Enterprise stent for symptomatic complex intracranial atherosclerotic stenosis: safety and efficiency

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Abstract

Purpose: To evaluate the safety and efficacy of Enterprise stent in the treatment of symptomatic complex intracranial atherosclerotic stenosis.

Methods and materials: 20 complex cases among 53 patients with symptomatic ischemic stroke who were treated with balloon angioplasty and enterprise stents in Department of Neuro-interventional Radiology, The First Affiliated Hospital of Zhengzhou University from Jan. 2014 to Dec. 2017 were retrospectively enrolled in this study. Diagnostic criteria for complex intracranial atherosclerotic stenosis were as follows: 1) intracranial atherosclerotic stenosis was $\geq$70% confirmed by digital subtraction angiography (DSA) using the formulas described by the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) method; 2) length of lesion was >10 mm. Basic characteristics of target lesions, technical success rate, perioperative safety, follow-up outcomes were investigated.

Results: 20 patients were enrolled in this study, including 15 males and 5 females from 44 to 70 years old with an average age of 57.20 ± 9.25. 20 lesions were treated with 20 enterprise stents. The average preoperative and postoperative residual stenosis was reduced from $(77.45 \pm 8.44)\%$ to $(24.89 \pm 16.61)\%$. The successful rate of operation was 100%. Among the perioperative complications, only 1 case (5%) experienced perforating branch event. The average clinical follow-up period was 13.15 ± 11.33 months (time range: 5–38). There were no ischemic events, no bleeding events and no various causes of death during the follow-up period. 8 lesions (40.0%) underwent DSA follow-up examinations and 12 lesions (60.0%) were checked by CT angiography during the follow-up period. 3 lesions (15.0%) developed ISR without any cerebral ischemia symptoms.

Conclusion: This retrospective, single-center study suggests that enterprise stent is effective in the treatment of symptomatic complex intracranial atherosclerotic stenosis with less perioperative complications. Prospective, multicenter, randomized controlled trials are expected.

Keywords: Enterprise stent; intracranial atherosclerotic stenosis; endovascular treatment

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INTRODUCTION

Intracranial atherosclerotic stenosis (ICAS) is one of the main causes of stroke, especially in the Asian population (1). The current guidelines for the treatment of ICAS are still antiplatelet aggregation drugs, but for moderate and severe ICAS patients with the drug treatment, the annual recurrence rate of stroke is 10–24% (2). Wingspan stents, self-expandable stents, were approved by FDA for the treatment of ICAS. However, the SAMMPRIS multicenter study was terminated early because the stroke and mortality rate in the wingspan stent group within 30 days were significantly higher than those in the drug treatment group, and the adverse events were twice as high as expected (3). There are few reports on the treatment of intracranial atherosclerotic stenosis with enterprise stents. This study reports the follow-up results of enterprise stent in the treatment of symptomatic complex intracranial atherosclerotic stenosis since 2014.

METHODS

Patient population

53 patients with symptomatic ischemic stroke were treated with enterprise stents in our department from Jan. 2014 to Dec. 2017 (27 patients with symptomatic intracranial stenosis, 21 patients with atherosclerotic intracranial large vessel occlusion and 5 patients with cerebral artery dissection). 20 lesions met the following inclusion criteria: 1) intracranial atherosclerotic stenosis was ≥70% confirmed by DSA using the formulas described by the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) method; 2) length of lesion is > 10 mm; 3) cerebral infarction in the blood supply area within 90 days; 4) still with recurrent symptoms under anti-platelet aggregation therapy. Patients with any of the following were excluded: 1) total occlusive lesion; 2) non-atherosclerotic stenosis; 3) preoperative modified Rankin Scale (mRS) score is over 3; 4) acute cerebral infarction within 24 hours.

Procedures

Preoperative preparation

1) preoperative evaluation of cerebral ischemia degree by cranial CT perfusion or MR perfusion-weighted imaging, and DSA were performed to evaluate path classification [referring to LMA classification (4)], the stenosis rate, the length of lesions, the diameter of proximal and distal vessels, relationship with branch blood vessels and collateral circulation compensation. 2) antiplatelet aggregation drugs (100 mg aspirin plus 75 mg clopidogrel daily) were given before operation for at least 5 days, and thromboela-stogram was used to detect the effect of antiplatelet aggregation drugs. The patients with insufficient platelet inhibition (AA < 50%, ADP < 30%) were given an intensive anti-platelet aggregation drug. During the perioperative period, lipid-regulating drugs (Atto vastatin 20 mg qd or Rosuvastatin 10 mg qd) were given for at least 3 months. At the same time, drug therapy for corresponding risk factors was given.

