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Clinical Efficacy of Superficial Temporal Artery-middle Cerebral Artery Bypass Grafting Surgery Combined With Temporal Muscle Patch on Patients With Moyamoya Disease

Feng Gao, PhD, Shiling Chen, MD, Jiajie Gu, MD, Zhengchun Wang, PhD, and Zhengzheng Wang, MD

Objective: To analyze the clinical efficacy of superficial temporal artery-middle cerebral artery (STA-MCA) bypass grafting surgery combined with temporal muscle patch and STA-MCA bypass grafting surgery alone on patients with moyamoya disease.

Methods: Totally 73 patients confirmed with moyamoya disease in our hospital between January 2019 and December 2021 were enrolled. Among them, 43 patients treated with STA-MCA bypass grafting surgery combined with temporal muscle patch were assigned to the experiment group, whereas 30 patients treated with STA-MCA bypass grafting surgery alone to the control group. The following items of the 2 groups were compared: clinical efficacy, total effective rate, and disease control rate 6 months after surgery, the changes of modified Rankin Scale (mRS) and Karnofsky performance scale (KPS) scores before and on the seventh day and 6 months after surgery, and changes of Glasgow coma scale scores before and 24 hours after surgery. In addition, the incidences of cerebral ischemia and cerebral hemorrhage within 1 year after surgery were counted. The cerebral perfusion-associated indexes including relative mean transit time (rMTT), relative time-to-peak, relative cerebral blood flow (rCBF), and relative cerebral blood volume (rCBV) on the seventh day and 6 months after surgery were compared between the 2 groups, and the predictive value of cerebral perfusion-associated indexes before surgery for clinical efficacy on patients was analyzed.

Results: The Glasgow coma scale score after surgery ($P > 0.05$) was similar between the 2 groups, but the clinical efficacy and total effective rate of the 2 groups were notably different (both $P < 0.05$). Compared with those before surgery, mRS scores of both groups declined, whereas KPS scores increased (both $P < 0.05$) on the seventh day after surgery. In addition, compared with those before surgery and on the seventh day after surgery, mRS scores of both groups decreased 6 months after surgery, whereas KPS scores increased (both $P < 0.05$). Both the groups showed decreased rMTT and rTPP, and increased rCBF and rCBV on the seventh day after surgery than those before surgery (all $P < 0.05$). In addition, both the groups still showed decreased rMTT and rTPP, and increased rCBF and rCBV 6 months after surgery than those before surgery and on the seventh day after surgery (all $P < 0.05$). Most notably, the experimental group displayed improved cerebral perfusion-associated indexes than the control group 6 months after surgery (all $P < 0.05$). The relief group showed notably higher rCBF and rCBV levels than the nonrelief group (both $P < 0.05$). According to ROC analysis, the areas under the curves of rCBF and rCBV in forecasting the clinical efficacy on patients were 0.842 and 0.823, respectively.

Conclusion: Superficial temporal artery-middle cerebral artery bypass grafting surgery combined with temporal muscle patch can deliver a higher total clinical curative rate for patients with moyamoya disease and can alleviate their coma.

Key Words: Clinical efficacy, moyamoya disease, superficial temporal artery-middle cerebral artery bypass grafting surgery, temporal muscle patch

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From the Department of Neurosurgery, The Affiliated People's Hospital of Ningbo University, Ningbo, Zhejiang, China.
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Address correspondence and reprint requests to Feng Gao, MD, Department of Neuro surgery, The Affiliated People's Hospital of Ningbo University, 251 Baizhang East Road, Ningbo, Zhejiang 315040, China; E-mail: rmgaofeng@nbu.edu.cn
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Moyamoya disease is a rare chronic brain disease with unclear etiology.[1] It is featured with chronic progressive stenosis or occlusion at the end of bilateral internal carotid artery, anterior cerebral artery, and middle cerebral artery.[2] The disease is named moyamoya disease because of its "smoky" image of cerebral angiography—the abnormal vascular network formed by collateral circulation.[3] Recent research has revealed a high incidence of moyamoya disease in East Asia, and its family aggregation that is probably due to genetic factors.[4] Cerebral ischemia and intracranial hemorrhage are the 2 main hazards of the disease, with the former mainly appearing in childhood and the latter appearing in adulthood.[5] With the popularization and the development of imaging technologies such as angiography, the detection rate of moyamoya disease in China is increasing annually,[6] but its diagnosis and therapy are still under disputes.

