ORIGINAL RESEARCH

Evaluation of the Treatment Effects of Intervention in Cortical Watershed Infarction Caused by Middle Cerebral Artery Stenosis

Jianjun Li, MM; Riming Huang, BM; Jia Li, MM; Wei Wu, BM

ABSTRACT

Objective • This study aims to evaluate the efficacy of interventional treatment in patients with hypoperfusion cerebral infarction in the territory of the lenticulostriate arteries caused by middle cerebral artery (MCA) stenosis.

Methods • A prospective, single-center, non-blinded research design was employed to assess the efficacy of interventional treatment for hypoperfusion cerebral infarction in the territory of the lenticulostriate arteries caused by MCA stenosis. Clinical and surgical data were collected from patients with MCA atherosclerotic disease who underwent interventional therapy at our hospital between January 2020 and December 2022. The intervention group consisted of 8 patients meeting the criteria for hypoperfusion cerebral infarction caused by MCA stenosis, while the control group comprised 8 patients with hypoperfusion cerebral infarction caused by middle cerebral artery stenosis who received conventional treatment. Clinical and imaging characteristics, perioperative complications, and follow-up outcomes were compared between the two groups.

Results • Pre-intervention cerebral perfusion imaging revealed significantly prolonged rMTT and rTTP, decreased rCBF, and altered rCBV within the territory of the lenticulostriate arteries in all 8 patients. Follow-up imaging showed restoration of blood flow and comparable perfusion to the healthy contralateral side. A case demonstrating successful restoration of vessel patency, good recovery, and absence of complications was presented. Both groups had favorable outcomes during follow-up, with no cases of stroke, transient ischemic attack (TIA), or death in the perioperative period. There were no significant differences in relative perfusion parameters, NIHSS scores, and mRS scores between the two groups.

Conclusion • Interventional treatment demonstrates good efficacy and low risk of complications in treating cortical watershed cerebral infarction caused by middle cerebral artery stenosis. It is an effective and safe alternative to conventional treatment. (*Altern Ther Health Med.* 2024;30(10):504-509).

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INTRODUCTION

Cerebral artery stenosis is one of the important causes of ischemic stroke.[1-3] The lenticulostriate arteries are vital blood supply arteries to the cerebral cortex, and stenosis or occlusion of these arteries can result in inadequate perfusion, leading to hypoperfusion cerebral infarction.[4,5] Cerebral infarction, commonly known as a stroke, occurs when there is a sudden loss of blood flow to a part of the brain, leading to damage or death of brain cells. This often results from a blockage or narrowing of the arteries that supply blood to the brain. The interventional therapy for cerebral infarction includes mechanical thrombectomy and intra-arterial thrombolysis, aiming to restore blood flow promptly, minimizing damage, and improving outcomes. Interventional therapy, including mechanical thrombectomy and intra-arterial thrombolysis, aims to promptly restore blood flow, minimize damage, and improve outcomes for patients with cerebral infarction. However, there are challenges in optimizing patient selection and developing advanced techniques and devices for interventional therapy. Overcoming these will advance interventional therapy for cerebral infarction. Hypoperfusion cerebral infarction is characterized by sudden onset and severe conditions, posing a significant threat to patients' quality of life and prognosis.[6] Currently, interventional treatment has been widely used as an important therapeutic approach for patients

with cerebral infarction related to arterial stenosis. Through interventional surgery, narrowed blood vessels can be dilated or stents implanted to restore blood flow and improve cerebral perfusion. However, research has shown that compared to medical treatment, interventional therapy carries a higher incidence of perioperative complications and does not yield superior long-term efficacy.[7] Particularly for patients with intracranial atherosclerotic stenosis presenting as infarction in the perforator artery territory, subgroup analysis suggests that interventional treatment may not be beneficial for this patient population.[7,8] The underlying mechanism may involve the occlusion of perforator artery origins caused by plaque displacement, thereby exacerbating perforator stroke.[9-11] Thus, most clinicians consider these patients unsuitable for interventional treatment. Hypoperfusion cerebral infarction is characterized by sudden onset and severe conditions, posing a significant threat to patients' quality of life and prognosis. While interventional treatment has been widely used for patients with cerebral infarction related to arterial stenosis, research has shown that it carries a higher incidence of perioperative complications and does not yield superior long-term efficacy compared to medical treatment. Particularly for patients with intracranial atherosclerotic stenosis presenting as infarction in the perforator artery territory, interventional treatment may not be beneficial due to the occlusion of perforator artery origins caused by plaque displacement.

