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The effects of interventional therapy with endovascular stents for ischemic cerebrovascular disease.

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Abstract

Objective: To explore the effects of interventional therapy using endovascular stents on the perioperative and long-term postoperative period for patients with Ischemic Cerebrovascular Disease (ICVD) induced by vertebral-basilar ischemia.

Methods: From January 2014 to August 2015, seventy-one patients with ICVD induced by vertebral-basilar ischemia were treated in our hospital and retrospectively analysed. According to the method of treatment, all patients were divided into the stent group (treated with endovascular stents, n=33) and drug group (treated with drug therapy, n=38). Baseline parameters, recurrence rate during the follow-up period, comprehensive scores of vessel lesions before and after treatment, and neurologic deficit scores at 1, 3, 6, and 12 months after treatment were compared between two groups to evaluate the clinical value of interventional therapy.

Results: The follow-up data showed that the recurrence rate of patients in the stent group (3/33, 9.09%) was significantly lower than that in the drug group (9/38, 23.68%) ($p<0.05$). There was no significant difference in the comprehensive scores of vessel lesions or neurological deficit scores before treatment between both groups ($p>0.05$). At 1 w and 12 months after treatment, the comprehensive scores of vessel lesions in the stent group were significantly lower than in the drug group ($p<0.05$). At 1, 3, 6, and 12 months after treatment, the neurological deficit scores in the stent group were significantly lower than in the drug group ($p<0.05$).

Conclusions: Both interventional therapy using endovascular stents and drug therapy are effective for the treatment of ICVD caused by vertebral-basilar ischemia. The perioperative and long-term follow-up effects of interventional stent treatment were more obvious than with drug therapy alone. Stenting intervention therapy is better for treatment of ICVD induced by vertebral-basilar ischemia.

Keywords: Vertebrobasilar artery, Ischemic cerebrovascular disease, Endovascular stent, Interventional therapy.

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Introduction

According to a survey, the annual incidence of cerebrovascular accidents in adults in the mainland of China may reach 150-200/100,000 people, of which Ischemic Cerebrovascular Disease (ICVD) accounts for 80% [1]. Intracranial large artery and extracranial carotid artery stenosis are common causes of ICVD. Notably, intracranial arterial stenosis is more common than extracranial stenosis in Easterners, the ratio is about 3:1 [2]. Lesions of the vertebrobasilar system are the most common cause of stenosis of the intracranial arteries. Currently, the treatment of ICVD primarily includes surgery, drug therapy, and interventional therapy. Among them, interventional therapy using endovascular stents has a wide range of applications in medical practice as it is least invasive, simple to operate, associated with short time of blocking blood flow, and causes little damage to nerve fibers in the brain [3]. However, reports on the use of interventional therapy for ICVD in the vertebrobasilar system are very limited. Thus, to evaluate the clinical effect of interventional therapy, we compared the curative effects of interventional therapy and drug therapy on patients with vertebrobasilar ICVD.

Patients and Methods

Patients

Patients with ICVD caused by intracranial vertebral vascular disorders admitted and treated in our hospital between January 2014 and August 2015 were selected for inclusion in the study. The 71 patients met the inclusion and exclusion criteria. According to method of treatment, the patients were divided

into the stent group (treated with endovascular stents, 33 cases) and the drug group (treated with drug therapy, 38 cases). Among the patients, vertebral artery lesions were the cause of ICVD in 69.7% of cases in the stent group and 63.2% in the drug group. There was no significant difference in the distribution of arterial lesions between the two groups. The proportions of males, smoking patients, and drinking patients between the stent group and drug group were 63.6% *vs.* 57.9%, 57.6% *vs.* 60.5%, and 36.4% *vs.* 39.5, respectively. Statistical analysis using a chi-square test showed no statistically significant differences between the two groups. Baseline parameters including age, systolic blood pressure, diastolic blood pressure, triglycerides, total cholesterol, high density lipoprotein, and low-density lipoprotein in the stent group and drug group were analysed (Table 1). There were no statistically significant differences according to analysis of variance.