There is no effective medicine for moyamoya disease at present. For patients in chronic stage or those with moyamoya syndrome, some drugs aiming at risk factors of stroke or comorbid diseases, such as vasodilators, antiplatelet aggregation drugs, and anticoagulants, are probably beneficial, but the adverse effects of these drugs need to be alerted.[7] According to guidelines in 2012, oral antiplatelet aggregation drugs for treating ischemic moyamoya disease lack supports from clinical data, and the long-term use of antiaggregation drugs such as aspirin could lead to a transition from ischemia to hemorrhage, which is not conducive to the prognosis of patients.[8] In addition to drug therapy, surgery can also be adopted to treat the moyamoya, and intracranial and extracranial vascular reconstruction is the primary treatment for moyamoya disease and moyamoya syndrome.[9] At the time of this writing, surgical treatment of moyamoya disease mainly based on direct or indirect revascularization.[10] Among them, direct revascularization is the most frequently adopted treatment in clinical practice. According to some data, cerebral revascularization can lower the 5-year rebleeding rate from 31.6% to 11.9%, which indicate its notably positive effect on the postoperative bleeding rate of patients.[11] However, the most ideal reconstruction method for adult patients is still under controversy.

Accordingly, the current study compared the short-term and long-term efficacy of combined vascular reconstruction and direct vascular bypass reconstruction in adult patients with moyamoya disease, with the purpose of exploring an effective surgical method of vascular reconstruction against moyamoya disease and providing the basis for clinical treatment.

METHODS

Clinical Data of Patients

Totally 73 patients confirmed with moyamoya disease in our hospital between January 2019 and December 2021 were enrolled. Among them, 43 patients treated with superficial temporal artery-middle cerebral artery (STA-MCA) bypass grafting surgery combined with temporal muscle patch were assigned to the experiment group, while the rest 30 patients treated with STA-MCA bypass grafting surgery alone to the control group. This study was performed with permission from the Medical Ethics Committee of our hospital.

Inclusion and Exclusion Criteria

The inclusion criteria: Patients meeting the diagnostic criteria of moyamoya disease released by the Ministry of Health of Japan in 2012,[12] patients whose computed tomography (CT) perfusion imaging indicated abnormal cerebral blood flow, patients who provided signature in informed consent forms after understanding the study, patients whose families provided signature after understanding it, and those 18 years old and above.

The exclusion criteria: Patients with comorbid tumor or congenital brain diseases; patients whose head magnetic resonance imaging or CT indicated the presence of acute cerebral hemorrhage and acute stroke; patients with systemic diseases, including infection, blood diseases, and immune system diseases; pregnant women; and lactating women.

