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ORIGINAL

MICROVASCULAR TRANSIT TIME OF THE RECIPIENT VESSELS DURING STA-MCA BYPASS SURGERY FOR ATHLETIC PATIENTS

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DECLARATIONS

Ethics approval: Written informed consent for the use of medical images was obtained from all participants prior to the start of this study. Other requirements for informed consent were waived since all information was anonymized before analysis. This study protocol was approved by the institutional review board at our hospital and was in accordance with the Declaration of Helsinki as revised in 1983.
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ABSTRACT

Purpose: We investigated the relationship between hemodynamic sources of recipient arteries and the microvascular transit time (MVTT) to explain the underlying mechanisms of cerebral hyperperfusion syndrome (CHS) in individuals with moyamoya disease (MMD). **Methods:** Forty-two adult individuals with MMD that underwent superficial temporal artery–middle cerebral artery (STA-MCA) bypass surgery between July 2020 and January 2021 were included in the analysis. Enrolled individuals underwent digital subtraction angiography (DSA) to diagnose MMD and determine the hemodynamic sources of recipient arteries (MCA or non-MCA), as well as intraoperative indocyanine green video angiography to measure MVTTs. Correlations between the hemodynamic sources of recipient arteries and the MVTT were analyzed. **Results:** Seventeen surgical hemispheres (40.5%) displayed a MCA-derived recipient artery and 25 hemispheres (59.5%) a non-MCA-derived recipient artery. Preoperative MVTT and DMVTT (the difference between preoperative and postoperative MVTTs) were significantly prolonged in the MCA-derived group (4.00±1.4 s and 1.96±1.48 s) compared to the non-MCA-derived group (2.79±0.79 s and 1.55±0.86 s). The incidence of CHS was 9.5% (4/42), with 3 CHS cases in the MCA-derived group and 1 CHS case in the non-MCA-derived group. Multivariate linear regression showed that hemodynamic sources of recipient arteries were related to preoperative MVTT ($P = 0.004$) and DMVTT ($P < 0.001$)**. Conclusions:** The MVTTs of recipient vessels in the MCA-derived group were in general longer than those in the non-MCA-derived group. This may be due to abnormal hemodynamics. As well, this could account for the higher incidence of CHS in MMD patients with MCA-derived recipient vessels compared to non-MCA-derived vessels after STA-MCA bypass surgery.

KEYWORDS: moyamoya disease; cerebral hyperperfusion syndrome; microvascular transit time; superficial temporal artery–middle cerebral artery

INTRODUCTION

Moyamoya disease (MMD) is a chronic progressive occlusive cerebrovascular disease of unknown etiology and pathogenesis. It is characterized by bilateral stenotic or occlusive changes at the terminal portion of the internal carotid artery (ICA) and the formation of an abnormal vascular network at the base of the brain, accompanied by severe hemodynamic alterations in collateral vessels (moyamoya vessels) (J. Yang, Song, Li, Zhang, & Yang, 2019) (Suzuki & Takaku, 1969). Direct revascularization performed by means of superficial temporal artery–middle cerebral artery (STA-MCA) anastomosis is the most common and successful therapy for improving cerebral

hemodynamics and blood flow. Individuals with MMD who undergo direct revascularization usually obtain improvement in intracranial blood perfusion, and the risk of transient ischemic attack and subsequent ischemic stroke is reduced (Kuroda & Houkin, 2008) (Miyamoto et al., 2014). Direct bypass surgery can also prevent recurrent hemorrhage in these individuals (Kawaguchi, Okuno, & Sakaki, 2000). However, cerebral hyperperfusion syndrome (CHS), which can cause transient neurological deficits (Kim et al., 2008) (Fujimura, Mugikura, Kaneta, Shimizu, & Tominaga, 2009) or delayed intracerebral hemorrhage (Fujimura, Shimizu, Mugikura, & Tominaga, 2009), are common postoperative complications (Fujimura et al., 2011). Importantly, CHS is challenging to predict before surgery. Risk factors for CHS include individual characteristics (Fujimura et al., 2012), adult onset, hemorrhagic onset, donor STA size, poor run-off, and low integrity of the blood–brain barrier (Horie et al., 2014) (Hu et al., 2020).

