


Endovascular treatment of cerebrovascular stenosis with stent for patients with ischemic cerebrovascular disease

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Abstract

This study aimed to investigate the therapeutic effect of cerebrovascular stent implantation in southwest Chinese patients with ischemic cerebrovascular disease and underlying risk factors for stent restenosis.

We made a retrospectively analysis of occurring risk, cerebrovascular lesion, stent implantation, complication treatment, and prognosis of 54 patients with ischemic cerebrovascular disease in our department.

A total of 85 stents were implanted into 54 patients, involving 44 of the internal carotid artery system, 34 of the vertebral-basal artery system and 7 of the subclavian artery system. All patients with stenosis were reduced by >70%, with all stenosis complete reduction in 5 (9%) patients and reduction of over 90% in 25 (46%) patients. A total of 50 patients were followed up for 28.5 (21–35) months. The stents in 42 patients exhibited satisfactory shape and location while restenosis occurred in 8 patients. Univariate analysis revealed that hyperlipidemia, hyperuricemia, surgery duration, and total length of hospital stay are significantly correlated with stent restenosis, and hyperlipidemia and hyperuricemia were proven to be independent risk factors for restenosis using logistic regression analysis.

Cerebrovascular stent implantation and balloon inflation surgery can assist in abating angiostenosis and improving blood supplement effectively in patients with ischemic cerebrovascular disease. Besides, an overall evaluation, strict care, and regular check-up in perioperative period may reduce the occurrence of complications. Finally, several clinical parameters may need to be highly focused on in surgery for better prognosis.

Abbreviations: CT = computed tomography, DSA = digital subtraction angiography, ICVD = Ischemic cerebrovascular disease, IV = intravenous, MRI = magnetic resonance imaging, SD = standard deviation, TCD = transcranial Doppler.

Keywords: cerebrovascular stenosis, endovascular stent, ischemic cerebrovascular disease (ICVD), risk factors

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KL and LC contributed equally to this work.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction.

Ischemic cerebrovascular disease (ICVD) is a pathological state of hypoperfusion and hypoxia in brain tissue, and is associated with high morbidity that originates from cerebrovascular occlusion or stenosis. Furthermore, a certain proportion of patients undergoing ICVD will experience an acute ischemic stroke if treatment is delayed or inappropriate, which severely endangers health. Atherosclerosis is a major cause of hypertension, hyperglycemia, and hyperlipemia, and results in different levels of stenosis in the cerebral arteries.^[1–5] Therefore, arterial sclerosis and stenosis may play a significant role in clinical investigation and treatment of individuals with ICVD.

Endovascular stenting and remodeling have been the primary methods of treating various types of cerebrovascular stenosis or occlusion. Such methods primarily aim to restore local blood supply by remodeling narrow vessels, thus preventing ischemic stroke.^[6–9] However, a series of potential complications using this surgical technique persist, including carotid sinus reaction, hyperperfusion syndrome, intracranial hemorrhage, and stent restenosis, among others. Regardless of whether patients comply with regular anti-plaque medication, stent location, and the extent of stenosis determine the incidence of complications after surgery. In summary, advanced surgical technologies, perioperative nursing, and postoperative follow-up are all important elements in preventing against surgical complications.

Table 1
Descriptive analysis of patient clinical characteristics.

	N (%)
Demographics	
Mean age, years (range)	58 (35–73)
Male	38 (70)
Chronic health conditions	
Cerebral infarction	27 (50)
Hypertension	31 (57)
Diabetes	9 (17)
Coronary heart disease	4 (7)
Hyperlipidemia	12 (22)
Hyperuricemia	4 (7)
Hyperhomocysteinemia	2 (4)
Smoking	21 (39)
Basic clinical symptoms	
Headache	18 (33)
Vertigo	9 (17)
Alalia	9 (17)
Limb paralysis	14 (26)
Limb numbness	4 (7)
Combined symptoms	12 (22)
No evident symptoms	12 (22)

Unless otherwise indicated, data are number (percentage).

