ORIGINAL RESEARCH

Long-Term Outcomes After Stenting in Extracranial vs. Intracranial Stenosis

Yi Zhang, MD, PhD; Yanan Hu, MM; Xiaochun Gu, PhD; Shuo Leng, MD; Degang Tang, MD; Jiayi Sun, BM; Jie Ding, PhD

ABSTRACT

Objective • The purpose of this pilot study is to explore the difference in safety and effectiveness after stenting in patients with extracranial or intracranial vertebral artery stenosis.

Methods • The study involved 26 patients treated with stents for ≥70% stenosis between January 1, 2017, and September 8, 2020. The patients were divided into intracranial and extracranial groups based on the location of the target vessel stenosis. The incidence of stroke or death within 30 days, long-term recurrence of ischemic symptoms, and restenosis during follow-up were monitored.

Results • Within 30 days, no stroke or death was observed in the 26 patients, During the follow-up period, the risk of recurrence of posterior circulation stroke or transient ischemic attack was 23.1% (6/26). Vascular-related complications were 5.6% vs. 12.5% (P = .529) in the intracranial vs. extracranial stenosis group. After 1 year, stroke or transient ischemic attack of posterior circulation was observed in 12.5% (1/8) vs. 16.7% (3/18) in the intracranial and extracranial stenosis group, respectively. The restenosis rate in the intracranial stenosis group was higher than the extracranial stenosis group (37.5% vs. 28.6%, P > .05). This trend was also found in the asymptomatic restenosis rate (25% vs. 7.1%, P = .527).

Conclusions • The study results showed that there was no significant difference in the safety and effectiveness after stenting in extracranial and intracranial vertebral artery stenosis, but intracranial vertebral artery stenosis has a low rate of symptomatic restenosis. Symptomatic restenosis may be an important problem that limits the efficacy of extracranial vertebral artery stenting. (*Altern Ther Health Med.* 2023;29(8):255-261).

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INTRODUCTION

Approximately 20% of acute ischemic strokes occur in the posterior circulation and 25% of posterior circulation ischemia is associated with atherosclerotic stenosis of the vertebrobasilar artery.[1] Despite the fact that symptomatic vertebral stenosis significantly increase the risk of early stroke recurrence, posterior circulation stroke or transient ischemic attack (TIA) diagnosis and treatment have received less attention than carotid ischemic events.[1] Stents are being utilized more frequently to treat stenosis in the aim of lowering the high risk of ischemia. Despite the ongoing search for optimal treatment, randomized trials in recent years have failed to demonstrate that stenting is more effective than best medicine treatment (BMT).[2,3] The Vertebral Artery Ischemia Stenting Trial (VIST), which included patients with both intracranial and extracranial vertebral artery (VA) stenosis, demonstrated that stenting in extracranial stenosis is both safe and has a low complication rate.[4] A similar result was observed in the clinical study of Wu-Qiang Che et al.[5] However, the results of Tanja Djurdjevic's study on high-risk symptomatic intracranial vertebrobasilar atherosclerotic stenosis after intravascular therapy showed that recurrent stroke was rare. 10% of patients experienced a recurrent stroke, and 6.7% had a posterior circulation transient ischemic attack during the 7-year follow-up period.[6] A small sample size study in China

had similar results, with a perioperative stroke rate of 1.11%, a posterior circulation TIA of 6.3%, and a posterior circulation mild stroke of only 3.8% during follow-up.[7] The real-world data from China shows that patients with symptomatic intracranial vertebrobasilar stenosis who receive percutaneous transluminal angioplasty and stenting (PTAS) have better functional outcomes and lower residual target vessel stenosis compared to patients who receive standard drug therapy.[8] Therefore, stenting may be advantageous in the long term for suitably selected individuals with vertebrobasilar atherosclerotic stenosis. These results appear to have rekindled interest in endovascular therapy among people who had become disillusioned with earlier clinical studies.

We believed that patients with intracranial vertebral stenosis had a greater risk of recurrent stroke or TIA than those with extracranial abnormalities.[9] It appears that the outcome of stent implantation differs depending on whether the stenosis is intracranial or extracranial. However, prior trials paid little attention to this and instead emphasized technological advancement. The purpose of this study was to determine whether patients with high-risk symptomatic vertebral atherosclerotic stenosis who had stenting experienced a long-term recurrence of symptoms, and whether the prognosis for patients with intracranial or extracranial stenosis was comparable. The ideal way to lessen the recurrence rate of ischemia episodes in the posterior circulation is further discussed.

