ischemic cerebrovascular event with sequelae was observed 24 hours after the procedure. This led to the suspicion of acute carotid artery thrombosis, and the CT angiography showed that the stent lumen in the left carotid artery was blocked entirely with thrombocytes. Because of the patient's resistance to acetylsalicylic acid and clopidogrel, the reason for the acute carotid artery thrombosis was thought to be a dual resistance to antiplatelet drugs. Based on the above observations and the recommendation from the Neurology Department, the patient was followed medically. With physical therapy, the patient's speech improved, and 2/5 paresis in the right extremities continued. Overall, TIA was observed in two symptomatic patients (1.7% of the total) 6 and 11 months after the procedure. Even though the carotid stent was open in the carotid Doppler USG of one of the patients who had TIA, the Holter monitoring prompted by the visualization of bilateral infarcts in the brain magnetic resonance im-

Table 2. Results of the procedures and complications

	n	%
Asymptomatic restenosis	3	2.5
Symptomatic restenosis	0	0
Stroke on the same side as CAS implanted ICA	1	0.8
Transient ischemic attack	2	1.7
Mortality	0	0
Myocardial infarction	0	0
Gastrointestinal system bleeding	1	0.8
Hyperperfusion syndrome	0	0

CAS: Carotid artery stenting; ICA: Internal carotid artery.

aging (MRI) revealed paroxysmal atrial fibrillation (PAF). As a consequence, warfarin therapy was initiated. No symptoms were observed in the 12th month follow-up. The other patient's carotid stents were open in the carotid Doppler USG, but a medical follow-up was decided since atherosclerosis was present in the intracranial segments in the CT and diagnostic angiography. In another patient, gastrointestinal bleeding not requiring transfusion developed. In this patient, acetylsalicylic acid was terminated and replaced with clopidogrel. Overall, asymptomatic restenosis was detected in three patients (2.5% of the total, with 2 in the asymptomatic and 1 in the symptomatic group) in the 12th month Doppler ultrasound screening, with additional confirmation in the CT angiography. The carotid artery intra-stent restenosis was 60% in one of the two restenosis patients and 80% in the other. CEA procedure was implemented, and the stent was removed in the patient with 80% restenosis, which we considered to be hemodynamically significant. In the Doppler USG during the 3rd month follow-up after CEA, upon detecting a severe flow velocity increase at the distal region from which the stent had been removed earlier, CT angiography was performed. After determining a severe stenosis with CT angiography, a stent was re-placed in this region. Symptomatic restenosis was not observed. Hyperperfusion syndrome was not observed in any of the patients (Table 2).

The 24 patients who had successful CAS procedures underwent coronary surgery no later than one week after the CAS procedure or no earlier than four weeks after the CAS procedure. No ischemic cerebrovascular events occurred. In patients taking acetylsalicylic acid and clopidogrel, treatment was continued

before and after the operation. No bleeding complications were observed in any of the patients.

DISCUSSION

Seventy-five percent of ischemic strokes originate from the anterior system and one-third of these are due to extracranial artery stenosis. In strokes due to symptomatic carotid artery, the rate of recurrence in the first year increases to 26% in cases treated with medications after the first event.^[4] Annual stroke incidence of asymptomatic patients with greater than 60% stenosis in the carotid artery is around 2.5% despite the patients being under medical treatment.^[5] Percentage of the stenosis (greater than 95) and characteristics of the lesion (ulcerated lesion) prominently increase the risk of stroke.^[5] Development of endovascular treatment methods began in the 1990s and accelerated recently with the production of balloons and stents and have become an important alternative treatment method to CAS technique and CEA, since they are less invasive yet as effective as surgery.^[6,7] CAS, which was applied to risk groups previously, has become an alternative treatment method to CEA for all patient groups with the recent advances, and it has appeared in the guidelines with class 1 indication in the treatment of extracranial CAS.