Table 1. *Baseline parameters in the two groups.*

Group	Age	Systolic blood pressure	Diastolic blood pressure	Triglycerides	Total cholesterol	High density lipoprotein	Low density lipoprotein
Stent	60.7 ± 11.2	156.63 ± 16.74	91.45 ± 13.17	5.44 ± 1.09	1.65 ± 0.78	1.07 ± 0.16	3.37 ± 0.95
Drug	63.5 ± 14.1	154.73 ± 18.92	91.92 ± 12.41	5.53 ± 1.08	1.68 ± 0.84	1.11 ± 0.18	3.26 ± 0.89

Inclusion criteria

Patients with ICVD caused by simple vertebral or basilar artery disorder; patients who met the criteria for endovascular stent placement, namely lumen diameter of asymptomatic stenosis ≥ 70%, lumen diameter of symptomatic stenosis ≥ 50%, or arterial stenosis with atherosclerotic plaque, intimal tear, dissection, or retention of contrast media after angiography; patients with residual stenosis after acute arterial thrombolysis; patients without serious cardiac and pulmonary dysfunction.

Exclusion criteria

Patients with other ischemic cerebrovascular diseases; patients with total arterial occlusion; patients with severe sclerosis and tortuous arteries resulting in the catheter being unable to pass through; patients with ICVD caused by tumor compression; patients with history of intracranial hemorrhage, or with simultaneous hemorrhagic diseases such as arterial tumors, arterial-venous fistula, or arteriovenous malformation in the corresponding blood supply area; patients with uncontrolled high blood pressure; contraindication to heparin, aspirin, or other antiplatelet drugs; allergy to contrast media; patients with other anticipated operations occurring within 30 d prior to interventional therapy; patients with myocardial-cerebral infarction that occurred within 2 w prior to interventional therapy; patients with severe heart, liver, or kidney disease; pregnant and perinatal women; patients with interrupted follow-up or less than 12 months of follow-up visits.

Treatment methods

This was a retrospective cohort study. Vascular neurological history and examination of all 71 patients was performed simultaneously by neurological and vascular specialists. Preoperative computed tomography and magnetic resonance imaging examinations were performed to exclude accompanying intracranial tumors, arteriovenous fistula, and new infarctions; transcranial Doppler examination was carried out to clarify intracranial arterial hemodynamics. Whole cerebral angiography was conducted to show the status of intracranial arteries, with or without other cerebral arterial lesions or collateral circulation. Interventional therapy in the stent group: 33 patients were examined by routine ECG, blood examination, liver and kidney function tests, and blood coagulation test prior to interventional procedures. Aspirin (300 mg/d) and clopidogrel (75 mg/d) were administered orally for 3 d before the surgical operation. Stent implantation was performed with the femoral artery approach, and systemic heparin administration and angiography were carried out to determine the location and extent of arterial stenosis and ischemic collateral circulation. Catheter, guide wires, microwares and the balloon catheter were performed in accordance of the order. Angiography was carried out to observe the status of stenosis, balloon post-dilatation was conducted if necessary, angiography of the intracranial and vertebral artery was repeated, and the stent was released to observe the arterial dilatation and blood supply of branches of intracranial vessels. 24 h after the procedure, the neurological symptoms and signs were comprehensively monitored. Aspirin (300 mg/d) and clopidogrel (75 mg/d) were administrated orally for no less than 6 months, followed by 100 mg/d aspirin as a maintenance dose. The patients in the drug group received drug therapy alone. Aspirin (300 mg/d) and clopidogrel (75 mg/d) were administered orally for no less than 6 months, followed by 100 mg/d aspirin as a maintenance dose.

Efficacy evaluation

The follow-up data of the two groups were analysed, including comparison of the comprehensive scores of vessel lesions before treatment and at 1 w and 12 months after treatment [4]. We also compared the incidence of transient ischemic attack and stroke, and the neurological deficit scores in patients with cerebral infarction (NIHSS) before treatment and at 1, 3, 6, and 12 months after treatment.

Statistical analysis

Data were analysed using SPSS 18.0 software. Numerical data are presented as mean ± SD, while categorical data are presented as percentage. Paired t-test was used to evaluate the curative effects before and after treatment. The curative effects at different time points between the two groups were evaluated

by analysis of variance, and a chi square test was used for comparisons of categorical data.

