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Original Article

Evaluation of Clinical and Radiological Results of the Perioperative and Postoperative Periods in the Endovascular Treatment of Vertebral Artery Stenosis

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ABSTRACT

Objective: The purpose of this study was to showcase the outcomes of endovascular treatment, assessing its safety and efficacy for patients with symptomatic severe atherosclerotic stenosis of the vertebral artery, who did not respond to medical management and were treated at our institution.

Methods: We performed a retrospective analysis on patients who had suffered a transient ischemic attack or ischemic stroke and received endovascular treatment for symptomatic vertebral stenosis despite being under medical care. The endovascular techniques utilized were cataloged as angioplasty alone, balloon-mounted stenting, or angioplasty with subsequent self-expanding stent insertion. We recorded both peri-procedural complications, such as in-stent thrombosis, dissection, and guide wire perforation, as well as post-procedural complications, including stroke and transient ischemic attack. The study focused on analyzing the endovascular treatment methodologies alongside clinical and radiological outcomes.

Results: From January 2020 to December 2022, 15 patients were treated, including 6 with V1 segment stenosis, 2 with V2, and 7 with V4 segment stenosis. The rate of successful stent placement was 100% (15 out of 15). Six patients (40%) received a balloon-expandable stent in addition to angioplasty, while the remaining nine (60%) were treated with a self-expanding stent following angioplasty. No peri-procedural complications were reported in patients who had extracranial stenting. However, during intracranial stenting, complications occurred in two cases: one patient had a dissection leading to occlusion of a perforator artery, and another experienced stent thrombosis. These complications resulted in ischemic strokes and subsequent mortality during hospitalization in two patients (13% of the cohort). The median follow-up duration was 15 months, with an interquartile range of 9 to 24 months. An improvement in the modified Rankin Score was noted in 10 patients, while no change was observed in 3 patients.

Conclusion: Our findings advocate for the safety and probable efficacy of endovascular treatment in patients with vertebral artery stenosis who are non-responsive to optimal medical therapies. Stenting, particularly for extracranial vertebral artery stenosis, can be performed with a low rate of complications and is deemed safe.

INTRODUCTION

Posterior circulation strokes account for approximately 20% of all ischemic strokes. Atherosclerosis of the posterior circulation arteries is also responsible for 25% of these strokes.[1,2] The Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) study showed that stroke rates at the same site as the stenotic artery were 10.7% in patients with basilar artery stenosis and 7.8% in patients with vertebral artery (VA) stenosis, with a twofold increase in stroke risk in patients with stenosis >70%.[1,2,3]

Treatment of symptomatic VA stenosis includes medical, surgical, and endovascular treatments. The stenosis site of the VA is mostly proximal to the artery. Surgical intervention on the VA in this region is technically challenging due to limited access to the vascular origin, thus it is often considered an unfeasible option.

Endovascular treatment (ET) of the VA stenosis comprises percutaneous transluminal angioplasty with or without stent deployment. Well-known international studies have demonstrated that stenting for symptomatic carotid stenosis can be effective in selected patients. However, the most effective approach to managing individuals with symptomatic VA stenosis has not yet been determined.

In patients with severe vertebral artery stenosis, despite standard medical treatments including antiplatelet agents and statins, the risk of recurrent stroke within 90 days may increase up to 33%.[4] Hence, aggressive treatment is of significant importance in the prognosis of patients. On the other hand, endovascular treatments are hopeful methods in these patients who do not respond to the best medical therapy (BMT). However, appropriate patient selection is important because of outcomes such as procedural stroke, intracranial hemorrhage, and death. In studies involving case series, it has been demonstrated that angioplasty and/or stenting can be effective treatment options in VA stenosis, and stenting has very low complication rates of 1-1.5%, particularly for Extracranial VA stenosis. This rate has been reported to be approximately 7-10% in intracranial vertebral artery stenosis. While examining randomized controlled trials, it is noteworthy that a clear consensus has not been reached.[2,4]