Operation process

Patients were performed under general anesthesia, the femoral artery was punctured with modified seldinger technique, a 6F envoy guiding catheter (Cordis, USA) was introduced through a femoral sheath. The whole body heparinization was achieved by injecting with heparin sodium (1 mg/ kg) through vein. Cerebral angiography was performed prior to the treatments. The stenosis, diameter and length of the target lesion were calculated again. Referring to the diameter of the target lesion, the gateway balloon catheter (Boston Scientific, USA) was selected with 80% of the "normal" parent artery proximal to the stenosis and the length was selected to match the stenosis. With the help of 0.014 in transend or synchro microguide wire (Stryker, USA), the gateway balloon catheter reached stenosis segment, the balloon was dilated slowly, with a final pressure of 6 atm for about 3 minutes. Withdraw the balloon catheter and feed into the select plus microcatheter (stryker, USA) along the microguide wire. Enterprise stent (Cordis, USA) was delivered through microcatheter, located accurately and released after crossing the narrow segment. If the residual stenosis rate was over 50%, the in-stent balloon expansion

was carried out. 5 minutes after the release of the stent, the anterior-posterior and lateral arteriography of the responsible artery was performed to confirm the presence of artery and its distal branches. Xper CT was performed to see whether there was hematencephalon. Successful stent placement was defined as complete coverage of the target lesion, no displacement and thrombosis in the stent, and residual stenosis was less than 50%.

Post operation management

After the operation, a dynamic monitoring of electrocardiogram and blood pressure was provided. We kept blood pressure to target value (10%–15% lower than basic blood pressure). A daily dose of aspirin (100 mg) and clopidogrel (75 mg) was recommended for half a year followed by only aspirin (100 mg). The risk factors, such as hypertension, diabetes mellitus and hyperlipoidemia, were given treatment.

Follow-up and definition of in-stent restenosis

Patients were followed up by telephone within 30 days, and mRS scale was used to evaluate prognosis (≤2, good prognosis; >2, poor prognosis). The first follow-up of DSA was 3–6 months later after the operation, followed by DSA or CTA each year. In the two-dimensional DSA image, ISR was well-defined as >50% stenosis within or immediately adjacent (within 5 mm) to the stent with >20% luminal loss.

Statistical methods

Statistics analysis was performed with the SPSS version 21.0 (IBM, Armonk, NY, USA). The baseline, imaging and stenting data of all patients were presented as means ± standard deviation for continuous variables and number for categorical data. Continuous variables were tested with the student t-test and Wilcoxon signed-rank test while categorical data with a Fisher exact test. Factors affecting restenosis were analyzed with the logistic regression method. The significant P value was set at <0.05.

RESULTS

Patient characteristics

From Jan.2014 to Dec. 2017, 20 patients with 20 lesions received treatment using the enterprise stent, 15 (75.0%) were men and 5 (25.0%) were women. Their mean age was 57.20 ± 9.25 years old (age range: 44–70 years old). The details of the 20 lesions included in this study are shown in Tables 1 and 2. Enterprise stent was performed within 90 days for patients with ischemic stroke. The mean stenotic vessel length was 17.46 ± 4.39 mm (length range:

Table 1 Basic preoperative clinical data of selected patients

Variables	N (%)	P value
Age, years	57.20 ±9.25	0.689[a]
Male gender	15 (75.0)	0.601[b]
Hypertension	13 (65.0)	0.270[b]
Hyperlipemia	4 (20.0)	0.491[b]
Diabetes mellitus	6 (30.0)	0.681[b]
Coronary artery disease	1 (5.0)	0.150[b]
Hyperhomocystinemia	2 (10.0)	0.716[b]
Smoking history	3 (15.0)	0.596[b]
NIHSS score before intervention		
≤3	19 (95.0)	0.850[b]
>3	1 (5.0)	
NIHSS score at discharge		
≤3	18 (90.0)	0.716[b]
>3	2 (10.0)	
mRS score at discharge		
≤2	20 (100.0)	-
>3	0 (0.0)	
mRS score of 3 months after discharge		
≤2	20 (100.0)	-
>3	0 (0.0)	

Note: [a] an Independent Wilcoxon test, [b] a Fisher exact test, NIHSS the National Institute of Health Stroke Scale, mRS modified Rankin Scale. Comparing with the value in group in-stent restenosis, the difference is insignificant (P>0.05).

