Elective carotid artery stenting with distal embolic protection

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Abstract

Objective: It is aimed to present our experience in carotid artery stenting with attention to the patient selection, technique, success rate, perioperative complications, and efficacy. *Methods:* Patients presented with carotid stenosis treated by stenting were included. Symptomatic patients were defined as having a history of transient ischemic attack or stroke in the last 6 months. Patients with symptomatic carotid stenosis of at least 50% or asymptomatic carotid stenosis of at least 70% detected by catheter angiography were accepted for treatment. Distal embolic protection devices were used in all patients. Technical success was defined as the luminal patency at least 70%. *Results:* The study consisted of 94 patients with 98 procedures and the mean age was 66.38±11.13 years. The mean stenosis rate was 74.52±13.44%. A total of 109 stents were used in 97 procedures, and closed-cell design was used in 87.2% versus open-cell design in 12.8%. Technical success and complication rate were 98.9% and 8.2%, respectively. The mean follow-up period was 14.92±10.76 months.
Conclusion: Carotid artery stenting with use of distal embolic protection devices is widely accepted, safe, feasible, less invasive when compared to surgery and can be performed successfully especially in patients with high risk factors.

Keywords: Carotid stenosis, embolic protection devices, endovascular procedures, stents

INTRODUCTION

Ischemic stroke is responsible for the majority of all strokes and accounts for 67-83%.[1] Carotid stenosis (CS) is the most important cause of ischemic stroke with a rate of 20-25% and predominantly occurring at the bifurcation of the internal and external carotid arteries.[2,3] Treatment options for CS include best medical treatment (BMT), carotid endarterectomy (CEA) and carotid artery stenting (CAS). The main purpose of treatment is to prevent stroke or stroke-related mortality and morbidity. The decision on management generally *depends* on several factors such as age, clinical symptoms, stenosis rates, plaque morphology, vessel anatomy, medical comorbidities and patient preferences.[4] The prevalence of the asymptomatic carotid stenosis with >70% luminal narrowing is reported as, 3.1% in the general population.[3] The annual risk of stroke in patients with asymptomatic

and symptomatic CS are reported as, 1–3% and 4–12%, respectively.[5] In most studies[4,6], carotid revascularization (CEA or CAS) is recommended in symptomatic carotid stenosis of at least 50% and asymptomatic carotid stenosis of at least 70%.

Since the development of new stent designs, distal embolic protection devices, increase in operator experience and centers performing endovascular treatments; CAS became an alternative and even the primer treatment method in selected patients with CS. In the last three decades, starting with the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS)[7], numerous randomized multicenter trials had been tried to find out which method is better. The answer still remains uncertain but the consensus point is that the treatment selection in CS must be done following patient and lesion-based analysis.

The purpose of this study is to present our clinical experience in carotid artery stenting

with attention to the patient selection, technique, success rate, perioperative complications, and efficacy.

METHODS

A total of 94 consecutive patients presented with symptomatic or asymptomatic CS between 2012 and 2017, treated by CAS with distal protection in our Interventional Radiology unit were included in the study. All data including demographic information, clinical findings, were obtained from the patients' medical records, our procedure form and digital subtraction angiography (DSA) images. The ethics committee approved our study design and written informed consents were obtained from all patients. Before the procedure; all patients were investigated in terms of stroke or TIA related symptoms, severity of CS detected by diagnostic imaging modalities such as Doppler ultrasound (US), computed tomography angiography (CTA) or DSA, medications, and comorbid diseases. Symptomatic patients were defined as having a history of transient ischemic attack or stroke in the last 6 months. Patients with symptomatic carotid stenosis of at least 50% or asymptomatic carotid stenosis of at least 70% detected by catheter angiography according to the NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria were accepted for CAS treatment. Annual follow up was recommended in asymptomatic patients with a rate of 50-69% CS detected by non-invasive imaging modalities. DSA was performed in patients with suspected or borderline CS rates detected by non-invasive imaging. Asymptomatic patients with >50% CS and contralateral carotid artery occlusion were also accepted for CAS treatment. In patients with recent stroke and having an infarct more than 3 cm in diameter, CAS procedure was delayed at least 4 weeks under medical treatment to prevent postoperative reperfusion hemorrhage. Dual antiplatelet therapy consists of acetylsalicylic acid 100 mg and clopidogrel 75 mg was started preferably 10 days before the procedure and antiplatelet drug resistance was investigated with laboratory tests.

