Carotid artery stenting in surgically unfit patients with symptomatic carotid artery stenosis: Does it worth?

Original Article

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ABSTRACT

Background: Carotid endarterectomy (CEA) is the gold standard for the treatment of patients with severe carotid stenosis (CS). However, carotid artery stenting (CAS) has emerged as an alternative to CEA in surgically unfit patients. The present study aimed to assess the role of CAS with an embolic protection device (EPD) in the management of symptomatic CS in patients who were deemed unfit surgically for CEA.

Patients and Methods: This is a retrospective study that encompassed the analysis of patients who presented with symptomatic CS and were treated with CAS using EPD. The patients' clinical data, procedure details, and procedure outcomes were obtained from the medical files and analyzed.

Results: This study included 40 patients. During the immediate postprocedural period, one case (2.5%) showed stroke due to early stent occlusion. The late adverse events were stent occlusion that occurred in 3 patients (7.5%), TIA (n=2; 5%), myocardial infarction (n=3; 7.5%), and stroke (n=2; 5%). The primary patency rate during the follow-up period was 89.5%, and the secondary patency rate was 94.8%. The presence of diabetes and the stenosis length were significant predictors of stent occlusion. The delayed mortality rate was 7.5%. The predictors of patients' mortality were the presence of diabetes mellitus, stent occlusion, and the occurrence of myocardial infarction (MI).

Conclusion: The one-year primary and secondary patency rates were encouraging at 89.5% and 97.4%. Diabetes and stenosis length were identified as significant predictors of stent occlusion. Mortality was predicted by diabetes, stent occlusion, and MI.

Key Words: Carotid artery stenting (CAS), carotid stenosis (CS), embolic protection device (EPD), stent occlusion.

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INTRODUCTION

Carotid stenosis (CS) is the encroachment upon the carotid artery lumen that is mostly caused by atheromatous plaques and can lead to cerebrovascular events. Currently, carotid stenosis has become a growing focus of current medical practice worldwide[1]. Patients with CS may present with stroke[2], which remains a main cause of mortality all over the world[3,4].

The principal axes of CS treatment are medical and interventional treatment, which mainly encompasses carotid endarterectomy (CEA) or carotid artery stenting (CAS)[3,5]. Carotid endarterectomy is the gold standard for the treatment of patients with significant CS. However, carotid artery stenting has emerged as an alternate choice to CEA in surgically unfit patients[6].

The acceptance of CAS as an alternative to CEA has been based on findings suggestive of its comparable safety and efficacy to CEA[7]. It has shown a lower risk for cranial nerve injury and a promising faster recovery in some studies[8–10]. Nevertheless, carotid artery stenting has been reported to be associated with a higher risk for periprocedural stroke, which most probably occurs due to the formation of debris during the manipulation of atherosclerotic plaques[10–12]. Therefore, embolic protection devices (EPDs) have been recommended to be used as an adjunct to CAS to reduce the risk of cerebrovascular accidents[10,13,14]. The value of using EPDs has been demonstrated during CAS for asymptomatic and symptomatic CS[15,16], with several EPDs being developed promising up to 50% reduced risk of periprocedural stroke[17,18].

The present study aimed to assess the role of CAS and EPD in the management of symptomatic CS in patients who were deemed unfit surgically for CEA.

PATIENTS AND METHODS:

This is a retrospective study that encompassed the analysis of prospectively maintained data of patients who

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presented with CS symptomatized as transient ischemic attacks (TIAs) or stroke and treated with CAS during the period from November 2017 until December 2022 and presented to khamis mushait general hospital and Aseer central hospital in Saudi Arabia. The study was conducted after approval by the institutional research ethics committee under number 2023R 16.

