Larger Posterior Revascularization Associated with Reduction of Choroidal Anastomosis in Moyamoya Disease: A Quantitative Angiographic Analysis

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ABSTRACT

BACKGROUND AND PURPOSE: Choroidal anastomosis, a hemorrhage-prone periventricular collateral manifestation in Moyamoya disease, outflows to the cortex posterior to the central sulcus. The objective of the present study was to test whether the angiographic extent of revascularization posterior to the central sulcus contributes to the postoperative reduction of choroidal anastomosis.

MATERIALS AND METHODS: This retrospective cohort study included choroidal anastomosis–positive hemispheres before direct bypass surgery. The postoperative reduction of choroidal anastomosis was determined by a consensus of 2 raters according to the previous research. An imaging software automatically traced the angiographic revascularization area, which was subsequently divided into anterior and posterior parts by an anatomic line corresponding to the central sulcus. Each area was quantitatively measured as a percentage relative to the whole supratentorial area.

RESULTS: Postoperative reduction of choroidal anastomosis was achieved in 68 (85.0%) of the 80 included hemispheres. The revascularization area posterior to the central sulcus was significantly larger in the hemispheres with reduction than in those with no reduction (mean, 15.2% [SD, 7.1%] versus 4.2% [SD, 3.4%], $P < .001$), whereas no significant difference was observed in the revascularization area anterior to the central sulcus. Multivariate analysis revealed that the revascularization area posterior to the central sulcus was the only significant factor associated with reduction (OR, 1.57; 95% CI, 1.21–2.03, for every 1% increase).

CONCLUSIONS: The results suggest that a larger revascularization posterior to the central sulcus is associated with postoperative reduction of choroidal anastomosis regardless of the extent of anterior revascularization. It might facilitate optimal selection of the revascularization site for preventing hemorrhage.

ABBREVIATIONS: CS = central sulcus; PCA = posterior cerebral artery; STA = superficial temporal artery

Choroidal anastomosis is one of the abnormal periventricular collaterals in Moyamoya disease.[1-5] The collateral is characterized by a connection between the choroidal and medullary arteries, which outflows to the cortex via retrograde flow in the medullary artery (Fig 1).[2,3,6] Choroidal anastomosis is commonly observed in hemorrhagic Moyamoya disease[7-9] and is associated with an extremely high risk of bleeding.[4,5,10] After bypass surgery, the normalized direction of flow in the medullary artery can induce angiographic reduction of choroidal anastomosis.[6,11] This change might explain the effectiveness of direct bypass in preventing bleeding.[12-14] However, only a few studies have focused on the factors contributing to this change.[15] A recent study revealed that choroidal anastomosis outflows to the cortex posterior to the central sulcus (CS).[16] We hypothesized that a larger angiographic extent of revascularization posterior to the CS is associated with the reduction of choroidal anastomosis. Testing this hypothesis might help to determine the optimal revascularization site for preventing hemorrhage.

MATERIALS AND METHODS

The present retrospective cohort study was approved by Kyoto University Hospital institutional ethics committee (R1600). The Strengthening the Reporting of Observational Studies in Epidemiology was followed. All participants gave opt-out

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From the Departments of Neurosurgery (T.F., A.M., K.Y., T.K., Y.M., M.O., Y.Y., S.M.) and Diagnostic Imaging and Nuclear Medicine (Y.F.), Kyoto University Graduate School of Medicine, Kyoto, Japan; Department of Neurosurgery (H.K.), National Cerebral and Cardiovascular Center, Osaka, Japan; Department of Neurosurgery (J.C.T.), Kindai University Faculty of Medicine, Osaka, Japan; and Department of Neurosurgery (Y.T.), Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan.

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Please address correspondence to Takeshi Funaki, MD, PhD, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan; e-mail: tfunaki@kuhp.kyoto-u.ac.jp

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consent in accordance with the ethical standards of the institutional and national research committees.

Patients and Setting

The present study included patients who had been diagnosed with Moyamoya disease according to the guidelines,[17] who had presented with ischemic and hemorrhagic symptoms, who had undergone superficial temporal artery (STA)-MCA anastomosis at our hospital in the past 5 years, and who had been deemed positive for choroidal anastomosis before the operation.

