Carotid arterial stent implantation follow-up and results in 50 patients: preliminary report

Alireza Khosravi1, Fereshteh Ziaee Bideh2, Farshad Roghani3, Mohammad Saadatnia4, Fariborz Khorvash5, Majid Nejati6, Nastaran Khoshpour6, Mohaddeseh Behjati7

1 Hypertension Research Center, Interventional Cardiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
2 Adjunct Professor, Department of Cardiology, Faculty of Medicine, Islamic Azad University, Yazd, Iran
3 Interventional Cardiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
4 Department of Neurology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
5 Anatomical Science Research Center, Kashan University of Medical Sciences, Kashan, Iran
6 Department of Pediatrics, Shahid Beheshti University of Medical Sciences, Tehran, Iran
7 Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

Type of article: Case series

Abstract

Background: Carotid artery stenting (CAS) is considered as a safe and effective procedure for treatment of carotid artery stenosis. Evaluation of this procedure's complications is essential for proper clinical decision-making.

Objective: This study aimed to evaluate the cardiovascular events after CAS among our patients in Isfahan, Iran.

Methods: This case-series study was conducted on fifty patients from December 2013 to May 2016. These patients were referred to the cardiology centers of Isfahan, Iran by a neurologist, for stenting of extracranial carotid arteries. The second step was examining the patients by cardiac interventionist. Stenting was performed on symptomatic patients with carotid artery stenosis of more than 50 percent or asymptomatic patients with more than 70 percent carotid artery stenosis on Doppler ultrasonography. Neurologic evaluation was performed at baseline, during hospital stay, and follow-up. Transient ischemic attack (TIA)/Stroke and Myocardial infarction (MI) questionnaires were filled out by a cardiologist over telephone interviews with the patients, for follow-up of one month, six months and at the end of study. Carotid Doppler ultrasonography was performed before and 6 months after stenting for evaluation of restenosis. Indeed, during the follow-up study, the major adverse cardiac events (MACE) were evaluated. All data were analyzed through SPSS v.17.

Results: The mean age of patients was 70.73 (±14.01) years old (range: 48-89 years old). Composite endpoint of death, stroke, and MI was totally 8 percent. The rate of carotid arterial restenosis (Luminal arterial narrowing>50%) was 8%.

Conclusions: Despite the fact that carotid stenting is new in our center, our results can be compared to other important studies.

Keywords: Carotid stenosis, Stents, Stroke care, Iran

1. Introduction

Stroke is the leading cause of death and the main cause of disability in humans (1). Atheroembolization from stenosed carotid arteries is one of the most important vascular causes of stroke. Atherosclerotic plaques occur at the site of a stenosis in the internal carotid artery. It could also develop at the junction of the carotid artery to the aorta. In conclusion, the consequent thromboembolic strokes lead to brain ischemia and subsequent neurological complications (2, 3). Due to the great impact of carotid artery stenosis on the development of stroke, United States
Preventive Service Task Force (USPSTF) advised against the routine screening of the general population for carotid artery stenosis in asymptomatic cases. In the case of significant carotid artery stenosis, removal of vessel occlusion improves a patient's symptoms. Also, medical treatment, interventional angioplasty, and carotid endarterectomy (CEA) are applied for cases with symptomatic carotid artery stenosis (4, 5). Carotid artery stenting (CAS) is a safe approved and maturing method for treatment of carotid artery stenosis, but there is still a greater risk of postoperative stroke after CAS compared to CEA (4). In various randomized trials, the safety and efficacy of carotid artery angioplasty and CAS have been approved. Development of restenosis after CAS has been reported to be low and most importantly, asymptomatic (6). Although the gold standard for the treatment of carotid artery stenosis is still CEA, performance facility of percutaneous angioplasty makes this procedure a preferred choice for both patient and physician (7). Some important randomized clinical trials such as Carotid Revascularization Endarterectomy versus Stenting Trial (CREST trial) (8) and Carotid Acculink/Accunet Post Approval Trial to Uncover Rare Events (CAPTURE) (9) registry showed no significant difference between the stenting and endarterectomy procedure in respect to composite primary endpoint of periprocedural stroke, MI or death and subsequent ipsilateral stroke (10).