METHODS

Patients and data collection

This is a single-center, retrospective, and pilot study. 29 individuals with extracranial and/or intracranial VA stenosis between January 1, 2017 and September 8, 2020 were analyzed at our institution (Figure 1). These patients were all treated with stents for ≥70% stenosis while the appropriate surgical procedure was selected by the same interventional physician. However, only 26 patients have undergone clinical follow-up, including one who died of a lung infection two months following the surgery. Three further participants were excluded from the study because they had received stenting for the intracranial segment of the vertebral artery and the vertebral artery origin at the same time. 22 of these patients received cerebral digital subtraction angiography (DSA) follow-up. The median duration of clinical follow-up was 22 months (quartile 9.25-36.75) and 10 months (quartile 4.0-20.5) for the extracranial group, and 26 months (quartile 15.0-34.25) and 6 months (quartile 3.25-17.75) for the intracranial group. By the end of the study, each patient had received at least three months of postoperative DSA monitoring.

Participants were chosen for the study based on the following inclusion criteria: (1) Stenosis ≥ 70% and recurrent typical symptoms of posterior circulation ischemia (such as vertigo, ataxia, and visual field abnormalities including hemianopia, eye movement disorders, bilateral weakness, loss of consciousness, and unilateral weakness; respiratory, heart rate, and blood pressure irregularities; and disorientation, confusion, and memory loss. (2) All diagnoses were verified by DSA. (3) The Modified Rankin Scale (MRS) value of ≤ 2. Patients with the following conditions were excluded: (1) Other non-atherosclerotic diseases (arterial dissection, aneurysm, or other hemorrhagic disease). (2) A previous history of stent placement, or an evaluation of unsuitable surgical treatment. (3) Cardiogenic stroke or potential cardiogenic embolism. (4) Severe vessel tortuosity or some other reason due to which the stent couldn't be implanted. (5) A history of severe drug allergy, especially heparin, aspirin, clopidogrel, etc. (6) Women during gestation or lactation period.

We obtained clinical and image data, including surgical records, postoperative complications, and other vascular events during follow-up from hospital records. Other baseline data, such as atherosclerotic risk factors like hypertension, hyperlipidemia, and diabetes, were collected at the time of admission. Hypertension was defined as blood pressure ≥ 140/90 mmHg before previous diagnosis or surgical treatment. Blood glucose levels of > 11.1 mmol/L or fasting blood glucose levels of > 7.0 mmol/L after a previous diagnosis or two random visits were used to define diabetes.

Hypercholesterolemia was defined as either known hyperlipidemia or fasting total cholesterol levels greater than 5.0 mmol/L.[3] A history of previous stroke or transient ischemic attack and smoking in the past or present were recorded. The MRS scores were also recorded at the end of the study. The prespecified primary outcomes were recurrent stroke in the symptomatic vertebral artery supply area during follow-up, and in-stent restenosis (ISR) during follow-up. Secondary outcomes were the recurrence rate of stroke or TIAs in the vertebral area within one year and death from any cause. Restenosis was defined as any residual or recurrent stenosis of at least 50% or occlusion of the vertebral artery on DSA during follow-up and an absolute lumen loss ≥ 20%. Stroke or death within 30 days after stent placement and cerebrovascular events within 30 days were recorded and statistically analyzed.

Procedures

Before the procedure, all individuals received at least three days of dual antiplatelet medication (aspirin 100 mg and clopidogrel 75 mg). To control risk factors, we attempted to individualize medicine and improve lifestyle choices. Thromboelastographic of 1 patient showed clopidogrel resistance. Therefore, the medication was changed to aspirin 100 mg combined with ticagrelor 90 mg. The patient was prescribed dual antiplatelet therapy for at least 3 months postoperatively. Heparin intravenous boluses (70-100 IU/kg) were given to initiate anticoagulation, which was maintained through intravenous administration to sustain an activated clotting time of > 250-300 seconds.