Microvascular transit time (MVTT) can reflect blood flow velocity. It is calculated from the time required for blood to flow from the arterial phase to the venous phase employing intraoperative indocyanine green (ICG) video angiography. MVTT was promulgated as a method for analysis of cortical microhemodynamics (Czabanka et al., 2008). In this regard, the early filling arteries (A1), their direct branches (A2) and the last draining veins (V1), and their direct branches (V2) are referred to as the cortical microvasculature. All vessels that appeared between A2 and V2 vessels are regarded as cortical microvasculature. By comparing the time points of peak fluorescence intensity in the arteries (A2 vessels) and veins (V2 vessels), the difference between arterial and venous peak time is defined as MVTT. Individuals with MMD and a DMVTT (the difference between preoperative and postoperative MVTTs) of more than 2.6 s in the recipient arteries tended to develop postoperative CHS (T. Yang et al., 2017). This suggested that the properties of recipient arteries are related to the occurrence of postoperative CHS. Related to this, we showed that direct anastomoses of recipient perisylvian cortical arteries (PSCAs) with as hemodynamic source the MCA was associated with a higher risk of postoperative CHS compared to non-MCA PSCAs (Zhang et al., 2019). We posited that the different characteristics of blood flow in recipient arteries with different hemodynamic sources could possibly account for this. Herein, we determined the incidence of CHS in forty-two individuals with MMD as related to preoperative MVTT (pre-MVTT) and DMVTT of recipient arteries with different hemodynamic sources (Burrichter, Chen, & Marco, 2022; Gnangnon, 2021).

MATERIALS AND METHODS

Patients

Forty-two recipient arteries of surgical hemispheres (20 left sides and 22 right sides) in 42 adult individuals with MMD (15 males and 27 females, average age 47.33±9.88 years, ranging from 24 to 65 years) who underwent STA-MCA bypass surgery between July 2020 and January 2021 were retrospectively analyzed. All subjects met the diagnostic criteria of the Research Committee on Spontaneous Occlusion of the Circle of Willis of the Ministry of Health, Labor, and Welfare, Japan (on the Pathology, 2012). The inclusion criteria were as follows: (1) each subject was diagnosed by digital subtraction angiography (DSA) before surgery; (2) no conditions associated with MMD such as intracranial atherosclerosis, intracranial aneurysms, meningitis, Down syndrome, systemic vasculitis, acute stroke, hyperthyroidism, neurofibromatosis, leptospiral infection, prior skull-base radiation therapy, or autoimmune disease.

Written informed consent for the use of medical images was obtained from all participants. Other requirements for informed consent were waived since all information was anonymized before analysis. The study protocol was approved by the Medical Ethics Committee of Zhongnan Hospital of Wuhan University and was in accordance with the Declaration of Helsinki as revised in 1983.

Surgical indication and procedure

The indications for surgery were symptomatic MMD (ischemic or hemorrhagic) with apparent hemodynamic compromise. All individuals underwent STA-MCA single anastomosis under general anesthesia. Procedures were performed by two individuals (J.J.Z. or J.C.C.). The proper recipient vessel was identified after craniotomy and was most often the M4 branch of the MCA. Before anastomosis, flow 800 ICG video angiography was performed. If the major source of the individual's recipient vessel blood flow was the MCA, matching donor and recipient vessels were selected for bypass surgery to reduce postoperative CHS [12]. If the major source of blood flow was non-MCA, standard bypass surgery was performed. After anastomosis, flow 800 ICG video angiography was performed to confirm the graft patency.

MVTT measurement

The region of interest (ROI) for the arterial phase was on the recipient artery (M_4), and the ROI for the venous phase was on the superficial middle cerebral vein or its branch vein near the bypass site. We performed an analysis of the ICG time intensity curve on the same ROIs before and after bypass surgery. Because the time period of peak intensity lasted several seconds, determining an accurate intensity peak was sometimes difficult. Therefore, we used the "time point of half-value peak fluorescence intensity" ($T_{1/2}$ peak) instead of the

"time point of peak fluorescence intensity" and calculated MVTT as the difference between the venous phase $T_{1/2}$ peak and the arterial phase $T_{1/2}$ peak. The difference between MVTTs before and after bypass surgery was defined as DMVTT.