Procedure

All patients were treated under local anesthesia and an anesthesia team accompanied the procedure for monitoring the patient and atropine administration in case of need. Transfemoral arterial access with 5 French (F) vascular sheath was preferred to obtain diagnostic angiograms by selective catheterization of the common carotid arteries with use of appropriate catheters depending on the type of arcus aorta. Carotid angiograms in different views such as antero-posterior (AP), oblique and lateral were obtained to figure out the stenosis location, tandem lesions, stenosis rate, presence of an ulceration in plaque and vascular anatomy. After planning of which devices (stent, distal protection device, etc.) will be used according to the measurements in carotid angiograms; cerebral angiograms were obtained for the detection of distal embolic events before and after CAS.

A 6F long sheat was exchanged with a stiff guide wire and positioned in distal common carotid artery (CCA) under the roadmap image. After verifying the optimal position of the long sheath and patency in arterial flow with an angiogram; 70 IU/kg of heparin was administered to achieve the optimal activated clotting time. Distal embolic protection devices (SpiderFX™, Medtronic, Dublin-Ireland or Emboshield NAV[6], Abbott, Illinois- United States) were used before stenting in all patients. Care was taken in luminal position of the distal protection device. Filter was positioned at least 3 cm distally from possible distal end of the stent and in the most straight location of internal carotid artery (ICA) petrous segment. After the placement of filter, a self-expandable stent with appropriate diameter, length, design and type was advanced to the carotid bifurcation to cover the stenosis and positioned as getting the distal end in the healthy segment of ICA with proximal end in the CCA. In cases of pre-occlusive stenosis and having difficulty in crossing the stent via stenosis; pre-dilatation with a diameter of 2 mm or 3 mm balloon was performed (Figure 1). In cases of residual stenosis more than a rate of 30% after stent placement; a balloon depending on the size of the ICA (5 mm or 6 mm x 20 mm) was used for post-dilatation (Figure 2). During the post-dilatation, care was taken to the heart rate monitorization due to the need of atropine administration in patients with marked vagal response. As a routine practice in our clinic, 0.5-1 mg atropine was administered in patients with a heart rate of <70 bpm before the balloon angioplasty to prevent asystole and severe bradycardia. In patients with normal heart rate before the procedure, a dose of 1 mg atropine was applied in occurrence of severe bradycardia (<50bpm) or asystole during balloon angioplasty. Before and after retrieval of distal protection device, carotid and cerebral angiograms were obtained for a potential vasospasm and distal
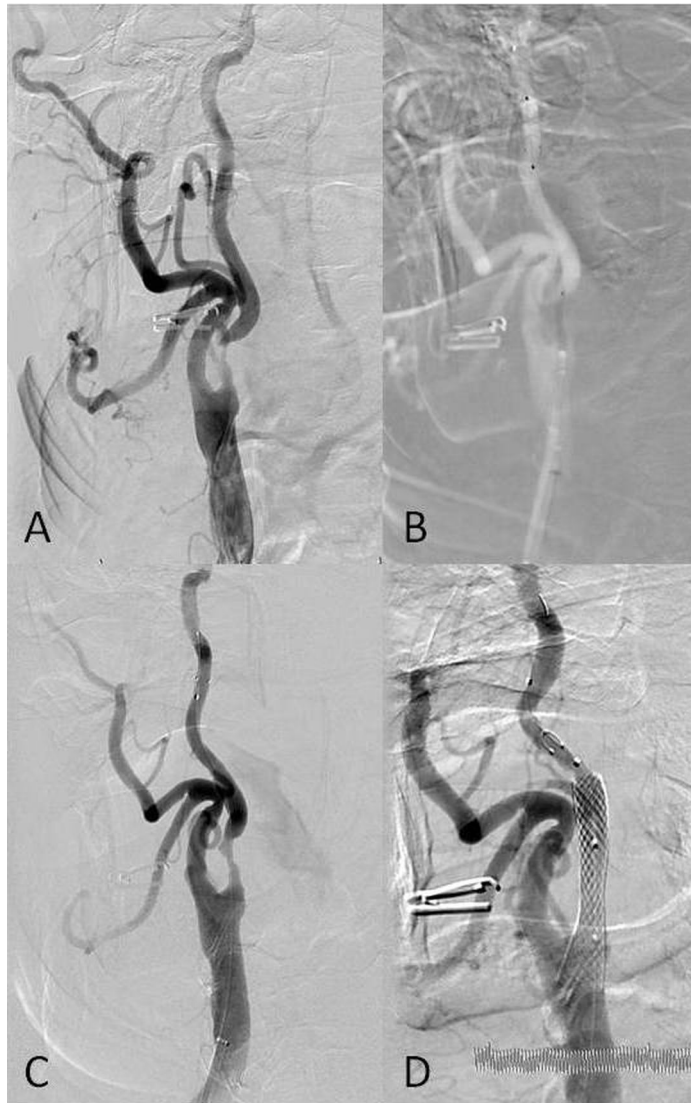
Figure 1: In a 68 years old male patient with severe stenosis starting from the origin of internal carotid artery (A); pre-dilatation with a 2 mm sized balloon (B) after filter deployment was performed. Sufficient luminal patency is provided for stent placement (C) and complete patency after stenting was obtained except a minimal residual vasospasm owing to the filter (D).