Our original surgical procedures for STA-MCA anastomosis have been described in detail elsewhere.[18] The addition of encephalomyosynangiosis was considered in pediatric patients.

Assessment of Choroidal Anastomosis

Patients routinely underwent MR imaging and conventional angiography before and after the operation. Postoperative angiographies were acquired at 3–6 months after completion of bilateral operations.

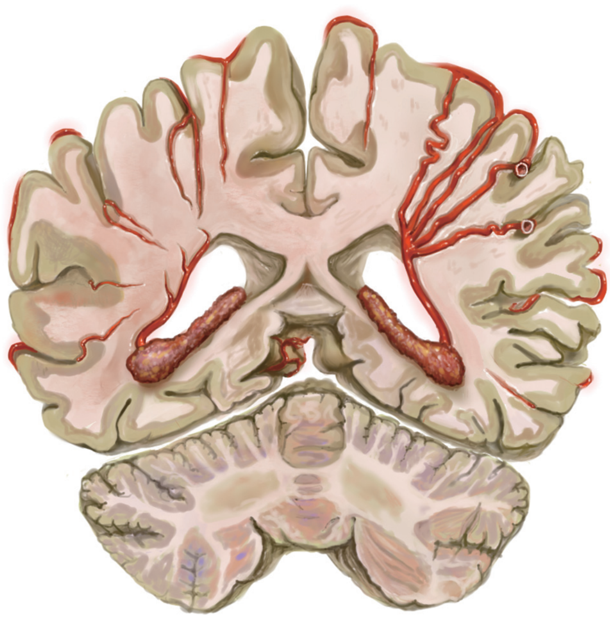

FIG 1. Schematic illustration showing choroidal anastomosis (*left hemisphere*) in the coronal plane.

Two raters (T.F. and A.M.), blinded to other clinical information to avoid biases, viewed conventional angiograms and the sliding-thin-slab MIP coronal MRA[2] to grade the development of choroidal anastomosis by hemisphere. The presence or absence of the anastomosis was determined by a consensus of 2 raters. The determinants for the presence of choroidal anastomosis were defined in the previous studies.[1,2] In brief, choroidal anastomosis is defined as an anastomosis between the choroidal artery, either anterior or posterior, and the medial end of the medullary artery. The positive angiographic indicator of choroidal anastomosis is dilation and extension of the choroidal artery beyond the level of the lateral ventricle.[1,5,9] This indicator corresponded to that of grade 2 choroidal anastomosis defined by Fujimura et al.[9]

According to previous research,[6] reduction of choroidal anastomosis was defined as no apparent anastomosis on a postoperative image, which corresponded to grade 0 or 1 defined by Fujimura et al.[9] Reduction was recorded as a dichotomous variable (yes/no). The study population partly overlapped with that of our previous study.[6] Recording of this variable had been completed for all hemispheres before the measurement of the revascularization area, to avoid making arbitrary decisions on the reduction of choroidal anastomosis.

Measurement of Revascularization Area

According to the method of Bang et al,[19] we quantitatively measured the revascularization area relative to the whole supratentorial area on the lateral views of postoperative external carotid angiography. To ensure objectivity, we used imaging software (ImageJ, Version 1.52a; National Institutes of Health), which facilitated binary image conversion and automatic tracing of the revascularization area (Fig 2). The threshold for binary image conversion was set as the "default." An unsubtracted angiographic image was also imported into the software for measuring the supratentorial area and determining the CS. We adopted the Rhoton method[20] to determine the location of the CS. In brief, the extended line of the CS was approximated to the line connecting the midportion of the zygomatic arch and the point located