The present study included 54 patients with ICVD who underwent endovascular stenting. We analyzed the corresponding primary hazard factors, locations of vascular lesions, existing complications, and prognosis in those who underwent treatment in our hospital between January 2015 and August 2018, and explored the risk factors for stent restenosis. Our results will provide information regarding valuable evaluations and summaries for the subsequent endovascular treatment.

2. Methods

2.1. General patient condition

Fifty four patients (38 male, 16 female) who underwent endovascular stenting and remodeling surgery in the authors hospital between January 2015 and August 2018 were included. All operations were performed with informed written consent from the patient and family members, and approved by ethics committee of the 75th Group Army Hospital of People's Liberation Army. Data were collected through available hospital records. Detailed information regarding clinical characteristics of the patients is summarized in Table 1.

Patients diagnosed with ICVD were divided into 2 groups—those with infarction and those with transient ischemic attack—based on the International Classification of Diseases, Ninth Revision, Clinical Modification (codes 433, 434, and 435). Definite infarction foci in the brain were found in 27 of the 54 patients on computed tomography (CT) or magnetic resonance imaging (MRI) examination. Thirty one patients had hypertension, 9 had diabetes, and 4 had coronary heart disease without acute coronary syndromes, which do not require urgent treatment in the cardiology department. Simultaneously, abnormalities in blood biochemistry indexes were found in some patients. Patients underwent transcranial Doppler (TCD) and cervical vascular ultrasound after admission for preliminary inspection of cerebrovascular lesions (stenosis, plaque, or

Table 2
Degree and location of stenosis, stent types and outcome of operation.

	N (%)
Degree of stenosis	
Intermediate-grade, >50% & <70%	15 (28)
High-grade, >70%	35 (65)
Occlusion	4 (7)
Location of stenosis	
Internal carotid artery system	37 (69)
Vertebral-basal artery system	29 (54)
Subclavian artery system	6 (11)
Multiple systemic locations	16 (30)
Stent types	
Wallsten	23 (43)
Apollo	29 (54)
SD	5 (9)
LD	3 (6)
Solitaier	2 (4)
AcculinK	1 (2)
Outcome of operation	
Stenosis reduction >70% & <90%	22 (41)
All stenosis reduction >90% & <100%	25 (46)
All stenosis reduction = 100%	5 (9)
Operation unfinished	2 (4)

Unless otherwise indicated, data are number (percentage).

sclerosis). Of 54 patients, 45 (83%) were diagnosed with definite stenosis and 17 (31%) with plaques.

All patients underwent digital subtraction angiography (DSA) of the cerebral artery system for further inspection before stent implantation. Of the patients, 37 patients had stenosis or occlusion in internal carotid artery system, 29 in the vertebral-basal artery system, and 6 in the subclavian artery system, while 16 patients had multiple lesions in ≥ 2 systems (Table 2). Surgical indications and contraindications were strictly defined in this study. Indications were as follows: specific clinical symptoms (paralysis, speech vague, dysdipsia, vertigo), in accordance with cerebral pathological and physiological characteristics dominated by the responsible artery ($\geq 50\%$ luminal stenosis); no specific symptoms of cerebral artery stenosis $\geq 70\%$; and cerebral artery stenosis suitable for stent implantation (i.e., implantation would effectively improve related cerebral blood supply). Contraindications were defined in patients with severe chronic diseases (heart, lung, liver, kidney), hemorrhagic disease, acute Takayass arteritis, and easily-shed large plaques. The degrees of luminal stenosis among patients in this study reported in Table 2.

2.2. Operative procedures

The method of anesthesia for endovascular surgery was based on location of the stent, operative difficulty, and basic condition of patients. Systemic administration of heparin was performed during the procedures, which were all via the transfemoral route. The angiography catheter was placed -3 cm to -5 cm proximal to the vascular lesion. Therein, a vascular filter would be placed at the distal site of lesion to prevent shedding plaque from embolizing. Balloons were used in the stenosis or occlusion to expand the vessel beforehand if operative conditions permitted. Different types, sizes, and numbers of stents (Table 2) were used, which were determined by the location and severity of the lesion, stability of the stent, and whether artery dissection existed. During the operation, heart rate, blood pressure, and patient

Table 3
Perioperative characteristics, complications, and prognosis.

