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Quantitative analysis of revascularization in ischemic moyamoya disease via whole-brain computed tomography perfusion

A retrospective single-center study

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Abstract

Ischemic moyamoya disease (MMD) can be treated with the revascularization of superficial temporal artery to middle cerebral artery (STA-MCA) bypass combined with encephalo-duro-arterio-myo-synangiosis (EDAMS) effectively. The purpose of the present study was to quantify the revascularization of STA-MCA bypass combined with EDAMS via whole-brain computed tomography perfusion (WB-CTP).

Seventy-nine consecutive patients with ischemic MMD who admitted to our hospital from August 2012 to October 2018 were carried out STA-MCA bypass combined with EDAMS. WB-CTP was performed at 24 hours prior to operation and 3 months following bypass with a follow-up WB-CTP, respectively. Both automatic analysis of WB-CTP (MIStar, Apollo Medical imaging Technology, Melbourne, Australia) for analyzing values of brain volume in delayed time (DT) >3 seconds and DT > 6 seconds, relative cerebral blood flow (γCBF) < 30% and its mismatch ratio or percentage and diffusion-weighted imaging of magnetic resonance imaging in the ischemic penumbra and the infarct core at the 2 time points were studied for verifying the effectiveness of the combined revascularization. Changes in DT values at MCA-terminal territory after revascularization had been investigated. The dynamic data were with reference to the individual cerebellar arteries.

All patients with ischemic MMD underwent STA-MCA bypass combined with EDAMS successfully. The preoperative brain volume in DT > 3 seconds in MCA-terminal territory was significantly larger than that of postoperative one ($P < .05$) in the ischemic penumbra in ischemic MMD. The mismatch ratio in brain volume of 24 hours prior to revascularization in MCA-terminal territory was significantly lower than that of 3 months ($P < .05$) following combined revascularization. The percentage of mismatch in brain volume of 24 hours prior to revascularization vs that of 3 months and the value of γCBF < 30% were similar to the above mismatch ratio ($P < .05$). The ratio of postoperative brain volume in DT > 3 seconds vs DT > 6 seconds indicated no significant differences compared with that of preoperative one ($P > .05$).

The WB-CTP can be regarded as a choice for quantifying the combined revascularization in the ischemic penumbra and the infarct core in ischemic MMD. As proposed methods, brain volume in DT > 3 seconds, the value of γCBF < 30% and mismatch ratio in brain volume in MCA-terminal territory should be paid more attention in assessing the validity of STA-MCA bypass combined with EDAMS in ischemic MMD.

Abbreviations: CBF = cerebral blood flow, DSA = digital subtraction angiography, DT = delayed time, DWI = diffusion-weighted imaging, EC-IC = extracranial-intracranial, EDAMS = encephalo-duro-arterio-myo-synangiosis, MMD = moyamoya disease, MRI = magnetic resonance imaging, STA-MCA = superficial temporal artery to middle cerebral artery, TIA = transient ischemic attack, WB-CTP = whole-brain computed tomography perfusion.

Keywords: whole-brain computed tomography perfusion, ischemic moyamoya disease, revascularization, quantitative analysis

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1. Introduction

Ischemic moyamoya disease (MMD) is considered as one kind of complicated and intractable cerebral vascular diseases, which includes the penumbra and the ischemic core in brain.[1] Generally, extracranial-intracranial (EC-IC) revascularizations, such as superficial temporal artery to middle cerebral artery (STA-MCA) bypass combined with encephalo-duro-arterio-myo-synangiosis (EDAMS), can be proposed as an effective method for ischemic MMD.[2,3] Due to the lack of explicit recognization of its etiology, the assessment of surgical effect in penumbra and the ischemic core in patients with ischemic MMD is always not well-defined. Some researchers tried to assess the outcomes of revascularization, but the results cannot be commonly accepted for semi-quantitative analysis or dissatisfactory specificity or sensitivity.[3]

Interestingly, neurologists made proper use of brain computed tomography perfusion (CTP) in assessing acute stroke for the time window of mechanical thrombectomy or intravenous thrombolis.[4,5] However, quantitative analysis of revascularization in ischemic MMD is still not achieved. To gain quantitative analysis of treatment in MCA-terminal territory in ischemic MMD, the present study analyzes the imaging data prior to and following the STA-MCA bypass combined with EDAMS via whole-brain CTP (WB-CTP).