The decision to proceed with CAS was taken by a collaborative, multidisciplinary team approach. Patients risky for surgery being aged above 80 years, having severe chronic obstructive pulmonary disease, a left ventricular ejection fraction of <30%, or having unstable angina were eligible for CAS if they had a stenosis grade ranging from 50 to 99%, as evidenced by the carotid artery duplex study. Patients with endovascular treatments for CEA complications were excluded. Informed written consents were obtained from patients or their authorized representative before performing the procedure. The patients‘ clinical data, procedure details, and procedure outcomes were obtained from the medical files.

Technique

All patients were admitted the day before the procedure. Clopidogril 300 mg was given before the procedure as a loading dose, followed by dual antiplatelet aspirin 75 mg and clopidogrel 75 mg once daily for 1 year, then aspirin 75 mg once daily for the long term.

The CAS procedure was performed through a trans femoral approach in a dedicated catheterization setting under local anesthesia and with conscious sedation for agitated patients. First, a 6-Fr sheath was inserted. The patients received intra-arterial 5000 IU of heparin immediately after insertion of the sheath. Under imaging guidance, 0.035-inch angled guidewire (Terumo Medical Corporation, Somerset, NJ) was carefully advanced into the aortic arch, An aortogram was obtained in 35 degree left anterior oblique position using pigtail catheter and a 5 Fr catheter was selected to engage the CCA. Catheter selection for CCA was chosen depending on the aortic arch anatomy. We use vertebral or simmon 2 catheter. The guidewire was then advanced into the ECA, followed by the catheter. Subsequently, a long, stiffer wire (Amplatz Super Stiff TM, Boston Scientific, USA) was introduced, over which a 90-cm-long sheath (Destination TM Guiding Sheath, Terumo, Japan) was advanced under careful fluoroscopy. The long sheath was meticulously positioned at the distal CCA, approximately 2–5 cm from the carotid artery bifurcation. A dedicated carotid angiography was performed in multiple views for the proper delineation of the lesion. A 0.014 wire was then used to traverse the lesion, and then a filter EPD (Emboshield NAV6 TM Embolic Protection System, Abbott, USA) was inserted and slowly advanced across the stenosis. A self-expanding nitinol stent system (Xact carotid stent system, Abbott, USA) was used. (Fig. 1A, B). The stent length depended on the lesion length. Post-balloon dilatation was used if there was a residual stenosis of 50% or more. Once the stent was successfully placed, the EPD was carefully retrieved under fluoroscopic observation, capturing any dislodged material.

