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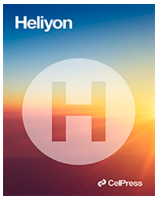

Risk prediction of CISS classification in endovascular treatment of basilar artery stenosis

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ABSTRACT

Objective: To investigate the incidence of ischemic stroke complications after endovascular treatment for basilar artery stenosis used preoperative high-resolution magnetic resonance vascular wall imaging (HRMR/VWI) and diffusion-weighted imaging (DWI).

Methods: The clinical data of 47 patients with severe symptomatic basilar artery stenosis (stenosis rate ≥70 %) treated with endovascular therapy at the Neuro-interventional Center from December 2017 to December 2021 were retrospectively analyzed. High-resolution magnetic resonance angiography (HRMR VWI) and DWI were used to evaluate the location of atherosclerotic plaque at basilar artery stenosis and the distribution of cerebral infarction lesions in all patients before surgery.

According to the CISS classification system for ischemic stroke, patients were divided into a perforation group and a hypoperfusion group, and the general situation, plaque distribution, and incidence of ischemic stroke complications 7 days after endovascular treatment in the two groups were analyzed.

Results: There was no significant difference in baseline data between the two groups. After 7 days of intravascular treatment, the incidence of ischemic stroke was higher in the perforation group (20.0 %) than in the hypoperfusion group (0.0 %), and the difference was statistically significant ($P = 0.027$). A significant association was found between the perforation group and the hypoperfusion group for the incidence of ischemic stroke at 7 days ($P = 0.003$, $OR = 2.347$; 95 % CI = 2.056–4.268). There were a higher proportion of ventral plaques (74.1 %) and a lower proportion of dorsal plaques (33.3 %) in the hypoperfusion group, which were 15.0 % and 90.0 % in the perforation group, respectively ($\chi2 = 16.045$, $P < 0.001$; $\chi2 = 15.092$, $P < 0.001$). There was no significant difference in the proportion of left and right plaques between the two groups.

Conclusions: The risk of ischemic stroke is greater in patients with perforator artery obstruction undergoing endovascular therapy, and lower in patients with hypoperfusion/embolus removal.

1. Introduction

In recent years, the incidence of ischemic stroke in China has been increasing, from 112/100,000 in 2005 to 156/100,000 in 2017, and ischemic stroke accounts for 70 % of the total number of new patients, so ischemic stroke has become a major factor endangering

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people's life safety [1]. Unlike anterior circulation stroke, which accounts for 25 % of all ischemic stroke cases, symptomatic vertebrobasilar atherosclerotic disease is more challenging; Despite standard antiplatelet and statin therapy, the annual recurrence rate of stroke remains relatively high [2–4]. And ischemic stroke due to narrowing or occlusion of the vertebrobasilar artery, is often devastating.

Endovascular therapy is a worldwide effective alternative to drug-refractory basilar artery (BA) atherosclerotic stenosis and has achieved positive results [5,6]. However, perioperative complications of endovascular treatment of BA atherosclerotic stenosis are high. The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) was a randomized, superiority, multi-center, clinical trial funded by the National Institute of Neurological Disorders and Stroke. Early results of the SAMMPRIS trial showed that, by 30 days, 14.7 % of patients in the stenting group and 5.8 % of patients in the medical group had died or had a stroke. Moreover, the long-term outcome of patients in this trial clarified that aggressive medical treatment is superior to percutaneous transluminal angioplasty and stenting (PTAS) with the Wingspan stent in patients with recent transient ischaemic attack or stroke (within the past 30 days) attributed to 70–99 % atherosclerotic intracranial arterial stenosis, especially in high-risk patients with atherosclerotic intracranial arterial stenosis. The most common complication of endovascular therapy is perforating artery occlusion, but BA atherosclerotic stenosis stenting is associated with stroke or mortality of up to 21.6 % [7]. In coronary artery and middle cerebral atherosclerosis, plaque naturally tends to form opposite the opening of the branch or perforating artery, and once the plaque is located near the opening of the perforating artery, symptoms are more likely to occur during stent implantation, which is associated with the "snow shovel" effect during stent implantation [8,9]. The distribution of basilar atherosclerotic plaques is long and evenly affects the ventral, dorsal, and lateral walls, and the plaques on the dorsal and lateral walls are associated with symptomatic pontine infarction and not with asymptomatic infarction [10]. High-resolution magnetic resonance vessel wall imaging (HRMR VWI) can be used to assess the location of plaques, vulnerability, and its relationship to important branch vessels in severe stenosis of the symptomatic basilar artery, helping to increase the safety of endovascular therapy [11,12].