2. Material and methods

2.1. Patients

A total of 79 consecutive patients with ischemic MMD were admitted to our hospital from August 2012 to October 2018. The mean age of all 79 was 45±12.8 (ranging from 18 to 78), including 52 males and 27 females. The medical history of 79 patients including 21 hypertension, 11 diabetes, 24 smoking, and 7 alcohol abusing (Table 1). Inclusion criteria of patients with ischemic MMD are as follows: ischemic symptoms, including transient ischemic attack and reversible ischemic attack, but without complete ischemic stroke; ischemic imaging data which preoperatively confirmed by digital subtraction angiography (DSA) or CT angiography (CTA) (Fig. 1A), diffusion-weighted imaging (DWI) of magnetic resonance imaging (MRI) (Fig. 1C) and CTP. The study was consented to the ethics committee of the First Hospital of Soochow University. Also, all patients and their families agreed with the procedures.

Table 1

Clinical characteristics of 79 patients with ischemic moyamoya disease.

	Male (n=52)	Female (n=27)	*P*-value
Age, yr, n (%)	47.3±12.2 (66)	45.5±13.1 (34)	>.05
Hypertension, n (%)	15 (29)	6 (22)	>.05
Diabetes, n (%)	7 (13)	4 (15)	>.05
Alcohol abuse, n (%)	5 (10)	2 (8)	>.05
Smoking, n (%)	19 (37)	5 (19)	
Clinical features			
TIA	40	22	
Reversible ischemic attack	12	5	
Preoperative mRS			
0–1	29	16	
2–3	23	11	
Bypass side			
1	49	23	
2	3	4	
Postoperative mRS			
0–1	48	24	
2–3	4	3	

mRS = modified Rankin scale score, TIA = transient ischemic attack.