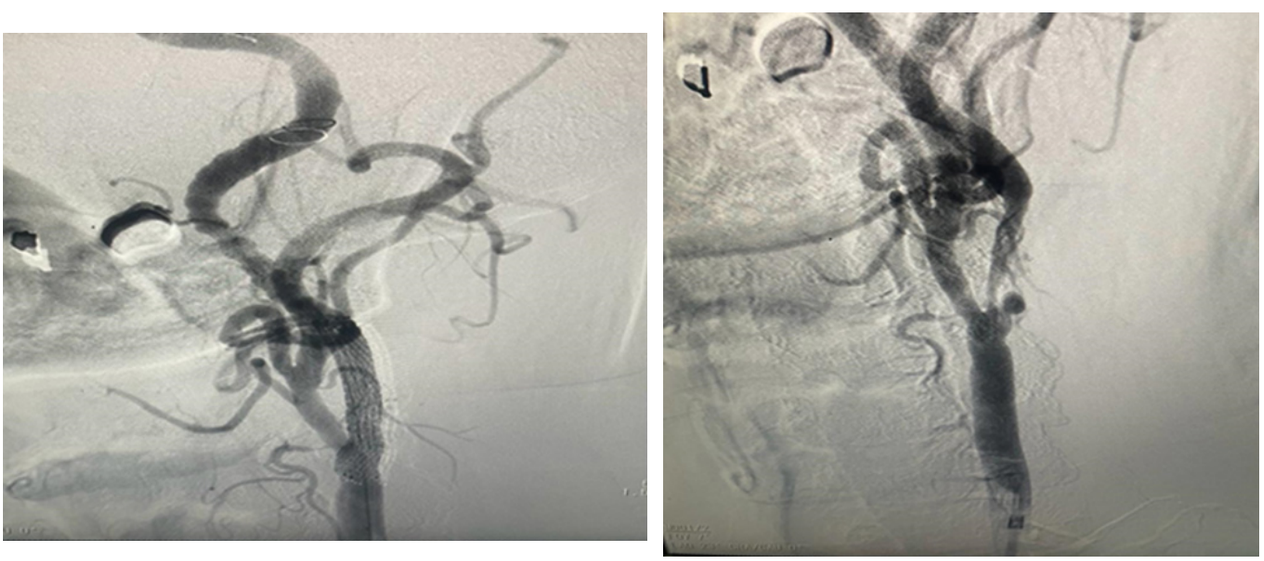

Fig. 1: A Left sided tight internal carotid artery stenosis, pre stenting. B. Left sided tight internal carotid artery stenosis, post stenting.

Follow-up and study outcomes

The patients received a clinical neurological examination and carotid duplex scan immediately after the intervention, then one, six, and twelve months later. The primary outcomes were technical success (≤30% residual stenosis) and early (30 days) major adverse events. The secondary outcomes were the one-year primary and secondary patency rates as well as the complications and mortality rates.

Statistical analysis

The data of the present study was analyzed using version 28 of the SPSS statistical software (IBM, Armonk, New York, United States). Qualitative data were presented as number and percentage, and numerical data were expressed as mean±SD. The probability of stent occlusion-free survival was analyzed with the Kaplan-Meier test. Predictors of occlusion-free survival were assessed using Cox regression, and the log rank was used to assess the difference in the one-year primary patency and occlusion-free survival in variables found to be significantly associated with stent occlusion. Predictors of one-year mortality were investigated using binary logistic regression. *P values* less than 0.05 were considered significant.

RESULTS:

This study included 40 patients who underwent CAS during the study period. The age of the patients ranged from 50 to 81 years, with a mean of 64.28±8.12. Most of the patients were males (n=32; 80%). The patients' mean body mass index (BMI) was 27.87±3.09 kg/m^2, with obesity (BMI ≥30 kg/m^2) prevalent in 12 patients (30%). Smoking was prevalent in more than half of the patients (n=23; 57.5%). The patients' comorbidities were dyslipidemia (n=40; 100%), hypertension (n=37; 92.5%), ischemic heart disease (n=32; 80%), and diabetes mellitus (n=10; 25%) (Table 1).

The study patients presented clinically with TIAs (n=33; 82.5%) or strokes (n=7; 17.5%). The treated vessel was predominantly left-sided (n=29; 72.5%). The degree of stenosis ranged from 50% to 95%, with a mean of 78.95±9.74. The stenosis length ranged from 7 to 21 mm, with a mean of 14.31±3.25 (Table 1). Post-balloon dilatation was indicated in 13 patients (32.5%).

Technical success was obtained in all patients (n=40, 100%). Postprocedural bradycardia occurred in 15 patients (37.5%). Access site complications were encountered in three patients (two cases of access site hematoma and one case of pseudoaneurysm). All were treated conservatively (Table 2).

During the immediate postprocedural period, one case (2.5%) showed stroke due to early stent occlusion and was managed by aspiration thrombectomy and extension of the stent . No other immediate adverse events or mortality occurred during the 30-day postprocedural period (Table 2).

During the remaining follow-up period up to one year, the adverse events were stent occlusion that occurred in 3 patients (7.5%), TIA (n=2; 5%), myocardial infarction (n=3; 7.5%), and stroke (n=2; 5%) (Table 2).

One case of delayed stent occlusion were managed with thrombectomy, stent removal and endarterectomy and one was died from massive stroke one case was asymptomatic and was managed conservatively.