In recent years, for stroke prevention, CAS has been considered in many studies (2, 11) as a less-invasive technique with high technical success and low compliance rate. Although many studies have been done to evaluate the outcome of CAS in the world, limited studies in this area have been done in Iran. An 8-year follow-up study of Simonetti (12) on CAS outcomes showed that this method is safe, and a similar study was done in Iran which considered this method safe and feasible too (13). Although, the results of various clinical trials and registries performed on CAS are so different, it seems that the success rate of this procedure is entirely operator-dependent. Knowledge about the complications of this procedure is essential for proper clinical decision-making. Since CAS is currently performed in Iran, the aim of this study was to evaluate the outcomes of CAS in our patients.

2. Material and Methods
2.1. Patient group
In this case-series study, 50 consecutive patients were enrolled. They were referred for stenting of the extracranial carotid arteries by a neurologist to the cardiology center of Isfahan, Iran between December 2013 and May 2016. In this study, we selected the symptomatic patients with more than 50% luminal internal carotid artery stenosis and asymptomatic patients with more than 70% stenosis on Doppler ultrasonography that was performed by a neurologist. Patients were considered to be symptomatic if they had a transient ischemic attack, amaurosis fugax, or minor non-disabling stroke. Patients with an earlier stroke history that was sufficiently severe to confound the assessment of end points were excluded from the study.

2.2. Carotid stent protocol
Before the procedure, history, physical examination and electrocardiography (ECG) interpretation was done by an interventional cardiologist for all patients, and blood samples were taken for laboratory tests such as, CBC, BUN, Cr, PT, PTT, INR, FBS, TG, Chl, LDL, HDL. The patients received Acetylsalicylic acid (ASA) 325 mg and Clopidogrel 600 mg before the procedure. In the cases of patients who had not received Clopidogrel and ASA; 600mg loading dose and 325mg was given, and those who had already received; Clopidogrel 75mg and ASA 80mg was given. The patients continued receiving ASA 80 mg and Clopidogrel 75 mg for 3 months after the procedure. In this procedure, self-expandable stents (RX Acculink and Cristallo) and embolic-protection devices (EZ Filter) were used. Carotid angioplasty was completed in all patients with femoral artery access, and a stent was placed in all, with a distal protection device. Patients undergoing procedure received medical therapy that was consistent with the current standard of care, including treatment of hypertension, hyperlipidemia and diabetes. At the time of CAS procedure, if the patient had any indication of coronary angiography, both were performed simultaneously. All events and any angiography complications such as, MI, retroperitoneal hemorrhage, stroke and death were recorded during hospitalization. We used five standard questionnaires for stroke, death, MI, unstable angina and sudden cardiac death (SCD). Neurologic evaluation was performed at baseline, during hospital stay, and follow-up by a neurologist. Also, ECG and carotid Doppler ultrasonography were performed before the procedure and 6-months after CAS for evaluation of carotid artery restenosis. A TIA/Stroke and MI questionnaire was filled out by a cardiologist over a telephone interview with the patients for a follow-up of one month, six months and at the end of study. Patients were asked to be examined by a neurologist if they had experienced any sudden episodes of weakness, blindness, numbness, or speech difficulty, including events similar to their index event and stroke, which was confirmed by brain CT scan. In addition, during follow-up study, MACE was assessed by a cardiologist.

2.3. Technique of CAS
The technique of CAS can be divided into an access phase and intervention phase. In access phase, in order to achieve local anesthesia, we used 1% Lidocaine (Xylocaine) subcutaneously, then femoral vein access was obtained
for pacemaker insertion (in cases when necessary). The femoral artery was punctured and a 6F vascular sheath was inserted. Loading dose of IV heparin (5000 unit or 70 unit/Kg) was administered. We inserted a diagnostic catheter (Cook, Bloomington, IN) using a guidewire (Wholey modified J, 175cm, Mallinckrodt, St. Louis, Mo) for selective cannulation of common carotid artery (CCA) and detection of the severity of carotid stenosis. Diagnostic catheter was removed and an 8F 100 cm long sheath was inserted. We used 0.035-inch guidewire 260 Cm Amplatz Super Stiff (Meditech/Boston Scientific, Natick Mass) for engagement of long sheath into CCA. The stenosis was crossed with 0.018-inch guidewire, and a monorail angioplasty balloon was advanced to the lesion over 0.014-inch guidewire which was attached to a distal protection embolic device (EZ filter) then a balloon (Balloon 4.30) was inflated and self-expandable stent was implanted. Eventually, carotid angiography for assessment of residual stenosis was performed.