Surgical Regimen

The experimental group was given STA-MCA bypass grafting surgery combined with temporal muscle patch. Specifically, based on the vascular reconstruction operation steps, after satisfactory anesthesia, each patient was let to lie in a supine position, with the blood pressure maintained relatively high and the head immobilized and slightly raised. Under the guidance of Doppler ultrasound, the shape of superficial temporal artery in the skin was marked, and then the vascular anastomosis point was selected in the shape area of superficial temporal artery. Subsequently, an "arc" skin incision was made in frontal-temporal lobe while avoiding the damage of the trunk, frontal branch, and parietal branch of superficial temporal artery. After the superficial temporal artery was found, 1 of the thicker branches was carefully separated as the donor vessel. To prevent the superficial temporal artery from being damaged, 5-mm thick tissue sheath was left, followed by wrapping with wet cotton sheets for protection. After dissection of the temporal muscle, a 12×10-mm frontotemporal bone flap was opened with a high-speed cranial drill and milling cutter. After opening of the dura mater, M3 or M4 was selected as the recipient vessel. The recipient vessel with a length of about 10 mm was freed and then temporarily clamped with a special vessel clamp to avoid the vessel twisting and damage. The recipient vessel was cut with a special microscissors to keep the cutting edge neat. A longitudinal incision about 1 cm was made at the root of temporal muscle, and the donor blood vessel (freed superficial temporal artery) was let to pass through the temporal muscle. Then, the blood vessel was intermittently anastomosed end-to-end with 10.0 prolene silk thread. After the anastomosis, the artery clamp was removed, and indocyanine green was injected, followed by the confirmation of unobstructed blood vessel under microscope. Finally, the dura mater was cutoff along the edge of the bone window, and the temporal muscle patch was applied to the frontal lobe and temporal lobe. The edge of the dura mater and the edge of the temporal muscle were tightly sutured. The part of the bone flap near the temporal part was resected about 1.5 cm with a milling cutter to prevent the edge of the bone flap from crushing the temporal muscle and the donor vessels passing through the superficial temporal artery, and then the bone flap was covered with the temporal muscle and immobilized.

The control group was given STA-MCA bypass grafting surgery alone. Specifically, each patient was treated with operation steps of STA-MCA bypass grafting surgery but without dural resection and application of temporal muscle patch. The 1.5 × 1 cm-sized bone window was removed at the site where the donor vessel passed through and then the bone flap was fixed in situ. The other steps were the same as those of combined vascular reconstruction.

Patients in both groups were given the same medication and other treatment schemes after operation including routine ECG and intracranial pressure monitoring, oxygen inhalation, dehydration to reduce intracranial pressure, nutrition of brain cells, active prevention and treatment of various complications, and symptomatic treatment.

Detection of Cerebral Perfusion-associated Indexes

Before surgery and 1 week after surgery, CT cerebral perfusion imaging was performed to each patient, with the superior frontal gyrus and middle frontal gyrus on the surgical side selected as the regions of interest with a diameter of 3 cm. The selected contralateral regions of interest was symmetrical with the surgical side. The relative mean transit time (rMTT), relative time-to-peak, relative cerebral blood flow (rCBF), and relative cerebral blood volume (rCBV) were calculated. The relative values of MTT and TTP were based on the contralateral side, that is, the difference between the surgical side and contralateral side. The relative values of CBF and CBV were also based on the contralateral side, that is, the ratio of the surgical side to the contralateral side.

Evaluation Criteria of Efficacy

The National Institutes of Health Stroke Scale and symptoms were adopted to classify the efficacy on patients into complete remission (CR), partial remission (PR), stable disease (SD), and disease progression;[13] CR: the patient's nerve injury was relieved by above 90%; PR: the patient's nerve injury was relieved by 46% to 89%; SD: the patient's nerve injury was relieved by above 18% to 45%; disease progression: the patient's nerve injury was relieved by 18% or less. The total clinical effective rate = (the number of patients with CR + that of PR) / the sum of patients ×100%. The disease control rate = (the number of patients with CR+that of PR + that of SD) / the sum of patients ×100%.

Evaluation of Clinical Symptoms and Quality of Life

Clinical symptoms and quality of life (QoL) of patients were evaluated by the same doctor. The patients were evaluated using the modified Rankin Scale (mRS) and Karnofsky performance scale (KPS), according to their clinical symptoms and signs.[14,15] The specific scores of mRS: 0 points: completely asymptomatic; 1 point: symptomatic, but without obvious dysfunction and with ability to complete all daily work and life activities; 2 points; mildly disabled, without ability to complete all preillness activities but without requirement of help in daily affairs; 3 points: moderately disabled, with partial help, but with ability to walk independently; 4 points: severely disabled, without ability to walk independently; 5 points: severely disabled and bedridden, with urinary incontinence, and total dependence on others in daily life. A higher score indicates worse recovery. The specific scores of KPS: 100 points: normal, no complaints, and no evidence of disease; 90 points: mildly symptomatic, with mild signs, and ability to carry on normal activity; 80 points: having some signs or symptoms of disease, with ability to carry on normal activity with effort; 70 points: with ability to care for self, but without ability to carry on normal activity or to do active work; 60 points: requiring occasional assistance, but with ability to care for most of their personal needs. 50 points: requiring considerable assistance and frequent medical care; 40 points: disabled with requirement of special care and assistance; 30 points: severely disabled without ability to care for their personal needs; 20 points: seriously ill, hospital admission necessary, and active supportive treatment necessary; 10 points: moribund; fatal processes progressing rapidly. 0 points: die. A higher score implies better health.