DSA images

The DSA images were blindly assessed by two senior neurosurgeons (J.C.C. and J.J.Z.). The Suzuki angiographic stage was first determined. The anterior–posterior and lateral views of the ICA, external carotid artery (ECA), and vertebral artery (VA) injections and the dynamic 3D DSA images were analyzed. Major feeding arteries to the frontal/parietal and temporal PSCAs were identified. Hemodynamic sources of PSCAs were divided into two types: MCA (M-PSCAs) and non-MCA (non-M-PSCAs).

Postoperative management

All patients recovered from anesthesia in the neurosurgical intensive care unit with blood pressure monitoring. Target of blood pressure values were based on the individual's blood pressure level: if they had a history of hypertension (≥140/90 mmHg), the target systolic pressure was 120–140 mmHg and if not, the target systolic pressure was 120–130 mmHg. Antiplatelet therapy and a hydration protocol were administered to all the patients. For MMD with hemorrhage onset, we determined the platelet aggregation rate. Antiplatelet therapy was not administered before bypass surgery. We performed head computed tomography (CT) and again determined the platelet aggregation rate on the first day after surgery. If the volume of new intracranial blood was less than 5 ml, aspirin was administered (0.1 g, daily) during the perioperative period. The patency of the anastomosis and the perfusion status were detected by magnetic resonance angiography (MRA) and ^{99m}Tc-ECD single-photon emission computed tomography (^{99m}Tc-ECD-SPECT). CHS was diagnosed using the following criteria (Sato et al., 2018): (1) seizure, alteration in the level of consciousness, and/or focal neurological signs such as aphasia, hemiparesis, and dysarthria that newly developed or worsened between 12 hours and 30 days after surgery; (2) presence of cerebral hyperperfusion on SPECT and magnetic resonance imaging (MRI); (3) a significant increase in focal cerebral blood flow (CBF) (from the lowest preoperative regional CBF [rCBF] value to the highest postoperative rCBF value of the supratentorial region of the bilateral hemispheres) at the site of anastomosis (qualitative observation of an intense focal increase in CBF confined to one major vascular territory); (4) apparent visualization of STA-MCA bypass by MRA; and (5) the absence of other pathologies such as compression of the brain surface by the temporal muscle for indirect pial synangiosis and increases in

CBF secondary to seizure. If CHS was confirmed, strict blood pressure control and edaravone administration were initiated [12].

STATISTICAL ANALYSIS

IBM SPSS Statistics Desktop, version 24 (IBM Corp.) was used for all statistical analyses. One-way ANOVA was used for parametric statistical analysis. Categorical variables were analyzed in contingency tables with Pearson's chi-square test and Fisher's exact test. Multivariate statistical analysis of the factors related to pre-MVTT and DMVTT, including sex, age, hemorrhagic/ischemic onset, surgical side, Suzuki stage, and recipient arteries with different hemodynamic sources, was performed using a multivariate linear regression model. $P < 0.05$ was considered statistically significant.

RESULTS

Patient population and clinical parameters

Forty-two adults with MMD (15 males and 27 females) were included in the study cohort and 42 recipient arteries of surgical hemispheres underwent analysis. The mean cohort age was 47.33±9.88 years (ranged from 24 to 65 years). Sixteen subjects had hemorrhagic onset and 26 had ischemic onset. Twenty individuals (47.6%) underwent STA-MCA bypass surgery on the left side and 22 patients (52.4%) on the right side. By analyzing DSA images in 42 surgical hemispheres, the results of Suzuki staging were stage 1 (1/42, 2.4%), stage 2 (3/42, 7.1%), stage 3 (16/42, 38.1%), stage 4 (14/42, 33.3%), and stage 5 (8/42, 19.1%). Different hemodynamic sources of selected recipient vessels in STA-MCA bypass surgery were analyzed in all 42 individuals with MMD based on preoperative DSA, and the hemodynamic source of 17 selected recipient arteries was MCA (40.5%), and the hemodynamic source of 25 recipient arteries was non-MCA (59.5%) (**Fig. 1**). During the bypass surgery, the mean MVTT on the recipient artery before anastomosis was 2.79±1.76 s, and the mean DMVTT was 2.05±1.03 s (**Table 1**).