The late expansion rates of the carotid stents and the larger diameter of the carotid artery lumen compared to the coronary artery maintain the lower restenosis rates. Self-expandable stents reach their largest diameter between six months and one year.^[8] The restenosis rate after carotid stent placement is less than 5%. Generally, the restenosis rates over a period

of five years are very low for procedures that were performed with appropriate technique, appropriate stent diameter selection, sufficient post dilatation, and avoidance of stent tips being left in the atheromatous plaques.^[9,10]

Many randomized studies performed about CAS are deficient in some aspects. Although it was mentioned in the SAPPHIRE study that experienced interventionists and distal EPDs are important, 70% of the patients were asymptomatic. EPD was not used in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) study, low rates of stent application and very low usage of EPD were present in the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study, and only 39% of the interventionists were experienced in the EVA-3S; thus, the success of EPD has been obscured. The CREST (Carotid Revascularization Endarterectomy and Stent Trial) study was a multicenter randomized controlled trial performed in order to determine which between CAS and CEA is a better treatment choice in symptomatic and asymptomatic patients; it considered patient selection, procedural experiences of the physicians and the patients' risk profiles.^[2-11]

In the CREST study, which until recently had the lowest risk among the randomized controlled trials, no significant difference was detected between the CAS and CEA groups regarding the primary endpoints (mortality, stroke, and MI development within the first 30 days and stroke on the same side as the intervention) at the end of four years (7.2% and 6.8%, respectively). Neither symptomatic or asymptomatic status nor patient gender was determined to be a distinguishing factor in terms of primary endpoints. Four-year stroke/mortality rates for all patients were 6.4% for CAS and 4.7% for CEA ($p=0.03$). After the intervention period, the incidence of stroke at the same time was found low in both treatment branches (2% and 2.4%). Interestingly, in the CREST trial, while the patients younger than 70 years of age benefited from CAS, CEA was found more beneficial in patients older than 70 years. These findings suggested that the increased vascular tortuosity and calcification made the CAS process riskier.

The ratio of symptomatic patients was 52% in the CREST study, and 42% of the patients had previous cardiovascular disease history. In our study, these ratios were 75% and 92%, respectively. Eighty percent

of the asymptomatic group consisted of the patients who were approved for coronary bypass surgery. Again, while the rate of patients with opposite-side carotid artery total occlusion was 2.7% in the CREST study, the same rate was 7% in our study. As can be seen, there was greater risk in our study with respect to the patients undergoing CAS and the characteristics of the lesions when compared to the previous studies.

Stroke, which is the most important and most feared complication of carotid stenting, was seen in only one patient after the procedure, which is a low rate when looking at the literature. Usage mainly of the proximal prevention method in our cases might have contributed to the lower rates of stroke due to the procedure and TIA complications.

When the two patients who developed TIA were evaluated in the follow-up, PAF was detected in one case, while in the other case, atherosclerotic lesions were determined as increased in distal segments of the internal carotid artery on the same side. No thrombus was visualized in the transthoracic and transesophageal echocardiographs of the patient with atrial fibrillation. Both patients had TIA before the CAS and had greater than 70% stenosis in the internal carotid arteries. Although the origin of the TIA was not detected clearly in the patients with visually open stents in the follow-up carotid angiographs, the fact that TIA did not develop after the warfarin treatment of the patient with PAF suggested that the symptoms may have been due to PAF.

Overall, three asymptomatic restenoses were seen in our study. When the initial lesions of the patients developing restenosis were evaluated, all three drew attention as being long and prominently calcific. With the approach to asymptomatic restenosis already a controversial subject, 60% of restenosis patients were followed medically, and CEA was performed in 80% of the restenosis patients.

Hyperperfusion syndrome, which can be the most serious complication of the CAS procedure, sometimes ending with mortality, was not observed in any of our cases. The most important causes of hyperperfusion syndrome are hypertension history of the patient and poor preparation for the procedure in terms of hemodynamics. Mean systolic blood pressure values of the patients in the CREST study were 141.6 ± 20.2 mmHg. The same mean value was 134.2 mmHg in

our study. We believe the absence of hyperperfusion syndrome among our patients can be attributed to our following the blood pressures of all patients before the procedure and preparing the patients for the procedure with standard follow-up in the cardiology and neurology clinics.

