

Percutaneous Interventional Treatment of Extracranial Vertebral Artery Stenosis with Coronary Stents

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Stenosis of extracranial vertebral artery (VA) is not an infrequent lesion, and it can pose a significant clinical problem. However, the standard treatment for a significant VA stenosis has still not been established. Here in this study, we report our experiences of VA stenting in 25 patients (age 56.2 ± 15.2 years, male 76%). The patients had comorbidities as follows: DM (36%), hypertension (64%), Takayasu's (12%) and Behcet's diseases (4%). There were combined involvement of other vessels such as the coronary artery (72%), carotid artery (36%), subclavian artery (32%) and the contralateral vertebral artery (24%). Indications for stenting were prior stroke or symptoms related to vertebrobasilar ischemia in 11 patients, and an asymptomatic but angiographically significant stenosis ($>70\%$ stenosis) in 14 patients. Twenty-three balloon-expandable stents and two self-expandable stents were deployed. A drug-eluting coronary stent and distal balloon protection device were each used in one case. A technically successful procedure was achieved in all patients. The baseline reference diameter was 4.7 ± 1.3 mm, minimal luminal diameter (MLD) 1.0 ± 0.6 mm (diameter stenosis $77.8 \pm 12.5\%$) and lesion length 6.4 ± 3.9 mm. After stenting and adjuvant dilation, the MLD was increased to 4.5 ± 0.9 mm (diameter stenosis $3.1 \pm 17.9\%$). There were no procedure-related complications. During the further follow-up period of 25 (3-49) months, no stroke or death occurred. Restenosis was observed in 4 (30.8%) of 13 eligible patients. In conclusion, VA stenting is feasible with a high degree of technical success, and this treatment is associated with a relatively low incidence of procedure-related complications. However, a relative high rate of in-stent restenosis remains as a problem to be resolved.

Key Words: Vertebral artery, vertebrobasilar artery insufficiency, percutaneous transluminal angioplasty, stenting

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INTRODUCTION

Vertebral artery stenosis is frequently encountered in the patients undergoing coronary or aortic arch angiography, and its incidence has been reported to be up to 20-40% in certain patient populations.^{1,2} However, its correlation with ischemia of vertebrobasilar system is not commonly accepted because most patients can tolerate occlusion of one of the two vertebral arteries. Often however, vertebrobasilar artery insufficiency is not recognized because these patients have only nonspecific symptoms or isolated spells of dizziness.³ Especially in the patients with combined stenosis of the carotid artery system or contralateral vertebral artery, the risk of posterior cerebral ischemia is higher, although these patients generally remain asymptomatic. In addition, there are indications that progressive disease will lead to vertebrobasilar ischemia and stroke. The risk of disease progression and development of a posterior fossa stroke within 5 years is estimated to range between 20% and 60%.⁴ Also, the risk of in situ thrombus formation and distal embolization remains a potential problem for patients with compensated brainstem perfusion from the contralateral vertebral artery.^{5,6} Therefore, the significance of the VA stenosis may be underestimated in current clinical practice.

Clinically significant vertebral artery stenosis has been treated with medical treatment or surgical procedures. However, the efficacy of medical management consisting of antiplatelet or anticoagulation medications is uncertain at best. Surgical procedures are associated with relatively high

rates of mortality (4.2%)⁷ and complications (10-20%) such as nerve injuries and pulmonary problems from thoracotomy.^{8,9} Reports on percutaneous endovascular management of vertebral artery stenosis have been sporadic, and most of these studies have included only a small numbers of clinically heterogeneous patients; but these studies have demonstrated good procedural results.¹⁰⁻¹³ In our present study, we report on our experience for extracranial vertebral artery stenting in our institution.

MATERIALS AND METHODS

Patient population

Between January 1997 and October 2003, 25 patients (25 vessels) underwent vertebral artery stenting at Yonsei Cardiovascular Center. There were 16 males and 9 females, and their ages ranged from 21 to 72 (mean 56.2 ± 15.2) years.

The study population included symptomatic patients found to have vertebral artery stenosis, and we also included asymptomatic patients with significant vertebral artery stenosis incidentally found on angiographic studies. Significant angiographic stenosis was defined as $> 70\%$ diameter stenosis when the stenotic artery was compared to the distal reference vessel diameter.

All patients underwent diagnostic aortic arch and four-vessel angiography that included selective carotid and vertebral angiography as well as brain magnetic resonance imaging or computerized tomography with contrast. An independent neurologic evaluation was performed on all patients before and after vertebral artery intervention.

Diagnostic angiography and vertebral artery intervention

Diagnostic angiography and vertebral artery intervention were performed via the femoral approach in all patients. Selective angiography of the target vessel was carried out using a 5 F Judkins right-4, internal mammary artery or multipurpose-shaped diagnostic coronary catheter.

