Endovascular Stenting with Drug-Eluting Stent for Symptomatic Ostial Vertebral Artery Stenosis

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Abstract: Objective: To evaluate the safety and efficacy of endovascular treatment with drug-eluting stent for symptomatic atherosclerotic ostial vertebral artery (VA) stenosis. Methods: Seventeen symptomatic patients (average age, 70.7±5.6 years) with 17 ostial vertebral artery lesions received 17 balloon-expandable drug-eluting stents. Follow-up angiography was performed when restenosis was suspected or during later catheterization for other indications. Restenosis was defined as 50% diameter narrowing. Results: The degree of stenosis ranged from 75% to 98% (mean 81 ± 5.2%). The technical success rate was 100%. Procedure-related complication rate, mortality rate, and permanent neurologic morbidity rate at 30-day follow-up were 0%. At 12-months follow-up, no patient was reported of having recurrent vertebrobasilar ischemic symptoms and all VA restenosis was ＜50%. Conclusion: This pilot study suggests that use of drug-eluting stents in angioplasty to treat symptomatic atherosclerotic ostial VA stenosis is feasible and promising in terms of potential safety and effectiveness on the prevention of recurrent ischemia and restenosis. These results could be helpful in the formulation of a larger prospective randomized controlled trial. [**Endovascular Stenting with Drug-Eluting Stent for Symptomatic Ostial Vertebral Artery Stenosis.** Life Science Journal. 2011;8(4):378-381] (ISSN: 1097-8135). http://www.lifesciencesite.com.

Key words: Vertebral Artery Stenosis; Drug-Eluting Stent; Stenting

1. Introduction

Approximately 20% to 25% of ischemic stroke are located in the posterior circulation involving the vertebrobasilar system (VBS) [1]. The prognosis for patients with atherosclerotic occlusion or thrombosis of the VBS is poor, with 80% to 100% mortality[2]. Medically refractory, symptomatic VBS disease carries a 5% to 11% incidence of stroke or death at 1 year[3]. Transient ischemic attacks (TIA) due to extracranial VBS disease are associated with a stroke rate of 30% at 5 years[4]. The Joint Study of Extracranial Arterial Occlusion examined 3,800 patients who presented for angiography due to symptomatic cerebrovascular disease and found a 40% incidence of veterbral artery (VA) stenosis and a 10% incidence of complete occlusion of either of the 1 vertebral artery[5]. The most frequently involved location of VA is ostium[6]. Endovascular intervention has been identified as an effective method for VB stenosis. Balloon angioplasty limited by elastic recoil and dissection, and restenosis rates reported in the literature was nearly 75%.[7] Stenting offers salvage following unsuccessful balloon angioplasty and primary stenting has been shown to be safe and effective[8]. However, the restenosis rate after stenting vary from 11.1% to 66.7%[9,10]. The major advantage of drug-eluting stent is to use the cytotoxic drug coatings on the stent to inhibit the occurrence of vascular restenosis due to intimal hyperplasia that is known to be associated with the use of stents. Drug-eluting stents are rationally superior to bare metal stents. The purpose of our study was to evaluate the feasibility and preliminary results of using paclitaxel-eluting stents for angioplasty and to treat symptomatic atherosclerotic ostial VA stenosis.

2. Methods

2.1 Study Design and Patient Population

With the approval of our institutional review board, a retrospective review of medical and radiological records was performed to identify patients referred to our tertiary center for endovascular treatment of symptomatic ostial VA stenosis refractory to adequate medication. The search identified 17 consecutive patients (11 men; mean age 70.7 years, range 54 to 88) who were treated with stent implantation for vertebral artery stenosis from March 2009 to October 2010. All patients presented with typical VBI symptoms (Table 1), such as severe dizziness, diplopia, vertigo, gait disturbance, or drop attacks, which was confirmed by a neurologist. Informed consent was obtained from every patient prior to the procedure, including follow-up angiography.

Table 1: Patient characteristics

	Male (n=11)	Female (n=6)
Age y	70±7	72±6
Hypertension	8	4
Diabetes	6	4
Hyperlipidemia	6	3
Smoking	7	1
Bilateral disease	2	1
Coronary artery disease	5	2
Symptoms		
Dizziness	7	3
Drop attack	2	0
Vertigo	2	1
Gait disturbance	3	1
Diplopia	5	2

2.2 Preprocedural Evaluation

The diagnosis of vertebral artery stenosis was made by cerebral angiography. Bilateral subclavian and nonselective vertebral artery angiograms were obtained to visualize the true vertebral ostium. The degree of stenosis in ostium was evaluated by using NASCET (North American Symptomatic Carotid Endarterectomy Trial) method (The diameter of a normal ipsilateral V2 segment was used as reference). The indications for stenting were: (1) diameter stenosis ＞ 75% in an artery with a reference diameter ＞3.5 mm or (2) diameter stenosis ＞50% in an artery with reference diameter ＞3 mm and contralateral occlusion. Lesions in an artery without continuation to the basilar artery or with severe stenosis beyond the V2 segment were excluded. Patients with severe stenosis in the basilar artery or its major branches were also excluded. Bilateral ostial vertebral artery stenting was allowed, as long as the stenting indications were fulfilled in individual lesions.