Intraoperative ICG video angiography and postoperative MRA confirmed bypass patency in all subjects. Postoperative CHS occurred in 4 (9.5%) individuals (**Fig. 2**) and symptoms included seizure, dysarthria, aphasia, and limb weakness (**Table 2**).

Comparison of MMD patients with recipient arteries with different hemodynamic sources

Pre-MVTT was significantly greater in the MCA-derived group (4.00±1.4 s) than in the non-MCA-derived group (1.96±1.48 s) (**Fig. 3**). The DMVTT was significantly greater in the MCA-derived group (2.79±0.79 s) than in the non-

MCA-derived group (1.55±0.86 s). In the MCA-derived group, postoperative CHS occurred in 3 patients (17.6%), while clinical symptoms included 1 instance of seizure, 1 of aphasia, and 1 of dysarthria. In the non-MCA-derived group, the incidence of postoperative CHS was 4% (1 patient), with limb weakness being the only clinical symptom (**Table 2** and **Table 3**).

Multivariate linear regression of pre-MVTT and DMVTT

Multivariate linear regression with sex, age, hemorrhagic/ischemic onset, surgical side, Suzuki stage, and recipient arteries with different hemodynamic sources showed that the different hemodynamic sources of the PSCAs significantly influenced pre-MVTT ($P = 0.004$) and DMVTT ($P < 0.001$) (**Table 4** and **Table 5**).

DISCUSSION

As one of the most serious complications of MMD revascularization surgery, CHS occurred in approximately 17% of MMD patients after STA-MCA bypass surgery. On meta-analysis, we found the incidence of CHS was 16.5% (ranging from 11.3 to 22.3%) (Yu, Zhang, Li, Zhang, & Chen, 2020). The clinical symptoms of CHS vary and include headache, aphasia, hemiparesis, paresis, facial palsy, limb weakness, dysarthria, and intracerebral hemorrhage (Cho et al., 2013). Most of these symptoms are caused by transient neurologic impairment, and usually resolve within 2 weeks without permanent cerebral damage. However, delayed intracranial hemorrhage and secondary subarachnoid hemorrhage can lead to irreversible neural damage (Ogasawara et al., 2005). Since CHS can have serious consequences, it is important to identify predictive indicators of CHS before surgery. Probable risk factors for CHS include patient characteristics, onset types, surgical methods, and surgical hemisphere. Adult onset, hemorrhagic onset, and increased preoperative cerebral blood volume are the most commonly reported risk factors for postoperative CHS. Several possible factors may contribute to of postoperative CHS, i.e., vessel diameter, blood flow speed, and blood flow direction (Uchino et al., 2012). First, because the diameter of arteries determines their blood transport capacity, an excessive difference in diameter between the donor and recipient vessels delays the effective dispersion of the relatively large blood volume from the external carotid system, leading to hyperperfusion around the anastomosis. We reported that selection of matching vessel diameters between donor and recipient vessels during revascularization surgery reduced the incidence of postoperative CHS in adult patients with MMD. We also noted that there are five major hemodynamic sources in PSCAs: the MCA, anterior cerebral artery (ACA), contralateral ACA, posterior cerebral artery (PCA), and ECA. The hemodynamic origin

determines the direction of blood flow in the recipient artery. We found that direct anastomoses of recipient arteries with as hemodynamic source the MCA were associated with a high risk of postoperative CHS for STA-MCA bypass surgery in adult patients with MMD. The above data show that the recipient vessel influences the incidence of CHS.