Evaluation of Consciousness State

The Glasgow coma scale (GCS) was used for evaluating the coma of patients.[16] It covers 3 items: eye response, verbal response, and motor response, with the highest score of 4 points for eye response and the lowest score of 0 points for eye response; the highest score of 5 points for verbal response and the lowest score of 0 points for verbal response, the highest score of 6 points for motor response, and the lowest score of 1 point for motor response. A higher score indicates better consciousness state.

Outcome Measures

Primary outcome measures: The following items of the 2 groups were compared: cinical efficacy, total effective rate, and disease control rate 6 months after surgery, the changes of mRS and KPS scores before surgery, on the seventh day and 6 months after surgery, and changes of GCS scores before surgery and 24 hours after surgery.

Secondary outcome measures: The clinical data of the 2 groups were compared, including sex, age, past medical history, mode of onset, and Suzuki staging of moyamoya disease on the operation side. The incidences of cerebral ischemia and cerebral hemorrhage within 1 year after surgery were counted, and cerebral perfusion-associated indexes (rMTT, rTPP, rCBF, and rCBV) on the seventh day and 6 months after surgery were compared between the 2 groups. The predictive significance of preoperative cerebral perfusion-associated indexes for clinical efficacy on patients was analyzed.

Statistical Analyses

Counting data (%) were analyzed using the χ^2 test, and measurement data (mean ± SD) were all in normal distribution. Their intergroups comparison were carried out via the independent samples *t* test, and their introgroup comparison at different temporal points was performed via the paired *t* test and presented by *t* value. Receiver operating characteristic (ROC) curves were adopted for analyzing the function of cerebral perfusion-associated indexes in forecasting the relief of patients. $P < 0.05$ suggests a notable difference. SPSS20.0 (SPSS Co., Ltd., Chicago, IL) was adopted for statistical analyses of collected data.

RESULTS

There was no difference between 2 groups in sex, past medical history, mode of onset, Suzuki staging of moyamoya disease on the operation side (all $P > 0.05$, as shown in Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/SCS/E504).

Comparison of Glasgow Coma Scale Scores After Surgery

According to the comparison results of the changes of GCS score between the 2 groups before and after surgery, before surgery, no difference was found between them in GCS score (P>0.05), whereas after surgery, GCS scores of both groups increased notably ($P < 0.05$), with no notable difference between the 2 groups in GCS score ($P > 0.05$, as shown in Supplemental Table 2, Supplemental Digital Content 2, http://links.lww.com/SCS/E505). (It was recommended to keep the original score, because there should be no notable difference in GCS between the 2 groups in a short time after operation.)

Evaluation of Efficacy

The clinical efficacy of all patients after surgery was evaluated. According to comparison, the experimental group showed was not greatly different from the control group in disease control rate ($P > 0.05$, as shown in Supplemental Table 3, Supplemental Digital Content 3, http://links.lww.com/SCS/E506), but the clinical efficacy and total effective rate of them were notably different (both $P < 0.05$, as shown in Supplemental Table 3, Supplemental Digital Content 3, http://links.lww.com/SCS/E506).

Evaluation of Clinical Symptoms and Quality of Life

According to the evaluation of patients' clinical cognitive status and QoL, before surgery, the control group and experimental group were not greatly different in mRS and KPS scores ($P > 0.05$), but on the seventh day after surgery, the mRS scores of both groups declined notably, whereas KPS score of them increased notably (both $P < 0.05$). In addition, the mRS scores of both the groups decreased notably 6 months compared with those before surgery and on the seventh day after surgery, whereas KPS scores of them increased (both $P < 0.05$, Fig. 1). However, no difference was observed between the 2 groups in mRS and KPS score at each time point (both $P > 0.05$).