	N (%)
Intraoperative characteristics	
Technical success	52 (96)
Additional balloon expansion applied	33 (61)
Additional vascular filter applied	25 (46)
Operating time, minutes, mean (SD)	96 (49)
Vasoactive drugs used	1 (2)
Operation-related typical complications	
Stress blindness	1 (2)
Secondary major epileptic seizures	2 (4)
Carotid sinus reaction	2 (4)
Intracranial hemorrhage	2 (4)
In-hospital data	
Overall hospital stay, days, mean (SD)	23 (7)
Mortality	0 (0)
Prognosis	
Stents restenosis	8*
Reintervention	3 (6)

* data are incomplete.

Unless otherwise indicated, data are number (percentage), SD = standard deviation.

consciousness were monitored closely. Meanwhile, medication was used to maintain vital signs, stabilize emotions, and mitigate various emergent symptoms (e.g., headache, vertigo, palpitation, nausea). Angiography at the lesion site was performed during and after the operation for inspection. Femoral artery puncture was oppressed for 20 minutes directly or 10 minutes using a vessel suture instrument after the operation, followed by compression bandaging for 24 hours or 12 hours when vessel suture instruments were used. Maintenance therapy including subcutaneous heparin 4000 IU was administered for 7 days. Meanwhile, aspirin 100 to 300 mg/day and clopidogrel 75 to 150 mg/day were administered for 4 to 8 weeks. Regular doses of aspirin (100 mg/day) and clopidogrel (75 mg/day) were recommended for a prolonged period. Based on the patients postoperative condition, maintenance of vital signs, balancing water and electrolytes, and preventing infection should be the focus.

2.3. Statistical analysis

Normally distribute data are expressed as mean \pm standard deviation (SD), while non-normally distributed data are expressed as median (Q1 – Q3), and enumerative data are expressed as frequency (percentage). The Kaplan–Meier method was used to estimate the percentage free from restenosis. Univariate analysis was used to assess the prognostic value of diverse clinical factors using the t (measurement data) or χ^2 (enumeration data) tests. Logistic regression analysis was used to determine independent risk factors. Differences with $P < .05$ were considered to be statistically significant. All statistical analyses were performed using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA).

3. Results

Details of surgical parameters are shown in Table 3. Eighty five stents were implanted in 54 patients, including 44 in the internal carotid artery system, 34 in the vertebral-basal artery system, and 7 in the subclavian artery system. Sixteen patients underwent implantation of ≥ 2 stents. Six representative implantation sites

for stents in 3 different cerebral artery systems photographed before and after the operation using DSA are shown in Figure 1. With extremely severe vascular stenosis, tortuosity or even complete occlusion, operations ceased in 2 patients because the microcatheter could not pass through the lesion site after repeated attempts. Following stent implantation and balloon expansion, DSA revealed that all stenoses were reduced by $>70\%$, with complete reduction in 5 (9%) cases and 90% partial reduction in 25 (46%) (Table 2).

Seven patients experienced postoperative complications, which are summarized in Table 3. One patient experienced stress blindness; however, the symptoms disappeared spontaneously 2 days later. Two patients experienced secondary major epileptic seizures, which were treated using anti-epileptic and sedative therapy, gradually alleviating symptoms within 2 days and never recurring in outpatient follow-up 1 month later. Two patients experienced a severe carotid sinus reaction, which is characterized by a decrease in heart rate and blood pressure when performed with stent implantation near the carotid sinus, with the lowest heart rate of 34 beats/minute and blood pressure of 64/40 mm Hg in a typical patient. In patients who were administered vasoactive drugs (dopamine and atropine), the heart rate returned to normal and blood pressure partly recovered, and completely 4 days after constant dopamine maintenance. Two patients experienced intracranial hemorrhage with stenting in the middle cerebral artery. One patient experienced subarachnoid hemorrhage, with symptoms including intense headache, nausea and dysphoria, which were characterized as hyperperfusion syndrome. The patients condition remained aggravated, even when hemostasis, anti-vasospasm, and vasoactive drugs were administered. Another patient experienced intracerebral hematoma in the basal ganglia and temporal lobe (DSA images before and after operation, postoperative CT scan 0.5 hour later, and reexamination 1 year later via enhanced CT scan are presented in Figure 2). Paralysis of the left upper limb without unconsciousness recovered to a certain extent when hemostasis, anti-vasospasm, and brain protective therapy for the hematoma were implemented. Hematomas were not enlarged on re-check. Finally, no patients experienced obvious discomfort at the return visit 1 month later, except for 1 who experienced subarachnoid hemorrhage, as mentioned above.