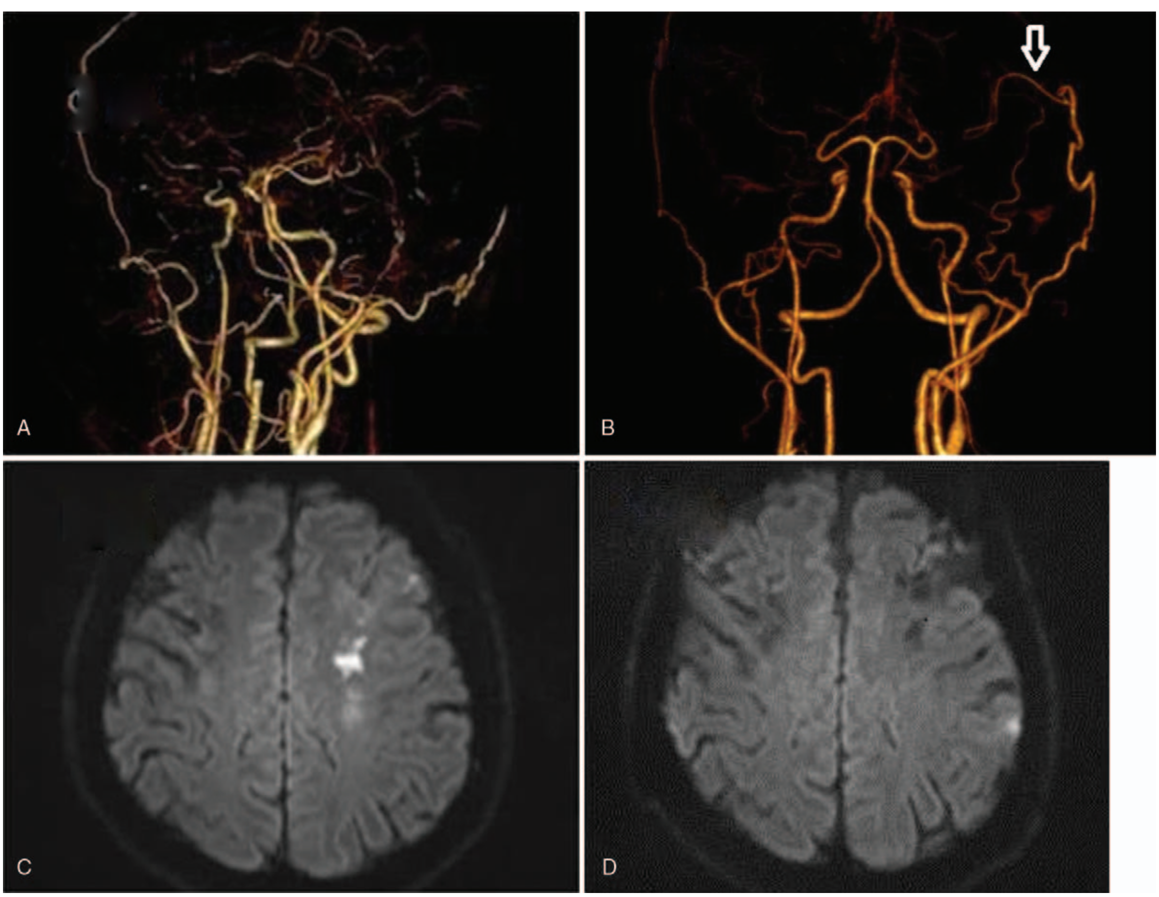

Figure 1. Typical imaging findings of patient before and after revascularization. (A) Preoperative computed tomographic angiography (CTA) showing moyamoya disease. (B) Postoperative CTA indicating patency of graft artery (white arrow) in moyamoya disease. (C) Preoperative diffusion-weighted imaging (DWI) illustrating ischemic stroke in the lobe. (D) Postoperative DWI showing the remission of the ischemic stroke in the lobe following the revascularization.

2.2. Combined revascularization in ischemic moyamoya disease

All 79 patients with ischemic MMD underwent 86 STA-MCA bypass combined with EDAMS. Seven of 79 patients were carried out bilateral revascularization.

2.3. Imaging data

Both automatic analysis of WB-CTP (MIStar, Apollo Medical imaging Technology, Melbourne, Australia) for analyzing values of brain volume in delayed time (DT) > 3 seconds and DT > 6 seconds, relative cerebral blood flow (γCBF) $< 30\%$ and mismatch ratio (volume of DT > 3 divide volume of γCBF $< 30\%$) or mismatch (volume of DT > 3 minus volume of γCBF), and DWI of MRI (Fig. 1D) in the ischemic penumbra and the infarct core at 24 hours prior to operation (Fig. 2A-1, A-2) and 3 months (Fig. 2B-1, B-2) following combined revascularization were respectively studied. Changes in DT values at MCA-terminal territory after revascularization had been investigated. The calculation of γCBF should abide by the rule: γCBF =

