Original Article

Carotid Artery Stenting: A Single-Center Experience

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Abstract

Background: *Carotid artery stenting is now used as an alternative to surgical endarterectomy. This study was done to assess the feasibility, safety, and immediate and late clinical outcomes in patients undergoing carotid stenting.*

Methods: *Between July 2008 and December 2009, a total of 40 patients (20 male, mean age: 65 ± 11 years, 19 symptomatic, and 90% high risk for endarterectomy) underwent carotid artery stenting with different embolic protection devices and carotid stents. Thirty-seven patients had coronary artery disease. Technical success rate, stroke/death/ myocardial infarction rate at 30 days, access-site complications, and contrast-induced nephropathy were assessed. For the evaluation of the influence of experience in carotid artery stenting on complications, the patients were divided into two groups: Group 1 included the first 20 treated patients and Group 2 comprised the remainder of the patients.*

Results: *The overall technical success rate was 100%. The cumulative in-hospital stroke death rate was 7.5% (n = 3: 2 deaths and 1 major stroke). Complications were more frequent in Group 1 (2/20, 10%; 2 deaths) than in Group 2 (1/20, 5%; 1 major stroke), but this was not statistically significant (p value = 0.09). No access-site complications occurred, and mild contrast-induced nephropathy occurred in 3 patients (7.5%). No major stroke or neurological deaths occurred during a mean follow-up of 12 months.*

Conclusion: *Carotid stenting seemed feasible and relatively safe in our experience. Advanced experience in carotid artery stenting appears to confer an acceptable peri-procedural stroke-death rate.*

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Introduction

Stroke is one of the leading causes of neurological disability and death. One fourth of cerebrovascular events are attributable to atherosclerotic carotid artery disease.[1]

Large population-based studies indicate that the prevalence of carotid stenosis ranges from approximately 0.5% in individuals above the age of 60 and 10% in those above 80 years old; however, stenosis remains asymptomatic in the majority of cases.[2-4] The incidence of stroke will probably increase in the next 20 years due to the aging of the population and the improved survival rate of patients with a history of stroke or myocardial infarction; these are people who are at increased risk of further vascular accidents.

Randomized controlled trials have shown that the surgical treatment of carotid artery stenosis is more efficient than medical therapy alone in terms of stroke prevention when treating carotid artery stenosis > 70% in asymptomatic patients or > 50% in symptomatic patients.[4, 7]

In recent years, carotid artery stenting (CAS) has gained worldwide attention as a less invasive treatment option for stroke prevention. Data from recent studies and registries show that CAS can be performed with excellent technical success and a 30-day stroke/death rate of 2.2% - 4.8%.[8-10]

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Although several registries and trials have assessed the feasibility and results of CAS in the world, such studies on this important procedure and its results in Iran are scarce.[10, 11]

In this study, we sought to evaluate CAS efficacy and safety in our center and report our short and long-term clinical results in the treatment of 40 consecutive patients.

Methods

The data of 40 patients with internal carotid artery stenosis who underwent CAS with the use of an embolic protection device between July 2008 and December 2009 were analyzed.

All the patients had evidence of carotid stenosis in non-invasive tests such as Doppler sonography, CT, or Magnetic Resonance Angiography. All the patients provided signed informed consent and agreed to undergo regular follow-up evaluations. All the patients referred to the clinic one month later and were, thereafter, followed up by clinic visits or telephone calls. They also underwent pre-procedural neurological examinations, performed by a neurologist.

Of the patients examined, 19 (47.5%) were classified as symptomatic because they had a history of transient ischemic attack or stroke within the 6-month period prior to the stenting procedure, and 21 (52.5%) were classified as asymptomatic. Carotid angiography was performed in all the patients before CAS. The stenoses were visually assessed and quantitated by two cardiologists. Quantitative analysis was employed only when the visual assessment of individual lesions approximated borderline stenosis. In-hospital neurological events were documented and were categorized as transient ischemic attack (a focal ischemic neurological deficit with an abrupt onset within 24 hours); minor stroke (focal neurological deficit lasting > 24 hours), with regression; and major stroke (focal neurological deficit lasting > 24 hours), without regression.