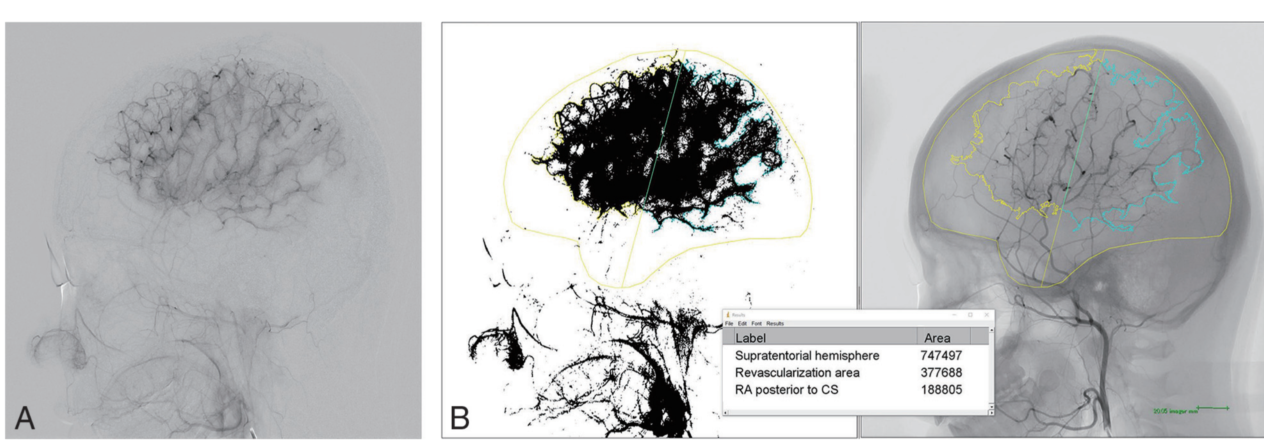

FIG 2. Quantitative measurement of revascularization areas. *A*, Original image of the postoperative external carotid angiography in the capillary phase. *B*, Images imported into the software (ImageJ, Version 1.52a). The revascularization area (RA) posterior to the CS (*blue line*) is 188805/747497 = 25.3%.

2 cm behind the midpoint between the nasion and inion. The accuracy of this topographic method has been confirmed in several studies.[21,22] The extended line of the CS divided the revascularization area into 2 areas, those anterior and posterior to the CS, and each pixel area was measured. Anterior and posterior revascularization areas were calculated as a percentage relative to the whole supratentorial area through setting each revascularization pixel area and whole supratentorial pixel area as the numerator and denominator, respectively (Fig 2). Revascularization areas were regarded as a continuous variable.

Other Variables

We measured 7 other variables as potential confounders: age at the operation, sex, symptom at onset, Suzuki stage,[23] the presence or absence of posterior cerebral artery (PCA) involvement,[24] the addition of encephalomyosynangiosis,[25] and the preoperative hemodynamic state assessed with SPECT.[26] According to Takahashi et al,[26] the hemodynamic state in the MCA territory was classified into 1 of the following 3 stages: stage 0, normal baseline with normal acetazolamide-challenged CBF; stage 1, normal baseline with reduced acetazolamide-challenged CBF; and stage 2, reduced baseline with reduced acetazolamide-challenged CBF. We also assessed the hemodynamic status in the posterior half of the MCA territory because this area might be more closely associated with choroidal anastomosis. A commercially available software (NEURO FLEXER; https://neuro-flexer.software.informer.com/) with the functions of NEUROSTAT (http://128.95.65.28/~Download/) developed by Ogura et al[27] was used to set the ROIs. The latest version of this software can automatically set ROIs including the anterior cerebral artery, MCA, anterior MCA, posterior MCA, PCA, basal ganglia, thalamus, pons, vermis, and cerebellar hemisphere. The hemodynamic status in the posterior MCA territory was classified into 1 of the 3 stages in the same manner as described above. All variables were recorded separately by hemisphere.

Statistical Analysis

The sample size was determined by the number of cases treated during the study period. All statistical analyses were performed for single hemispheres. For comparison of baseline characteristics (univariate analysis), the *t* test, Wilcoxon rank-sum test, χ^2 test, or Fisher exact test was used as appropriate. To identify independent factors associated with the reduction of choroidal anastomosis, we used a multiple logistic regression analysis. Variables with a P value $< .1$ in univariate analyses were incorporated into the multiple logistic regression analysis. P values $< .05$ were considered significant. Neither loss to follow-up nor missing data occurred. All analyses were performed using JMP software (Version 15; SAS Institute).