The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) study has reported worse outcomes for stenting compared to BMT in patients with stenosis in various intracranial cerebral arteries. The Vertebral Artery Stenting Trial (VAST) study, which included patients with intracranial and extracranial VA stenosis, found no significant difference between stenting and BMT.[2-4] However, the Vertebral Artery Ischaemia Stenting Trial (VIST) study concluded that stenting is effective and reliable, particularly in cases of extracranial vertebral artery stenosis. The variability in study outcomes can be attributed to several factors such as differences in the location and severity of stenosis, variations in devices and procedural techniques employed, and the level of experience of the operators.[2-4]

The aim of our study was to share the perioperative and postoperative outcomes, complication management, clinical and radiological results of patients who underwent endovascular treatment due to severe extra and intracranial vertebral stenosis.[2,5,6]

MATERIALS AND METHODS

This study was conducted prospectively and analyzed retrospectively between January 2020 and December 2022. Patients aged 18–85 who exhibited symptoms of transient ischemic attack (TIA) or mild stroke in the posterior circulation and had a 70% or greater degree of stenosis in the vertebral artery due to atherosclerotic disease were included in the study consecutively. Other inclusion criteria involved a recent non-disabling stroke or TIA that occurred within 90 days in the VA vascular territory, refractory to standard medical therapy, and stroke or TIA recurrence due to severe stenosis of the VA under intensive risk factor control, such as hypertension and diabetes mellitus. The symptomatic duration was determined as 3 months, based on data indicating the highest stroke risk within this period.

Exclusion criteria included:[1] VA artery stenosis caused by dissection;[2] non-atherosclerotic stenosis;[3] known contraindications to heparin, aspirin, clopidogrel, anesthesia, and contrast agents;[4] pregnancy and lactation in women;[5] a life expectancy of less than 1 year due to other medical conditions. The study was approved by the institutional ethics committee on 19/07/2023. The study procedure was conducted in accordance with the Declaration of Helsinki and regulations for human studies.

Management of risk factors, antiplatelet therapy, and lipid-lowering therapy formed the basis of medical treatment, with individual treatments for comorbidities such as hypertension or diabetes also being important. The recommended antiplatelet therapy for the procedure was a combination of clopidogrel and acetylsalicylic acid. If not already on dual therapy, a loading dose of 300-600 mg of clopidogrel was administered at least 12 hours before the procedure. Resistance to acetylsalicylic acid and clopidogrel was assessed in all patients prior to the procedure.

Endovascular treatment (ET) options included angioplasty alone, the placement of a balloon-mounted stent, and the placement of a self-expanding stent with angioplasty. Clinical complications such as stroke, transient ischemic attack (TIA), and mortality were recorded following the procedures.

The primary outcome was the occurrence of ischemic or hemorrhagic stroke, TIA, or death related to the endovascular procedure during hospitalization. The secondary outcome included successful revascularization (residual stenosis <30%) and periprocedural complications such as vessel dissection, stent dislocation, or acute stent occlusion noted on the 90th day following stenting.

The primary safety outcome encompassed a combination of stroke within 30 days post-randomization, TIA in any region between 2 and 30 days, all-cause mortality within the first 30 days post-procedure, and intracranial hemorrhage within 30 days post-randomization.

Dual antiplatelet therapy was continued for a minimum of 3 months following ET. Clinical evaluation was performed by two independent interventional neurologists who assessed the patients immediately before treatment, at discharge, and at 3 months.

The National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) were used for assessment. Stenosis was gauged based on the distal normal vessel diameter as defined by the North American Symptomatic Carotid Endarterectomy Trial (NASCET).