In MMD, cerebral cortical vessels proliferate and expand to compensate for the reduction of local cerebral perfusion by decreasing peripheral vascular resistance. Related to this anatomical alteration, MVTT is prolonged in patients with MMD [13]. Prolonged MVTT in individuals with MMD was reduced after bypass surgery, and the difference in MVTT before and after bypass surgery in these subjects influenced the incidence of postoperative CHS [14]. It is conceivable that the prolongation of pre-MVTT and the reduction of MVTT after bypass surgery was secondary to microvascular vasodilation in the cortex which could have predisposed individuals to postoperative CHS. However, the authors did not distinguish the blood flow source of recipient vessels, thus making it difficult to explain the difference in DMVTT of recipient vessels. We found that recipient vessels of different hemodynamic sources are also associated with differences in the incidence of postoperative CHS. Still, why this is remains to be determined.

The microvascular density and the microvascular diameter of cortical vessels in MMD are significantly increased and associated with prolonged microvascular hemodynamics suggesting a compensatory process [13]. The recipient PSCAs with as hemodynamic source the MCA are extremely dilated because of their poor collateral establishment, so the blood flow from the stenosis- or MMD-altered MCA is accompanied by prolonged microvascular hemodynamics while the blood flow speed of M-PSCAs is significantly reduced. The slow blood flow in M-PSCAs may retard flow of the relatively large blood volume from the STA and so contribute to postoperative CHS. On the contrary, the blood flow in non-M-PSCAs is from established collateral vessels with stable microvascular hemodynamics and are sufficient to disperse the large blood volume from the STA. In consequence, the incidence of CHS is significantly decreased in MMD patients with non-M-PSCAs after STA-MCA bypass surgery. MVTT can be easily measured during bypass surgery by flow 800 ICG video angiography. However, as a predictor of postoperative CHS, DMVTT was associated with false-negative results [14].

The present study contains a number of limitations. First, our analysis was post hoc and by its nature likely to be impacted by selection bias and limitations inherent in single center studies. Second, the investigation methods were limited to measuring microvascular hemodynamics, such as blood flow direction, blood flow speed, and blood flow sources. However,

blood flow directly at the site on microvascular anastomosis was not characterized. This is important as anastomotic blood flow alters the MVTT after bypass surgery. Nonetheless, the blood flow techniques employed herein were representative of the capacity of our medical center. Lastly, the assessment of hyperperfusion with SPECT is less precise than some other modalities.

CONCLUSIONS

Analysis of blood flow recipient vessels with different hemodynamic sources of MMD individuals that underwent surgical vascular bypass surgery there were significant differences in pre-MVTT and DMVTT. The preoperative MVTT and DMVTT of MCA-derived recipient arteries were longer compared to those of non-MCA-derived recipient arteries. This variation was associated with CHS risk.

ABBREVIATIONS

MMD: moyamoya disease
CHS: Cerebral hyperperfusion syndrome
ICA: internal carotid artery
ACA: anterior cerebral artery
MCA: middle cerebral artery
STA: superficial temporal artery
DSA: digital subtraction angiography
MRI: magnetic resonance imaging
CBF: cerebral blood flow
TIA: transient ischemic attack
PSCA: perisylvian cortical artery
MVTT: microvascular transit time

REFERENCES

Burrichter, K., Chen, B., & Marco, G. (2022). Evaluation of modern technology on human resources management and sustainable development in Pharma industries. *Journal of Commercial Biotechnology, 27*(2). doi:https://doi.org/10.5912/jcb1296

Cho, W.-S., Lee, H.-Y., Kang, H.-S., Kim, J. E., Bang, J. S., & Oh, C.-W. (2013). Symptomatic cerebral hyperperfusion on SPECT after indirect revascularization surgery for Moyamoya disease. *Clinical Nuclear Medicine, 38*(1), 44-46.

Czabanka, M., Pena-Tapia, P., Schubert, G. A., Woitzik, J., Vajkoczy, P., & Schmiedek, P. (2008). Characterization of cortical microvascularization in adult moyamoya disease. *Stroke, 39*(6), 1703-1709.