2.3 Stent Implantation

Procedural heparin was given at 70 U/Kg, and the activated coagulation time was kept at 250 to 300 seconds. A 6-F guiding catheter was placed via a femoral sheath into the proximal subclavian artery without engaging the vertebral ostium. A 0.014-inch coronary guidewire was carefully passed across the stenosis into the distal cervical vertebral artery, and no embolic protection devices were used in this series of patients. Predilation, if considered necessary by the operator, was done with an undersized coronary angioplasty balloon. A balloon-expandable drug-eluting coronary stent (Fire Bird Microport company, China) sized to match the reference diameter was positioned at the ostium and deployed at high pressure (9 to 12 atm). The goal was to achieve ＜ 20% residual stenosis, with complete lesion coverage. Aspirin (100 mg/d), combined with clopidogrel (75 mg/d), were started 5 days prior to stenting and was kept continued for 3 months.

2.4 Follow-up

All patients were followed for change in symptom and neurological status with monthly clinic visits. If new posterior stroke was suspected, CT or MRI was arranged for documentation. Recurrent VBI symptoms were carefully recorded and validated by a neurologist. Neck ultrasonography were done at 1 and 6 months post stenting to evaluate the stenosis of treated vessel by an independent neurologist. If restenosis was suspected, angiography was mandated to confirm the diagnosis. Vertebral angiography was also obtained in patients undergoing angiographic workup or intervention in other vascular territories, but no systematic angiographic follow-up was planned in the protocol. Angiographic restenosis was defined as diameter stenosis .50% at the stented site.

2.5 Statistical Analysis

The VA diameter, degree of stenosis, and length of the stenotic segment were measured, and the range, median, mean, and standard deviation were determined for each measurement. Since this was a single-arm study and the number of patients being small, statistical analysis was not performed.

3. Results

Technical success was 100%. The mean reference diameter was 4.0±0.6 mm and the pretreatment diameter stenosis was 92%±5% for the 17 target lesions. Predilation was done in only 22% (4/17) of the lesions before implantation of stents. No periprocedural death occurred. No patients suffered a periprocedural posterior stroke. One patient presented with nystagmus and severe vertigo just after stent implantation; of whom the MRI revealed multiple acute ischemic infarcts in the cerebellum, left thalamus, and bilateral occipital regions. The symptoms improved within 1 week, and no permanent neurological sequela remained thereafter. In the follow-up of angiogram 12 months later. One patient (5.9%) who had an episode of minor left hemispheric stroke 3 weeks prior to the procedure suffered from worsening right sided weakness on the day after the intervention. MRI revealed recent stroke in the left periventricular white matter, but no posterior infarction was found. The condition improved 5 days later, with complete neurological recovery. No patient had experienced recurrent vertebrobasilar stroke or transient ischemic attack at either the treatment-related vascular territory or the

treatment-unrelated vascular territory within 12 months follow-up after stenting. No patient had a VA restenosis of 50% or more. The degree of stenosis of the vessel lumen ranged from 0% to 45% (median, 25.5%; mean, 25.8% ±13.4). The management of stenting with drug-eluting stent is shown in Table 2. The degrees of VA stenosis measured before and immediately after stent placement and at 12-month follow-up of individual patients are shown in Table 3.

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Table 2: Angiographic Measurements in 17 Ostial Vertebral Arteries

Predilation	4
Balloon diameter, mm	3.8 ± 0.5
Reference vessel diameter, mm	4.0 ± 0.6
Lesion length, mm	8.2 ± 2.5
Initial diameter stenosis, %	81 ± 5.2
Stent diameter, mm	4.0 ± 0.5
Stent length, mm	11.6 ± 3.8
Residual stenosis, %	25.8 ±13.4

Table 3: Proportional Distribution of Degree of VAS before and after Stent Placement

	Degree of VAS			
	⩽25%	25% ～50%	50%～＜70%	⩾70%
Before stent placement	0	0	5	12
Immediately after stent placement	12	5	0	0
At 12-month follow-up	9	8	0	0

4. Discussion

The present study demonstrates the feasibility and relative safety of primary stenting for ostial vertebral artery stenosis using balloon expandable drug-eluting coronary stents exclusively. Ostial VA stenoses are highly elastic lesions that require stents with high radial force. Accurate positioning is also necessary for complete lesion coverage and avoidance of stent protrusion into the subclavian artery. The shape-recovery capability of self-expanding stents is very important in the mobile cervical carotid artery to avoid the stent displacement that has been reported with balloon-expandable stents.

Current experiences with angioplasty and stent placement in the treatment of extracranial vertebral stenosis have almost exclusively been based on the use of balloon-mount coronary stents. The rate of recurrent ischemic attacks after stent placement varied from 3.8% to 28.5% of patients for a mean follow-up period of 11 months to 20.7 months [11,12]. Restenosis of the vessel in which the stent was placed at angiographic follow-up is usually defined as a degree of luminal narrowing of at least 50% [12,13]. In a retrospective study, Gupta et al.[14] reported on the off-label use of drug-eluting coronary stents in the endovascular treatment of VA. However, the exact location of the lesions in the extracranial VA was not specified.

Our early results showed that both the rate of recurrent ischemic symptoms and the rate of vascular restenosis ＞50% stenosis were 0% at 12-month follow-up. Drug-eluting stents were considered a major medical advance when they first appeared. The drugs released by these stents reduce the risk of restenosis by limiting macrophage accumulation and smooth muscle cell proliferation around the stent. However, such actions also inhibit re-endothelialization of the stent surface, and investigators became concerned that persistent exposure of the stent could increase the risk of delayed stent thrombosis due to localized hypersensitivity and that delayed endothelialization might occur and lead to vascular restenosis at longer-term follow-up.[15]

Our study had some limitations, namely, the small number of patients and the short follow-up period. To evaluate the clinical value of drug-eluting stents as opposed to bare metal stents or medical therapy in the treatment of VA stenosis would require a randomized controlled trial of a much larger scale.

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