A total of 50 patients were followed up, of which 23 underwent DSA and 27 underwent CT angiography for reexamination. The follow-up duration was 28.5 (21–35) months, with a minimum of 6 months and a maximum of 46 months. Stents in 42 patients exhibited satisfactory shape and location, while restenosis occurred in 8 patients. Three patients underwent secondary endovascular surgery due to new stenosis in other parts of the cerebral artery (Table 3). The Kaplan–Meier curve for the percentage free of restenosis is presented in Figure 3.

Combining clinical parameters with occurrence of stent restenosis, hyperlipidemia, hyperuricemia, surgery duration, and total length of hospital stay were significant factors that posed risks for restenosis according to univariate analysis (Table 4). Parameters with $P < .10$ in the univariate analysis were then extracted for further logistic regression analysis, which revealed that hyperlipidemia and hyperuricemia were independent risk factors for restenosis (Table 5).

4. Discussion

An increasing number of individuals ignore good dietary habits (i.e., balanced diet) and healthy lifestyle as current living

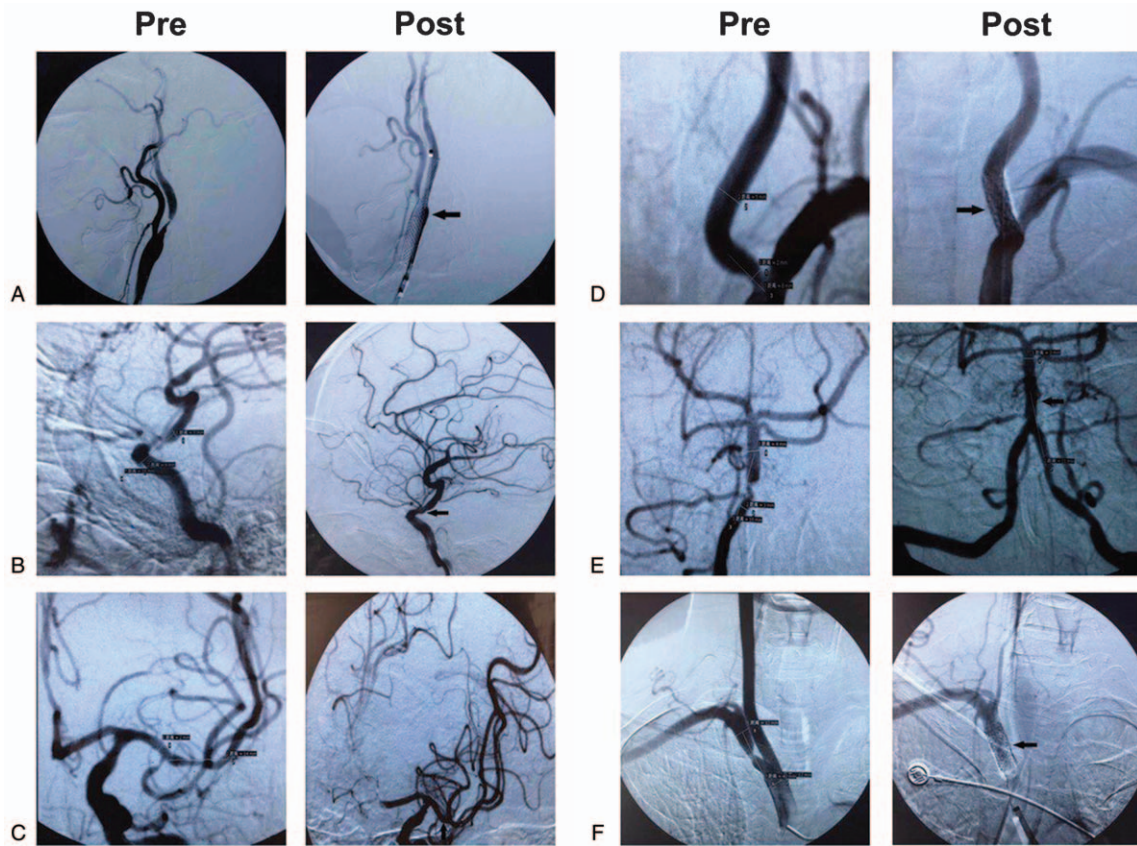