embolic events. The procedures were terminated by using vascular closure systems (Angioseal™ St. Jude Medical Inc. Minnetonka, MN, USA) that provide protection against bleeding that may occur in the arterial vascular access region and cause postoperative morbidity and mortality. No platelet activity test such as light transmittance aggregometry was performed before the procedures.

Follow-up

After each procedure, patients were anticoagulated with heparin for 24 hours and admitted to the neurology clinic for the follow up of either hemodynamic and neurologic conditions. Systolic blood pressure between 100-150 mmHg was recommended to prevent cerebral hypoperfusion or hyperperfusion. All patients were prescribed daily 75 mg clopidogrel for at least six months and daily 100 mg acetylsalicylic acid lifelong to prevent stent thrombosis and thromboembolism. Technical success was defined as the placement of the stent with at least 70% luminal patency. All patients were followed up until discharge from the hospital.
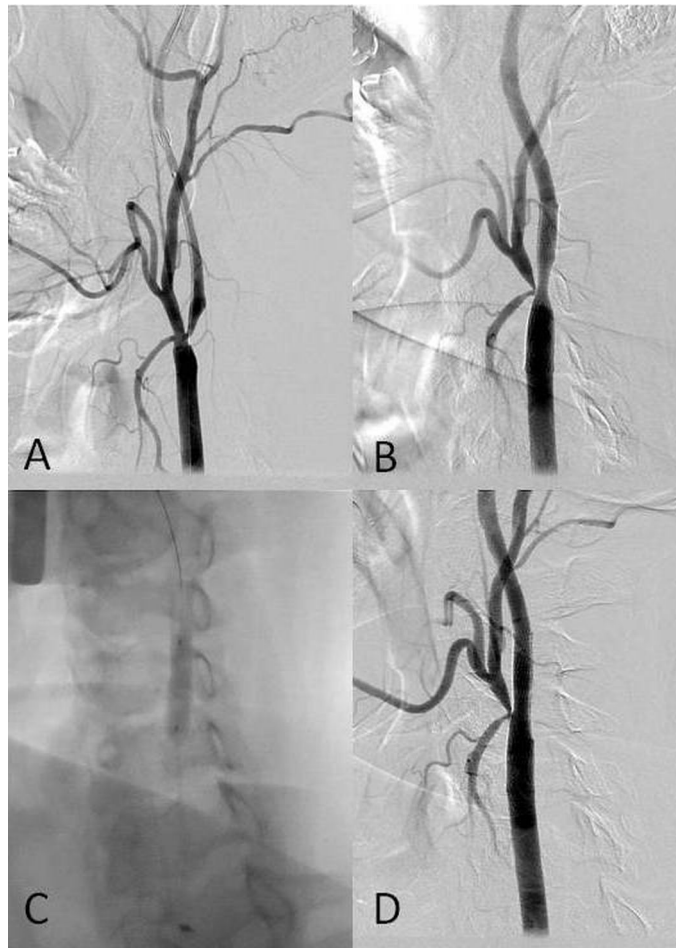
Figure 2: A standard carotid artery stenting procedure: placement of the distal embolic protection device (A), and stent (B), post stent dilatation with a balloon (C) and complete patency in the carotid artery (D).

Statistical analysis

Mean, median, standard deviation, minimum and maximum values were used as descriptive statistics for numerical data whereas number and percentages were used for categorical data. Statistical significance was set at $p < 0.05$. Statistical data editing and analysis were performed using SPSS 25.0 software (IBM Corp.).