All operations were conducted by an interventional surgeon with at least five years of experience doing intracranial and extracranial interventions. All patients with intracranial stenosis were operated under general anesthesia, while those with extracranial stenosis received local anesthesia. After catheter sheath placement at the femoral artery puncture

point, a guidewire was routinely inserted into the stenosis segment, and then stenting was placed in the lesioned vessel after adequate pre-dilatation by the Gateway balloon. Depending on the characteristics of the vessel, the surgeon chose to implant an Enterprise or Apollo stent in order to carry the stent safely to the site of the disease. DSA determined the degree of stenosis promptly. Postoperative residual stenosis was defined as stenosis of more than 30 percent. We encouraged the patient to adhere to double antiplatelet and antilipidemic medication therapy for at least three months after surgery to prevent thrombosis. The incidence of restenosis was observed by DSA follow-up. An angiographic calculation of the VA stenosis was calculated with the following formula (% VA stenosis = (1– [narrowest VA diameter/diameter normal distal VA]×100).[10] A degree of stenosis of 70-99% of the VA was classified as high grade. When a normal distal vessel is unavailable, as in the case of distal stenosis, the proximal normal arterial diameter is utilized as the denominator. This approach is based on the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) assessment of intracranial stenosis.[11]

Statistical analysis

Continuous numeric variables were represented by means, medians, and quartiles, whereas classification variables were represented by proportions. Since there were less than 40 cases, Fisher's exact test and an independent sample *t* test were employed to compare the differences between classification variables and continuous numerical variables. A statistically significant difference between the two groups was considered only when $P \leq .05$. This statistical study was conducted using the SPSS 20.0 program.

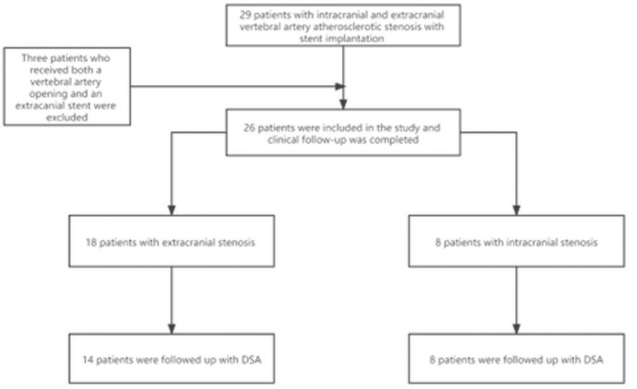
RESULTS

Clinical information was collected from 29 patients who satisfied the criteria. Three individuals who had both vertebral artery openings and intracranial vertebral artery stents were excluded from the analysis. Finally, 26 patients with moderate to severe vertebral artery stenosis were included in the study conducted in our hospital (Figure 1). Among the 18 patients with extracranial stenosis, 4 patients had stenosis in the V2 segment, and the stenosis of the rest was in the vertebral artery origin (VAO). In the remaining 8 individuals, intracranial stenosis was observed. Table 1 displays demographic data and basic clinical features.

Baseline characteristics and clinical features

Among the 26 patients, nineteen were male (73%) and seven were female (27%), with a mean age of 65 years (±8.67). All patients had ≥70% severe stenosis, including 8 patients with intracranial stenosis and 18 with extracranial stenosis. The rate of stroke on admission was significantly higher in the intracranial stenosis group compared to the extracranial stenosis group (75.0% vs. 22.2%, $P = .026$). However, this does not raise the incidence of recurrence in intracranial stenosis patients during follow-up. 50% (9/18) of the cases in the extracranial stenosis group were admitted for TIA of the posterior circulation, despite the fact that 78% (7/9) of the participants had old ischemic infarcts or lacunar ischemic lesions, diagnosed using brain magnetic resonance imaging (MRI) after admission. For the remaining two patients MRI was not conducted in a timely manner. One patient had a history of lacunar cerebral infarction; however, an MRI was not conducted on this occasion since the patient suffered a stroke three years ago. For another patient, the right arm was affected by mild hemiplegia. One patient in the extracranial stenosis group had developed viral meningitis 1 month before and improved before the vascular intervention. Among the four stroke patients, three had experienced either a brainstem, cerebellar, or occipital infarction before administration, and only one had new onset ischemic. Five patients presented with anterior circulation ischemia also received endovascular treatment due to severe VA stenosis which may be associated with a high risk of stroke recurrence in the posterior circulation.