Statistical Analysis

Continuous variables were expressed as median and in-

Table 1. Patient clinical and technical results

Case	Clinical before procedure	Age/Sex	Vessel	Contralateral stenosis or occlusion	Stenosis before procedure (%)	Restenosis	Stent	Diameter (mm)	Intervention method	MRS before	MRS in 3 months
1	Stroke	70/M	V1	YES	85	0	CS	3.5	Balloon mounted stent	1	0
2	Stroke	67/M	V1	YES	95	0	CS	3.0	Balloon mounted stent	1	0
3	Stroke	69/M	V1	YES	70	0	CS	3.5	Balloon mounted stent	3	1
4	Stroke	68/M	V1	YES	90	0	CS	4.0	Balloon mounted stent	3	1
5	Stroke	67/M	V1	NO	80	0	CS	3.5	Balloon mounted stent	2	0
6	TIA	80/M	V1	YES	85	0	CS	3.0	Balloon mounted stent	0	0
7	Stroke	49/M	V2	YES	90	0	ICS	4	Self-expending stent	3	1
8	TIA	79/M	V2	YES	80	0	ICS	4	Self-expending stent	0	0
9	Stroke	68/F	V4	YES	80	1	ICS	4	Self-expending stent	1	0
10	Stroke	43/M	V4	YES	90	0	ICS	4	Self-expending stent	6	6
11	Stroke	51/M	V4	YES	75	0	ICS	4	Self-expending stent	6	6
12	Stroke	54/M	V4	YES	95	0	ICS	4	Self-expending stent	0	0
13	Stroke	71/M	V4	YES	80	0	ICS	3	Self-expending stent	3	1
14	Stroke	67/M	V4	YES	90	0	ICS	4	Self-expending stent	1	0
15	Stroke	72/M	V4	YES	80	0	ICS	4	Self-expending stent	2	0

CS: Coronary stent (Alvimedica); ICS: Intracranial stent (Neuroform Atlas, Stryker, California, USA); TIA: Transient ischemic attack.

terquartile range (IQR), and categorical variables as n (%). Statistical analyses were performed using IBM SPSS Statistics Software version 21 (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the 15 patients who experienced a stroke or TIA due to VAS, 14 were male with a median age of 68 years (IQR 60.5–70.5). Of the 9 patients with extracranial VAS stenosis, 7 were located in the V1 segment, 2 in the V2 segment, and all 6 intracranial stenoses were in the V4 segment. Patient data, along with clinical and technical results, are summarized in Table 1.

The rate of successful stent deployment was 100% (15/15). The overall complication rate, considering all adverse events, was 13% (2/15). Complications included one case of dissection following balloon angioplasty during the procedure (Case 10), and one instance of stent thrombosis (Case 11), both occurring in patients with V4 segment stenosis. Within 24 hours post-procedure, two ischemic events were noted: one related to stent thrombosis and the other to perforator injury subsequent to dissection. The patient with stent thrombosis suffered extensive ischemia involving the pons and medulla oblongata and succumbed to bulbar ischemia, while the patient with perforator injury also died during hospitalization.

Balloon-mounted stents were utilized in 6 patients with V1 stenosis (6/6, 100%), and self-expanding stents were used in all patients with V2 (2/2, 100%) and V4 stenosis (7/7, 100%) (Figure 1 and Figure 2). In one instance of V4 stenosis (Case 9), a restenosis rate of 60% was observed, yet retreatment was not deemed necessary during follow-

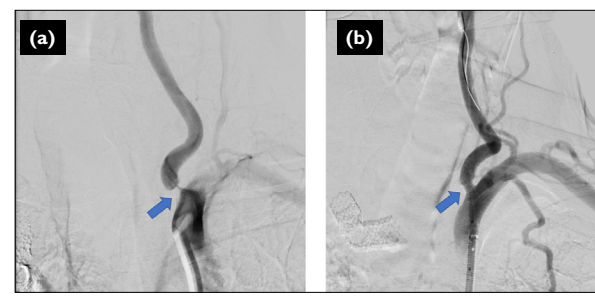

Figure 1. Angiographic Imaging Findings of a Patient with Proximal Vertebral Artery Stenosis Before and After Treatment, **(a)** Preprocedural left subclavian artery angiography from the frontal oblique view reveals high-grade ostial stenosis in the left vertebral artery (indicated by a blue arrow). **(b)** Postprocedural control angiography following primary stent placement with a balloon-mounted stent shows adequate restoration of the vessel lumen.