To evaluate the influence of experience in CAS on in-hospital neurological complications, the patients were divided into two groups: Group 1 comprised the first 20 treated patients and Group 2 consisted of the remaining 20 patients. Data on the procedural details were also collected, including the use of embolic protection devices, type of stents and balloons, technical success rate, and causes of technical failure. Furthermore, complications at the access site and contrast medium amount were evaluated. For the evaluation of contrast-induced nephropathy, serum creatinine values were determined before and after the intervention. Baseline creatinine values of 1.8 - 2.5 and > 2.5 mg/dl were defined as moderate and severe renal insufficiency, respectively. Contrast-induced neuropathy was defined as an increase of 0.5 mg/dl in the baseline serum creatinine value. Myocardial infarction was defined as the occurrence of a new Q-wave in two leads. The primary end-point was the rate of 30-day major or minor stroke and/or death and/or myocardial infarction.

Acetylsalicylic acid (100 mg) and clopidogrel (75 mg per day) were administered at least 3 days prior to the procedure and those patients who were not on an antiplatelet medication received a 300-mg clopidogrel loading dose on the same day. During the intervention, 5000-7500 units of heparin were administered to maintain an activated clotting time of 200-250. Nearly all the interventions were performed under local anesthesia via a trans-femoral access; only in one case was the brachial artery chosen due to the severe occlusive disease of the distal abdominal aorta (right brachial approach for left carotid angioplasty). The routinely used contrast medium was Visipaque 270. After an angiogram of the aortic arch, selective carotid angiography was done with a 6-Fr right Judkins catheters and Vitek and Sidewinder Simmons I & II catheters for type III and bovine aortic arch. Finally, intra-cerebral angiography was also performed. Subsequently, long sheaths (6 or 7 Fr) or guiding catheters (7 - 8 Fr) were utilized to engage the common carotid artery. In both approaches, the catheters were advanced into the common carotid artery on support of 0.035-inch stiff wires. Different embolic protection devices were thereafter employed. To prevent a baroreceptor reaction, 1 mg of atropine was given intravenously before dilation. In all the cases, a self-expandable stent was implanted to cover the entire lesion, and in 2 patients two overlapping stents were placed. Pre-dilation was performed occasionally and was followed, in most cases, by post-dilation. To confirm the correct position of the stent and to rule out complications, a final angiogram of the cerebral circulation was performed in all the patients. Residual stenosis < 30% with no alteration in the brain circulation was considered a satisfactory result. The patients were monitored continuously both during the intervention and during the whole in-hospital period. All the patients were repeatedly examined by residents, and all the symptomatic patients were examined by neurologists. Post-procedural brain CT was performed if the neurological status of the patient changed. Uncomplicated patients were discharged 2 days later. All the patients were prospectively asked to undergo clinical 30-day follow-up. The patients were discharged on dual antiplatelet therapy (aspirin 100 mg and clopidogrel 75 mg per day) at least for 1 month and aspirin was continued indefinitely.

This study was a prospective case series study. All the analyses were carried out using SPSS version 16.0. The continuous data are presented as mean ± standard deviation (SD) or, if adequate, as median and range. The comparisons between the groups were analyzed for significance using the Fisher exact test or the chi-square test, as appropriate. All the tests were two-sided, and significance was assumed at p value < 0.05.

Results

In total, there were 40 patients comprised of 20 men and 20 women at an average age of 65 ± 11 years (range 38 - 88 years). Amongst the study population, 4 (10%) patients were ≥ 80 years old; 35 (90%) were at high surgical risk (Table 1);[12] 8 (20%) suffered from significant (> 70%) bilateral carotid artery disease; 13 (32.5%) had old myocardial infarction; and 37 (92.5%) had evidence of coronary artery disease, 32 (80%) of whom had multi-vessel (≥ two vessels) involvement. All the lesions were due to atherosclerosis. Nearly half of the asymptomatic patients, who were referred by cardiovascular surgeons, required surgery in the following 4 - 6 weeks. Table 2 summarizes the baseline demographic and clinical characteristics of the patient population.