This study aimed to use preoperative HRMR VWI and preoperative magnetic resonance weighted imaging (DWI) technology [12], combined with the Chinese ischemic stroke subclassification (CISS) [13] typing system. The incidence of ischemic stroke and the distribution of plaque at basilar artery stenosis were retrospectively analyzed to provide safety guidance for subsequent endovascular treatment of basilar artery stenosis.

2. Methods and material

2.1. Participant

The clinical data of 47 patients with symptomatic basilar artery stenosis who received endovascular therapy at Shanxi Cardiovascular Hospital Neurointerventional Center from December 2017 to December 2021 were retrospectively analyzed, and all patients underwent preoperative high-resolution magnetic resonance vascular wall imaging and magnetic resonance diffusion-weighted imaging. According to the Chinese ischemic stroke sub Chinese classification (CISS) system [13], the pathogenesis is that the carrier artery plaque blocks the perforating artery because its lesions are distributed in the brainstem part of the basilar artery stenosis, which is called the perforation group (Fig. 1a); Patients whose pathogenesis is low perfusion/emboli clearance are called hypoperfusion group because the distribution of lesions in such patients is mostly located in arterial branches far from the basilar artery stenosis (such as a posterior cerebral artery, superior cerebellar artery, and other branches) (as shown in Fig. 1b). At the same time, the general information of the enrolled patients, such as gender, age, history of tobacco and alcohol, history of hypertension, dyslipidemia, diabetes history, and family history were collected. This study is in line with the Declaration of Helsinki.

Inclusion criteria: (1) Age 22–80 years old. (2) The time from the first onset to endovascular treatment ≥3 weeks, and the ischemic

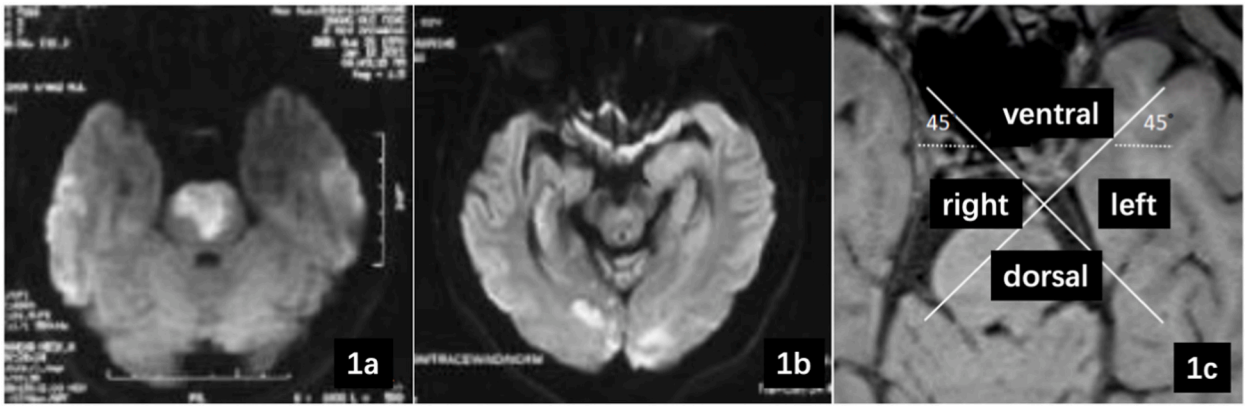

Fig. 1. Typical cases for grouping and imaging analysis. 1a. Typical case for perforation group; 1 b. Typical case for the hypoperfusion group. 1c. Typical case for the description of the distribution of basilar artery plaque. There is a greater risk of perforating branch occlusion after dorsal plaque balloon dilation.