Figure 1. Flow Chart of Included Case Data



Among the patients with intracranial stenosis, two were admitted with TIA and six with posterior circulation stroke, as confirmed by craniocerebral MRI. Despite past aggressive medical treatment, two of them experienced recurrent stroke or TIA worsened by neurologic sequelae such as dizziness or limb paralysis. The patients were at high risk for developing a severe infarction in the future. Contralateral VA stenosis was observed in 12 (66.6%) extracranial patients and 5 (62.5%) intracranial patients, with no statistically significant difference ($P > .05$).

The median time from the first event to the procedure was 30 days (interquartile range, 13.75-95.75) in patients with extracranial stenosis and 30 days (interquartile range, 10.50-52.25) in patients with intracranial stenosis. The time between the most recent event and surgery was 9 (7.0- 15.5) and 11 (5.75- 18.75) days in patients with extracranial and intracranial vascular stenosis, respectively ($P = .717$). One patient in the extracranial stenosis group had the intervention due to sporadic but recurring dizziness during a two-year period and an increase in frequency within a week. An angiographic evaluation of a second patient indicated a VAO stenosis of greater than 70% and contralateral VA blockage prior to the surgery. The MRI of the patient's brain revealed acute lacunar infarctions in the right parietal and frontal lobes; the first symptom was developed two years prior to treatment.

Table 1. Baseline Characteristics of Patients

Baseline characteristics, n (%)	Total n = 26	Extracranial stenosis n = 18	Intracranial stenosis n = 8	*P* value
Age (mean)	65 (± 8.67)	66 (±7.59)	62 (±10.78)	.290
Male sex	19 (73.1)	13 (72.2)	6 (75.0)	>.999
Hypertension	24 (92.3)	18 (100)	6 (75.0)	.086
Diabetes	11 (42.3)	8 (44.4)	3 (37.5)	>.999
Dyslipidemia	7 (26.9)	5 (27.8)	2 (25.0)	>.999
Coronary heart disease	4 (15.4)	3 (16.7)	1 (12.5)	>.999
Smoking history	13 (50.0)	9 (50.0)	4 (50.0)	>.999
Index event				
Stroke	10 (38.5)	4 (22.2)	6 (75.0)	.026
TIA	11 (42.3)	9 (50.0)	2 (25.0)	.395
Time from the first event to procedure in days(median, interquartile range)	30 (12.75-60.25)	30 (13.75-95.75)	30 (10.50-52.25)	.472
Time from most recent event to procedure	10 (7.0-15.5)	9 (7.00-15.5)	11 (5.75-18.75)	.362
Contralateral vertebral artery	18 (69.2)	12 (66.7)	6 (75.0)	>.999

Table 2. Outcomes of 2 Groups

	Total n = 26	Extracranial stenosis n = 18	Intracranial stenosis n = 8	*P* value
Outcomes within 30 days				
Residual stenoses	1 (3.8)	0	1 (12.5)	.308
Vascular-related Complications	2 (7.7)	1 (5.6)	1 (12.5)	.529
Stroke or death	0 (0)	0(0)	0 (0)	
Follow-up Outcomes				
Stroke or TIAs of posterior circulation	6 (23.1%)	4 (22.2%)	2 (25.0)	>.999
Stroke or TIAs of posterior circulation at 1 year	4 (15.4)	3 (16.7)	1 (12.5)	>.999
Posterior circulation ischemic stroke	1 (3.8)	1 (5.6)	0	>.999
Restenoses	7 (31.8)	4 (28.6)	3 (37.5)	>.999
Asymptomatic restenosis	3 (13.6)	1 (7.1)	2 (25.0)	.527
Symptomatic restenosis	4	3 (21.4)	1 (12.5)	>.999
Death from any cause	1 (3.8)	1 (5.6)	0	>.999

Procedures and complications

In 22 patients, there were no statistically significant differences in surgical success rate, recurrence of stroke or death within 30 days, recurrence of stroke or TIA during follow-up, or incidence of restenosis between intracranial and extracranial vertebral artery stenosis. Within 30 days of intervention, the intracranial group experienced significantly more vascular problems than the extracranial group (12.5% vs. 5.6%, $P = 0.529$). On the contrary, stroke or TIA of the posterior circulation at 1 year was relatively low (12.5%, 1/8) in the intracranial stenosis group, compared to 16.7% (3/18) in the extracranial group. Posterior circulation ischemic stroke was only observed in one of the extracranial groups during follow-up. Successful surgery was defined as no intraoperative complications or death. The success rate was 100% in both groups. The overall complication rate was 7.7% (2/26).