Table 1. Criteria for high-risk patients

Age>80 years
History of open heart surgery
Need for open heart surgery within 30 days
History of myocardial infarction
Known multi-vessel disease
Left ventricular dysfunction with left ventricular ejection fraction <40%
Severe bronchopulmonary disease
Severe renal disease
Significant contralateral carotid disease
Previous endarterectomy

Table 2. Baseline demographic and clinical characteristics[*]

Age, y (mean±SD)	65±11
Male gender	20 (50)
Symptomatic	19 (47.5)
Asymptomatic	21 (52.5)
History of myocardial infarction	13 (32.5)
Prior CABG	11 (27.5)
Prior PCI	4 (10)
Known multi-vessel coronary artery disease	32 (80)
EF<40%	8 (20)
Moderate renal insufficiency	4 (10)
Severe renal insufficiency	2 (5)
Current smoker	11 (27.5)
Hypertension	28 (70)
Hyperlipidemia	20 (50)
Diabetes mellitus	21 (52.5)
Contralateral carotid disease	8 (20)

[*]Number are presented as n (%)
CABG, Coronary artery bypass graft; PCI, Percutanceus coronary intervention; EF, Ejection fraction

Table 3. Embolic protection devices

Embolic protection device	Procedures	Percentage
Filterwire EZ	17	42.5
Mo.Ma	2	5
Spider RX	3	7.5
EmboShield	15	37.5
Angioguard RX	3	7.5

Table 4. Stent type

Self-expandable stents	Procedures	Percentage
Carotid Wallstent	9	21.4
RX Acculink	10	23.8
Xact	5	11.9
Protegè	7	16.6
Precise RX	7	16.6
Cristallo	4	9.7

Overall, neurological complications during hospital stay included 1 (2.5%) transient ischemic attack in an asymptomatic 71-year-old man during the procedure and 1 (2.5%) major stroke in a symptomatic 88-year-old man 3 days after the procedure with a much calcified aortic arch. Two (5%) patients died during the in-hospital course; one of them was a symptomatic 57-year-old woman who expired during the first 24 hours due to hyper-perfusion syndrome and evidence of intracranial hemorrhage in CT. She also had percutaneus coronary intervention (PCI) on the right coronary artery in the same session and intra-procedural activated clotting time (ACT) was 400. The other case was a symptomatic 77-year-old man with ischemic heart failure (ejection fraction = 20%) who died a few hours after the procedure due to hypotension and intractable ventricular tachycardia (VT) and finally ventricular fibrillation (VF). It appears that post-stenting hemodynamic instability must have decompensated the cardiovascular status. Therefore, the overall in-hospital stroke/death rate was 7.5% (Table 5), with all the cases being symptomatic. With respect to the learning curve, there were 1(5%) transient ischemic attack and 2 (10%) deaths in Group 1; whereas in Group 2, there was only 1(5%) major stroke. The difference, however, was not statically significant (p value = 0.09).

There were no access-site complications. The average amount of contrast medium consumed during angiography was 325 ± 120 ml. A mild reversible contrast-induced nephropathy after intervention was found in 3 (7.5%) patients, two of whom were diabetics and the other one suffered from severe renal failure.

The mean follow-up was available in 34 patients for a mean period of 12 ± 9 months. In this interval, 2 patients died after the surgical procedures: one patient after coronary artery bypass graft surgery due to pump failure and the other

one after mitral and aortic valve replacement surgery due to abdominal complications. There was no major stroke, and the major stroke/neurological death rate was 0%.

Table 5. Incidence of major adverse events within 30-day follow-up[*]

Number of procedures	40
Death	2 (5)
Major stroke	1 (2.5)
Minor stroke	0
Myocardial infarction	0
Transient ischemic attack	1 (2.5)
Primary end-point (stroke, death, or myocardial infarction)	3 (7.5)

[*]Numbers are presented as n (%)

Discussion

In our experience, the overall technical success rate was 100%, which compares well with the published data. Given that one fourth of our cases had a difficult aortic arch and that more than half of the CAS procedures were on the left side, which is clinically more difficult, this high technical success rate is important. In our study, none of the selected patients was excluded due to comorbidities; consequently, all the patients considered high surgical risk (90%) were treated. Therefore, of the 40 procedures, the combined complication rate (death/stroke) at 30 days (including intra- and post-procedural complications) was 7.5%. As was mentioned earlier, 80% of the patients in our study had evidence of multi-vessel coronary artery disease; still, no myocardial infarction occurred and the combined death/ stroke/myocardial infarction rate was 7.5%.

These results compare well with two recent EVA-3S and SPACE trials.