stroke (transient ischemic attack (TIA) or cerebral infarction) patients with ≥BA stenosis as the responsible vessel twice before surgery has relapsed even after strict drug treatment; Modified Rankin score mRS ≤3. (3) The stenosis rate of BA is 70 %~99 %. Measurement method of narrowed blood vessels: based on digital subtraction angiography DSA images, using WASID method: (Warfarin-Aspirin Symptomatic Intracranial Disease), It is usually measured with a reference to the normal arterial diameter distal to the stenosis segment: stenosis rate (%) = 100 % to (diameter of stenosis segment/diameter of normal segment distal to stenosis) × 100 % [14]. (4) The patient and his family have full informed consent and sign the informed consent form for surgery.

Exclusion criteria: (1) BA occlusion. (2) BA stenosis caused by non-atherosclerotic causes, such as vasculitis, myofiber dysplasia, and BA dissection. (3) Patients with intracranial aneurysm, intracranial tumor, systemic tumor, coagulation mechanism disorder, severe heart, lung, liver, kidney dysfunction, and expected survival time <1 year. (4) Patients who cannot tolerate general anesthesia and postoperative dual antiplatelet aggregation therapy. (5) Lack of clinical and imaging data.

2.2. Imaging examination

All patients were preoperatively treated with head DWI to determine the distribution location of symptomatic cerebral infarction lesions and HRMR VWI (3.0 T magnetic resonance instrument, Siemens AG, Germany) to evaluate the stenosis of blood vessels, the distribution location of plaques and their position relationship with perforating blood vessels; Digital subtraction angiography (DSA) is used to assess the degree and location of narrowing of blood vessels.

2.3. Treatment

After the patient completes the preoperative examination and assessment, and at the same time completes the clopidogrel gene test, at least 4 days before the operation, continuous administration of clopidogrel tablets (75 mg/day) and aspirin (100 mg/d) dual antiplatelet aggregation therapy, if clopidogrel gene detection is intermediate metabolism or slow metabolism, it is replaced with ticagrelor.

Surgical operation: (1) After general anesthesia is satisfactory, femoral artery puncture is performed, the femoral artery sheath is inserted, and systemic heparinization is given. (2) Balloon dilation and/or stent plasty under general anesthesia. 3) Regular oral administration of double antiplatelet therapy drugs after surgery.

3. Efficacy and adverse event evaluation methods

Intraoperative observation for complications such as arterial dissection, perforation, downstream vascular embolism, acute or subacute stent thrombosis, and death events. The NIHSS score was performed by two neurologists before surgery, immediately after postoperative awakening anesthesia, 24 h after surgery, and 7 d after surgery (National Institute of Health stroke scale NIHSS score), and the 7 d NIHSS score after surgery was regarded as not aggravated as before surgery, and the NIHSS score after 7 d after surgery was ≥1 point higher than before surgery, and the head CT was further performed to screen for bleeding, and the distribution of ischemic stroke lesions was determined by head DWI.

3.1. Image analysis

The collected images are processed using Siemens processing systems. All patient images were blinded by two experienced clinical imaging physicians with intermediate or higher professional titles. When the results are inconsistent, the decision is made after discussion. For the description of the distribution of basilar artery plaque, select the cross-sectional image of the blood vessel with the most severe stenosis in the lumen of the vessel, as shown in Figure (Fig. 1c) in the cross-section of the basilar artery at an angle of 45° to the sagittal line and coronary line, divide the basilar artery into four equal parts, and name: left, right, dorsal, ventral. When plaques are distributed in two or more quadrants, the count of each quadrant in which the plaque is located is increased by 1 [15,16].