One developed a lung infection and type I respiratory failure 2 days after the operation, cerebral computed tomography (CT) examination also found a right frontal temporal subdural hematoma. The patient eventually died two months later. The pulmonary infection that occurred shortly after surgery was considered strongly associated with aspiration pneumonia diagnosed 20 days ago. General anesthesia may exacerbate its deterioration. In addition, the patient also had a history of chronic renal insufficiency.

Two patients with intracranial stenosis developed active hemoptysis and pulmonary Haemophilus influenzae infection on the postoperative day, and one of them experienced a sudden onset of unconsciousness on the 15th postoperative day, with an emergent head CT scan revealing hemorrhage transformation following left middle cerebellar peduncle infarction. They all recovered after aggressive medical treatment. Patients who experienced vasospasm during the operation resolved without sequelae. Several patients who developed skin rashes after surgery were prescribed anti-allergy drugs and the rashes subsided.

According to the surgeon's preference, all patients with extracranial VA stenosis received balloon-expandable stents, while two patients with intracranial stenosis received self-expanding stents. Only one patient had a 50% residual stenosis. The rate of technical success was 96%.

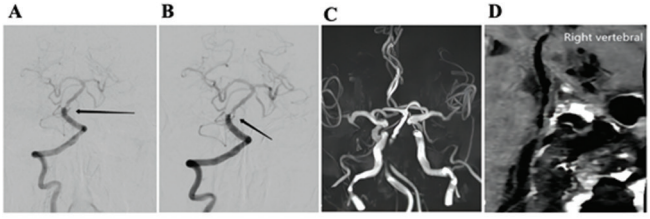
Follow-up

MRS scores were recorded by telephone in 22 patients, with 2 patients in the extracranial group scoring MRS 4, 1 scoring MRS 1, and the rest scoring MRS 0. The risk of recurrence of posterior circulation stroke or TIA was 23.1% (6/26) during follow-up (Table 2). However, the incidence of any stroke or TIA was 30.8% (8/26), including four patients who developed symptoms of anterior circulation ischemia.

Acute ischemic infarction lesions on the left cerebral hemisphere, the right side of the hippocampus, the right centrum semiovale acute lacunar infarction, and decreased perfusion of the right cerebral hemisphere were observed in four patients with anterior circulation ischemic stroke at later follow-up. They were administered the most potent lipid-lowering medications based on dual antiplatelet treatment. After recurring tingling and weakness in the left limb, one of four patients elected to undergo a right superficial temporal artery-middle cerebral artery bypass four months later. One patient (1/18, 5.6%) in the extracranial group experienced a stroke in the posterior circulation. This patient acquired a fresh infarction in the pontine and right occipital lobe with concomitant symptoms one year after the intervention and was managed conservatively. However, the symptoms of dizziness due to lacunar infarction in the right hippocampus

still recurred after 1 year. In fact, the patient's DSA four months post-surgery revealed a 40% of ISR, and he was only treated with aggressive medical management. In contrast to the 30-day results, the incidence of posterior circulation stroke or TIA at 1 year was relatively lower in the intracranial stenosis group (12.5%, 1/8) than in the extracranial group (16.7%, 3/18). There were no stroke events in the intracranial group during the follow-ups. However, two patients (25%, 2/8) had a transient ischemic attack in the 19th and 6th month, respectively. The incidence of recurrent TIA in the extracranial stenosis group was 11.1% (2/18). Regarding imaging results, the intracranial stenosis group had a greater restenosis rate than the extracranial stenosis group (37.5% vs. 28.6%, $P > .05$). This trend was also found in the asymptomatic restenosis rate. Patients with intracranial stenosis were more likely to have asymptomatic restenosis (25%, 2/8) than patients with extracranial stenosis (7.1%, 1/14, $P = .527$) (Figure 2). In other words, only 57.1% of the patients with restenosis experienced a recurrence of symptoms. On the basis of the patient's symptoms and signs, dual antiplatelet and lipid-lowering statins were administered to all patients with restenosis.