RESULTS

The study consisted of 94 patients (27 women, 67 men) with 98 CAS procedures and the mean age was 66.38 ± 11.13 years (range: 36-85 years). Patient distribution considering the age group as 18-69 years, 70-79 years and ≥80 years was 54.3% (n: 51), 37.2% (n: 35) and 8.5% (n: 8), respectively.

Of the 32.7% (n: 32) CS, had no stroke or TIA related symptoms, and diagnosed by non-invasive modalities (Doppler US or CTA) during the follow up of other vascular diseases or incidentally. Two patients (2%) had a history of CEA (Figure 3). Most of the patients had a history of transient ischemic attack or stroke in the last 6 months with a rate of 65.3% (n: 64) thus categorized as symptomatic CS.

Of the 79.6% (n: 78) CS were detected by Doppler US imaging with CS rates of 50-69% in 26 carotid arteries (33.3%) and 70-99% in 52 carotid arteries (66.7%). CTA was the primary imaging modality in 7.1% (n: 7) of the CS with a mean stenosis rate of 71.71 ± 11.37 (range: 50%-95%). Twelve patients with 13 CS (13.3%) were referred to our Interventional Radiology Unit from other hospitals and no data of pre-procedural diagnostic modality report was found in our archives. The mean stenosis rate calculated according to the criterion of NASCET during in all CAS procedures was 74.52 ± 13.44% (range: 50%-

Figure 3: Carotid artery stenosis in patient with prior endarterectomy operation (A) and complete patency after carotid stenting (B).

99%). The mean stenosis rates in asymptomatic and symptomatic patients were, $73.13 \pm 9.39\%$ and $75.20 \pm 15.27\%$, respectively with no statistically significant difference (p>0.05). Ulcerated plaques were found to accompanied by 22.4% (n: 22) in patients with CS.

Side of the CS was found to be almost equal [right 51% (n: 50), left 49% (n: 48)]. Carotid bifurcation was the most involved localization in 86 CS (87.8%). Other involvements were as; multiple lesions in different localizations, only in ICA and only in CCA with a rate of 6.1% (n: 6), 5.1% (n: 5) and 1% (n: 1), respectively. In 10 patients (10.6%) contralateral ICA (right: 4 patients, left: 6 patients) were occluded totally, thus CAS was required although these patients were symptom-free and had CS at least 50%. Four patients (0.04%) had bilateral CAS procedure, 3 in different sessions and one in same session.

CAS procedures in 97 (98.9%) CS were performed using distal protection system routinely with two different devices SpiderFX™ (Medtronic, Dublin-Ireland) and Emboshield NAV[6] (Abbott, Illinois- United States) with the rates of 54.2% (n: 52) and 45.8% (n:44), respectively. One procedure completed without using distal protection device. In a young patient with CS caused by dissection and pseudoaneursym in ICA; distal protection device was not used due to lack of plaque. Dilatation of the stenosis before the stent placement was required in 10.2% (n: 10) of the procedures and post dilatation was performed in all CS (100%) to obtain the optimal stent patency.

Of the 93 patients and 97 CAS procedures, a total of 109 stents were used. Among all stents, closed-cell design was used in 87.2% (n: 95) versus open-cell design in 12.8% (n: 14). All stents were self-expandable and bare-metal. Tapered and non-tapered stent designs were used with a rate of 53.2% (n: 58) and 46.8% (n: 51), respectively. The diameters of the stents mostly used in our study were; 8x6 mm tapered (43.1%, n: 47), 7 mm non-tapered (24.8%, n: 27), 9 mm non-tapered (11%, n: 12), 9x7 mm tapered (9.2%, n: 10) and 8 mm non-tapered (8.3%, n: 9). Stent diameters used in the procedures were 30 mm or 40 mm, selected based on the length of the stenotic segment.

In one patient with symptomatic and severe CS (pre-occlusive); crossing the stenosis and stenting was failed despite pre-dilatation and using different type of stents. Upon this, carotid endarterectomy was recommended for carotid revascularization. Technical success of CAS in our study was 98.9% (97/98).