3.2. Statistical analysis

SPSS 22.0 software is used for statistical analysis, the measurement data is described by (mean ± standard deviation), and the statistical analysis adopts two independent samples *t*-test; The counting data were described by frequency and percentage, and the chi-square test was used for comparison between groups. Logistic regression was used to compute odds ratios adjusted for baseline characteristics to evaluate the incidence of ischemic stroke at 7 days after endovascular therapy. $P < 0.05$ indicated that the difference was statistically significant.

4. Results

4.1. Basic information

The clinical characteristics of the participants are listed in Table 1. The mean age of the 20 patients in the perforation group was 62.00 ± 8.27 years, that in the hypoperfusion group was 59.67 ± 6.83 years. There was no significant difference in baseline data between the two groups, including percent of hypertension, diabetes, and atrial fibrillation.

4.2. Surgical results and complications of the two groups of patients

Balloon dilation was performed in 22 cases and balloon dilation + stenting was performed in 25 cases. None of the patients had complications such as basilar artery perforation, stent thrombosis, and cerebral hemorrhage after surgery. Two cases had arterial dissection-like manifestations after balloon dilation, and the dissection disappeared after stent implantation, and there were no obvious symptoms after surgery. Four patients with increased NIHSS scores were patients in the perforation group, and the new DWI lesion suggested a new perforated infarction of the pontine. New-onset ischemic stroke 7 days after surgery: the perforation group (20.0 %) had a hypoperfusion group (0.0 %), and the difference was statistically significant (P = 0.027) (as shown in Table 2).

As shown in Table 3, in the binary logistic regression model, age and history of hypertension were significantly associated with the incidence of ischemic stroke at 7 days. A significant association was found between the perforation group and the hypoperfusion group for the incidence of ischemic stroke at 7 days (P = 0.003, OR = 2.347; 95 % CI = 2.056–4.268).

4.3. Comparison of plaque location distribution between the two groups

The proportion of ventral plaques (74.1 %) in the hypoperfusion group was higher than that in the perforation group (15.0 %), and the proportion of dorsal plaques (33.3 %) was lower than that in the perforation group (90.0 %), and the difference was statistically significant ($\chi 2 = 16.045$, $P < 0.001$; $\chi 2 = 15.092$, $P < 0.001$) (Detailed in Table 4). There was no significant difference in the proportion of left and right plaques between the two groups. Typical diseases type as shown in Fig. 2.

5. Discussion

Complications of ischemic stroke following endovascular treatment of basilar artery stenosis often led to severe disability and even life-threatening. However, there are certain reasons for the occurrence of perioperative ischemic stroke during endovascular treatment of basilar artery stenosis. In the current study, we mainly showed that the risk of ischemic stroke is greater in patients with perforator artery obstruction undergoing endovascular therapy, and lower in patients with hypoperfusion/embolus removal.

Early results of the SAMMPRIS trial showed that, by 30 days, 14·7 % of patients in the stenting group had died or had a stroke [17]. And the 30-day safety end point of any stroke within 30 days or hard TIA within 2–30 days was 24.1 % in the stent group in the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) trials [18]. Whereas in the Miao et al. study, only 4.3 % of patients had TIA or stroke, and only seven (2.3 %) had ischemic stroke complications [19]. One important reason is that, unlike the inclusion criteria for the SAMMPRIS and VISSIT trials, the patients enrolled in the Miao study were hypoperfusion etiologies, effectively excluding patients with perforating artery stroke. Chinese scholar Yang Yi et al. released a single-center study of stent treatment of symptomatic intracranial vertebral basilar artery stenosis in Northeast China, and the results showed that 7 ischemic events occurred within 24 h after surgery, including 1 TIA and 6 strokes (7.2 %, 7/97), all caused by perforating damage [20]. An analysis of perioperative complications of the SAMMPRIS trial showed that perforating infarction was the most common complication of balloon dilation and stenting of symptomatic BA stenosis [21]. Patients with basilar artery stenosis and pontine infarction are at high risk of postoperative complications due to perforating and occlusion of these parts due to plaque dissection, stent coverage, vascular straightening or curvature, thromboembolism, and other reasons. Therefore, intraoperative avoidance of perforating artery injury is critical to the success of endovascular therapy.