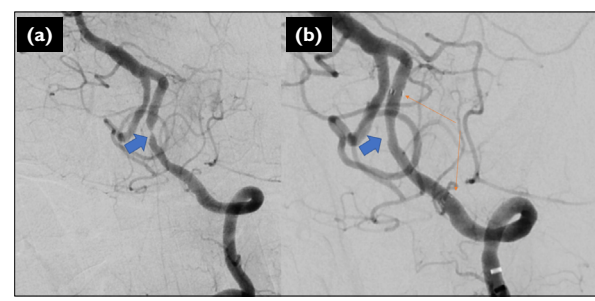

Figure 2. Angiographic Imaging Findings of a Patient with Distal Vertebral Artery Stenosis Before and After Treatment **(a)** Preprocedural intracranial angiogram of the left vertebral artery in the anterior view displays high-grade distal V4 stenosis. **(b)** Postprocedural control angiography illustrates significant improvement in the distal V4 stenosis of the vertebral artery (highlighted by a blue arrow). The proximal and distal ends of the stent are denoted by orange arrows.

up. Two patients who underwent self-expanding stenting for V4 stenosis experienced complications related to the interventional technique (2/7, 29%), one of which was dissection due to balloon angioplasty.

For patients who survived, the median follow-up duration was recorded as 15 months (IQR 9–24). During post-treatment follow-up, these patients did not develop new infarcts nor did they exhibit any worsening in NIHSS scores. The mRS scores of the 13 surviving patients showed improvement over the three-month follow-up period.

DISCUSSION

The clinical and treatment processes related to extracranial and intracranial segment stenosis of the vertebral artery differ. VA stenosis most commonly occurs at the orifice, specifically in the V1 segment, which is why there is more experience and research on extracranial vertebral artery stenosis. Stenting for extracranial VA stenosis demonstrates a 1% complication rate. In our study, none of the 8 patients with extracranial VA stenosis developed major or minor complications.[2,7,8]

The technical failure rate for endovascular treatment of vertebral artery extracranial segments is generally low.[9] Challenges are more likely in patients with anatomical complexities, such as those with a type 3 aortic arch or tortuous subclavian artery. Both intracranial and extracranial interventions have been shown to be effective.[9]

Percutaneous transluminal angioplasty (PTA) was the initial endovascular procedure of choice for treating vertebral artery stenosis.[9] However, high restenosis rates post-PTA have been reported. Cloud et al.[10] found restenosis rates of up to 100% in patients treated with balloon angioplasty alone. Stayman et al.[3] reported nearly identical rates of TIA and stroke at 0.8% and 1.1%, respectively, in 993 patients who underwent PTA and stenting, leading to a preference for combining stenting with PTA.[9,10] We applied both PTA and stenting to all our patients.

For extracranial VAS treatment, pre-dilation with a smaller balloon catheter than the lesion followed by stenting is common. The stent choice depends on the vertebral artery's diameter, ranging from 3 to 6 mm. Coronary stents are suitable for VA in terms of diameter and flexibility, but their radial force is not optimal. They are preferred for short segment stenosis like orifice lesions.[9,11] In our patients with V1 stenosis, we initially performed PTA, followed by placement of a balloon-expandable coronary stent.

Due to the vertebrobasilar junction, basilar artery stenosis and V4 segment stenosis are frequently observed simultaneously, presenting higher risks of morbidity and mortality. However, variability in these rates exists across studies due to factors such as sample size, stenosis severity, presence of contralateral stenosis, endovascular technique, and operator experience. For instance, the SAMMPRIS and VISSIT trials showed primary outcome rates of 14.7% and 24.1% within 30 days.[2] A comprehensive meta-analysis covering 23 studies indicated a stroke recurrence or death risk of 8.9 per 100 person-years in the endovascular group.[9,10] In our study, stroke and mortality were observed in two hospitalized patients.

Intracranial arteries are more vulnerable as they contain fewer elastic fibers, traverse the subarachnoid space, and lack surrounding protective tissue. Hence, vessel rupture or perforation may occur during intracranial PTSA due to microwire manipulation or excessive balloon inflation. The risk of vessel rupture significantly increases with rapid balloon inflation or use of unsuitably sized balloons or stents.[12,13] One of our intracranial cases experienced an ischemic event following PTSA due to dissection and related perforator artery occlusion.

In-stent restenosis is another potential complication. Factors such as stent type, initial vertebral artery segment tortuosity, atherosclerotic lesion length, smoking, and diabetes can elevate restenosis rates. A meta-analysis of 9 non-randomized studies showed significantly lower restenosis rates (8.2%) with drug-eluting stents (DES) compared to bare-metal stents (BMS) (23.7%).[9] Additionally, a direct correlation between restenosis and recurrence of VBI symptoms has not been established. Patients with restenosis often remain asymptomatic during follow-up.[14] After a median follow-up of 2.5 years, VA stenting was shown to provide lasting symptomatic relief in roughly 70% of patients. No recurrent symptoms or complaints were reported by our patients during a 15-month follow-up period.[15] Significant improvement in mRS scores was observed post-procedure and at the 3-month follow-up.