Figure 1. Stents implantation in six typical sites before and after operation using DSA. (A) Right internal carotid sinus. (B) Siphon section of the left internal carotid artery. (C) Left middle cerebral artery. (D) Starting section of the left vertebral artery. (E) Basal artery. (F) Right subclavian artery. Lines show measurement of the vessels, arrows show the location of the stents.

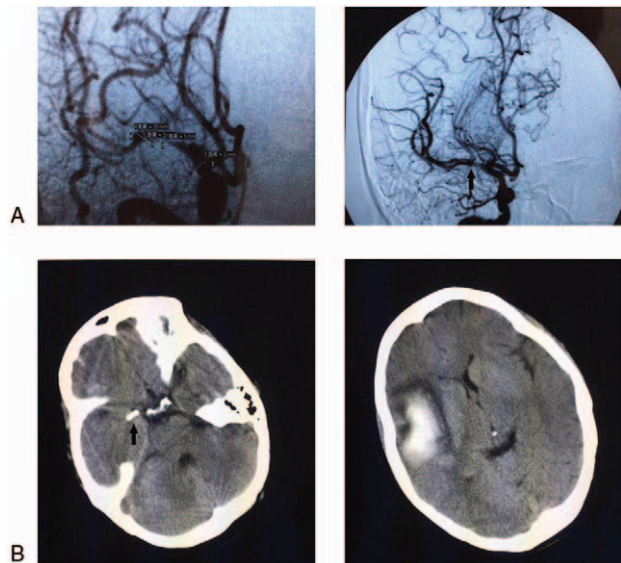


Figure 2. Clinical data of 1 typical patient experienced postoperative intracranial hemorrhage. (A) Stents implantation in the right middle cerebral artery before and after operation using DSA. (B) Postoperative CT 0.5 hour later and enhanced CT as reexamination 1 year later of intracranial stent and related hemorrhagic foci. Lines show measurement of the vessels, arrows show the location of the stents.

standards develop and social stress accumulates. The incidences of chronic diseases and sub-healthy conditions (such as hypertension, diabetes, hyperlipidemia and hyperuricemia, among others) have increased, and both are the obvious result of inappropriate lifestyle and dietary habits, especially in growing aging populations. All of these factors increase the risk for the occurrence of cardio-cerebrovascular diseases. Nearly 60% of the 54 patients (31 cases) with ICVD in the present study had hypertension, diabetes, or coronary heart disease. ICVD is

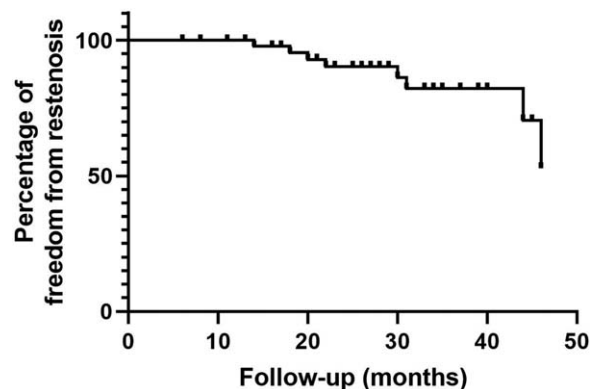


Figure 3. Kaplan-Meier curve of percentage free of restenosis during follow-up period.