Currently, pan-cerebral angiography (DSA) is the “gold standard” for evaluating the degree of luminal stenosis of arteries, showing only the location and extent of luminal stenosis [22]. However, the success of intracranial atherosclerotic stenosis is not limited to this, and the relationship between the position of atherosclerotic plaque and perforating vessels is also a key factor influencing the occurrence of postoperative complications [23]. High-resolution magnetic resonance imaging can determine plaque stability, plaque location, and the relationship between plaque and perforating vessel position by showing the degree of plaque strengthening [24,25]. The distribution of atherosclerotic plaques in symptomatic middle cerebral is mostly ventral wall, and the upper wall and dorsal wall

Table 1
Comparison of the two groups of baselines.

	Perforation group (n = 20)	Hypoperfusion group (n = 27)	χ^2/t	p
Age (year)	62.00 ± 8.27	59.67 ± 6.83	1.059	0.296
male (n, %)	16 (80 %)	21 (77.8 %)	0.034	0.854
Hypertension (n, %)	14 (70.0 %)	25 (92.6 %)		0.057[a]
Diabetes (n, %)	11 (55.0 %)	10 (37.0 %)	1.500	0.221
Coronary artery disease (n, %)	2 (10.0 %)	3 (11.1 %)		0.644[a]
Stroke (n, %)	10 (50.0 %)	8 (29.6 %)	2.018	0.155
Atrial fibrillation (n, %)	1 (5.0 %)	0 (0.0 %)		0.426[a]
Smoker (n, %)	12 (60.0 %)	18 (66.7 %)	0.221	0.638
Drinker (n, %)	11 (55.0 %)	13 (45.1 %)	0.216	0.642
Total cholesterol (mmol/L)	4.22 ± 1.22	4.51 ± 1.00	0.871	0.389
Triglycerides (mmol/L)	1.92 ± 0.81	1.78 ± 0.70	0.641	0.525
high-density lipoprotein Cholesterol (mmol/L)	0.89 ± 0.15	0.89 ± 0.27	0.007	0.994
low-density lipoprotein Cholesterol (mmol/L)	2.40 ± 0.68	2.35 ± 0.62	0.302	0.764

[a] Fisher exact probability method results.

Table 2
The incidence of ischemic stroke at 7 days after endovascular therapy in both groups.

	Perforation group (n = 20)	Hypoperfusion group (n = 27)	P[a]
Diffusion-weighted imaging (+)	4 (20.0 %)	0 (0.0 %)	0.027
Diffusion-weighted imaging (-)	16 (80.0 %)	27 (100.0 %)	

[a] Fisher exact probability method results.

Table 3
Multivariate analysis of independent risk factors for the incidence of ischemic stroke at 7 days after endovascular therapy.

Variable retained in the model	Odds Ratio (OR)	95 % Confidence Interval (CI)	P
Age (year)	1.031	1.020–1.320	0.032
Hypertension	1.073	1.060–1.249	0.045
Perforation artery	2.347	2.056–4.268	0.003

Table 4
Comparison of plaque positions between the two groups.