The evaluation and research on the efficacy of interventional treatment for hypoperfusion cerebral infarction in the territory of the lenticulostriate arteries still remain inadequate. Currently, the primary approach for the management of patients with intracranial atherosclerotic stenosis is medical therapy, as supported by current clinical guidelines and evidence.[12,13] However, for those patients who have recently experienced a transient ischemic attack (TIA) or stroke and exhibit severe vascular stenosis in the intracranial atherosclerotic lesions, there remains a substantial risk of recurrence even with optimal medical management and risk factor control.[14,15] Consequently, interventional treatment has emerged as a promising therapeutic modality, serving as an alternative option for patients in such situations who may benefit from a more aggressive approach to reestablish adequate cerebral blood flow and reduce the likelihood of further ischemic events. It is important to note that further studies are still needed to comprehensively evaluate the effectiveness and long-term outcomes of interventional treatment in this specific patient population. Medical therapy is currently the primary approach for managing patients with intracranial atherosclerotic stenosis, but for those at a high risk of recurrence despite optimal medical management, interventional treatment offers a promising alternative. This approach aims to reestablish adequate cerebral blood flow and reduce the likelihood of further ischemic events. However, further studies are needed to comprehensively evaluate the effectiveness and long-term outcomes of interventional treatment in this specific patient population.

Therefore, this study aims to evaluate the efficacy of interventional treatment for hypoperfusion cerebral infarction in the territory of the lenticulostriate arteries caused by middle cerebral artery stenosis. The study will assess symptom improvement, cerebral blood flow perfusion status, and prognosis after treatment through clinical observations and relevant measurements. The necessity, safety, and effectiveness of interventional treatment in this specific patient population will be explored. The findings of this study will provide valuable references and guidance for treating hypoperfusion cerebral infarction in the lenticulostriate artery territory, offering more effective treatment options and facilitating patient recovery.

PATIENTS AND METHODS

Patient Recruitment and Selection Criteria:

Patients with MCA atherosclerotic disease who received interventional therapy at our hospital between January 2020 and December 2022 were identified through retrospective review of clinical and surgical data. Patients meeting the inclusion criteria for hypoperfusion cerebral infarction caused by MCA stenosis in the territory of the lenticulostriate arteries were screened and approached for participation. Additionally, data on patients with hypoperfusion cerebral infarction caused by middle cerebral artery stenosis receiving medical treatment were collected and included as a control group.

This study employed a prospective, single-center, non-blinded study design. All patients voluntarily participated in the study and provided informed consent by signing the consent form. Furthermore, the study protocol has been approved by the hospital's ethics committee.

Inclusion Criteria. Age ≥ 18 years and hospitalization duration exceeding 7 days; (2) Ischemic stroke within the territory of the lenticulostriate arteries confirmed by diffusion-weighted imaging (DWI); (3) Digital subtraction angiography (DSA) confirming severe proximal stenosis of the M1 segment of the MCA with a stenosis degree ranging from 70% to 99%, or poor opacification of the lenticulostriate arteries with severe stenosis in the M1 segment of the MCA, identified by absence or poor visualization of the lenticulostriate arteries at the stenotic site, as indicated by high-resolution MRI findings in the axial and ventral quadrants of the M1 segment; (4) Reduced perfusion within the territory of the lenticulostriate arteries validated by whole-brain CTP; (5) Voluntary participation in the study and cooperative completion of related examinations.