Results

Observation of the recurrence rate at follow-up visits after treatment

Twelve months of follow-up data showed that there was one case of cerebral infarction and two cases of transient cerebral ischemia in the stent group, and the recurrence rate was 9.09% (3 cases); in contrast, there were three cases of cerebral infarction and six cases of transient cerebral ischemia in the drug group, and the recurrence rate was 23.68% (9 cases). The rate of ICVD recurrence in the drug group was significantly higher than in the stent group ($p<0.05$) by chi-square test (Table 2).

Table 2. Follow-up observation of recurrences.

Recurrence	The stent group (33)	The drug group (38)
Total recurrences (n)	3	9
Non-recurrences (n)	30	29

Analysis of vascular assessment scores during the follow-up period

The vascular comprehensive scores between the stent group and drug group at 1 w and 12 months of follow-up were compared. The scores of vessel lesions were significantly decreased after treatment in both groups, suggesting that both drug therapy and stent intervention can significantly improve blood circulation. Compared with the drug group, the vascular scores in the stent group were significantly lower at 1 w and 12 months after treatment, suggesting that stenting intervention can significantly improve circulatory status ($p<0.05$). The arterial vascular scores at different time points were compared for different vessels that underwent the same treatments. The vascular comprehensive scores of the basilar artery were higher than those of the vertebral artery before treatment; after treatment, there was no statistically significant difference in the stent group, although in the drug group, the overall scores of the basilar artery were higher than those of the vertebral artery, suggesting that treatment by endovascular stenting for different arterial lesions was better than with drug therapy (Table 3).

Table 3. Comparison of vascular assessment scores in the preoperative, perioperative, and postoperative.

	The stent group			The drug group		
	Before treatment	1 w	12 months	Before treatment	1 w	12 months
Vertebral artery	205.61 ± 27.34	88.72 ± 29.38	92.39 ± 24.34	210.66 ± 25.91	203.18 ± 26.88	205.56 ± 21.95
Basilar artery	215.73 ± 29.72	91.37 ± 31.38	92.95 ± 32.68	224.46 ± 28.59	219.34 ± 29.58	215.26 ± 32.03

Comparison of neurological deficit scores (NIHSS) during the follow-up period

The neurological deficit scores in the stent group and drug group were compared at 1, 3, 6, and 12 months after treatment using a paired t-test. The neurological deficit scores of the two groups were significantly decreased after treatment, suggesting that both drug therapy and stent intervention can significantly improve neurological function. Compared with the drug group, the neurological deficit scores in the stent group were significantly lower at 1, 3, 6, and 12 months after treatment ($p<0.05$), suggesting that stenting intervention can significantly improve neurological function ($p<0.05$). The neurological deficit scores were compared at the same time points for different vessels that underwent the same treatment. The neurological deficit scores of basilar artery lesions were higher than those of the vertebral artery before treatment; after treatment in the stent group, the comprehensive scores of basilar artery lesions were higher than those of the vertebral artery at 1 and 3 months ($p<0.05$). However, there was no significant difference between the basilar artery and vertebral artery in terms of neurological deficit score at 6 and 12 months after treatment ($p>0.05$). This suggests that stenting therapy may be more beneficial than drug therapy alone for different arterial lesions (Table 4).

Table 4. Analysis of NIHSS scores of patients with ischemic cerebrovascular disease during the follow-up period.

	The stent group					The drug group				
	Before treatment	1 month	3 months	6 months	12 months	Before treatment	1 month	3 months	6 months	12 months
Vertebral artery	11.61 ± 3.31	5.24 ± 2.79	4.16 ± 2.08	2.86 ± 1.16	2.49 ± 1.26	11.52 ± 2.95	9.27 ± 3.06	8.06 ± 2.49	7.89 ± 3.14	7.91 ± 3.03
Basilar artery	14.12 ± 2.61	5.97 ± 2.58	4.89 ± 2.37	3.22 ± 1.38	2.72 ± 1.48	12.99 ± 2.60	10.65 ± 3.34	8.77 ± 2.79	8.81 ± 3.71	8.37 ± 3.56

Discussion

ICVD is a disorder of blood supply caused by short-term stenosis or occlusion of the cerebral artery. Consequently, the corresponding brain tissues undergo ischemic anoxic degeneration, death, or cerebromalacia, resulting in impaired neurological function [5]. With the increasing incidence of ICVD, the incidence of ICVD caused by disorders of posterior cerebral circulation has been increasing, mostly because of vertebrobasilar artery stenosis [6]. Modern treatments for