	Perforation group (n = 20)	Hypoperfusion group (n = 27)	χ^2/t	P
Ventral side	3 (15.0 %)	20 (74.1 %)	16.045	<0.001
Left side	13 (65.0 %)	11 (40.7 %)	2.706	0.100
Right side	14 (70.0 %)	16 (59.3 %)	0.571	0.449
Dorsal side	18 (90.0 %)	9 (33.3 %)	15.092	<0.001

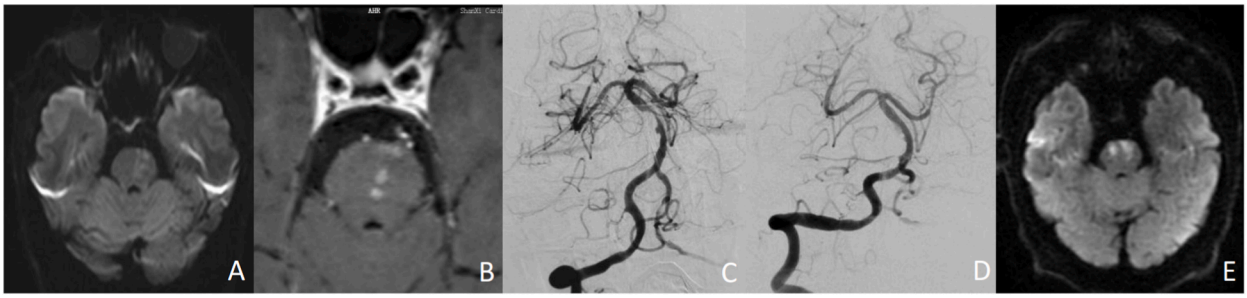

Fig. 2. A typical case of acute cerebral infarction is severe stenosis of the middle basilar artery. Male, 64 years old, main reason: "dizziness with right limb weakness for 5 days" admission, history: diabetes, smoking, alcohol history, diagnosis of acute cerebral infarction, severe stenosis of the middle basilar artery. Preoperative physical examination: clear consciousness, fluent speech, limb muscle strength level 5, NIHSS score 0, mRS score 0 points; Preoperative DWI (Fig. A) shows: acute stage of left cerebral infarction of pontine hematosis; The preoperative axial position HRMR—VWI (Fig. B) showed that the basilar artery plaque was eccentric, and the surface was punctate and significantly strengthened, and the plaque mainly affected the dorsal and right sides of the basilar artery wall. Preoperative digital silhouette angiography (Fig. C) showed severe stenosis in the middle of the basilar artery; Endovascular treatment showed significant improvement in stenosis with a balloon dilation at basilar artery stenosis and implantation of one Enterprise2 4.0 × 23 mm stent (Fig. D). 24 h postoperative review DWI showed that the acute stage of bilateral cerebral infarction of the pontine (as shown in Figure E), 7 d postoperative physical examination: clear consciousness, unable to speak, right limb muscle strength level 0, left upper limb muscle strength level 4, left lower limb muscle strength grade 2, NIHSS score 16 points, mRS score 4 points.

are less distributed [26,27]. This may be because vascular endothelial damage due to hypertensive shock is the main causative factor of atherosclerosis, and for the middle intracranial cerebral artery, the ventral wall is subjected to the greatest pressure on the blood flow side, so it is a common site for atherosclerosis. Then grasping the distribution of arterial plaque provides the possibility for protecting perforating vessels during endovascular treatment.

In patients with atherosclerosis in the middle cerebral period, plaque tends to form opposite the opening of the branch or perforating artery, and once the plaque is located near the opening of the perforating artery, symptoms are more likely during endovascular treatment, which is associated with the "snow shovel" effect during balloon or stent implantation [28]. The pontine branches of the basilar artery originate from both sides of the basilar artery and the back, about a dozen, varying in length. When basilar atherosclerotic stenosis, from an anatomical point of view, if the plaque is located near the perforating artery orifice, the squeeze process of the plaque during endovascular therapy, balloon dilation, or stent release, will also block the pontine perforating vessel due to the "snow shovel" effect, resulting in serious complications. The results of this study showed; Four patients had symptoms of increased NIHSS score after endovascular treatment, all of whom were patients in the perforation group, and the perfect head DWI examination showed perforating ischemic stroke; The incidence of ischemic stroke at 7 days after endovascular treatment in the two groups: the