Exclusion criteria. (1) Preoperative modified Rankin Scale (mRS) score ≥ 3; (2) Within 30 days prior to enrollment, patients who underwent intracranial or extracranial intra-arterial balloon angioplasty, stent implantation or endarterectomy; (3) Inability to tolerate oral aspirin or clopidogrel (due to allergy or gastrointestinal intolerance); (4) Non-atherosclerotic lesions; (5) Presence of concurrent intracranial tumors, aneurysms, or intracranial arteriovenous malformations; (6) Unwillingness to participate in the study or premature withdrawal.

Observation indicators

Clinical data collected included age, gender, history of hypertension, diabetes, coronary heart disease, dyslipidemia, smoking history, pre- and post-intervention mRS scores, National Institutes of Health Stroke Scale (NIHSS) scores, relative perfusion parameters within the territory of the lenticulostriate arteries before and after interventional therapy, including relative mean transit time (rMTT), relative time to peak (rTTP), relative cerebral blood volume (rCBV), relative cerebral blood flow (rCBF), and vascular characteristics.

Imaging methods

To ensure standardization and consistency in imaging techniques, the following settings and protocols were employed:

MRI-DWI Sequences: The location of the infarct area was determined using standardized MRI-DWI sequences. Lenticulostriate artery territory infarction was defined as the infarct area located within the radiations of the corona radiata and the centrum semiovale, including specific anatomical landmarks. This definition required involvement of at least three planes on horizontal DWI images.

High-Resolution MRI: High-resolution MRI techniques were utilized to investigate the relationship between the lenticulostriate arteries and the plaque. A standardized approach involved drawing two straight lines on the axial image of the M1 segment of the middle cerebral artery to divide the lumen into quadrants.

Preoperative Digital Subtraction Angiography (DSA): DSA findings were used to determine important parameters related to the stenosis, lenticulostriate arteries, and plaque. The evaluation included assessing the length and severity of the stenosis, the relationship between the lenticulostriate arteries and the filling defect, the number of main lenticulostriate arteries, and the distribution type of the lenticulostriate arteries.

CT Perfusion (CTP): CTP was utilized to evaluate perfusion status in the territory of the lenticulostriate arteries. A standardized approach involved selecting two consecutive levels in the affected side's lenticulostriate artery territory. Regions of interest (ROI) were delineated, excluding areas of infarction. The software automatically outlined mirrored regions on the contralateral side. Absolute and relative perfusion parameters were measured, including mean transit time (MTT), time to peak (TTP), cerebral blood volume (CBV), cerebral blood flow (CBF), relative MTT (rMTT), relative TTP (rTTP), relative CBV (rCBV), and relative CBF (rCBF).

Inter-Observer Variability: To address potential inter-observer variability in image analysis, two experienced neurointerventional or neuroimaging physicians independently analyzed the radiological images of the patients. In cases of disagreement, consensus was reached through discussion to ensure reliable interpretations and minimize variability..

Interventional therapy and perioperative drug therapy

During the interventional therapy, specific techniques will be employed to address the arterial stenosis and restore the patency of the lenticulostriate arteries. The choice of technique, whether balloon angioplasty or stent implantation, will be determined based on the individual condition of each patient and the decision-making of the medical team. For balloon angioplasty, a balloon catheter will be used to dilate the stenotic segment of the artery. The size and type of the balloon will be selected according to the characteristics of the stenosis. Wire navigation and vascular imaging techniques will guide the placement and inflation of the balloon to achieve optimal results. In cases where stent implantation is deemed necessary, a stent suitable for the diameter and length of the stenotic segment will be selected. The stent will be deployed at the site of the arterial stenosis to provide structural support and maintain the patency of the lenticulostriate arteries. Similar to balloon angioplasty, wire navigation and vascular imaging techniques will be utilized to ensure accurate stent placement. Intra-operative imaging, such as digital subtraction angiography (DSA), may be performed to visualize the arterial anatomy and confirm the success of the intervention. Additionally, intra-operative monitoring will be employed to assess the patient's hemodynamic parameters and neurological status throughout the procedure. Prior to the interventional therapy, all patients will receive standard dual antiplatelet therapy for a minimum of 5 days. This therapy consists of daily doses of clopidogrel (75 mg) and aspirin (100 mg). Thromboelastography, a laboratory test, will be utilized to evaluate the response to antiplatelet therapy. Criteria for appropriate response include arachidonic acid > 50% and adenosine diphosphate > 30%. The interventional procedures and perioperative drug therapy will be performed by experienced medical professionals following established guidelines and protocols.