2.4. Statistical analysis
The statistical analysis was done by using the Stat statistical software (version 10, Stata Corporation, College Station, Texas, USA). The mean and standard deviation, frequency, and percent were used in the descriptive analysis.

3. Results
The mean age of participants was 74±7.1 years (range 48-89 years old). The mean follow-up duration was 674±318 days. The researchers encountered a 20% follow-up loss of carotid Doppler ultrasonography participants. Mean volume of contrast agent for each patient was 100cc. The percentage of male participants was 68%. Baseline characteristics are reported in Table 1. Hypertension was the most common (78%) cardiac risk factor among patients in the carotid stenting group. In total, 36% and 42% of the participants had hyperlipidemia and diabetes respectively. These risk factors did not change during the study period. Most of the patients (82%) had neurological symptoms before carotid angioplasty and the most common neurologic sign was hemiparesis (76%). Also, 100% of patients had no residual stenosis after the angioplasty procedure. This means the success rate was 100%. In total, 56% of patients had significant stenosis of Right Internal Carotid Artery (RICA) and 2% had involvement of both carotid arteries (Table 2). On the whole, 8% of our follow-up patients developed restenosis i.e. 2% and 6% developed severe and moderate restenosis respectively. Periprocedure complications (up to 30 days) were 4%. Combination rate of MI, death and stroke (MACE) were totally, 8% (Table 3). There was a loss of a participant who was an 82-year old man with a history of hypertension and ischemic heart disease (IHD) and a previous coronary artery bypass graft (CABG). He underwent simultaneous stenting of cut of left anterior descending (LAD) artery and right coronary artery (RCA) due to gastrointestinal bleeding. ASA and Plavix were discontinued which resulted in occurrence of acute stent thrombosis. He expired due to acute MI and cardiogenic shock. This death was not related to the procedure. Another death was in an 83-year old diabetic male without IHD, who expired one year later due to aspiration pneumonia following cerebro vascular accident (CVA).

Table 1. Comorbidities and main risk factors for atherosclerosis in 50 treated patients

| Variables                        | Frequency | Percent |
|----------------------------------|-----------|---------|
| Hypertension                     | 39        | 78.0    |
| Hyperlipidemia                   | 18        | 36.0    |
| Diabetes mellitus                | 21        | 42.0    |
| Smoking                          | 10        | 20.0    |
| Insulin injection                | 7         | 14.0    |
| Ischemic heart disease           | 20        | 40.0    |
| Three vessels (CAD*)             | 13        | 26.0    |
| Two vessel disease               | 3         | 6.0     |
| Single vessel disease            | 4         | 8.0     |
| Previous CAS**                   | 1         | 2.0     |
| Previous CEA***                  | 2         | 4.0     |
| Contralateral carotid artery stenosis> 70% | 1 | 2.0 |
| Prior PCI****                    | 10        | 20.0    |
| Prior CABG*****                  | 10        | 20.0    |
| Renal insufficiency (Cr > 2.5)   | 1         | 2.0     |
| Pacemaker                        | 3         | 6.0     |

CAD: Coronary artery disease; CAS: Carotid Arterial Stenting; CEA: Carotid Endarterectomy; PCI: Percutaneous coronary intervention; CABG: Coronary Artery Bypass Graft
Table 2. Initial neurologic symptoms before carotid artery stenting in 50 patients

| Neurological Symptoms before Stenting | Frequency | Percent |
|--------------------------------------|-----------|---------|
| Symptomatic patients                 |           |         |
| CVA*                                 | 33        | 66.0    |
| TIA**                                | 7         | 14.0    |
| Amaurosis Fugax                      | 1         | 2.0     |
| Total                                | 41        | 82.0    |
| Asymptomatic Patients                | 9         | 18.0    |