The primary patency rate during the follow-up period was 89.5% (34/38) as two patients died from MI and were excluded from follow up , and the secondary patency rate was 94.8% (36/38) as one patient died from stent occlusion and massive stroke (Table 3). The estimated mean occlusion-free survival was 11.48 months. Cox regression for the stent occlusion was the presence of diabetes (HR=1.529, CI: 1.032–2.267, *P=0.034*) and the stenosis length (HR=10.353, CI: 1.075–99.711, *P=0.043*) (Table 4). ROC curve analysis revealed that a stenosis length of ≥17 mm was able to predict stent occlusion with a sensitivity of 7% and a specificity of 88.9% (Fig. 2). Log rank analysis for the occlusion-free survival rates according to the presence of diabetes mellitus and the stenosis length showed statistically significant differences (*P=0.011* and *0.001*, respectively). Comparisons are shown in (Figs. 3 and 4).

Delayed mortality was encountered in 3 patients (7.5%). two patients from MI and one patient from massive stroke after stent occlusion Binary logistic regression analysis for the predictors of patients' mortality demonstrated that statistically significant predictors were the presence of diabetes mellitus (OR=12.429, CI: 1.117–138.238, *P=0.04*), stent occlusion (OR=105.0, CI: 5.164–2134.802, *P=0.002*), and the occurrence of MI (OR=35.0, CI: 2.146–570.712, *P=0.013*) (Table 5). Multivariate regression showed that only stent occlusion remained statistically significant (OR=61.46, CI: 2.65–1426.36, *P=0.01*).

Table 1: Sociodemographic and clinical data of the study patients

	Study patients (*n*=40)
	Mean±SD
Age (years)	64.28±8.12
BMI (kg/m^2)	27.87±3.09
Stenosis degree (%)	78.95±9.74
Stenosis length (mm)	14.31±3.25
	Count (%)
Sex	
Female	8 (20)
Male	32 (80)
Smoking	23 (57.5)
Obesity (BMI ≥30 kg/m^2)	12 (30)
Comorbidities	
Diabetes mellitus	10 (25)
Hypertension	37 (92.5)
Dyslipidemia	40 (100)
IHD	32 (80)
Clinical presentation	
TIAs	33 (82.5)
Stroke	7 (17.5)
Affected side	
Right	11 (27.5)
Left	29 (72.5%)
Post balloon dilatation	13 (32.5)

BMI, body mass index, IHD, ischemic heart disease, TIA, transient ischemic attack.

Table 2 Post-procedural complications in the study patients

Complication	Group A (*n*=195)
Postprocedural bradycardia	15 (37.5%)
Access site complications	3 (7.5%)
Immediate stent occlusion (up to 30-day)	1 (2.5%)
Immediate mortality (up to 30-day)	0 (0.0%)
1-year stent occlusion	3 (7.5%)
1-year TIAs	2 (5%)
1-year stroke	2 (5%)
1-year Myocardial infarction	3 (7.5%)
1-year mortality	3 (7.5%)

TIA, transient ischemic attack.

Table 3: Life table for the primary patency in the study patients

Interval start time	Number entering interval	Number exposed to risk	Number of terminal events	Proportion terminating	Proportion surviving
0	40	40.000	1	0.03	0.98
1	39	39.000	0	0.00	1.00
2	39	39.000	0	0.00	1.00
3	39	39.000	1	0.03	0.97
4	38	38.000	0	0.00	1.00
5	38	38.000	0	0.00	1.00

6	38	38.000	0	0.00	1.00
7	38	38.000	0	0.00	1.00
8	38	38.000	0	0.00	1.00
9	38	38.000	0	0.00	1.00
10	38	38.000	0	0.00	1.00
11	38	38.000	0	0.00	1.00
12	38	20.000	2	0.10	0.90