The use of an EPD was not 100% in any of the previous studies, including CREST. We believe that one of the most important reasons for our lower complication rate due to the procedure was the thorough and persistent use of either proximal or distal EPDs in all procedures. Another distinguishing aspect of our study was the preference for the proximal blockade method rather than distal protection method. In a previous study, it was demonstrated that compared to distal protection, proximal protection is related more frequently to non-clinical brain infarcts.^[12] If we consider that our patients were evaluated by a neurologist before and after the procedure and that cranial imaging methods were used, we believe that our complication rates due to the procedure are reliable.

In our study, CAS and CEA were not compared; rather, the effectiveness and reliability of carotid stenting and midterm results were evaluated. The reason for this is that initially, only 10% of all patients were approved for CEA.

In conclusion, the success rate and complication ratio of the CAS method, which has been accepted as an alternative to CEA in light of the recent guidelines, are closely related to patient selection and preparation of the patient for the procedure in terms of medical and hemodynamic aspects. Patient selection for revascularization should be made according to the characteristics of the patient and lesion and experience of the center. Consideration of surgical treatment primarily for long and calcific lesions and reexamination of the non-carotid causes in patients with TIA after stenting will be beneficial.

One of the most important results of our study is that it presents evidence for the CAS procedure being effectively and reliably applicable to patients with asymptomatic carotid lesions before coronary bypass surgery. Consequently, we believe that the CAS procedure can be performed safely in symptomatic and asymptomatic patients with low complication and high success rates.

Conflict-of-interest issues regarding the authorship or article: None declared

REFERENCES

1. Gresham GE, Fitzpatrick TE, Wolf PA, McNamara PM, Kannel WB, Dawber TR. Residual disability in survivors of stroke-the Framingham study. *N Engl J Med* 1975;293:954-6.
2. Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010;363:11-23.
3. Aydinler O, Boztosun B, Sirvanci M, Akçakoyun M, Karaman K, Aksoy T, et al. Early and late outcomes of carotid artery stenting. *Anadolu Kardiyol Derg* 2007;7:152-7.
4. Ferguson GG, Eliasziw M, Barr HW, Clagett GP, Barnes RW, Wallace MC, et al. The North American Symptomatic Carotid Endarterectomy Trial : surgical results in 1415 patients. *Stroke* 1999;30:1751-8. [CrossRef](#)
5. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA* 1995;273:1421-8. [CrossRef](#)
6. Ricotta JJ 2nd, Malgor RD. A review of the trials comparing carotid endarterectomy and carotid angioplasty and stenting. *Perspect Vasc Surg Endovasc Ther* 2008;20:299-308. [CrossRef](#)
7. Vogel TR, Dombrovskiy VY, Haser PB, Scheirer JC, Graham AM. Outcomes of carotid artery stenting and endarterectomy in the United States. *J Vasc Surg* 2009;49:325-30. [CrossRef](#)
8. Clark DJ, Lessio S, O'Donoghue M, Tsalamandris C, Schainfeld R, Rosenfield K. Mechanisms and predictors of carotid artery stent restenosis: a serial intravascular ultrasound study. *J Am Coll Cardiol* 2006;47:2390-6. [CrossRef](#)
9. Vogel TR, Dombrovskiy VY, Haser PB, Graham AM. Carotid artery stenting: Impact of practitioner specialty and volume on outcomes and resource utilization. *J Vasc Surg* 2009;49:1166-71. [CrossRef](#)
10. Verzini F, De Rango P, Parlani G, Panuccio G, Cao P. Carotid artery stenting: technical issues and role of operators' experience. *Perspect Vasc Surg Endovasc Ther* 2008;20:247-57.
11. Sheffet AJ, Roubin G, Howard G, Howard V, Moore W, Meschia JF, et al. Design of the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST). *Int J Stroke* 2010;5:40-6. [CrossRef](#)
12. Schmidt A, Diederich KW, Scheinert S, Bräunlich S, Olenburger T, Biamino G, et al. Effect of two different neuroprotection systems on microembolization during carotid artery stenting. *J Am Coll Cardiol* 2004;44:1966-9. [CrossRef](#)

Key words: Angioplasty, balloon, coronary; carotid stenosis/complications; patient selection; stents.

Anahtar sözcükler: Anjiyoplasti, balon, koroner; karotis darlığı/ komplikasyonlar; hasta seçimi; stent.