Of the 97 technically successful CAS procedures, 8 (8.2%) complications were encountered. Distal protection device related complications were occurred in 3 patients. In

one patient, the wire of the filter was broken whilst advancing the filter and immediately replaced with a new filter to avoid any potential problem in advancing the stent or balloon over the wire. In another patient the filter moved back to the stenosis segment while advancing the stent due to vascular tortuosity. In the third patient, a *flow-limiting vasospasm* was developed at the site of the distal embolic protection device after the stent placement. Normal flow with no residual vasospasm after intra-arterial nimodipine administration was proven by control angiograms in the ICA. In 2 patients, minimally flow-limiting dissection in the distal edge of the stent after post-

dilatation was occurred and treated by additional stenting. A non-flow limiting dissection at distal CCA occurred in one patient whilst advancing the long vascular sheath. Although it is not a flow-limiting dissection, it was treated by a second stent to avoid the potential embolic risk due to the dissection that might lead to a thrombus (Figure 4). Distal embolic events in 2 patients were encountered. Motor aphasia and facial paralysis in one patient, and hemiparesis in other; healed without sequelae by anticoagulant therapy.

Follow up data were reached in 60.8% (n: 59) of the CAS procedures. The mean follow-up period was 14.92 ± 10.76 months, ranged from 1 to 50
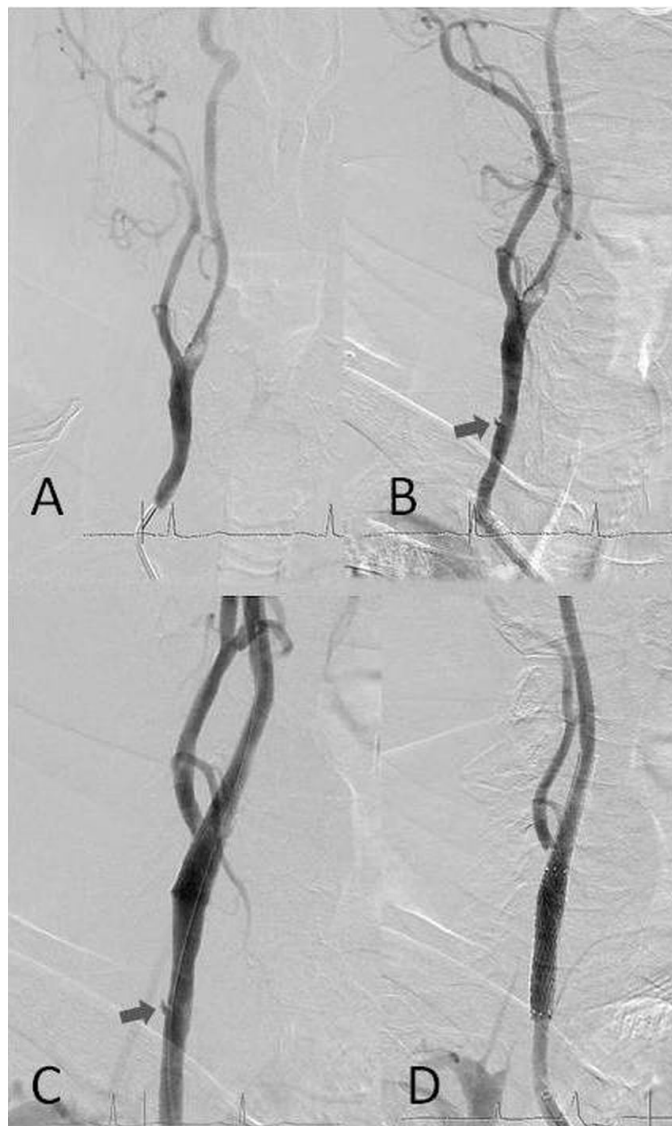

Figure 4: Selective carotid angiogram revealed the stenosis in the origin of the internal carotid artery (A). While advancing the long sheath, minimal dissection (black arrow) in distal common carotid artery was occurred (B). The first stent placed in the stenosis (C) was extended with a second stent to cover the dissection (D).

months. Intimal proliferation in 2 patients (3.4%), restenosis in 6 patients (10.2%) and occlusion in one patient (1.7%) were detected by Doppler US. Mean duration of restenosis in 6 patients was 9.33 ± 3.93 months (range: 3-13 months). Restenosis rates in Doppler US were 50-69% in 2 patients (33.3%) and ≥70% in 4 patients (66.7%).

Patient's demographic data, features of the lesions, procedure related data are shown in Table 1.