perforation group (20.0 %) had a higher incidence and the perfusion group (0.0 %) had a lower incidence. Our results are consistent with those of MIAO et al. [19], which excluded patients with perforating arterial stroke and effectively avoided the risk of re-exacerbation due to endovascular therapy in patients with perforating artery stroke. Then there is no doubt that the preoperative grasp of the location of atherosclerotic plaques through high-resolution magnetic resonance imaging can reduce or avoid perforating ischemic stroke caused by perforating occlusion.

At present, the preoperative evaluation of endovascular treatment of basilar atherosclerotic stenosis is still mainly based on imaging examination, and rarely combined with the pathogenesis of symptomatic cerebral infarction. In this study, patients were divided into a perforation group and a hypoperfusion group according to the CISS classification system. The results showed that there were 23 cases of ventral plaque, 24 cases of left plaque, 30 cases of right plaque, and 27 cases of dorsal plaque in the two groups. There were a higher proportion of ventral plaques and a lower proportion of dorsal plaques in the hypoperfusion group, while no significant difference was observed in the proportion of left and right plaques between the two groups, which was consistent with the results of Jin et al. [10]. Combined with the results of the incidence of ischemic stroke 7 days after the previous two groups of endovascular treatment, this study believes that the incidence of ischemic stroke in patients in the hypoperfusion group after endovascular treatment of the basilar artery is lower than that in the perforation group, because the plaque at the stenosis of the basilar artery in this group is mostly located on the ventral side of the basilar artery, while the pontine branches of the basilar artery mostly originate from the dorsal and left and right sides of the basilar artery, and the ventral vascular branches are relatively few. On the contrary, the atherosclerotic plaques in the perforation group were distributed on the left and right sides and dorsal sides of the basilar artery, where there were more perforating vessels, and its "snow shovel effect" was obvious when undergoing endovascular treatment of the basilar artery, and the risk of blocking the perforating vessels was greater. This statement is also confirmed by studies such as Abe A [25], which suggest that stent plastic can produce a "snow shovel" effect, in which intraoperative balloons or stents can push athero-form in plaque near the opening of the perforating artery into the perforating vessel, resulting in perforating vascular occlusion events.

6. Limitations

The study had a few limitations. Firstly, this study is a single-center retrospective study, which only explores the changes of NIHSS score and preoperative in patients 7 days after surgery, without long-term follow-up, and the sample size is small, which has a certain impact on the research result. Secondly, the factors affecting the success of endovascular treatment surgery also include the nature of atherosclerotic plaque, whether it is strengthened or not, as well as basilar artery remodeling, endovascular treatment device selection, and many other factors, which we will further explore in future studies.

7. Conclusions

The risk of ischemic stroke is greater in patients with perforator artery obstruction undergoing endovascular therapy, and lower in patients with hypoperfusion/embolus removal. In the future, preoperative HRMR VWI technology and head DWI imaging technology can be used to evaluate the distribution of plaque at the basilar artery stenosis and the distribution of ischemic stroke lesions, and then analyze the pathogenesis of patients according to the CISS classification method.

Combined with the above theory, screening patients with greater benefits from endovascular therapy for treatment can be used for risk prediction. This will provide a relatively intuitive and concise preoperative assessment method for our future endovascular therapy of the basilar artery.

Data availability statement

The data associated with my study is not available or deposited into a publicly available repository. Please contact the corresponding author if you are interested.

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CRediT authorship contribution statement

Guiquan Wang: Conceptualization. **Tao Cheng:** Conceptualization. **Heng Niu:** Conceptualization. **Jing Ma:** Conceptualization. **Jianhong Wang:** Conceptualization. **Weirong Li:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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