Table 4**Univariate analysis of risks for restenosis.**

	Restenosis (n=8)	Patency (n=42)	P value
Age (y)	55.6±11.7	58.9±8.8	.063
Male	7 (87.5)	27 (64.3)	.381
Cerebral infarction,	3 (37.5)	21 (50.0)	.793
Hypertension	4 (50.0)	24 (57.1)	1.000
Diabetes	2 (25.0)	6 (14.3)	.817
Coronary heart disease	1 (12.5)	3 (7.1)	1.000
Hyperlipidemia	4 (50.0)	5 (11.9)	<.05
Hyperuricemia	4 (50.0)	0 (0.0)	<.05
Hyperhomocysteinemia	0 (0.0)	2 (4.8)	1.000
Smoking	3 (37.5)	14 (33.3)	1.000
Surgery duration (min)	150.3±86.8	85.0±32.1	<.05
Total length of stay (d)	29.1±11.9	21.2±5.8	<.05

characterized as a series of pathological changes due to the long-term effects of abnormal hemodynamics, which further result in the accumulation of atherosclerotic plaque,^[2,10] vascular stenosis,^[5] and cerebral infarction.^[11] Therefore, early diagnosis and intervention of cerebrovascular lesions can effectively improve the ischemic condition of cerebral tissue, preventing the occurrence and progression of cerebral infarction.

Imaging findings from examinations of the head (e.g., CT, MRI, TCD, and cervical vascular ultrasound) provide important early evidence supporting the diagnose of various cerebrovascular lesions, such as stenosis, occlusion, and malformation. In particular, cervical vascular ultrasound primarily identifies the location, size, and the degree of luminal stenosis.^[12,13] More than 80% of patients in the present study were diagnosed with different degrees of cerebrovascular lesions using cervical vascular ultrasound and subsequent DSA. Therefore, cervical vascular ultrasound provides important clinical value in preliminary inspections of ICVD.

Endovascular treatment for cerebrovascular diseases is a minimally invasive operation in numerous cerebrovascular lesions (stenosis, occlusion, arterial dissection, aneurysm, etc.). The implantation of stents and balloons at lesion site can relieve vascular stenosis, improve vascular reformation, and promptly restore blood supply in the brain compared with traditional medications.^[14,15] All patients included in the present study experienced apparent alleviations of cerebrovascular stenosis and clinical symptoms, which demonstrates the significant effect of endovascular treatment. However, 2 patients in whom stent implantation failed suggests that the treatment would fail if vascular lesions could not be treated in timely manner and the degree of stenosis was extremely severe. Therefore, the rapidity at which disease is detected, diagnosed, and treated is important in those with ICVD.

Endovascular treatment remains associated with some post-operative complications due to operative technology, instant pathophysiological changes, and patient compliance to anti-plaque medications after surgery.^[16–20] Complications include the following. First, intracerebral hemorrhage is one of the most severe complications caused by catheter or guidewire, resulting from severe vessel sclerosis, or distortion. It occurs frequently in the secondary cerebral arteries (middle cerebral artery, basal artery). In the present study, 2 patients with intracerebral hemorrhage underwent stent implantation in the middle cerebral artery. Consequently, 1 required bleeding control and the other died due to the inhibition of respiratory and circulatory centers in the brain. These cases indicate that careful preoperative assessment, appropriate operative procedures, and perioperative nursing care should be performed. Second, carotid sinus reaction is a kind of vessel-nerve reflex caused by the tearing of carotid intima or sclerotic plaque, and the stimulus of carotid sinus baroreceptors due to the stretching action of stents and balloons. The common clinical symptoms are a drop in heart rate and blood pressure. They most commonly occur in endovascular treatment at the bifurcation of the carotid artery. The duration and the severity of these symptoms are related to the degree and length of stenosis, the type of stents, and whether patients have underlying conditions such as heart failure and/or hypotension. In the present study, carotid sinus reaction occurred in 2 patients, both of which received implantation of self-expandable stents at the bifurcation of the carotid artery. Patients with hypertension did not experience heart failure; however, their blood pressure normalized before the operation after the administration of antihypertensive drugs. Both were found to have intermediate and severe degrees of vascular stenosis in the carotid sinus according to DSA before the operation. Subsequently, the more severe the degree of stenosis is, the more evident carotid sinus reaction in the patients will be. Heart rate returned to normal by the immediate administration of intravenous (IV) dopamine and atropine. Blood pressure recovered completely to the preoperative levels via continuous (i.e., pump) intravenous administration of dopamine. Consequently, stents at the carotid sinus have smaller oppression of vessel walls. The selection of stents and availability of conventional first-aid medications during the operation help reduce the incidence and severity of this reaction. Third, hyperperfusion syndrome is caused by damage to the blood-brain barrier and vasogenic cerebral edema after relieving vascular stenosis where cerebral blood flow rises abruptly. It is characterized by rising blood pressure, perioperative headache, focal or generalized seizures, and transient focal neurological impairment (paralysis, sensory disturbance, unconsciousness, aphasia). The degree of vascular stenosis, basic blood pressure, and severity of cerebral ischemic impairment before surgery all contribute to the incidence and degree of hyperperfusion