Outcome evaluation and follow-up

Patients will undergo outpatient or telephone follow-up at 1, 3, 6 months, and annually postoperatively. The modified Rankin Scale (mRS) will be utilized to assess the clinical prognosis. Patients will be categorized into two groups based on the difference between their preoperative and follow-up mRS scores: those with a score difference≥0 will be classified as having a favorable prognosis (indicating improvement or stability). In contrast, those with a score difference<0 will be categorized as having an unfavorable prognosis. Digital subtraction angiography (DSA) will be employed to evaluate residual stenosis postoperatively and the number of main lenticulostriate arteries. Imaging follow-up, including DSA, computed tomography angiography (CTA), or magnetic resonance angiography (MRA), will be conducted to assess the condition of the affected blood vessels. Good vessel patency during follow-up will be defined as less than 50% stenosis compared to the reference segment. CT perfusion (CTP) will be employed to evaluate improvements in cerebral blood flow perfusion.

Figure 1. Flow chart of cerebral infarction with hypoperfusion of the psammostriate artery due to middle cerebral artery stenosis

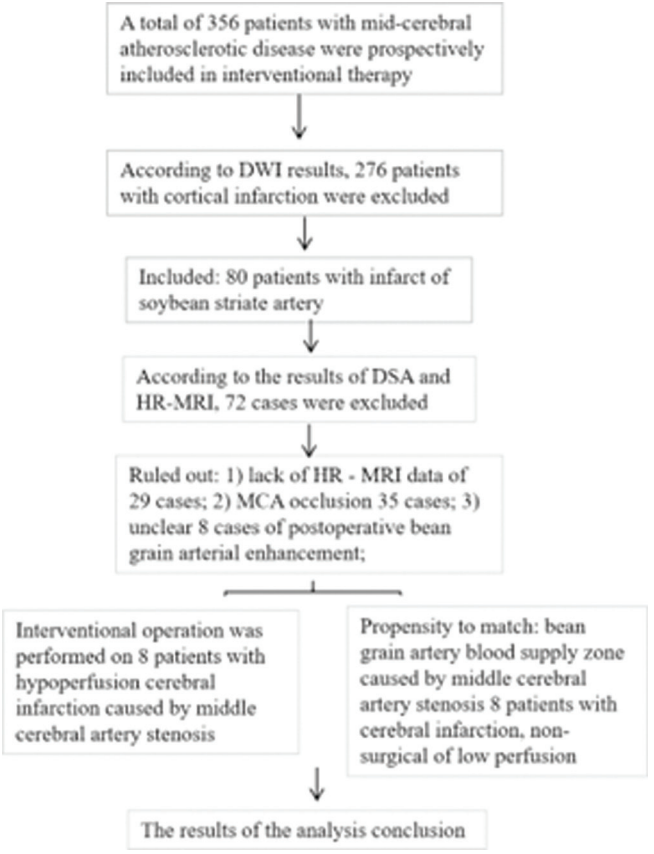

Table 1. Basic data of patients undergoing surgery for hypoperfusion cerebral infarction caused by middle cerebral artery stenosis