ICVD include surgery, drug therapy, and interventional therapy. Surgery mainly involves carotid endarterectomy, however it is not the preferred method because of strict indications and contraindications, and high rates of perioperative adverse events. In contrast, drug therapy is a traditional and conservative method, and is presently the primary method of treatment. The aim of drug therapy is to control blood glucose, blood pressure, blood lipid levels, and platelet aggregation [7-9]. Although drug therapy can effectively prevent the occurrence of transient ischemic cerebrovascular disease, many cases of ICVD still occur or relapse. The use of drug therapy alone is not very effective for the prevention and treatment of ICVD, and therefore has several limitations. Interventional therapy, as a new method of treatment, has been used by many scholars because of its minimal trauma, ease of use, safety, efficacy, few complications, and short hospital stay. After years of development, interventional therapy has become a pillar of medical treatment. Cerebrovascular interventional therapy is primarily for intracranial arterial stenosis, and has been widely used in medical practice because it causes short interruption of blood flow and less damage of cerebral nerve fibers during the operation [3,10]. For vertebrobasilar arterial ICVD, drug therapy is still the main method of treatment and includes antiplatelet therapy, anticoagulation therapy, antiarteriosclerotic therapy, and blood vascular expansion. Administration of clopidogrel and aspirin for antiplatelet therapy is beneficial to prevent transient ischemic attack of the vertebral arterial system and cerebral infarction [11,12]. Anticoagulant therapy and the use of prophylactic aspirin can achieve the same effect [13]. However, endovascular stenting in patients with symptomatic vertebral artery stenosis is more effective for improving blood supply to the basilar artery [14-16].

In the present study, if the comprehensive scores of vascular lesions and neurological deficit scores of the two groups before treatment are considered as the baseline values, the scores in both the stent group and drug group were decreased after treatment. This suggested that both stenting therapy and drug therapy are effective treatments for ICVD of the basilar artery. This conclusion is consistent with previous studies [17,18]. Additionally, the follow-up results showed that the comprehensive scores of vascular lesions and neurological deficit scores in the stent group were significantly lower than those in the drug group, suggesting that interventional therapy improved neurological function more rapidly for patients with ICVD. The results showed that vascular stenting is more effective than traditional drug therapy alone for patients with vertebrobasilar arterial disorder. This observation was slightly different from those in the study by Wei et al. [18], who showed that there were no significant differences in the comprehensive scores of vascular lesions before and after treatment. This may have been because of differences in patients and vessels observed. In the present study, the follow-up data of the two groups showed that the recurrence rate of stent therapy (9.09%) was significantly lower than that of drug therapy (23.68%), which was consistent with the studies by Wei et al. [19-21]. The results suggested that the clinical effects of vascular interventional therapy were more obvious than those of drug therapy alone in both the perioperative and long-term follow-up period. Therefore, vascular stenting interventional therapy was more suitable for the treatment of vertebrobasilar ICVD.

Conclusions

In our study, because of the relatively small sample-size, the synergistic effects of interventional therapy and drug therapy were not sufficiently explored. Only the patients in the drug group met the interventional indications. Therefore, the study introduced “gold standard bias” and the conclusions of this study need to be further validated. Furthermore, this study was not a randomized multicenter study, thus the clinical effect of interventional treatment using endovascular stenting for patients with vertebrobasilar ICVD needs to be further confirmed by large-sample, multicenter, long-term follow-up studies. Despite these limitations, low rate of recurrence and rapid recovery of neurological function were observed in the interventional group in this study. Therefore, interventional treatment with vascular stenting is more suitable than drug therapy alone for vertebrobasilar IVCD when the patients are eligible for its indications.