Figure 2. Ten days after the initial symptoms, the patient underwent intracranial basilar artery stent placement under general anesthesia. The patient had an 80% narrowing of the right distal vertebral artery (A) and there were no complications during the procedure, including the perioperative period for the first 30 days postoperatively. The MRS score at discharge was 1. DSA imaging (B) revealed restenosis in the stent after 3 months, but the patient did not develop any symptoms of ischemia. After 1 year of conventional antiplatelet therapy (i.e., lipid-lowering drugs), the patient's MRA showed mild to moderate restenosis in the stent without any symptoms of ischemia (C, D). Currently MRS was 0.



DISCUSSION

Few studies have specifically analyzed and compared the risks of stroke recurrence over a longer period after intracranial and extracranial VA stenosis stenting. This study compared the results of intracranial and extracranial VA stent implantation and found that there may be differences in symptomatic restenosis between the two groups. For extracranial VA, more attention should be paid to the occurrence of symptomatic restenosis. Intensive drug therapy and the application of a drug-coated balloon or drug-eluting stent may be needed.

An earlier meta-analysis of two prospective experiments by Gulli et al. showed that intracranial stenosis is associated with a higher risk of early recurrence, with a surprisingly high 33% probability of recurrence within 90 days after the first event.[1] The results of the SAMMPRIS study for intracranial spinal stenosis revealed a 21.1% probability of recurrence within two years of a stroke that was successfully treated.[12] The primary outcome within 30 days after stenting was observed in 22% of patients with intracranial VA stenosis stenting and 2% of those with extracranial stenosis in the Vertebral Artery Stenting Trial (VAST) experiment. Similarly, the risk of recurrent stroke in patients with intracranial vertebral artery stenosis was higher during follow-up.[13] VIST and VAST showed a higher rate of perioperative stroke for intracranial stenosis.[14] It seems that intracranial VA stenting puts patients at greater risk of perioperative and recurrent stroke than patients with extracranial VA stenosis. The higher risk of perioperative vascular complications and general anesthesia after endovascular treatment for intracranial stenosis is one of the reasons for the low benefit of endovascular treatment for intracranial stenosis at present. We also observed higher vascular complications within 30 days in the intracranial stenosis of the posterior circulation group compared to the extracranial group (12.5% vs. 5.6%, $P = .529$). This is similar to the results of previous studies.[13] Our results do not record any stroke or death during the perioperative period irrespective of the subgroup, which is quite a positive result.

In addition to comparing differences in perioperative risk, we compared differences in the long-term risk of stroke recurrence. Our retrospective study revealed that the long-term risk of posterior circulation stroke or TIA recurrence after VA stenting was 23.1% and that there was no statistically significant difference between the long-term risks of extracranial VA stenosis and intracranial VA stenosis. Patients with extracranial stenosis had a 5.6% incidence of ischemic stroke in the posterior circulation during follow-up, whereas in the intracranial group, no recurrent ischemic stroke was identified. 9 (7%) of 122 patients (randomized trial VAST,[3] VIST[4]) with extracranial stent placement had a recurrent stroke which was reported in a meta-analysis[1] and this was found to be consistent with our results. However, we found that the results obtained for the intracranial group were more positive than previous studies[3,4].

On one hand, we discovered that the majority of ischemia recurrences (15.4%, 4/26) occurred within one year. In the extracranial group, more recurrent strokes or TIAs were detected over the course of one year. In recent investigations, long-term follow-ups of patients treated endovascularly for symptomatic cerebral posterior circulation stenosis revealed minimal incidence of recurrent stroke.[6] It is suggested that we should pay more attention to patients' outcomes within one year in subsequent studies. On the other hand, our outcomes present a relatively high rate of ISR. However, no elevated rate of symptom recurrence was observed. This phenomenon is more obvious in intracranial stenosis. All patients with extracranial stenosis were treated with balloon-dilated stents,