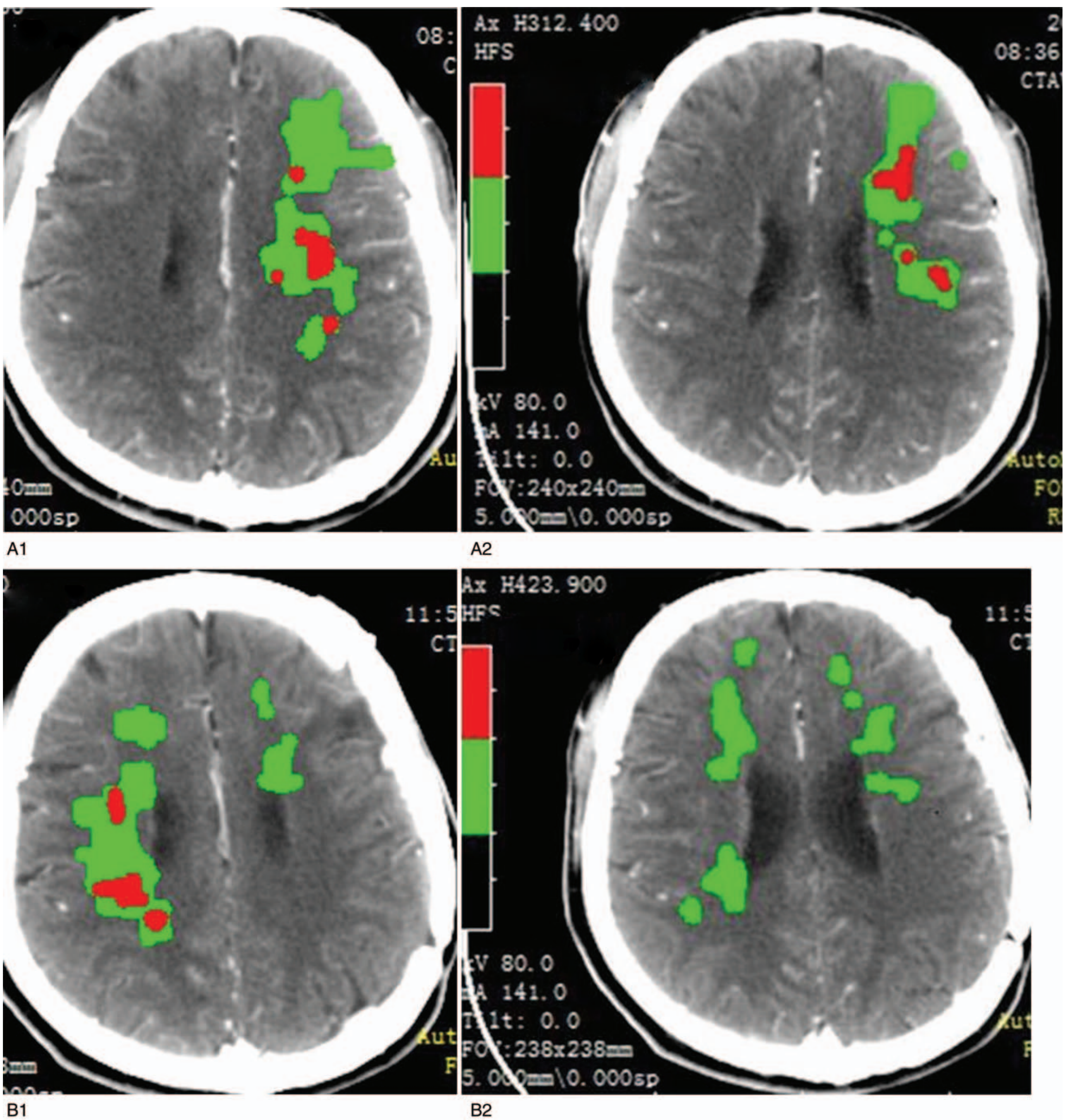

Figure 2. Comparison of whole-brain computed tomography perfusion (CTP) map before and after revascularization. (A) Preoperative CTP showing the volume of ischemic penumbra (delayed time > 3 s, green) and infarct core (relative cerebral blood flow $< 30\%$, red) in ischemic moyamoya disease (2A-1, 2A-2). (B) Postoperative CTP indicating the volume decrease of ischemic penumbra (green) and infarct core (2B-1, 2B-2) in the lobe following the revascularization.

absolute values of CBF in cerebral arteries in MCA-terminal territory/absolute values of CBF in cerebellar arteries. The reference cerebellar arteries were not altered before and after combined revascularization in individual patients.

First, intravenous injection of contrast material and other modalities such as deconvolution calculation in WB-CT was similar to the procedure mentioned in the literature.[6]

Second, the DWI of MRI in the ischemic penumbra and the infarct core was performed simultaneously at 24 hours prior to operation and 3 months following combined revascularization.

In addition, DT > 3 seconds stand for ischemic penumbra and γCBF < 30% indicated the infract core.

2.4. Imaging analysis

Quantitative analysis of dynamic data was carried out by 2 different neuroradiologists blind to the patients and surgical revascularization, respectively.

2.5. Statistical analysis

Student *t* test was utilized to estimate the data. – Chi-squared test was applied to evaluate the categorical data. All data were analyzed by statistical software SPSS version 22.0. $P < .05$ was regarded as significant differences.