	1	2	3	4	5	6	7	8
gender	male	male	male	female	female	male	female	male
age (years)	56	65	63	70	69	67	59	68
diseased region	LM1	RM1	LM1	LM1	RM1	RM1	LM1	LM1
narrow length (mm)	10.78	11.26	9.67	7.89	15.22	8.5	12.89	15.26
stenosis (%)								
preoperation	74	95	82	78	76	72	86	88
postoperation	22	10	16	10	30	30	22	28
image number of main lenticular artery								
preoperation	0	2	3	3	2	3	2	3
postoperation	2	2	3	3	2	2	2	3
modus operandi	**PTAS**	**PTA**	**PTAS**	**PTAS**	**PTA**	**PTAS**	**PTAS**	**PTA**
NIHSS scores								
preoperation	3	5	4	4	6	4	5	4
postoperation	1	0	2	0	3	2	0	2
mRS scores								
preoperation	0	0	2	2	2	2	2	2
postoperation	0	0	2	0	1	1	0	1

Abbreviations: LM1, M1 segment of left middle cerebral artery; RM1, M1 segment of right middle cerebral artery; PTAS, balloon dilation + stent implantation; PTA, simple balloon dilatation; NIHSS score, National Institutes of Health Stroke Scale; mRS scores, Modified Rankin scale.

Table 2. Basic data of control patients with hypoperfusion cerebral infarction caused by middle cerebral artery stenosis

	1	2	3	4	5	6	7	8
gender	female	male	female	male	male	male	female	male
age (years)	65	66	69	68	59	71	65	69
diseased region	LM1	LM1	LM1	RM1	LM1	LM1	RM1	LM1
narrow length (mm)	8.78	5.26	6.35	7.56	8.24	6.87	9.37	10.21
Stenosis (%)								
preoperation	56	45	63	42	56	56	30	62
postoperation	26	18	23	18	30	34	10	48
image number of main lenticular artery								
preoperation	0	3	2	2	1	3	1	3
postoperation	0	2	2	1	2	2	0	1
NIHSS scores								
preoperation	2	3	2	3	3	4	3	4
postoperation	1	0	1	0	2	3	0	1
mRS scores								
preoperation	0	1	1	2	2	1	1	2
postoperation	0	0	2	0	0	0	0	1

Abbreviations: LM1, M1 segment of left middle cerebral artery; RM1, M1 segment of right middle cerebral artery; NIHSS score, National Institutes of Health Stroke Scale; mRS scores, Modified Rankin scale.

Follow-up of complications

Efficacy endpoints included clinical follow-up (occurrence of stroke or death within 1 year in the responsible vessel territory) and imaging follow-up (improvement in cerebral perfusion within the territory of the lenticulostriate arteries, changes in lenticulostriate artery opacification and main trunk number observed on DSA). Safety endpoints include the incidence of stroke and death within 30 days postoperatively.

Statistical analysis

Statistical analysis was performed using Statistic Package for Social Science (SPSS) 26.0 software (IBM, Armonk, NY, USA). Normally distributed continuous data were presented as (mean ± standard deviation). Two-sample *t* test was used to analyze continuous data, and the results were presented as mean difference [n (%)]. For categorical data, chi-square tests or Fisher's exact tests would be used. Differences in ranked data were analyzed using the Mann-Whitney U test. A $P < .05$ was considered statistically significant, indicating a significant difference.

RESULTS

Baseline information

A total of 8 patients with hypoperfusion cerebral infarction caused by middle cerebral artery (MCA) stenosis who underwent interventional surgery were included in this study. An additional 8 patients receiving conventional treatment were selected as the control group using propensity score matching. In the interventional treatment group, there were 5 male and 3 female patients with a mean age of 65.85±7.86 years. Among them, 6 patients presented with severe stenosis in the left M1 segment of the middle cerebral artery, while 2 patients had severe stenosis in the right M1 segment. In terms of comorbidities, 6 patients had coexisting hypertension, 5 had hyperlipidemia, 2 had diabetes, and 3 had coronary heart disease. Please refer to Figure 1 for a detailed depiction of the patient selection and inclusion process. The baseline characteristics of the patients in both the interventional surgery group and the control group, including gender, age, lesion location, stenosis length, pre- and post-operative stenosis percentage, number of main lenticulostriate arteries, pre-and post-operative NIHSS scores, and mRS scores, can be found in Table 1. For the baseline characteristics of the patients in the control group receiving conventional treatment, please refer to Table 2.