DISCUSSION

Stroke is a major and global health problem owing to its high rates of mortality and morbidity. Atherosclerotic CS can lead ischemic

Table 1: Patients demographic data, features of the lesions, procedure related data

	n	%
Gender		
Female	27	28.7
Male	67	71.3
Age		
18-69 years	51	54.3
70-79 years	35	37.2
≥80 years	8	8.5
Symptomatic CS		
Yes	64	65.3
No	32	32.7
Prior CEA	2	2
Primary imaging modality		
Doppler US	78	79.6
CTA	7	7.1
DSA	13	13.3
Severity of CS in Doppler US		
50-69%	26	33.3
70-99%	52	66.7
Ulcerated plaque		
Yes	22	22.4
No	76	77.6
CS localization		
Bifurcation	86	87.8
Proximal ICA	5	5.1
CCA	1	1
Multipl	6	6.1
CS side		
Right	50	51
Left	48	49
Stent-design		
Open-cell	14	12.8
Closed-cell	95	87.2
Predilatation		
Yes	10	10.2
No	88	89.8

stroke with the mechanism of distal embolism or hemodynamic changes due to cerebral hypoperfusion.[8] The randomized clinical trials have been comparing the treatment methods of CS (BMT, CAS and CEA) for the last three decades, both in symptomatic and asymptomatic patients with or without high risk factors, by using several design and shape of stents, distal or proximal embolic protection devices and balloons using for pre- or post-dilatation. As a result in trials, the association of periprocedural stroke and death with CAS, and periprocedural MI with CEA is commonly stated.[3] In our study, elective CAS procedure in patients with symptomatic and asymptomatic CS was investigated.

Although it is still unclear; stroke or TIA related symptoms, severity of CS detected by imaging modalities and presence of comorbid diseases are the main factors in patient selection for CAS. The patients with clinically severe cardiac and pulmonary disease, contralateral carotid occlusion, restenosis after CEA, age ≥80 year, previous neck surgery or radiotherapy are defined as high-risk for CEA, thus CAS is recommended as the primary treatment method in revascularization.[9,10] Patients with high-risk factors analyzed in our study were as, contralateral ICA occlusion, restenosis after CEA and age≥80, with the rates of 10.6%, 2% and 8.5%, respectively.

Beside the carotid revascularization with either CEA or CAS; best medical treatment is considered as the gold standard treatment for CS in asymptomatic patients in some guidelines.[11] Baker et al.[12] stated that, contralateral carotid occlusion in patients with asymptomatic CS and managed by medical therapy are at lower risk of stroke when compared to patients with asymptomatic CS and patent contralateral carotid artery, thus shows the importance of the treatment preference. In our Interventional Radiology Unit, we recommend follow up under best medical treatment in asymptomatic patients having <70% CS with annual Doppler US.

Pre-procedural diagnostic imaging is essential for the patient selection of carotid revascularization. In a meta-analysis; CE-MRA (contrast enhanced-magnetic resonance angiography) was found to be the most sensitive noninvasive imaging technique in both patient groups of 50-69% CS and 70-99% CS compared with DSA.[13] Gough et al.[14] stated Doppler US as the optimum screening method due to its low cost and availability with the use of appropriate velocity rates and CE-MRA as the most accurate noninvasive imaging technique in the assessment of CS. In our study, Doppler US

was primarily used as the pre-procedural imaging method in 79.6% of the patients. Atherosclerotic lesions might be seen in any segment of the carotid artery system. Carotid bifurcation is the most affected location in patients with CS[15], and similar frequency was detected with a rate of 87.8% in our study.

The stroke rates tend to increase with the severity of CS. Marthur *et al*.[16] reported the stroke rates in patients with <70%, 70-89% and ≥90% CS as; 3.5%, 5.1% and 14.9%, respectively. In our study, mean stenosis rate in all patients were 74.52% and we have found no significant difference (p>0.05) in CS rates of symptomatic (75.20%) and asymptomatic patients (73.13%).

A staged CAS approach is recommended in patients with bilateral severe carotid stenosis owing to the risk of; bradycardia and hypotension as a result of baroreceptor irritation, contrast induced nephropathy, increase in complications related to the length of the procedure and cerebral hyperperfusion syndrome.[17,18] In our study, 4 patients had bilateral CAS, and staged approach was performed in 3 of them. In the patient with simultaneous bilateral CAS; a day lasting hypotension has occurred after the procedure and healed without sequelae. Thus, we preferred a staged approach in the next 3 patients with bilateral CS.