Table 4: Cox regression analysis for the predictors of stent occlusion

					95.0% CI	
Variable	B	SE	*p* value	Exp(B)	Lower	Upper
Age	0.085	0.063	0.174	1.089	0.963	1.232
Sex	0.371	1.155	0.748	1.450	0.151	13.944
BMI	0.064	0.171	0.711	1.066	0.762	1.491
Hypertension	1.586	1.159	0.171	4.885	0.504	47.349
diabetes	2.337	1.156	0.043*	10.353	1.075	99.711
IHD	0.371	1.155	0.748	1.450	0.151	13.944
Smoking	0.246	1.000	0.806	1.278	0.180	9.079
TIA	0.413	1.155	0.721	1.511	0.157	14.529
Treated side	3.528	4.686	0.452	34.051	0.003	331871.204
degree of stenosis	0.026	0.057	0.648	1.026	0.918	1.147
Stenosis length	0.425	0.201	0.034*	1.529	1.032	2.267
post ballon dilation	−0.834	1.001	0.404	.434	0.061	3.085

*: Statistically significant.
BMI, body mass index; IHD, ischemic heart disease; TIA, transient ischemic attack.

Table 5: Binary logistic regression analysis for the predictors of mortality

					95.0% CI	
Variable	B	S.E.	*p* value	Exp(B)	Lower	Lower
Age	0.122	0.072	0.090	1.130	0.981	1.301
Sex	0.323	1.229	0.793	1.381	0.124	15.360
BMI	0.196	0.198	0.323	1.216	0.825	1.792
Hypertension	1.735	1.365	0.204	5.667	0.390	82.237
IHD	1.609	1.095	0.142	5.000	0.584	42.797
Diabetes	2.520	1.229	0.040*	12.429	1.117	138.238
Smoking	−0.875	1.202	0.467	0.417	0.039	4.398
TIA	0.511	1.238	0.680	1.667	0.147	18.874
Treated side	19.370	12.1×103	0.999	0.258×109	0.000	
Degree of stenosis	−0.002	0.054	0.965	0.998	0.897	1.110
Stent length	1.825	1.110	0.100	6.200	0.704	54.612
Post ballon dilation	−2.054	1.213	0.090	0.128	0.012	1.382
Procedure related bradycardia	−0.571	1.058	0.590	0.565	0.071	4.500
Access site complication	19.093	23205.423	0.999	0.196×109	0.000	
Stent thrombosis	4.654	1.537	0.002*	105.000	5.164	2134.802
Myocardial infarction	3.555	1.424	0.013*	35.000	2.146	570.712
Postprocedural stroke	2.457	1.537	0.110	11.667	0.574	237.200
Postprocedural TIA	−19.155	17974.843	0.999	0.000		

*: Statistically significant.
BMI, body mass index; IHD, ischemic heart disease; TIA, transient ischemic attack.