Fujimura, M., Inoue, T., Shimizu, H., Saito, A., Mugikura, S., & Tominaga, T. (2012). Efficacy of prophylactic blood pressure lowering according to a standardized postoperative management protocol to prevent symptomatic cerebral hyperperfusion after direct revascularization surgery for moyamoya disease. *Cerebrovascular Diseases, 33*(5), 436-445.

Fujimura, M., Mugikura, S., Kaneta, T., Shimizu, H., & Tominaga, T. (2009). Incidence and risk factors for symptomatic cerebral hyperperfusion after superficial temporal artery-middle cerebral artery anastomosis in patients with moyamoya disease. *Surgical neurology, 71*(4), 442-447.

Fujimura, M., Shimizu, H., Inoue, T., Mugikura, S., Saito, A., & Tominaga, T. (2011). Significance of focal cerebral hyperperfusion as a cause of transient neurologic deterioration after extracranial-intracranial bypass for moyamoya disease: comparative study with non-moyamoya patients using N-isopropyl-p-[123I] iodoamphetamine single-photon emission computed tomography. *Neurosurgery, 68*(4), 957-965.

Fujimura, M., Shimizu, H., Mugikura, S., & Tominaga, T. (2009). Delayed intracerebral hemorrhage after superficial temporal artery–middle cerebral artery anastomosis in a patient with moyamoya disease: possible involvement of cerebral hyperperfusion and increased vascular permeability. *Surgical neurology, 71*(2), 223-227.

Gnangnon, S. K. (2021). Wages in the Manufacturing Sector and Remittances Outflows from High-Income Countries. *Remittances Review, 6*(2), 115-132. doi:https://doi.org/10.33182/rr.v6i2.1659

Horie, N., Fukuda, Y., Izumo, T., Hayashi, K., Suyama, K., & Nagata, I. (2014). Indocyanine green videoangiography for assessment of postoperative hyperperfusion in moyamoya disease. *Acta neurochirurgica, 156*, 919-926.

Hu, M., Zeng, X., Su, K., Tian, X., Chen, J., & Zhang, J. (2020). Matching selection of donor-recipient vessels in revascularization surgery effectively reduce the incidence of postoperative hyperperfusion syndrome in adult moyamoya disease: a retrospective comparison study. *Cerebrovascular Diseases, 49*(4), 361-368.

Kawaguchi, S., Okuno, S., & Sakaki, T. (2000). Effect of direct arterial bypass on the prevention of future stroke in patients with the hemorrhagic variety of moyamoya disease. *Journal of neurosurgery, 93*(3), 397-401.

Kim, J. E., Oh, C. W., Kwon, O.-K., Park, S. Q., Kim, S. E., & Kim, Y. K. (2008). Transient hyperperfusion after superficial temporal artery/middle cerebral artery bypass surgery as a possible cause of postoperative transient neurological deterioration. *Cerebrovascular Diseases, 25*(6), 580-586.

Kuroda, S., & Houkin, K. (2008). Moyamoya disease: current concepts and future perspectives. *The Lancet Neurology, 7*(11), 1056-1066.

Miyamoto, S., Yoshimoto, T., Hashimoto, N., Okada, Y., Tsuji, I., Tominaga, T., . . . Tomata, Y. (2014). Effects of extracranial–intracranial bypass for patients with hemorrhagic moyamoya disease: results of the Japan Adult Moyamoya Trial. *Stroke, 45*(5), 1415-1421.

Ogasawara, K., Komoribayashi, N., Kobayashi, M., Fukuda, T., Inoue, T., Yamadate, K., & Ogawa, A. (2005). Neural damage caused by cerebral hyperperfusion after arterial bypass surgery in a patient with moyamoya disease: case report. *Neurosurgery, 56*(6), E1380-E1380.

on the Pathology, R. C. (2012). Guidelines for diagnosis and treatment of moyamoya disease (spontaneous occlusion of the circle of Willis). *Neurologia medico-chirurgica, 52*(5), 245-266.