For the vertebral artery intervention, a 7 F long sheath was advanced over a long diagnostic catheter just prior to the vertebral artery origin. The stenotic lesion of the vertebral artery was crossed with a floppy-tipped 0.014 inch coronary guide wire. The lesions (n=22) were dilated with a coronary balloons (2.5-4.0 mm diameter) before the stent placement. All the lesions were treated with balloon-expandable tubular type (n=23) or self-expandable coronary stents (n=2). After stent deployment, postdilation was performed, if indicated, with a high-pressure non-compliant balloon (n=11). Fig. 1 shows the angiograms of a stenotic left

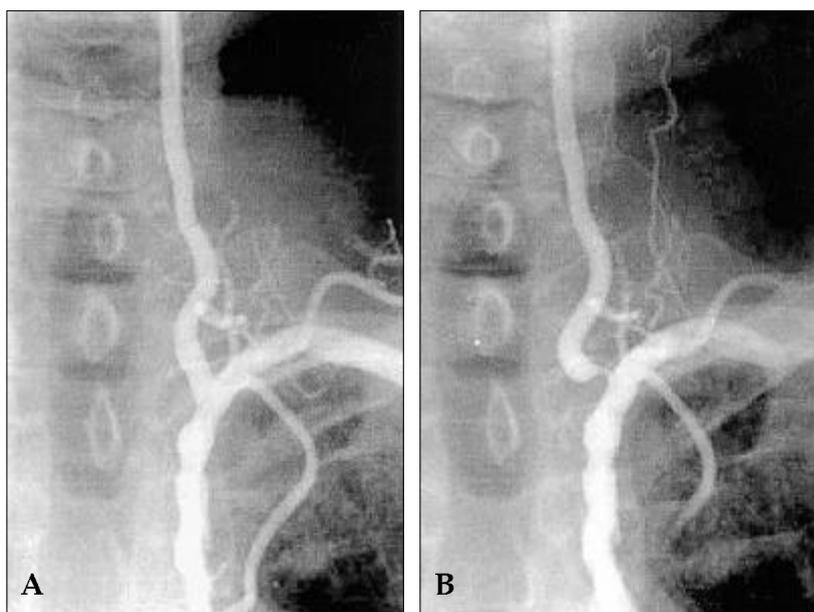


Fig. 1. Angiograms demonstrating left vertebral artery ostial stenosis (A) and the final appearance of the vertebral artery after stenting (B).

vertebral artery before and after stenting. In one patient with suspected thrombi, a distal balloon occlusion protection device (PercuSurge Guard Wire, Medtronic AVE, Santa Rosa, California) was applied.

All patients received aspirin 100 mg daily and ticlopidine 500 mg or clopidogrel 75 mg daily for at least two days prior to the VA intervention. This combination therapy of antiplatelet agents was continued for at least for 4 weeks. Thereafter, only aspirin was given. 5,000 to 10,000 units of intravenous heparin were administered after arterial access to maintain an activated clotting time ≥ 200 seconds.

Endpoint and data analysis

All clinical, laboratory and angiographic data were entered to a standard database. Patients were followed at 1 month after their discharge from the hospital and regularly thereafter at every 3 months. The clinical endpoints were any minor or major stroke, myocardial infarction, or death within the first 30 days and 6 months. Major stroke was defined as a new neurologic deficit that persisted 30 days after the stroke or an increase on the National Institute of Health Stroke Scale (NIHSS) score of four points or more. Minor stroke was considered if a new neurologic deficit resolved within 30 days, or if there was increases of the NIHSS scores of less than three points. Myocardial infarction was defined as the development of new pathologic Q-waves or elevation of creatinine kinase to more than twice the normal value or the cardiac troponin T value was over 0.1 ng/mL. Angiographic success was defined as $\leq 20\%$ residual stenosis after stent placement and postdilation. Restenosis was defined as a stenosis of $\geq 50\%$ upon the follow-up angiogram.

RESULTS

Patients characteristics

Nine patients (36%) had type II diabetes mellitus and 16 patients (64%) had hypertension. Most patients (88%) showed the combined involvement of other vessels as follows: coronary

artery (72%), carotid artery (36%), subclavian artery (32%) and contralateral vertebral artery (24%). Vertebral artery stenosis was associated with Takayasu's disease in 3 patients and with Behcet's disease in one patient. Indications for vertebral artery stenting were a prior stroke in 5 patients, symptoms related to vertebrobasilar ischemia (≥ 2 episodes of dizziness or vertigo attacks) in 6 patients, and asymptomatic but angiographically significant stenosis ($> 70\%$ stenosis) in 14 patients. Of the 14 asymptomatic patients, 8 patients had combined carotid, subclavian or contralateral vertebral artery stenosis, and 2 patients underwent vertebral stenting prior to a planned coronary artery bypass graft. The patient clinical characteristics and demographics are shown in Table 1.