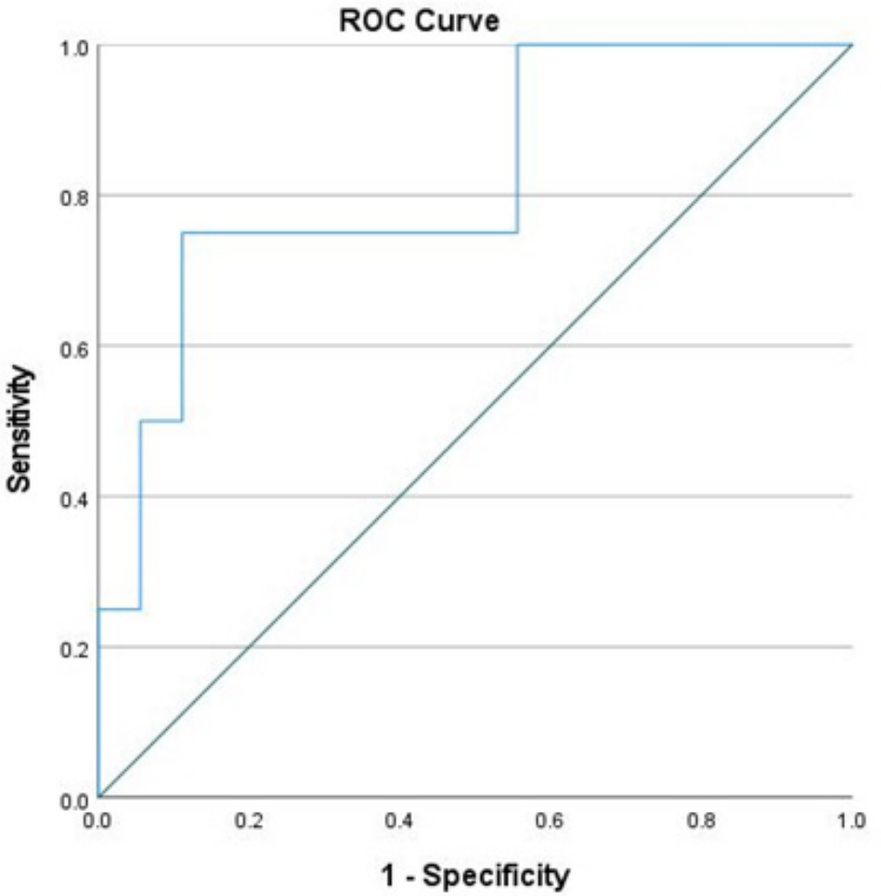

Fig. 2: ROC curve for the predictive value of stenosis length for stent occlusion.

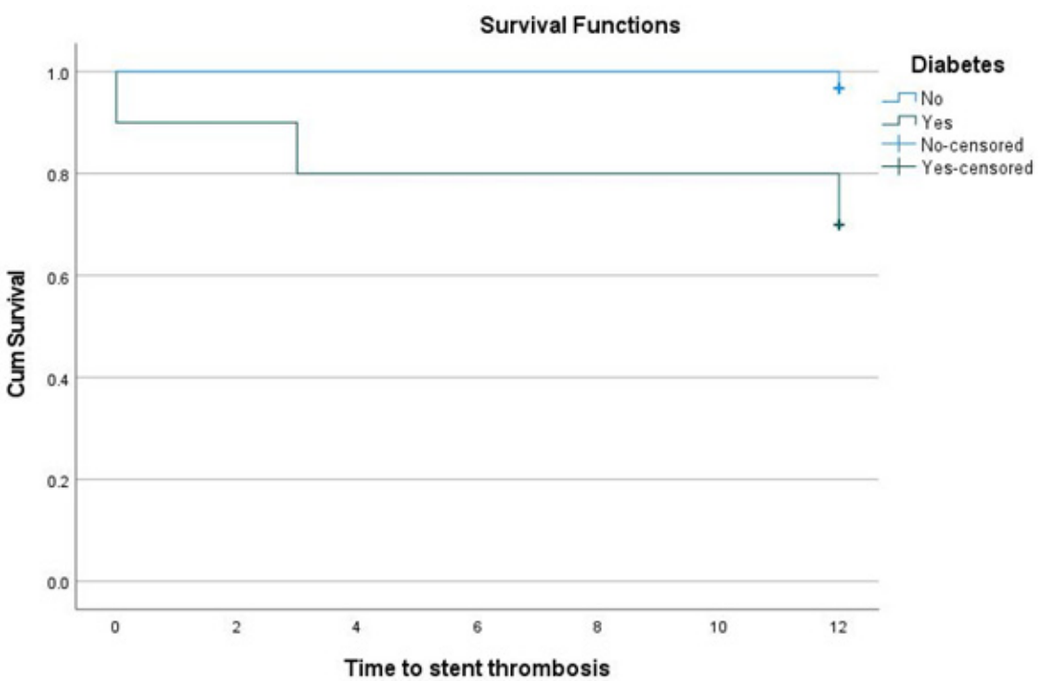

Fig. 3: Occlusion-free survival according to the presence of diabetes.