Table 2 Characteristics of diseased vessels in selected patients.

Variables	N (%)	P value
Location (i)		
Anterior circulation	7 (35.0)	0.730b
Posterior circulation	13 (65.0)	
Location (ii)		
ICA	3 (15.0)	0.447b
MCA	4 (20.0)	
VA	8 (40.0)	
BA	5 (25.0)	
Stenosis grade, %		
70–79	12 (60.0)	-
80–89	4 (20.0)	
90–99	4 (20.0)	
Vascular lesion length, mm	17.46 ±4.39	0.546a
Reference artery stenosis, mm	77.45 ±8.44	0.689a
Post-stent residual stenosis rate, %	24.89 ±16.61	0.416a
Classification of access (4)		
I	9 (45.0)	-
II	10 (50.0)	
III	1 (5.0)	

Note: ICA internal carotid artery, MCA middle cerebral artery, VA vertebral artery, BA basilar artery, Classification was according to the morphology and access criteria system. Comparing with the value in group in-stent restenosis, the difference is insignificant (P>0.05).
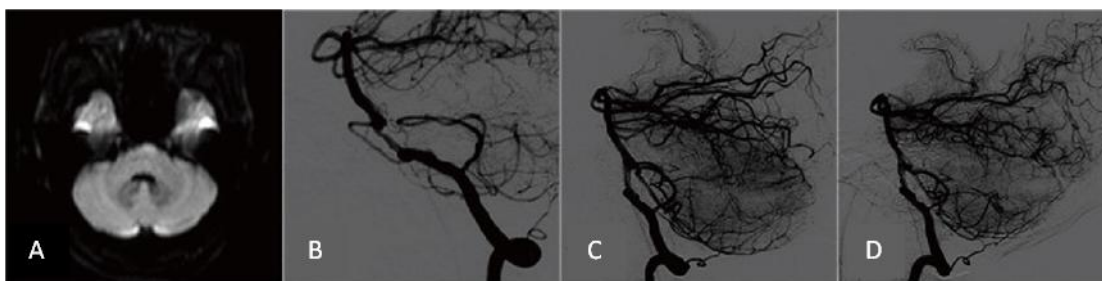
Figure 1. Images of procedure and follow-up for a patient. The patient presented with vertigo. New infarcts was found in the brainstem on DWI (A); preoperative DSA (B) and successful blood flow was achieved after stenting (C). At 28-month follow-up, angiography showed good patency of the BA (D).

11.06–26.98 mm). The mean stenosis rate was 77.45 ± 8.44% (rate range 70.10–94.52%) and the mean post-stent residual stenosis rate was 24.89 ± 16.61% (rate range: 0.00–48.68%). Images of procedure for a patient was showed in Figure 1.

Perioperative complications and follow-up results

Success rate of the operation reached 100%. There was only 1 case (5%) with distal arterial embolism which was treated with increasing fluid infusion.20 patients were available for the clinical follow-up 5–38 (13.15 ± 11.33) months after treatment. No patient experienced recurrent TIA or stroke. Overall, 8 lesions (40.0%) underwent DSA follow-up examinations and 12 lesions (60.0%) were checked by CT angiography during the follow-up period. 3 lesions (15.0%) developed ISR without any cerebral ischemia symptoms.