Cerebral Hemorrhage and Cerebral Ischemia in Patients After Surgery

One year follow-up was conducted to the 2 groups. The follow-up results showed 2 cases of frontal lobe ischemia at the operation side and no intracranial hemorrhage and death after surgery in the control group, and no intracranial hemorrhage and death in the experimental group after operation. The 2 groups were similar in the incidences of intracranial hemorrhage and cerebral ischemia ($P > 0.05$).

Changes of Cerebral Perfusion-associated Indexes

According to the analysis and comparison of cerebral perfusion-associated indexes between the control group and experimental group before and after treatment, the 2 groups were not greatly different in rMTT, rTPP, rCBF, and rCBV before surgery and on the seventh day after surgery ($P > 0.05$, Fig. 2), but 6 months after surgery, the experimental group showed notably decreased rMTT and rTPP and notably increased rCBF and rCBV compared with the control group ($P < 0.05$, Fig. 2). According to introgroup comparison, the 2 groups showed notably decreased rMTT and rTPP and notably increased rCBF and rCBV on the seventh day after surgery than those before surgery (all $P < 0.05$). And the 2 groups showed notably decreased rMTT and rTPP and notably increased rCBF and rCBV 6 months after surgery than those before surgery and on the seventh day after surgery (all $P < 0.05$, Fig. 2).

Predictive Value of Cerebral Perfusion-associated Indexes for Disease Alleviation

The predictive value of cerebral perfusion-associated indexes before surgery for clinical efficacy on patients was analyzed. The patients were assigned to the relief group (n = 55) and nonrelief group (n = 18) based on their disease relief. According to comparison, before surgery, the relief group showed notably higher rCBF and rCBV levels than the nonrelief group (both $P < 0.05$, Fig. 3), but rMTT and rTPP of the 2 groups were not greatly different ($P > 0.05$, Fig. 3). According to ROC curve-based analysis, rCBF and rCBV had areas under the curves of 0.842 and 0.823, respectively, in forecasting the clinical efficacy on patients (Fig. 4 and as shown in Supplemental Table 4, Supplemental Digital Content 4, http://links.lww.com/SCS/E507).

DISCUSSION

At the current stage, the etiology of moyamoya disease is still a mystery. According to a recent report, the disease has familial and racial heritability.[17] Among patients with moyamoya disease, first-degree relatives of 6% to 10% of them suffer moyamoya disease.[18] In addition, the disease is more frequently seen in Asian races, especially Japan, South Korea, and China.[19] Searching for an effective treatment is the key to alleviate moyamoya disease, and the selection of treatment plan is still under controversy.

At the time of this writing, 2 clinical methods are available to treat moyamoya disease, namely drug therapy and surgery. The purpose of both schemes is to maintain the effectiveness of cerebral blood perfusion and to improve the function of nervous system.[20] Among them, drug therapy includes calcium antagonist (nicardipine, nimodipine, verapamil, etc.) and aspirin.[21]