Carotid stent devices are mainly divided into two groups depending on the cell-designs; open cell stents and closed cell stents. The size of the cell area and the number of interconnections specify the stent design. The main advantages of each cell design are stated as the flexibility in open cell stents and better target lesion coverage in closed cell stents. In a recent meta-analysis, although higher incidence (25% more compared to closed cell stents) of subclinical new ischemic lesions after open-cell stenting is reported; no significant difference in short or intermediate-term procedure related cerebrovascular complications was observed respect to the cell design.[19] In our center, we mainly preferred closed-cell stents (87.2%) owing to smaller free cell area and lower potential risk of atherosclerotic material protrusion through the strut interconnections. Open cell stents (12.8%) were especially preferred in stenosis with having tortuous anatomy in carotid arteries (Figure 5).

In the literature periprocedural stroke is found to be significantly lower with the use of embolic protection devices.[20,21] In our study, distal embolic protection devices are used during all CAS procedures except one patient mentioned in results section. In patients where advancing the filter is not possible due to severe or angled narrowing of lesion and lack of proper segment of petrous

Figure 5. CAS procedure in a patient with mild tortuous anatomy: severe internal carotid artery stenosis (A) and complete patency after the placement of an open cell stent (B).

ICA to place the filter, and having a stenosis with a clot hanging off the plaque; CAS with proximal balloon protection or CEA is recommended for the revascularization of CS. Filters may induce flow-limiting vasospasm or dissection and cause periprocedural stroke in cases of not regressed.[22] In only one patient flow-limiting vasospasm treated with intra-arterial vasodilator was encountered in our study.

Restenosis rates following CEA is reported as 10-25% and re-surgery has a potential cranial nerve injury and stroke risk when compared with primary CEA.[23] Therefore in 2 patients of CS with a prior history of CEA, revascularization was provided by successful CAS procedures.

In patients with acute stroke, additional ipsilateral ICA stenosis or occlusion with a rate of 10-20% is detected and necessitates CAS. In the literature, timing of the stent placement before or after the clot retrieval is controversial.[24] In our center, we prefer CAS without filter before the clot retrieval to save time in urgent revascularization of the cerebral circulation. The management of CAS in patients with acute stroke differs in such terms of antiplatelet therapy before and after CAS, timing of stent placement (before/after clot retrieval) and need of general anesthesia. In this study only elective CAS patients were included due to unlike management as mentioned above.

Another issue about CS is the debate on timing of carotid revascularization after onset of symptoms. Although performing CAS in the early period after acute stroke is controversial, current guidelines recommend CEA within 14 days of symptom onset in symptomatic patients with 50-99% stenoses.[25] In our department, we perform CAS procedure at least 4 weeks after onset of symptoms especially in patients with infarct more than 3 cm in diameter, unless emergency intervention is required.

Platelet adhesion and thrombosis due to intimal injury triggered by stent is an important complication of CAS. Dual antiplatelet therapy of acetylsalicylic acid and clopidogrel (ticlopidine if intolerant of clopidogrel) pre- and post-stent deployment is recommended in guidelines of American Stroke Association, Society for Vascular Surgery and European Society for Vascular Surgery with different doses and duration.[3] In our clinic, dual antiplatetel therapy with daily doses of 100 mg acetylsalicylic acid and 75 mg clopidogrel starting 10 days before the CAS procedure, and daily doses of 100 mg acetylsalicylic acid lifelong with 75 mg clopidogrel together at least 6 months after the CAS procedure is recommended.

Next-generation stent devices mainly focus on prevention of periprocedural stroke in CAS procedures. Although large studies with long-term outcomes are needed; recent stents with dual-layer micromesh structures (The Roadsaver, Terumo Corp., Tokyo, Japan and C-Guard, The InspireMD, Israel) are promising for continuous embolic protection owing to reduce in prolapse of plaque.[26]

The major limitations of our study are its retrospective nature and the lack of follow-up data needed for the clinical success, periprocedural complications of the procedure.

In conclusion, CAS with use of distal embolic protection devices is widely accepted, safe, feasible, less invasive when compared to CEA and can be performed successfully especially in patients with high risk factors. The main advantage is that CAS can be performed under local anesthesia thus avoids the complications of general anesthesia. Also management of the tandem lesions detected during the procedure is crucial. Controversial data about patient selection, different carotid revascularization techniques, devices and antiplatelet therapy require further and stronger guidelines for evidence-based management.

DISCLOSURE

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