and 3 patients in the intracranial group were treated with self-dilated stents according to the situation. The rates of restenosis were 28.6% and 37.5% in extracranial and intracranial groups respectively during follow-up. Seifert et. al. observed 62% restenosis in VAO at 6 months follow-up, significantly higher than 32% restenosis in the intracranial group.[15] However, related studies in recent years have observed a lower rate of VAO restenosis (13%), similar to the 13.8% rate of intracranial vertebrobasilar artery restenosis reported in real-world data in China.[8,16] Currently, the risk of restenosis is comparable for intracranial and extracranial VA stents. In our study, the incidence of symptomatic restenosis was lower in the extracranial group than in the intracranial group (21.4% vs. 12.5%). Although patients with complex intracranial vertebral stenosis have a higher incidence of restenosis, lower recurrent symptoms were recorded. Restenosis alone cannot accurately assess vascular status, and more factors need to be combined to accurately assess the risk of cerebrovascular events. A more immediate cause associated with symptoms may be tissue perfusion. More and more researchers believe that distal blood perfusion plays an important role in the occurrence of ischemic symptoms.[17-19] We discovered that symptomatic patients with extracranial restenosis had contralateral vertebral artery stenosis or even occlusion, whereas this did not occur in patients with restenosis who did not experience symptom recurrence during follow-up. Contralateral VA occlusion is a major risk factor for ISR at VAO.[20] However, the influence of contralateral vertebral artery lesions on blood flow and perfusion in the posterior circulation following vertebral artery stenosis stenting may require additional investigation. We also observed that all symptomatic patients had moderate to severe ISR (50-99%).

Our current findings suggest that stenting in intracranial lesions was not associated with a higher risk of recurrent ischemic symptoms, despite a higher restenosis rate than extracranial vertebral stenosis, during long-term follow-up. In our study, although there was a higher incidence of in-stent stenosis in the stenting group during the follow-up period (31.8%), part of them were asymptomatic restenosis (13.6%), which was more common in patients with stenosis of the intracranial group. As is known to all, ISR is a major problem in the interventional treatment of cerebrovascular stenosis, and its recanalization is more difficult, and the prognosis is worse than that of primary stenosis *in situ*.[21] But in fact, we found that some patients with ISR could live asymptomatic for a long time, especially with intracranial stenosis, and the secondary intervention for ISR in these patients is not necessary.

Some studies suggested that stent type and stent diameter were independent risk factors for ISR.[22,23] Initial application of drug-eluting stents in coronary arteries was to reduce restenosis owing to intimal hyperplasia. A meta-analysis by Tank et al. suggested that drug-eluting stents (DES) also reduced the high restenosis rate after vertebral stent placement compared with bare metal stent (BMS).[24] However, there are limited data on whether DES has any advantage over BMS in terms of VA stenosis. A recent study did not support a remarkable difference in ISR rates between DES and BMS in extracranial vertebral artery stenting.[25] This result differs from the conclusions of randomized controlled trials comparing DES and BMS in intracranial atherosclerotic stenosis.[26] It was recently reported that drug-coated balloons have a lower restenosis rate in their cerebrovascular applications and their safety and feasibility have also been confirmed.[27-29] Drug-coated balloons may also become a feasible and effective option for intracranial artery stenosis or occlusion.[30]

Limitations

Our research has a number of limitations. Firstly, it was a retrospective single-center study with limited sample size, so avoiding bias in data collection was difficult. Second, other factors such as stent type may cause the difference between intracranial and extracranial VA stent restenosis, and further analysis with a larger sample size is needed, in addition to stenosis location. Thirdly, imaging follow-up was shorter than that anticipated in our study. In the future, more rigorous prospective trials are needed to refine the results of imaging follow-up.

CONCLUSIONS

In conclusion, our results show that there is no significant difference in long-term outcomes after stenting in extracranial and intracranial stenosis, but intracranial vertebral artery stenosis has a low rate of symptomatic restenosis. Symptomatic restenosis may be an important problem that limits the efficacy of extracranial vertebral artery stenting. Exploring more possible methods to reduce restenosis is one of the research directions of extracranial vertebral artery endovascular intervention.

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AUTHOR DISCLOSURE STATEMENT

The authors have no potential conflicts of interest to report relevant to this article.

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YZ and JD designed the study and performed the experiments, YH and XG collected the data, SL, DT and JS analyzed the data, YZ and JD prepared the manuscript. All authors read and approved the final manuscript.

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