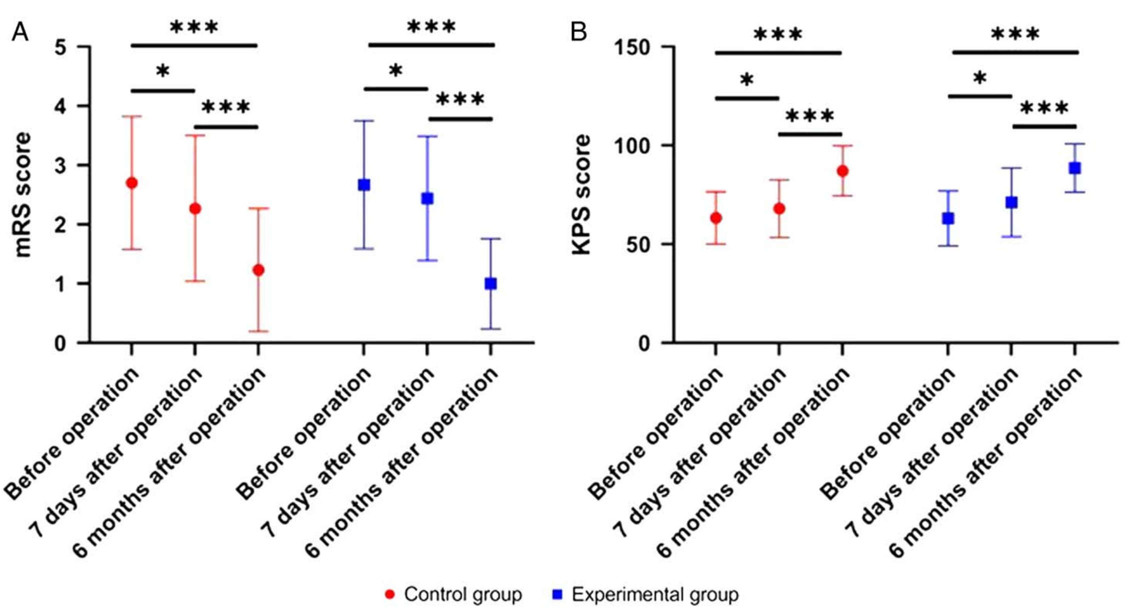

FIGURE 1. mRS and KPS scores at different time points. (A) Changes of mRS scores before surgery, on the seventh day and 6 months after surgery. (B) Changes of KPS scores before surgery, on the seventh day and 6 months after surgery. KPS indicates Karnofsky performance scale; mRS, modified Rankin Scale. *$P < 0.05$, ***$P < 0.001$.

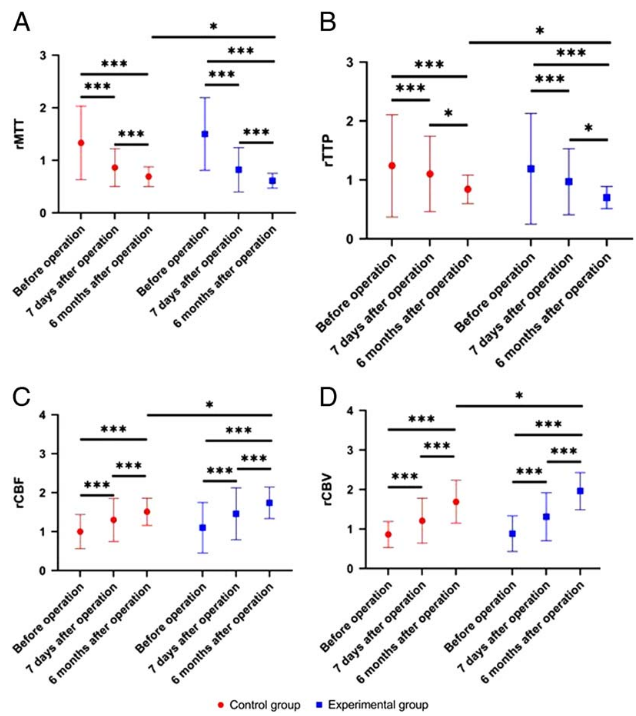

FIGURE 2. Cerebral perfusion-associated indexes of patients at different time points. (A) Changes of rMTT in the 2 groups before surgery, on the seventh day and 6 months after operation. (B) Changes of rTTP in the 2 groups before surgery, on the seventh day and 6 months after operation. (C) Changes of rCBF in the 2 groups before surgery, on the seventh day and 6 months after operation. (D) Changes of rCBV in the 2 groups before surgery, on the seventh day and 6 months after operation. rCBF indicates relative cerebral blood flow; rCBV, relative cerebral blood volume; rMTT, relative mean transit time; rTTP, relative time-to-peak. *$P<0.05$, ***$P<0.001$.