Conclusion

Current literature has not yet proven the superiority of endovascular therapy over medical therapy. With optimal medical management, angioplasty and stenting might be a safe approach for managing recurrent strokes in extracranial vertebral artery stenosis. In cases of intracranial vertebral artery stenosis, patient selection should be particularly cautious, especially due to the risk of perforator artery occlusions.

Ethics Committee Approval

This study approved by the Dr. Lutfi Kırdar City Hospital Ethics Committee (Date: 19.07.2023, Decision No: 2023/5141254/30).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.G., A.O.; Design: E.G., A.O.; Supervision: E.G.; Fundings: A.O.; Materials: A.O.; Data: A.O.; Analysis: E.G., A.O; Literature search: E.G., A.O; Writing: A.O.; Critical revision: E.G.

Conflict of Interest

None declared.

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Vertebral Arter Stenozlarının Endovasküler Tedavisinde Perioperatif ve Postoperatif Dönem Klinik ve Radyolojik Sonuçlarının Değerlendirilmesi

Amaç: Bu çalışmanın amacı, merkezimize başvuran ve medikal tedaviye yanıt vermeyen, semptomatik ciddi aterosklerotik vertebral arter hastalığı olan hastalarda endovasküler tedavinin sonuçlarını sunmak, güvenliliğini ve etkinliğini araştırmaktır.

Gereç ve Yöntem: Medikal tedavi altında geçici iskemik atak veya iskemik inme geçiren, semptomatik vertebral arter stenozuna bağlı endovasküler tedavi uygulanan hastalar geriye dönük olarak analiz edildi. Uygulanan endovasküler yöntemler tek başına anjiyoplasti, balona monteli stentleme ve anjiyoplasti ardından kendiliğinden genişleyen stent yerleştirilmesi olarak kaydedildi. İşlem sırasında stent içi tromboz, diseksiyon, kılavuz tel perforasyonu gibi perioperatif komplikasyonlar ve inme, geçici iskemik atak gibi işlem sonrası komplikasyonlar kaydedildi. Endovasküler tedavi yöntemleri, klinik ve radyolojik sonuçlar analiz edildi.

Bulgular: Ocak 2020-Aralık 2022 tarihleri arasında V1 darlığı olan 6 hasta, V2 darlığı olan 2 hasta ve V4 darlığı olan 7 hasta olmak üzere toplam 15 hastaya endovasküler tedavi uygulandı. Başarılı stent yerleştirme oranı %100'dü (15/15). Bu hastaların 6'sına (%40) balon anjioplasti ardından balonla genişleyen stent, geri kalan 9 (%60) hastaya ise balon anjıoplasti ardından kendiliğinden genişleyen stent uygulandı. Ekstrakranial stent uygulanan hastaların hiçbirinde periprosedürel komplikasyon görülmedi. İntrakraniyal stentleme sırasında, bir hastada perforatör arterde diseksiyon ve bunun sonucunda tıkanma görülürken, başka bir hastada stent trombozu gelişti. Bu iki hastada komplikasyonlara bağlı iskemik inme gelişti ve hastanede yatış sırasında mortalite görüldü (2/15, %13). Hastaların ortanca takip süresi 15 aydı (çeyrekler arası aralık, 9-24). Modifiye Rankin Skorunda (mRS) 10 hastada iyileşme gözlenirken, 3 hastada değişiklik görülmedi.

Sonuç: Bu çalışma, optimal tıbbi tedaviye dirençli vertebral arter stenozu olan hastalarda endovasküler tedavinin güvenliğini ve potansiyel etkinliğini desteklemektedir. Özellikle ekstrakranial vertebral arter darlıklarında stentleme işlemi düşük komplikasyon oranları ile uygulanabilinir.

Anahtar Sözcükler: Komplikasyon; semptomatik vertebral arter stenozu; stentleme.