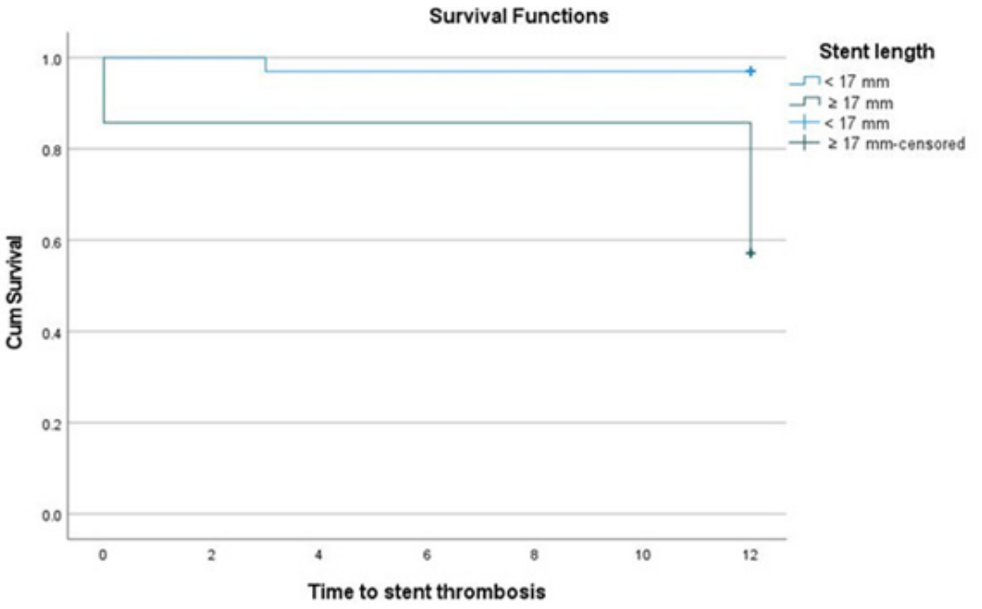

Fig. 4: Occlusion-free survival according to the stenosis length.

DISCUSSION

Several studies have assessed CAS as a method of treatment for patients requiring carotid revascularization. However, it has been difficult to reach a consensus due to the heterogeneity of the studied populations, techniques of treatment, and experience of the physicians. Overall, there have been encouraging trends towards CAS with a current improvement in procedure-associated morbidity and mortality[7], particularly with the use of EPDs that have led to a significant decline in the rates of periprocedural stroke, promoting declaring guidelines that obligate using EPD during CAS[10,13,14,17].

In this study, we present our experience in performing CAS with EPD for patients with CS who were ineligible to have surgery. In our study, we achieved technical success for all patients. There was a 2.5% rate of immediate postprocedural occlusion, with no 30-day morbidity or mortality. These findings are consistent with the fact that, despite advancements in CAS, including EPDs, carotid artery stenting is not free from adverse events[19]. Immediate postprocedural stent occlusion has shown various rates among studies. Similar to our results, Yoon *et al*.[20] reported a 2.2% rate of immediate postprocedural stent thrombosis. Relatively higher rates were described by Mpotsaris *et al*.[21] (6%), Rangel-Castilla *et al*.[22] (4.4%), and Pop *et al*.[23] (4.1%).

Our low rate of immediate periprocedural complications aligns with the broader evidence landscape about the safety of CAS, where a landmark trial comparing CAS to CEA, the Carotid Revascularization Endarterectomy versus Stent Trial (CREST), found that the rates of immediate periprocedural morbidity and mortality, despite being slightly higher in the CAS group, showed no statistically significant differences between the two treated groups (7.2 compared to 6.8%, respectively)[9]. On the other hand, an earlier trial by Mas *et al*.[24], Endarterectomy versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis (EVA-3S), was terminated early due to CAS-associated remarkably higher rates of death and stroke at 30 days (9.6 compared to 3.9%, respectively). Also, the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) trial failed to prove CAS non-inferiority in the 30-day morbidity and mortality[25]. It is most likely that these contradictory results are attributed to the variation in EPD utilization, where in CREST[9], like the current work, there was universal use of EPD, while in EVA-3S[24] and SPACE[25], EPD was used late in the trial and in 27% of patients only, respectively.