However, drug therapy has been found to be with no definite therapeutic effect on moyamoya disease in recent years, but can only alleviate the disease to a certain extent.[22] At the current stage, surgery is still deemed as the primary treatment for moyamoya disease.[23] It covers cerebral revascularization based on its type, including direct revascularization, indirect revascularization, and combined revascularization.[24] Each of the 3 operations has its own advantages and disadvantages. Direct vascular bypass technique is difficult, with a high rate of postoperative bleeding, but it can improve cerebral blood perfusion quickly and effectively.[24] Indirect vascular bypass surgery is relatively simple, requiring short operation time, but during it, collateral circulation formation is slow, and cannot even complete, so the effect of improving cerebral blood flow perfusion is poor.[25]

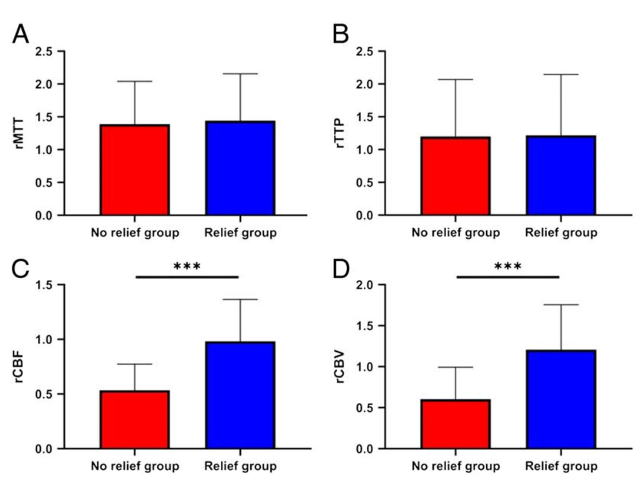

FIGURE 3. Cerebral perfusion-associated indexes in the relief group and nonrelief group before surgery. Comparison of rMTT, rTPP, rCBF, and rCBV between the relief group and nonrelief group was displayed in A, B, C, and D, respectively, before surgery. rCBF indicates relative cerebral blood flow; rCBV, relative cerebral blood volume; rMTT, relative mean transit time; rTTP, relative time-to-peak. ***$P<0.001$.

Superficial temporal artery-middle cerebral artery bypass grafting surgery combined with temporal muscle patch is a surgical scheme for clinical treatment of moyamoya disease in children, which has outstanding performance in alleviating children's disease.[26] However, the application of combination of them in adults with moyamoya disease is still rarely studied. Our study adopted STA-MCA bypass grafting surgery combined with temporal muscle patch for adults with moyamoya disease. Moyamoya disease in most patients is ischemic, so the surgical treatment is primarily to effectively improve the local blood supply of the brain in a short time and maximize the use of external carotid artery blood supply meantime.[27] In our study, GCS scores of both the experimental group and control group increased notably after surgery compared with those before surgery, without notable difference between the 2 groups. The results imply that both schemes can alleviate coma of patients. In addition, 6 months after surgery, the experimental group showed notably better improvement of cerebral perfusion pressure and higher clinical efficacy and total effective rate than the control group. We believe that intracranial and extracranial vascular bypass alone is not effective enough even when the blood flow is unobstructed. According to clinical cerebral angiography, some of the bypass vessels may be chronically occluded at different stages after operation, and the intracranial blood supply is insufficient again, resulting in poor late treatment effect. Temporal muscle patch can pastes the muscle tissue rich in blood vessels on the surface of the cerebral cortex to stimulate the cerebral cortex and to promote the growth of new blood vessels, thus effectively establishing the collateral circulation. The combination of the 2 can reconstruct the cerebral vessels and maximize the blood perfusion in the ischemic area. (The same as those mentioned above). In addition, the mRS and KPS scores of the 2 groups under different treatment schemes after surgery were compared in our study. modified Rankin Scale is a scale used to evaluate the recovery of neurological function in patients with stroke, and it is also adopted for evaluating the recovery of neurological function in patients with moyamoya disease after surgery in clinical practice.[28] Karnofsky performance scale is a scale used to evaluate the functional status, which can directly reflect the patient's mobility.[29] In our study, both surgical schemes have improved the neurological function and mobility of patients, and no difference has been found in the scores at each time point between the 2 schemes, suggesting that both schemes have improved the neurological function and mobility of patients, without difference. The primary reason is that both schemes can improve the patient's mobility and neurological function by restoring the blood supply to the brain. In addition, according to 1-year follow-up, both schemes did not increase the incidence of postoperative cerebral hemorrhage and cerebral ischemia.