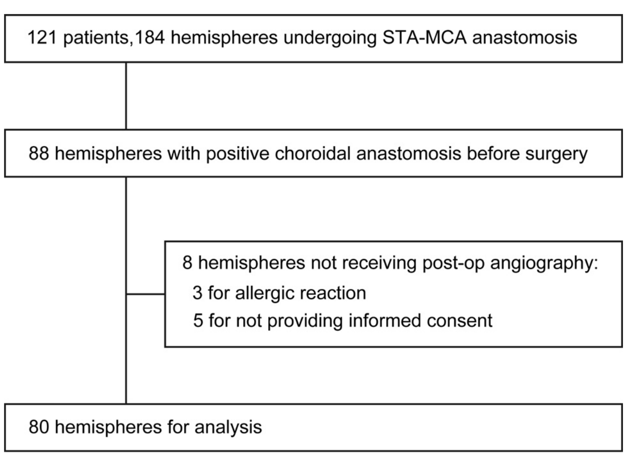

FIG 3. Flow chart for patient inclusion.

RESULTS

Of a total of 121 patients (184 hemispheres) who underwent STA-MCA anastomosis in the study period, 88 hemispheres were identified as positive for choroidal anastomosis with preoperative MR imaging and conventional angiography. Postoperative angiography was not performed in 8 hemispheres for the following reasons: allergic reaction to the contrast medium occurring after the first angiography (3 hemispheres) and patients not providing informed consent for the second angiography (5 hemispheres). The remaining 80 hemispheres were included in the analysis (Fig 3). Baseline characteristics of the 80 hemispheres, including 43 left and 37 right hemispheres, are summarized in Table 1.

Table 1: Baseline variables

		Reduction of Choroidal Anastomosis		
	Total	Yes	No	*P* Value
No. of hemispheres	80	68	12	NA
Revascularization area (mean) (%)[a]				
Posterior to CS	13.6 (SD, 7.7)	15.2 (SD, 7.1)	4.2 (SD, 3.4)	<.001
Anterior to CS	12.6 (SD, 7.0)	12.5 (SD, 6.7)	13.2 (SD, 8.9)	.74
Median age (yr) (IQR)	12 (8–36)	11 (8–33)	19.5 (5.25–47.5)	.57
Female (%)	47 (58.8)	43 (63.2)	4 (33.3)	.05
Hemorrhagic presentation (%)	17 (21.3)	12 (17.7)	5 (41.7)	.06
Median Suzuki stage (IQR)	3 (3–3)	3 (3–3)	3 (2–3)	.33
PCA involvement (%)	10 (12.5)	10 (14.7)	0	.34
SPECT stage 2				
MCA territory (%)	37 (46.3)	32 (47.1)	5 (41.7)	.73
Posterior MCA territory (%)	27 (33.8)	25 (36.8)	2 (16.7)	.17
Addition of EMS (%)	21 (26.3)	16 (23.5)	5 (41.7)	.19

Note:—EMS indicates encephalomyosynangiosis; IQR, interquartile range; NA, not applicable.
[a] Percentage relative to whole supratentorial area.

Reduction of choroidal anastomosis after the operation was confirmed in 68 (85.0%) of the 80 hemispheres with postoperative conventional and MR angiographies. Conventional and MR angiographies were performed an average of 148.7 and 129.3 days after ipsilateral surgery, respectively.

Revascularization Area and Choroidal Anastomosis Reduction

The relationship between each revascularization area and reduction of choroidal anastomosis is shown in Table 1 and Fig 4. The revascularization area posterior to the CS was significantly larger in the hemispheres exhibiting reduction than in those exhibiting no reduction (mean, 15.2% [SD, 7.1%] versus 4.2% [SD, 3.4%]; $P < .001$), whereas no significant difference was observed in the revascularization area anterior to the CS ($P = .74$). The cutoff value of the revascularization area posterior to the CS for predicting reduction was 10.7% according to the analysis of the receiver operating characteristic curve (Fig 4, dotted line). All 52 hemispheres in which the area exceeded 10.7% showed reduction, whereas only 16 of the 28 hemispheres (57.1%) with the area below 10.7% showed reduction.