The present study demonstrated that, during the first year, the primary and secondary patency rates were 89.5% and 94.8%, respectively. Despite several studies assessing the CAS outcome, only a few studies could be reached assessing stent patency in all the studied patients beyond 30 days after the procedure. Malik *et al*.[26] and Pop *et al*.[23] reported long-term stent occlusion rates of 7.4% and 19.1%, respectively. The rate of stenting occlusion found in our study (10%) lies within the range of rates reported in the described studies. The notable achievement in maintaining vessel secondary patency is similar to the 100% secondary patency rate at the one-year follow-up reported by Pop

et al.[23] and highlights the efficacy of CAS with EPD in patients ineligible for surgical intervention due to carotid stenosis.

The presence of diabetes was a significant predictor of stent occlusion in the current study. This is supported by findings from major trials such as CREST[9] and corroborated by research, including the work of Pop *et al*.[23], which observed that stent thrombosis was more common in patients with diabetes. The association of diabetes with higher rates of stent occlusion was also described in the context of cardiology interventions[27]. The association between diabetes and an increased risk of stent occlusion can be attributed to multiple interrelated factors. Diabetes contributes to endothelial dysfunction, compromising vascular integrity[28]. Elevated blood glucose levels in diabetes promote inflammation and atherosclerosis, collectively enhancing the likelihood of stent thrombosis[29]. The link between diabetes and accelerated platelet turnover time adds a burden to this association, as the altered platelet dynamics may compromise the efficacy of antiplatelet therapies such as aspirin[30].

The length of stenosis emerged as another significant predictor of stent occlusion in the current study. In a similar context, the study of Gröschel *et al*.[31] found that stent length, reflecting the lesion length, posed a risk marker for stent thrombosis. The association between the lesion length and CAS worse outcome was attributed to the longer lesions associated with technical complexity, deeming use of a longer stent that would have an increased surface area, promoting platelet adhesion and activation, and having a higher potential for incomplete apposition to the artery wall, leading to disturbed flow of blood flow and thrombus formation[31].

Finally, the present study revealed a mortality rate of 7.5% that was predicted by the presence of diabetes mellitus, stent occlusion, and the occurrence of MI, all of which indicate a worse thrombotic state. Only stent occlusion remained significant after adjusting for the confounding factors. Comparable results were found by previous researchers[23,32–34], who reported that stent occlusion was related to worse clinical outcomes. The incorporation of these insights into risk assessment and intervention planning is crucial for optimizing patients' outcomes. It seems reasonable to exert all conceivable effort to prevent stent thrombosis.

It is noteworthy that our study contributes to the broader discourse on carotid interventions, particularly in patients ineligible for surgery, by providing real-world insights into the CAS procedure using EPD. The low rate of 30-day morbidity and the absence of 30-day mortality in our cohort suggest a favorable short-term safety profile, reinforcing the feasibility of CAS with EPD in this specific patient population. Nevertheless, the observed rates of stent occlusion and delayed events underscore the ongoing challenges and the imperative need for vigilant monitoring, refinement of procedural techniques, and ongoing research endeavors.

CONCLUSION

This study demonstrated technical success with the relative short-term safety of CAS with EPD in patients with CS who were not fit for surgery. One-year primary and secondary patency rates were encouraging at 90% and 100%, respectively. Diabetes and stenosis length were identified as significant predictors of stent occlusion. Mortality, predicted by diabetes, stent occlusion, and myocardial infarction, underscores the importance of addressing a worse thrombotic state.

CONFLICT OF INTEREST

None.

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