Hemodynamic index is a crucial index for evaluating the prognosis and treatment of moyamoya disease.[30] The postoperative benefit on patients with moyamoya disease is strongly bound up with the degree of vascular stenosis and ischemia.[31] In our study, the cerebral perfusion-associated indexes of the

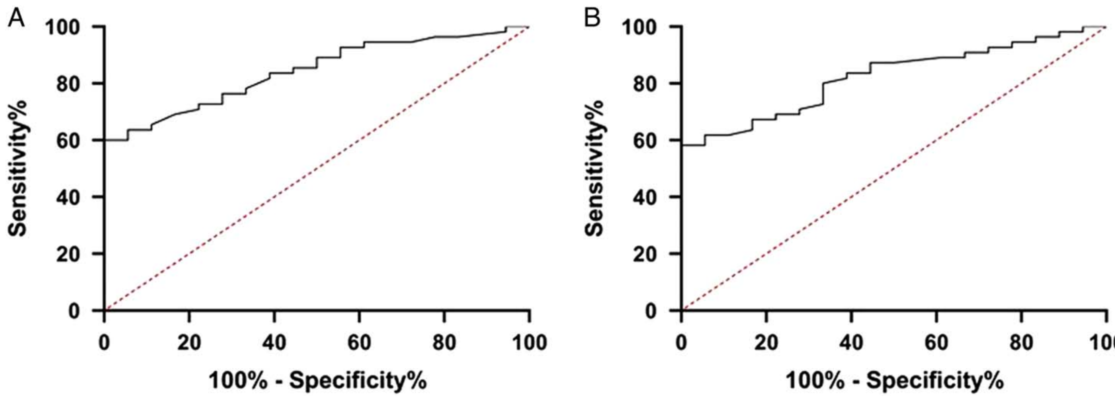

FIGURE 4. Relative cerebral blood flow (ROC) curves of relative cerebral blood flow and relative cerebral blood volume of patients. (A) ROC curve of relative cerebral blood flow in forecasting the improvement of clinical efficacy on patients. (B) ROC curve of relative cerebral blood volume in forecasting the improvement of clinical efficacy on patients.

2 groups were compared after surgery, and the results revealed that both schemes improved the blood supply of patients' brains. Moreover, the predictive value of preoperative cerebral perfusion-associated indexes for clinical efficacy on patients was analyzed in our study. At the time of this writing, there lack reference indexes for predicting the therapeutic effect on moyamoya disease clinically. Our study has revealed low levels of preoperativer CBF and rCBV in patients who were relieved after surgery, indicating their potential ability to predict patients' remission. To verify their function, we drew corresponding ROC curves. As a result, the areas under the curves of rCBF and rCBV in predicting the curative effect on patients were both larger than 0.8, suggesting their higher clinical value.

Our study has determined the clinical efficacy of STA-MCA bypass grafting surgery combined with temporal muscle patch and STA-MCA bypass grafting surgery alone on patients with moyamoya disease and found that preoperative rCBF and rCBV can be adopted as outcome measure to predict the degree of remission of patients. However, this study still has some limitations. First of all, in this study, only a short-term follow-up was conducted, so how the 2 kinds of operations affect patients for a longer period needs further observation. Second, the samples of this study are mainly ischemic patients, due to few cases of hemorrhagic type, which may lead to biased results. Finally, we hope to extend our follow-up time in the future and increase different types of cases for analysis to supplement our research conclusions.

To sum up, STA-MCA bypass grafting surgery combined with temporal muscle patch can deliver a higher total clinical curative rate for patients with moyamoya disease and alleviate their coma.

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