Table 3. Complications of 50 patients with carotid arterial stent placement

| Complications                        | Frequency | Percent |
|--------------------------------------|-----------|---------|
| Periprocedure (30 days)              |           |         |
| MI                                   | 1         | 2.0     |
| Death                                | 1         | 2.0     |
| Retroperitoneal hemorrhage           | 1         | 2.0     |
| Total                                | 3         | 6.0     |
| During 6-month                       |           |         |
| Carotid stenosis (<50%)              | 19        | 38.0    |
| Carotid stenosis (>70%)              | 1         | 2.0     |
| Total                                | 23        | 46.0    |
| During 12-month                      |           |         |
| Stroke                               | 11        | 2.0     |
| Death                                | 1         | 2.0     |
| CVA                                  | 1         | 2.0     |
| Total                                | 2         | 4.0     |
| MACE                                 | 4         | 8.0     |

4. Discussion

Morbidity and mortality following CAS may have improved since the first introduction of these devices. Combined 30-day stroke and death rates for carotid stenting in randomized trials for symptomatic patients was about 9.6 percent (14). However, the 30-day death and stroke rate was 3.6 percent in an analysis of two multicenter post market surveillance registries of CAS (EXACT, CAPTURE-2) that included 6,320 high-risk patients (15). Registry reports (16) showed a 98.4% CAS success rate, and various studies have shown that CAS is performed with low complication rate worldwide. Although the technique is different between operators and centers, CAS can be achieved with acceptable results. In the present study, the mean age of patients was 74±7.1 years, although the mean age of other studies, such as stenting and angioplasty with protection in patients at high risk for endarterectomy population (SAPPHIRE) (17), Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis (EVA-3S) (18), Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) (19) and Stent Protected Angioplasty versus Carotid Endarterectomy (SPACE) (20), was 72.6, 69.7, 67 and 67.9 respectively. Although the study shows that our patients were older than in most studies and they had many comorbidities, MACE was not higher than in other studies. In our study the mean duration of follow-up was considered 674±318 days (56±26 months); although in other studies, it was 25±16 (21), 18±10 (22) months respectively. The follow-up duration of our study was longer than most studies. 30-days MACE in our study was 4%, in other studies such as, SAPPHIRE, Veterans Affairs Cooperative Study (VACS) (23) and European Carotid Stent Trial (ECST) (24), it was 4.8% and 6.5% and 7% respectively. It shows that MACE in our study is lower than other studies and this important result can be due to the fact that CAS had been performed by an experienced interventionist. Although the restenosis rate (Stenosis>50%) was 8% in our investigation, in the study done by Ellie Y. Chakhtoura et al. (22), the restenosis rate was 12%. In our registry, the occurrence of severe degrees of restenosis was rare (2%), but in most studies such as the study mentioned above (22), Restenosis after Carotid Angioplasty, Stenting, or Endarterectomy in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATUST) (25) and a secondary analysis of CREST (26), severe carotid restenosis was 8%, 18.5% and 6% respectively. Preliminary studies for safety assessment of CAS showed high rate of stroke and death (27-29) A randomized trial which compared CAS with CEA for symptomatic carotid stenosis came to an end due to the high rate of stroke and death (71%) (30). It was reported that the cause of this could be due to limited experienced interventionist in doing CAS, often using balloon expandable stent and inadequate antiplatelet therapy. In current times, increasing operator experience and using self-expandable stent has led to better results and low complication rates. Therefore, we suggest that CAS can be used as an alternative treatment method for patients who have many comorbidities. Regarding the limitations, the main limitation of this study is small sample size and 20% loss of follow-up of Carotid Doppler ultrasonography participants.
5. Conclusions
According to the results, although carotid stenting started in our center in more recent years, cardiovascular complications can be comparable to those of other important studies. In high-risk patients, if performed by an expert operator, it can be associated with high success rates and low cardiovascular complications. Also, this procedure is less invasive and better tolerated, and can be performed with local anesthesia. CAS is also a safe and effective method compared to CEA for the treatment of patients with carotid artery stenosis with more surgical comorbidities. In the near future, a rapid shift to CAS is expected.

Acknowledgments:
We appreciate the kind help of the catheterization laboratory of Chamran Hospital, Isfahan, Iran.

Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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