Sato, S., Kojima, D., Shimada, Y., Yoshida, J., Fujimato, K., Fujiwara, S., . . . Terasaki, K. (2018). Preoperatively reduced cerebrovascular contractile reactivity to hypocapnia by hyperventilation is associated with cerebral hyperperfusion syndrome after arterial bypass surgery for adult patients with cerebral misery perfusion due to ischemic moyamoya disease. *Journal of Cerebral Blood Flow & Metabolism, 38*(6), 1021-1031.

Suzuki, J., & Takaku, A. (1969). Cerebrovascular moyamoya disease: disease showing abnormal net-like vessels in base of brain. *Archives of neurology, 20*(3), 288-299.

Uchino, H., Kuroda, S., Hirata, K., Shiga, T., Houkin, K., & Tamaki, N. (2012). Predictors and clinical features of postoperative hyperperfusion after surgical revascularization for moyamoya disease: a serial single photon emission CT/positron emission tomography study. *Stroke, 43*(10), 2610-2616.

Yang, J., Song, G.-f., Li, H.-b., Zhang, S.-h., & Yang, F.-y. (2019). Clinical efficacy of extracranial-intracranial bypass for the treatment of adult patients with moyamoya disease: A protocol of systematic review of randomized controlled trials. *Medicine, 98*(49).

Yang, T., Higashino, Y., Kataoka, H., Hamano, E., Maruyama, D., Iihara, K., & Takahashi, J. C. (2017). Correlation between reduction in microvascular transit time after superficial temporal artery–middle cerebral artery bypass surgery for moyamoya disease and the development of postoperative hyperperfusion syndrome. *Journal of neurosurgery, 128*(5), 1304-1310.

Yu, J., Zhang, J., Li, J., Zhang, J., & Chen, J. (2020). Cerebral hyperperfusion syndrome after revascularization surgery in patients with moyamoya disease: systematic review and meta-analysis. *World neurosurgery, 135*, 357-366. e354.

Zhang, J., Li, S., Fujimura, M., Lau, T. Y., Wu, X., Hu, M., . . . Li, X. (2019). Hemodynamic analysis of the recipient parasylvian cortical arteries for predicting postoperative hyperperfusion during STA-MCA bypass in adult patients with moyamoya disease. *Journal of neurosurgery, 134*(1), 17-24.

Figure legends

Figure 1. Analysis of the major blood sources of the PSCAs. Representative figures of M-PSCAs and non-M-PSCAs. These are defined as the PSCAs (white circles and ovals) with blood flow from the MCA and non-MCA. A1–4 (the anterior–posterior and lateral views of the right ICA and the right VA) indicate the major hemodynamic sources of PSCAs originating from the MCA; B1–4 (the anterior–posterior and lateral views of the left ICA and the left VA) indicate the major hemodynamic sources of PSCAs originating from the non-MCA (PCA).

Figure 2. Representative result of SPECT study in an individual with HPS. A1–3: SPECT images of a representative individual with MMD in the M-PSCA group showed hypoperfusion in the right frontal lobe and temporal lobe before operation. B1–3: The perfusion states of the right frontal lobe and temporal lobes were significantly improved after operation, while focal hyperperfusion was noted in the right temporal lobe.

Figure 3. Representative result of measuring MVTT. The red marks indicate ROIs in the recipient artery, the green marks indicate ROIs in the superficial middle cerebral vein. The white arrow indicates the STA. The red number at the right side highlights the arterial phase $T_{1/2}$ peak, and the green one highlights the venous phase $T_{1/2}$ peak. MVTT is the difference between the venous phase $T_{1/2}$ peak and the arterial phase $T_{1/2}$ peak. (A) Time intensity curves before bypass surgery; preoperative MVTT was 3.13 s. (B) Time intensity curves after bypass surgery; postoperative MVTT was 2.65 s. DMTT = 3.13 − 2.65 = 0.48 s.