Table 1. Baseline Patient Characteristics

Characteristics	Number	%
Patients	25	100%
Mean age (year)	56.2 \pm 15.2	
Male	16	64%
Diabetes	9	36%
Hypertension	16	64%
Hypercholesterolemia	10	40%
Smoker (within 1 year)	9	36%
Takayasu's arteritis	3	12%
Behcet's disease	1	4%
Stroke or symptoms*	11	44%
Bilateral vertebral artery disease	6	24%
Coronary artery disease	18	72%
Carotid artery disease	9	36%
Subclavian artery disease	8	32%

*Stroke or symptoms related to ipsilateral stenotic vertebral artery.

Angiographic results

Most lesions (88%) were located at the ostium and the other lesions were located in the proximal proportion of vertebral artery. A technically successful procedure was achieved in all patients.

The mean reference diameter was 4.7 ± 1.3 mm, the mean baseline MLD was 1.0 ± 0.6 mm (diameter stenosis $77.8 \pm 12.5\%$) and mean lesion length was 6.4 ± 3.9 mm. After stenting and adjuvant dilation, the MLD was increased to 4.5 ± 0.9 mm (diameter stenosis $3.1 \pm 17.9\%$). Twenty-two of the lesions (88%) were treated with balloon predilatation. Balloon expandable tubular type stents were implanted at 23 lesions (92%) and self-expandable stents were implanted at two lesions via the femoral artery approach. A drug-eluting coronary stent was deployed in one case. Follow-up angiography was performed in 13 patients (52%) at 22 ± 6 months after vertebral stenting. In-stent restenosis was documented in 4 (30.8%) patients and these lesions were asymptomatic. One of these patients with in-stent restenosis had Takayasu's arteritis. The mean MLD at follow-up angiography was 2.3 ± 1.0 mm (diameter stenosis $43.3 \pm 26.1\%$). The angiographic characteristics and results are shown in Table 2.

Clinical outcome

No immediate neurological problems or other procedure-related complications occurred after vertebral artery stenting. No stroke, death or myocardial infarction occurred at 30-day follow-up. Twenty-two of 25 patients were eligible for clinical follow-up at 25 (3-49) months. During this period of further follow-up, one patient developed a left major cerebral artery infarction at 19 months and another patient developed a right posterior cerebellar infarction at 32 months after vertebral artery intervention. The patient with right posterior infarction previously had right

vertebral artery stenting; however, this patient refused the angiography follow-up. There was no myocardial infarction, but one patient died due to stomach cancer at 32 months.

DISCUSSION

The most common cause of vertebral artery stenosis is atherosclerosis, and the less frequent etiologies are vasculitis, vertebral artery dissection, extrinsic compressions, etc.¹⁴ Our study included mostly atherosclerotic lesions, but there were also three cases with Takayasu's arteritis and one case with Behcet's disease. Most lesions were located at the origin or proximal proportion of the vertebral arteries and were accompanied by stenosis of other vessels such as carotid, subclavian and coronary arteries. Although the majority of the subjects in this study were asymptomatic, we performed percutaneous interventional treatment of vertebral artery stenosis because the risk of further progression of vertebral artery lesion, and the risk of stroke was considered to be increased due to the involvement of multiple vessels. Furthermore, despite the possible differences in plaque appearance between extracranial vertebral and internal carotid artery disease, it is generally considered that the two sites share a common pathogenesis resulting from the formation of emboli at the site of the atherosclerotic plaque. Hemodynamic stroke due to vertebral artery stenosis, however, occurs less frequently.¹⁵

The standard therapy of symptomatic vertebral artery stenosis has been empirical medical treat-

Table 2. Angiographic Characteristics and Results

Reference diameter	4.7 ± 1.3 mm
Lesion length	6.4 ± 3.9 mm
MLD, baseline (% diameter stenosis)	1.0 ± 0.6 mm ($77.8 \pm 12.5\%$)
MLD, poststent (% diameter stenosis)	4.5 ± 0.9 mm ($3.1 \pm 17.9\%$)
Patients at angiographic follow-up	N=13 (52%)
MLD, follow-up (% diameter stenosis)	2.3 ± 1.0 mm ($43.3 \pm 26.1\%$)
In-stent restenosis*	n=4 (30.8%)

MLD, minimal lumen diameter.