CT relative perfusion parameters before and after intervention

The CTP results showed that in the 8 patients before the procedure, there was a significant prolongation of rMTT and rTTP, a significant decrease in rCBF, and an increase or slight decrease in rCBV within the territory of the lenticulostriate arteries. Follow-up CTP revealed that rMTT, rTTP, rCBF, and rCBV in the affected lenticulostriate artery territory of the 8 patients were close to 1, indicating restoration of blood flow perfusion similar to that of the contralateral healthy side. For specific results, please refer to Table 3.

Table 3. Relative CT perfusion parameters before and during follow-up in patients with hypoperfusion cerebral infarction caused by middle cerebral artery stenosis

		1	2	3	4	5	6	7	8
rTTP	preoperation	1.28	1.25	1.18	1.20	1.22	1.08	1.14	0.98
	postoperation	1.12	1.08	1.09	1.12	1.07	0.89	1.02	0.92
rMTT	preoperation	1.86	1.59	2.12	1.49	1.58	2.02	1.68	1.89
	postoperation	1.25	1.06	1.36	1.05	0.99	1.58	1.23	1.48
rCBF	preoperation	0.85	0.72	0.59	0.85	0.63	0.74	0.78	0.83
	postoperation	1.08	1.21	0.98	1.12	1.08	1.06	1.23	1.16
rCBV	preoperation	0.89	0.97	0.96	1.29	1.05	1.48	1.26	1.35
	postoperation	0.90	0.91	1.01	1.06	0.98	1.12	1.12	1.20

Abbreviations: rTTP, relative peak time; rMTT, relative average transit time; rCBF, relative cerebral blood flow; rCBV, Relative cerebral blood volume.

CT relative perfusion parameters before intervention and at follow-up

There were no significant differences in the pre-intervention rMTT, rTTP, rCBF, and rCBV parameters between the two groups of patients. After intervention, both groups showed improved relative perfusion parameters on CT. However, there were no significant differences in post-intervention rMTT, rTTP, and rCBV between the intervention group and the control group. The post-intervention rCBF in the control group was slightly higher than that in the surgical treatment group. For specific results, please refer to Table 4.

Table 4. Preoperative and follow-up comparison of CT relative perfusion parameters between surgical and control groups ($\bar{x} \pm s$)

	Interventional group				control group			
	pre-intervention	post-intervention	*t* value	*P* value	pre-intervention	post-intervention	*t* value	*P* value
rTTP	1.17±0.056	1.04±0.068	2.571	.021	1.16±0.316	1.02±0.192	3.025	0018
rMTT	1.79±0.145	1.21±0.210	1.892	.012	1.74±0.271	1.16±0.452	2.891	.021
rCBF	0.75±0.067	1.20±0.156[a]	1.268	.005	0.85±0.163	1.36±0.248	1.589	.031
rCBV	1.16±0.216	1.04±0.128	2.348	.015	1.09±0.258	0.97±0.156	1.492	.002

[a]$P < .05$, compared to the control group post-intervention.