Characteristic		
Sex	Male	15 (35.7%)
	Female	27 (64.3%)
Age, yrs (mean ± SD)		47.33±9.88
Onset	Hemorrhagic	16 (38.1%)
	Ischemic	26 (61.9%)
Surgical side	Light	20 (47.6%)
	Right	22 (52.4%)
Suzuki stage		3.60±0.96
Recipient arteries with different hemodynamic sources	M-PSCAs	17 (40.5%)
	Non-M-PSCAs	25 (59.5%)
Pre-MVTT, s (mean ± SD)		2.79±1.76

DMVTT, s (mean ± SD)	2.05±1.03
CHS	4 (9.5%)

Table 1 Cohort demographics and physiologic parameters

Pre-MVTT = preoperative microvascular transit time;
DMVTT = the difference between MVTTs before and after bypass surgery;
CHS = cerebral hyperperfusion syndrome.

Table 2 Demographics and physiologic parameters of individuals that developed postoperative CHS

	1	2	3	4
Sex	Male	Male	Female	Female
Age, yrs	37	51	29	52
Onset	Hemorrhage	Ischemia	Hemorrhage	Ischemia
Surgical side	Right	Light	Right	Right
Suzuki stage	3	3	4	5
Recipient arteries with different hemodynamic sources	M-PSCAs	M-PSCAs	M-PSCAs	Non-M-PSCAs
Pre-MVTT, s	3.00	3.47	7.39	0.45
DMVTT, s	2.23	2.02	2.35	1.89
Symptoms of postoperative CHS	Seizures	Aphasia	Dysarthria	Limb weakness

M-PSCAs = recipient PSCAs with as hemodynamic source the MCA;
Non-M-PSCAs = all recipient PSCAs with blood flow not supplied by the MCA;
Pre-MVTT = preoperative microvascular transit time;
DMVTT = the difference between MVTTs before and after bypass surgery;
CHS = cerebral hyperperfusion syndrome.

Table 3 Demographics and physiologic parameters according to the hemodynamic sources of the recipient arteries

Characteristic	Classification of recipient arteries according to their hemodynamic sources		*P*-value
	M-PSCAs (*n* = 17)	Non-M-PSCAs (*n* = 25)	
Male sex	3 (17.6%)	12 (48%)	0.045
Age, yrs (mean ± SD)	43.00±1.44	50.28±7.57	0.017
Hemorrhagic/ischemic onset	6/11	10/15	0.765
Surgical side (left/right)	10/7	10/15	0.241
Suzuki stage (mean ± SD)	3.06±0.90	3.96±0.84	0.002

Pre-MVTT, s (mean ± SD)	4.00±1.41	1.96±1.48	<0.001
DMVTT, s (mean ± SD)	2.79±0.79	1.55±0.86	<0.001
CHS	3 (17.6%)	1 (4%)	0.146

M-PSCAs = recipient PSCAs with as hemodynamic source the MCA;
Non-M-PSCAs = all recipient PSCAs with blood flow not supplied by the MCA;
Pre-MVTT = preoperative microvascular transit time;
DMVTT = the difference between MVTTs before and after bypass surgery;
CHS = cerebral hyperperfusion syndrome.

Table 4 Multivariate linear regression analysis of pre-MVTT.

Variable	Correlation coefficient (95% CI)	*P*-value
Sex	0.07 (−0.82 to 1.32)	0.638
Age, yrs	−0.02 (−0.06 to 0.05)	0.913
Onset	−0.05 (−1.31 to 0.98)	0.772
Surgical side	−0.08 (−1.45 to 0.87)	0.615
Suzuki stage	−0.01 (−0.64 to 0.62)	0.970
Recipient arteries with different hemodynamic sources	0.54 (0.65 to 3.13)	**0.004**

P < 0.05 was considered as significant difference.

Table 5 Multivariate linear regression of DMVTT.

Variable	Correlation coefficient (95% CI)	*P*-value
Sex	0.02 (−0.54 to 0.63)	0.887
Age, yrs	−0.01 (−0.04 to 0.02)	0.913
Onset	0.19 (−0.24 to 1.01)	0.772
Surgical side	0.12 (−0.39 to 0.88)	0.442
Suzuki stage	0.24 (−0.09 to 0.60)	0.140
Recipient arteries with different hemodynamic sources	0.68 (0.73 to 2.08)	**<0.001**

P < 0.05 was considered significant.

Número de citas totales / Total references: 20 (100%)

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