*In-stent restenosis: $\geq 50\%$ diameter stenosis.

ment including antiplatelet agents or systemic anticoagulation, but its efficacy remains at best uncertain.¹⁴ Surgical management options such as endarterectomy or reconstruction are associated with considerable mortality and complication rates.^{7,8} There have been several reports on the percutaneous interventional treatment of vertebral artery stenosis. The largest trial of balloon angioplasty procedure alone was conducted by Higashida et al.¹⁰ They showed that 8.8% of the 34 patients included in their study developed transient neurologic complications after PTA without permanent neurologic deficits. Chastain et al.⁶ performed vertebral artery stenting in 55 vessels of 50 patients, and they reported a success rate of 98% and no procedure-related complications. Jenkins et al.¹¹ investigated the efficacy of vertebral artery stenting in 38 vessels of 32 patients. One patient (3%) experienced a transient ischemic attack after the procedure. Another trial reported by Albuquerque et al.¹² (n=33) also showed a high technical success rate (97%) and a low incidence of complications. Therefore, it can be concluded that vertebral artery stenting with a low incidence of complications is feasible and the outcome of vertebral artery stenting is more favorable compared to that of balloon angioplasty alone. This reduction of thrombus formation and thromboembolism is believed to be due to a protective layer of fibrous and neo-intimal tissue overgrowing the stent mesh and covering the atherogenic tissues of the vessel wall. Also, the complications due to intimal dissection by angioplasty can be reduced by stent deployment.^{6,11,14}

There are, however, discrepancies in different studies regarding the restenosis rates after vertebral artery stenting. Chastain et al.⁶ reported a restenosis rate of 10% at 6-month angiographic follow-up, which was available in 90% of the eligible patients. The restenosis rate was 3% in the study by Jenkins et al.¹¹ In contrast to these reports, Albuquerque et al.¹² observed a significantly higher restenosis rate (43.3%), which is comparable to the result of our investigation. As possible explanations for the different restenosis rates, Albuquerque et al.¹² suggested that several factors were responsible such as the small numbers of included patients, differing patient spectrums regarding disease severity, different time

points of angiographic follow-up and the influence of bias on the data analysis. More patients with symptoms (91% vs. 78%) and contralateral vertebral artery disease (82% vs. 54%) had been included in their study compared to those of Chastain et al.,⁶ and angiographic follow-up was carried out at a later time point (6 vs. 16.2 months). In our study, the proportion of patients with vertebrobasilar ischemic symptoms or bilateral vertebral artery stenosis was much lower than those of the both other studies. However, most of the patients enrolled in our study showed the combined involvement of other vessels (88%). Also, a follow-up angiography in our study was obtained at a later time point (22.0 months) than the study of Chastain et al.⁶

There are also other factors such as the vascular nature and angioarchitecture of the vertebral arteries that could contribute to a higher restenosis rate. Since the diameter of a vertebral artery ranges from 3 to 5 mm in general, most of the proximal vertebral artery lesions are thought to behave like coronary or renal artery ostial lesions having higher recoil forces and higher shear stress.^{12,14} Furthermore, the straightening of the tortuous vertebral origin by placement of stents may accelerate a restenosis because of possible change of blood flow and greater vessel wall injuries caused by the stenting.¹³ Therefore, drug-eluting stents or technically improved stent devices may help to significantly reduce the restenosis rate after vertebral artery stenting. In our study, a sirolimus-eluting stent was implanted in one patient. Follow-up angiography obtained 6 months after vertebral stenting showed no detectable restenosis in this patient.

The major concern in the endovascular treatment of vertebral artery stenosis is the risk of embolism during the procedure, although there have been no reports of procedure-related permanent stroke or death. The use of protection devices such as PercuSurge GuardWire in one of our cases can minimize possible complications due to distal embolization during the procedure.

The present study was a non-controlled single-arm study with a small number of subjects and a relative low rate of angiographical follow-up. Despite these major limitations, the results of this study serve to deliver a significant message. As

previous trials have reported,^{6,12,13} vertebral artery stenting can be carried out safely with a low complication rate. However, the in-stent restenosis rate at mid- or long-term follow-up was found to be relatively high, and the rate of this complication needs to be reduced by drug-eluting stents or technical improvement of stent design in the future.

The most controversial issue remaining about vertebral artery stenosis is which patients need to have interventional or surgical management. Since most of in-stent restenosis reported in the literatures are not associated with symptom persistence or recurrence, the indications for vertebral artery stenting should be defined and standardized.^{6,12,13} However, considering the fact that many of the patients who are believed to be asymptomatic may actually have nonspecific symptoms, and that risk of in situ thrombus formation and distal embolization is not eliminated by adequate collateral flow,^{5,6} vertebral artery stenosis may be underestimated and undertreated in current clinical practice. Therefore, large scale epidemiologic studies are necessary to address this issue, and prospective randomized data comparing medical treatment and interventional management of vertebral artery stenosis are essential to resolve this problem.

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