3. Results

All patients with ischemic MMD underwent STA-MCA bypass combined with EDAMS successfully (Fig. 1B). The postoperative brain volume in DT > 3 seconds in MCA-terminal territory (95 ± 14 mL) was significantly less than that of preoperative one (130 ± 15 mL) ($P < .05$) in patients with ischemic MMD (Table 2). The mismatch ratio in brain volume of 24 hours prior to revascularization (6.62 ± 1.21) in MCA-terminal territory was significantly lower than that of 3 months (16 ± 1.83) ($P < .05$) following combined revascularization (Table 2). The DT > 6 seconds brain volume of 24 hours prior to revascularization in MCA-terminal territory (57 ± 14) vs that of 3 months (45 ± 13) shown no significant differences ($P > .05$). The value of γCBF < 30% (58 ± 16 mL vs 20 ± 11 mL) in MCA-terminal territory was similar to the mismatch ratio ($P < .05$). The ratio of postoperative brain volume in DT > 6 seconds vs DT > 3 seconds indicated significant differences compared with that of preoperative one (0.69 ± 0.15 vs 0.75 ± 0.16) ($P > .05$).

4. Discussion

The MMD is characterized by progressively chronic steno-occlusion referring to the terminal portion of the internal carotid arteries, and/or proximal portion of the anterior cerebral arteries and/or the MCAs together with abnormal collateral vessels near the skull base.[1] On the basis of typical symptoms as to MMD, the cerebrovascular lesions are at least classified into 2 types: ischemic MMD and hemorrhagic MMD. EC-IC revascularizations, taking STA-MCA bypass combined with EDAMS as an example, are proposed as effective measurements for preventing ischemic stroke recurrence in ischemic MMD.[7] But quantitative analysis and assessment of surgical revascularization in penumbra and the ischemic core in MCA-terminal territory in ischemic MMD is still not achieved, which impacts the evaluation of effectiveness concerning EC-IC revascularizations. As to the present study, all 79 patients with ischemic MMD underwent WB-CTP 24 hours before and 3 months after STA-MCA bypass combined with EDAMS.

Varieties of radiologic methods have been carried out in assessing hemodynamic in the ischemic penumbra and the infarct core in ischemic MMD following the surgical revascularization. Without injections of intravenous contrast agent, hypercapnic BOLD MRI is regarded as a promising method for evaluating the hemodynamic following surgical bypass in MMD, but variable arterial circulation and patients' cooperation making the quantitative analysis difficult to achieve.[8] Single-photon emission computed tomography (SPECT) shown favorable correlation with DSA with regard to quantitative assessment in MMD, due to its drawbacks high expense and inconvenience, SPECT in less developed nations is inapplicable.[9] Multidelay arterial spin labeling perfusion MRI is suitable for monitoring the patients with MMD associated with renal diseases, hyperthyroidism, or allergic constitution, regardless of assessing instability for low signal to noise ratio or limited detecting points.[10] Owing to various transformations of the raw perfusion data into the ischemic penumbra or infarct core volume, conventional CTP map makes use of cerebral blood volume (CBV) for defining infarct core which in turn underestimating the scale of CBF and overestimating the corresponding mean transit time.[6] In addition, conventional CTP regards intracranial vessels as referring point for assessing cerebral arteries dynamic. But when it comes to the ischemic MMD, the cerebral arteries, such as intracranial segment of ICA, proximal portion of MCA, and ACA, have suffered chronic steno-occlusion, which affects the accuracy of CTP. So the reliability of conventional CTP in evaluating cerebral perfusion and arteries dynamic, guiding the surgical intervention concerning ischemic stroke is disturbing and questionable.

Automatic analysis of WB-CTP (MIStar, Apollo Medical imaging Technology, Melbourne, Australia), acting as a quantitative software concerning perfusion of cerebral arteries, can get the cerebral hemodynamic in the whole brain with one CTA and CTP examination and detect the onset and degree of ischemic stroke. The WB-CTP is usually utilized to assess the perfusion of hemodynamic status in the ischemic penumbra and the infarct core in acute stroke caused by occlusion or severe stenosis of ICA of intracranial segment or proximal branches of MCA, and then to guide the following reperfusion (mechanical thrombectomy or thrombolysis).[5,11] Due to its higher sensitivity, concerning patients suffering ischemic stroke with mild symptoms or even unable to being clearly assessed in the first hours following stroke occurrence, WB-CTP could offer mismatch rate.[4] Some researchers proposed <30% thresholded CBF of normal hemisphere as the standard of infarct core in WB-CTP.[12] It is noted that WB-CTP has the advantage of confirming

Table 2

Parameters of CTP concerning preoperative and postoperative outcomes in the 79 patients with ischemic moyamoya disease (n = 79).