Table 5. NIHSS scores and mRS Scores of patients in the two groups before intervention and during follow-up

	Interventional group				control group			
	pre-intervention	post-intervention	*t* value	*P* value	pre-intervention	post-intervention	*t* value	*P* value
NIHSS score	3.0±0.76	1.0±0.65	1.872	.016	3.0±0.89	0.97±0.65	2.183	.021
mRS score	1.25±0.56	0.37±0.25	2.361	.003	1.53±0.78	0.35±0.31	1.673	.045

Comparison of NIHSS scores and mRS scores before intervention and at the last follow-up

There were no significant differences in NIHSS scores and mRS scores between the two groups of patients before intervention. After intervention, both groups showed improved scores on NIHSS and mRS scales. However, there were no significant differences in NIHSS scores and mRS scores between the two groups post-intervention, indicating that both interventional surgery and conventional treatment have similar effects. For specific results, please refer to Table 5.

Comparison of surgical treatment and complications in control group

Both groups of patients were followed up, with an average clinical follow-up period of 296±56 days. The primary outcomes assessed during follow-up included the occurrence of complications such as non-target vessel territory stroke, transient ischemic attack (TIA), and death. Both groups of patients showed favorable prognosis, and good vessel patency was observed in both groups.

DISCUSSION

This study aimed to assess the effectiveness of interventional therapy in patients diagnosed with cortical watershed infarction resulting from middle cerebral artery stenosis. A carefully selected cohort of 8 eligible patients underwent a comprehensive analysis of their imaging data, complications, and clinical outcomes. The results demonstrated a notable absence of perioperative complications and clinical events such as stroke, transient ischemic attack (TIA), or mortality during medium to long-term follow-up, indicating favorable clinical outcomes associated with this treatment approach.

The intervention surgery primarily led to significant improvements in cerebral perfusion within the affected cortical region, highlighting its efficacy in restoring blood supply and reducing tissue damage, thereby improving patient prognosis. Moreover, the intervention approach exhibited a commendable safety profile with a low incidence of complications. This finding has important implications for the holistic management and care of patients suffering from cortical watershed infarction caused by middle cerebral artery stenosis. The remarkably low rate of perioperative complications observed in this study aligns with the lower rates of complications reported in similar investigations (ranging from 2.0% to 4.3%). 16-18 In conclusion, these findings underscore the potential of intervention surgery to enhance therapeutic outcomes for patients with cortical watershed infarction resulting from middle cerebral artery stenosis. However, it is crucial to expand the sample size and conduct more rigorous prospective studies to further validate these results and explore other factors that may influence successful intervention in this specific patient population.

Other studies findings indicate that for patients with intracranial large artery atherosclerosis presenting as infarction in the perforating artery supply region, pharmacological treatment alone often fails to sustain blood supply to the perforating arteries, leading to recurrent or worsening symptoms. If timely intervention is not implemented, and recanalization is attempted after complete occlusion of the parent artery, the perioperative risks escalate significantly, and therapeutic outcomes are often suboptimal.[19,20] Therefore, timely intervention targeting the underlying pathophysiology may yield greater clinical benefits for these patients. It is noteworthy that, following a meticulous imaging evaluation, intervention therapy conducted in high-volume stroke centers may serve as a safe and effective approach for patients with cortical watershed infarction resulting from middle cerebral artery stenosis. It is worth noting that, following a thorough imaging evaluation, intervention therapy performed in high-volume stroke centers can serve as a safe and effective approach for patients with cortical watershed infarction resulting from middle cerebral artery stenosis.

In summary, the results of this study suggest that intervention surgery shows promise in improving treatment outcomes for patients with cortical watershed infarction caused by middle cerebral artery stenosis. However, it is important to acknowledge the limitations of this study, including the small sample size and lack of a control group. Future research should aim to address these limitations by increasing the sample size and employing more rigorous prospective study designs to further validate these conclusions.

CONFLICT OF INTEREST

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

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This study did not receive any funding in any form.

AUTHOR CONTRIBUTIONS

JianL and RH designed the study and performed the experiments, RH and JiaL collected the data, JiaL and WW analyzed the data, and JianL prepared the manuscript. All authors read and approved the final manuscript.

ETHICAL COMPLIANCE

The ethics committee of Xi'an International Medical Center Hospital approved this study. Signed written informed consent were obtained from the patients and/or guardians.

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