References

1. Miyachi S, Izumi T, Tsurumi A, Hososhima O, Matsubara N, Naito T, Wakabayashi T. Endovascular treatment for ischemic cerebrovascular diseases. Rinsho Shinkeigaku Clin Neurol 2009; 49: 807-809.
2. Miao Z, Ning MA. Endovascular therapy of ischemic cerebrovascular disease. Chinese J Contemp Neurol Neurosurg 2013; 13: 170-173.
3. Helft G, Helft G. Optimal duration of dual antiplatelet therapy after drug-eluting stent implantation. Circulation 2014; 130: 161-162.
4. Olmez I, Ozyurt H. Reactive oxygen species and ischemic cerebrovascular disease. Neurochem Int 2012; 60: 208-212.
5. Chawalparit O, Chareewit S. Ischemic cerebrovascular disease and calcified intracranial vertebrobasilar artery: A case-control study by using cranial CT. J Med Assoc Thai 2013; 96: 346-350.
6. Ntalas IV, Milionis HJ, Kei AA, Kalantzi KI, Goudevenos JA. Antiplatelet treatment in the secondary prevention of coronary and cerebrovascular disease: is there any place for novel agents. Angiology 2014; 65: 473-490.
7. Lai SW, Lin HF, Lin CL, Liao KF. Long-term effects of pioglitazone on first attack of ischemic cerebrovascular disease in older people with type 2 diabetes: A case-control study in Taiwan. Medicine 2016; 95: 4455.
8. Liu J, Wang W, Wang M, Sun J, Liu J, Li Y, Qi Y, Wu Z, Zhao D. Impact of diabetes, high triglycerides and low HDL cholesterol on risk for ischemic cardiovascular disease varies by LDL cholesterol level: A 15-year follow-

up of the Chinese multi-provincial cohort study. Diabetes Res Clin Pract 2012; 96: 217-224.

9. Reynolds MR, Derdeyn CP, Grubb RL, Powers WJ, Zipfel GJ. Extracranial-intracranial bypass for ischemic cerebrovascular disease: what have we learned from the carotid occlusion surgery study. Neurosurg Focus 2014; 36: 9.
10. Hankey GJ. Replacing aspirin and warfarin for secondary stroke prevention: is it worth the costs. Curr Opin Neurol 2010; 23: 65-72.
11. Karlinski M, Bembenek J, Kobayashi A, Anna C. Hospital-initiated prevention of recurrent ischemic stroke: changes from 1995 to 2013. Eur J Neurol 2015: 602.
12. Ding D. Implications of aspirin biochemistry in the pathobiology of ischemic cerebrovascular disease. J Neurol Sci 2014; 336: 290.
13. Singh J, Nguyen TN. Iconography: endovascular and neurosurgical management of acute ischemic stroke. Emerg Med Clin North Am 2012; 30: 695-712.
14. Wang QH. The application of endovascular covered stents in the treatment of cerebrovascular diseases. Cerebrovasc Dis Foreign Med Sci 2005.
15. Menon BK, Almekhlafi MA, Pereira VM. Optimal workflow and process-based performance measures for endovascular therapy in acute ischemic stroke: analysis of the Solitaire FR thrombectomy for acute revascularization study. Stroke J Cerebr Circ 2014; 45: 2024-2029.
16. Chiam PT, Mocco J, Samuelson RM, Siddiqui AH, Hopkins LN, Levy EI. Retrograde angioplasty for basilar artery stenosis: bypassing bilateral vertebral artery occlusions. J Neurosurg 2009; 110: 427-430.
17. Ralea IC, Nighoghossian N, Tahon F, Derex L, Cakmak S, Trouillas P, Turjman F. Stenting of symptomatic basilar and vertebral artery stenosis in patients resistant to optimal medical prevention: the lyon stroke unit experience. Eur Neurol 2008; 60: 127-131.
18. Balousek PA, Knowles HJ, Higashida RT. New interventions in cerebrovascular disease: the role of thrombolytic therapy and balloon angioplasty. Curr Opin Cardiol 1996; 11: 550-557.
19. Weber W, Mayer TE, Henkes H, Kis B, Hamann GF, Schulte-Altedorneburg G, Brueckmann H, Kuehne D. Stent-angioplasty of intracranial vertebral and basilar artery stenoses in symptomatic patients. Eur J Radiol 2005; 55: 231-236.
20. Abuzinadah AR, Alanazy MH, Almekhlafi MA, Duan Y, Zhu H, Mazighi M, Lutsep HL, Donnon T, Hill MD. Stroke recurrence rates among patients with symptomatic intracranial vertebrobasilar stenoses: systematic review and meta-analysis. J Neurointerv Surg 2016; 8: 112-116.

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