	Preoperative CTP	Postoperative CTP (3 mo)	*P*-value
DT > 3s	130 ± 15	95 ± 14	<.05
DT > 6s	57 ± 14	45 ± 13	>.05
Mismatch ratio	6.62 ± 1.21	16 ± 1.83	<.05
DT > 6s/DT > 3s	0.75 ± 0.16	0.69 ± 0.15	>.05
γCBF < 30%	58 ± 16	20 ± 11	<.05

γCBF = relative cerebral blood flow, CTP = computed tomography perfusion, DT = delayed time.

minor ischemic stroke tissue (especially lacunar infarcts), but its sensitivity in supratentorial lesions higher than that of infratentorial one should be taken into consideration.[4] The brain CTP map increase the accuracy of detecting the small arteries occlusion including the distal branches or posterior circulation, which can learn more about the occurrence of intracranial vessels occlusion or stenosis and collateral level, and then perform the proper revascularization.[13]

As to the present study, quantitative analysis of dynamic data was carried out by 2 different neuroradiologists blind to the patients and surgical revascularization, respectively. DT > 3 seconds in MCA-terminal territory and γCBF < 30% shown the ischemic penumbra and the infarct core in brain tissue, respectively. The results were confirmed by DWI. The data of γCBF < 30% in MCA-terminal territory verified the infarct volume which were overestimated by the volume CBF < 30%. The postoperative volume of DT > 3 seconds in MCA-terminal territory decreased significantly compared with that of preoperative one ($P < .05$). But the volume of DT > 6 seconds did not show significant decrease following EC-IC revascularization. In addition, the volume of γCBF < 30% in MCA-terminal territory decreased dramatically. The decrease of volume in ischemic penumbra indicated the efficacy of STA-MCA bypass combined with EDAMS. EC-IC revascularization supply reperfusion in ischemic lesions in those patients with MMD. The volume of mismatch or mismatch ratio in MCA-terminal territory after bypass was higher than that of before bypass. In other words, the patency of revascularization and reperfusion achieved. And then the collateral vessels become more following bypass.

Owing to MMD with progressively chronic steno-occlusion in the terminal portion of the ICAs, and/or proximal portion of the ACAs and/or the MCAs associated with collateral arteries, the CBF of the ischemic penumbra and the ischemic core shows dramatic reduction compared with normal brain tissue. CBV and TTP indicated obvious rising tendency in MCA-terminal territory, but CBF decreased in injured penumbra in ischemic MMD. In other words, the dynamic data including CBF, CBV, and other values are convenient to evaluate the status of perfusion in ischemic penumbra and the ischemic core. This may be in connection with the procedure of ischemic MMD in our present study.

4.1. Limitations

However, the present study had several aspects to be further explored. First, owing to limited experience and single-center study, our research needed multicenters studies and large case–control study to certify the results in revascularization in ischemic MMD. Second, more data concerning DT > 6 seconds, even DT > 10 seconds in MCA-terminal territory should be given more attention. Third, sensitivity of WB-CTP in infratentorial vessels lesions in ischemic MMD was dissatisfactory and WB-CTP had not achieved the noninvasive optimal vessel analysis.

5. Conclusion

The WB-CTP can be regarded as a choice for quantifying the combined revascularization in the penumbra and the ischemic core in ischemic MMD. As proposed methods, brain volume in DT > 3 seconds, the value of γCBF < 30% and mismatch ratio in brain volume in MCA-terminal territory should be paid more attention in assessing the validity of STA-MCA bypass combined with EDAMS in ischemic MMD.

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Writing – review & editing: Qingdong Han.

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