Table 5**Logistic regression analysis of independent risk factors for restenosis.**

	B	SE	Wald	Exp (B)	P value
Age (y)	-.049	0.096	0.261	0.952	.609
Hyperlipidemia	17.039	4139.106	0.000	25126138.545	.997
Hyperuricemia	-41.450	0.000	0.000	9.964E-019	<.05
Surgery duration (min)	-.034	0.017	4.002	0.967	<.05
Total length of stay (d)	-.092	0.135	0.466	0.912	.495

syndrome. Furthermore, there were 2 patients with evident hyperperfusion syndromes in this study. They experienced transient unconsciousness and generalized seizures within 24 hours after surgery. Intracranial CT was performed to exclude hemorrhage. Valproic acid, diazepam, and phenobarbital IV were administered to control seizures and calm the patients, nimodipine IV to lower blood pressure and to relieve vasospasm, and mannitol IV to reduce cerebral edema. All patients symptoms were controlled and no one experienced recurrence in return visits. The mechanism of hyperperfusion syndrome has been extensively investigated; however, there is still no systemic and effective measure to prevent it. Therefore, all existing preventive focus on preoperative precautions including controlling blood pressure and postoperative symptomatic treatment. Fourth, stent restenosis always occurs in the long-term because patients do not comply with a healthy diet, lifestyle, and regular anti-plaque medications. Meanwhile, the stent itself may stimulate vessel intima and cause plaque again. There were 6 patients who experienced plaque recurrence and re-occlusion found restenosis in stents via DSA re-check 6 months to 2 years after the operation. In addition, patients reduced the dosage of aspirin and clopidogrel without doctors permission in this year. With the exception of management during the perioperative period, re-examination of stents and maintenance of anti-plaque medications are also needed. In addition, we performed risk factor analysis to assess the correlation between numerous clinical parameters and occurrence of stent restenosis, investigating potential risk factors that exacerbate restenosis, thereby establishing a more optimized regulation of endovascular surgery.

A recent survey demonstrated that inflammation may be an important factor in the pathogenesis of cerebrovascular disease. Antonino et al found that several pro-inflammatory factors were significantly associated with a diagnosis of acute ischemic stroke,^[21] which also exerted negative influence on diabetic-food-syndrome-related cerebrovascular events.^[22] Simultaneously, increased levels of selected pro-inflammatory cytokines were examined after intracranial and cervical stent implantation.^[23] These indicate that inflammation is also a key point to be addressed during the perioperative period. Incidentally, Antonino et al also found that long-term aerobic physical activity could reduce these systemic inflammation in sedentary individuals.^[24] These data offer a clue that sufficient exercise may be conducive to better recovery in patients who undergo endovascular surgery.

In summary, endovascular treatment of the cerebral artery may be a novel and effective method to treat cerebrovascular stenosis and occlusion. It improves the therapeutic efficacy and avoids worsening infarction combined with traditional thrombolytic, anti-plaque, promotion of blood circulation, and cerebral protective therapy. At the same time, strict surgical indications and contraindications, detailed preoperative assessment, skilled manipulation, careful perioperative management, periodic reexamination, and precautions in operative complications are important to ensure safety and effectiveness.

Author contributions

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