The most recent randomized trial, EVA-3S, showed a CAS stroke/death rate of 9.6% at 30 days. This study showed post-carotid endarterectomy (CEA) complication results comparable with those in the literature (3.9% stroke/ transient ischemic attack at 30 days). It is clear that the biggest limitations of the study were the scarce endovascular technique experience of the operators (12 carotid artery stenting procedures or 35 procedures performed on supra-aortic trunks, five of which were carotid) and the pre-procedural anti-platelet therapy, which was only recommended and not always homogeneously administered. Double anti-platelet therapy was administered to 82.9% of the patients and only 85.4% were administered anti-platelet therapy after the intervention.[13] The SPACE trial failed as well to demonstrate the "non-inferiority" of the endovascular treatment compared with CEA, reporting a complication (stroke/death) rate at 30 days of 7.68% for CAS and 6.51% for CEA.

Such high rates may be due to the limited use of cerebral protection devices, as well as to the insufficient operator's experience required (25 consecutive successful angioplasty or stent procedures).[14] Our results are inferior to those of other studies such as the SAPPHIER and AHA guidelines. In the SAPPHIER trial, 156 patients were treated with CAS with the use of a cerebral protection device and 151 with CEA. The death/stroke rate in the group of patients treated with CAS was 4.5% and in those treated with CEA was 6.6%; such results were beyond the limits of the AHA guidelines, which are based on the ACAS and NASCET. This may be explained by the fact that these latter studies excluded high-risk patients such as those with contra lateral carotid occlusions, restenosis after CEA, age above 80 years, or the presence of concomitant cardiovascular pathologies.[15]

In our experience, 10% of the study patients were ≥ 80 years; 20% had contralateral involvement, which increased the adverse results; and 90% had concomitant cardiovascular disease. Thus, the most important reasons for the higher adverse results in our study are more high-risk patients and the inadequate experience of the operators. It is, therefore, prudent that lower-risk patients be selected in an early learning curve. It is also recommended to avoid coronary PCI and CAS concomitantly, which would require higher ACT. In the Kassaian et al. experience in Iran, age ≥ 70 years, three-vessel disease, hypertension, plaque ulceration, Type C lesion, and a score of ≥ 22 were the independent predictors of adverse events after CAS.[10]

Numerous clinical reports have highlighted the importance of the operator's experience as a crucial factor in the clinical success of CAS.[7, 16, 17] Recent published data by Theiss et al.[7] demonstrated a peri-procedural stroke/death rate of 5.9% at centers with < 50 interventions, whereas at centers with > 150 patients, the stroke/death rate was significantly lower (3.0%). In addition, procedural time and contrast volume decreased significantly with increased physician's experience.[18] The effect of the learning curve was demonstrated, as well, in randomized studies such as the EVA-3s trial.[13] In our experience, in Group 1, which included the first 20 patients, the death/ stroke rate was 10% and in Group 2, which included the remaining 20 patients this rate was 5%. This difference was not statically significant, probably due to the small size of the study population. Apart from neurological complications, there are other procedure-related complications such as puncture-site complication and contrast-induced nephropathy. Despite heparinization and antiplatelet therapy and the use of 8 Fr guiding catheters in the majority (82.5%) of cases, no access-site complication was detected. The incidence of mild contrast-induced nephropathy in our study was 7.5%, which returned to the previous values in all the cases.

Amongst patients with diabetes mellitus and pre-existing renal disease, the incidence of contrast-induced nephropathy is estimated to be as high as 50%.[19] Nevertheless, despite the fact that 52.5% of our patients had diabetes mellitus and 15%

had a renal insufficiency, we had an acceptable incidence of contrast-induced nephropathy. The amount of dye in our study was relatively high, mostly due to the unavailability of road map technology in our Cath. lab. At the one-year follow-up, which was available in 34 patients, there was no major stroke or neurological death, which is definitely promising.

Admittedly, our study had limitations. This was an analysis of a small-sized, single-center patient population and thus had all the limitations of such a study which results in a low statistical power. Validation of these results requires larger studies.

Conclusion

We achieved a good technical success and a relatively acceptable in-hospital stroke/death rate. However, as was explained earlier, the occurrence of neurological complications may be associated with the learning curve. The major stroke/neurological death rate was also promising in the long-term follow-up. Finally, this study can be a guide to our colleagues in the country who are interested in CAS. Not only is it advisable that lower-risk patients be selected in an early learning curve but also concomitant coronary PCI and CAS should be avoided in that it would necessitate higher ACT.

Acknowledgment

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