DISCUSSION

The optimal treatment for symptomatic intracranial atherosclerotic stenosis (sICAS) remains controversial. The results of WASID and SAMMPRIS studies show that drug therapy can reduce the stroke recurrence rate. Intracranial stenting can also reduce the stroke recurrence rate by improving the blood flow of responsible lesions (5,6). Wingspan stent is the only self-expandable stent approved by FDA in the United States for the treatment of sICAS. But Lutsep et al. (6) shows that SAMMPRIS results cannot provide evidence to support that wingspan stent angioplasty is superior to intensive drug therapy. Clinical practice shows that

the manipulation of winspan is complex, its unique delivery system may not be able to pass through the circuitous lesions and the head of the wingspan stent has lower softness, which can easily cause vascular injury. In addition, the radial support force of wingspan stent is larger and its continuous stimulation to endovascular membrane may lead to in-stent restenosis. It is reported in the literature that the rate of in-stent restenosis by wingspan can be as high as 31.2% (7). Feng et al. (8) considered that it was safer and more effective for long lesions (>15 mm) treated with enterprise stents than wingspan stents. Apollo stent (McroPort, Shanghai) is an intracranial dedicated ball-expanding stent with stent diameter of 2.5–4.0 mm and a stent length of 8–23 mm. In 2015, the VISSIT test results did not support that the treatment of sICAS with ball-expanding stent was better than anti-platelet aggregation drugs (9). Jiang et al. (10) consider the flexibility of apollo stent delivery system was poor. For intracranial vessels with circuitous pathway and longer than 10 mm, its operation failure rate was high, and the light transmittance of stent itself was poor. It was difficult to observe the stent under X-ray after balloon dilatation. Stent shift might occur during withdrawal of guide wire.

Enterprise stents are self-expandable stents produced by Codman Company in the United States, which were expected to work with coils in the treatment of intracranial wide-necked aneurysms (11). The diameter of the stent is 4.5 mm, and the length ranges from 14 to 37 mm, which provides more choices for operators. The results of Krischek et al. (12) show that enterprise, which has a closed loop design, less radial support, and soft support conduit,

is easy to be placed under the guide wire, easy to be released, and to be located more accurately, compared with wingspan.

At present, enterprise stent therapy for sICAS is reported in few articles, showing that the restenosis rate of enterprise stent is from 3% to 24.7% (8,13-15). Vajda et al. (15) treated 189 patients with ICAD (with 209 lesions) using the enterprise stent, and had a DSA follow-up rate of 83%; they found that the in-stent restenosis rate was 24.7%, lower rate than that of wingspan (31.2%). Duffis et al. (16) considered a high sensitivity and specificity of CTA compared to DSA for the diagnosis of both any intracranial stenosis and for the diagnosis of 50% stenosis, so in our follow-up, 8 lesions (40.0%) were detected by DSA, the rest (60.0%) were checked by CTA, there was 3 (15.0%) in-stent restenosis. Wang et al. (13) considered that the large radial force of the wingspan stent could stimulate intimal hyperplasia and lead to restenosis in the stent, while enterprise was a self-expandable stent with less radial force. It can effectively reduce the rate of in-stent restenosis. At the same time, the continuous and small radial force of enterprise stent was conducive to the gradual recovery of the narrow vascular lumen.

Miao et al. (17) carried out a prospective study of targeted PTA or PTAS treatment in different types of sICAS patients. They considered that the Mori A lesions of the type I pathway were suitable for apollo stent and Mori B, C type lesions with the type III path were suitable for self-expandable stent. The Mori A lesion with a tortuous path is suitable for simple balloon dilatation with a total technical success rate of 96.3%. In this study, complex lesions were treated with balloon angioplasty and enterprise stent implantation. The technical success rate was 100%, and only 1 patient (5.0%) had ischemic cerebrovascular complications in perioperative period, which was less than 14.7% of perioperative complications reported by SAMMPRIS.

Jiang et al. (4) reported that the mortality of Mori A, B and C were 0, 0 and 25%, respectively. And the operation success rate of Access I was significantly higher than III. In this study, there are 9 (45.0%) Access I, 10 (50.0%) Access II and 1 (5.0%) Access III, and the high success rate of operation might be related to the fewer Access III.

In this study, there are 3 cases of in-stent restenosis (including 2 in-stent occlusion and 1 restenosis). The rate of restenosis was 15.0%, which

was lower than wingspan's in-stent restenosis that was registered by American multi-center enterprise in-stent. However, our study had several limitations. The patients enrolled in the study was relatively small, and the follow-up duration was not long. Besides, our study is a single-center experience, a prospective, multicenter, randomized controlled trial is required in the future.

Conclusion

For symptomatic intracranial atherosclerotic stenosis, especially patients with complex lesions, enterprise stent implantation is safe and effective. There is few data in our center due to strict criteria for intracranial stent. Prospective, multicenter, randomized controlled trials against optimal medical treatment are expected.

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