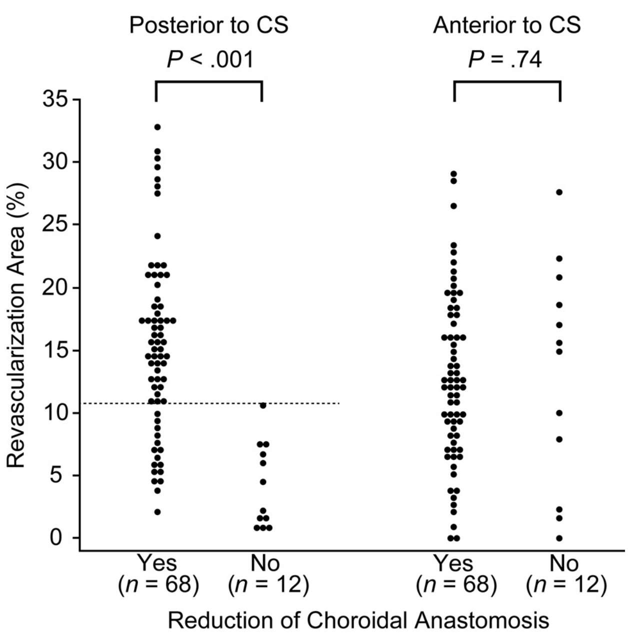

FIG 4. Comparison of each revascularization area between hemispheres exhibiting reduction of choroidal anastomosis and those exhibiting no reduction. The *dotted line* indicates the cutoff value (10.7%).

Figure 5 shows a representative case in which choroidal anastomosis responsible for hemorrhage has been markedly reduced after bypass surgery. The revascularization area posterior to the CS was relatively large (16.1%), whereas that anterior to the CS was small (3.4%).

Factors Associated with Choroidal Anastomosis Reduction

In the univariate analysis, the revascularization area posterior to the CS was the only significant factor associated with reduction of choroidal anastomosis (Table 1). Although the proportion of the hemisphere with stage 2 hemodynamic compromise in the posterior MCA territory was larger in the reduction group than in the no-reduction group (36.8% versus 16.7%), the difference was not statistically significant ($P = .17$). Three variables with a P value $< .1$ (the revascularization area posterior to the CS, sex, and hemorrhagic presentation) were incorporated in the multiple logistic regression analysis, revealing that the revascularization area posterior to the CS remained statistically significant (OR, 1.57; 95% CI, 1.21–2.03, for every 1% increase; Table 2).

We performed a sensitivity analysis in which we incorporated SPECT stage 2 in the posterior MCA territory in the multivariate analysis together with the above 3 variables. This analysis also revealed that the revascularization area posterior to the CS remained statistically significant (Online Supplemental Data).

Outcome

No subsequent intracranial hemorrhage associated with choroidal anastomosis occurred after the operation in the study population. However, there was a patient in whom de novo bleeding from the remaining choroidal anastomosis occurred 13 years after the operation (Fig 6). In this case, the revascularization area anterior to the CS was relatively large (12.3%), but that posterior to the CS was very small (1.5%). This patient's data were not included in the statistical analyses because the patient did not fulfil the inclusion criteria in terms of the operation date.

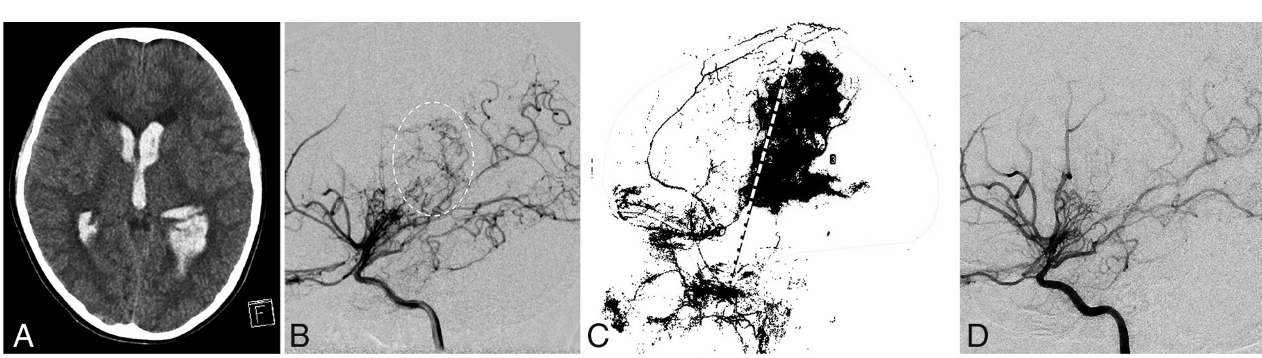

FIG 5. Case 1 (a 9-year-old girl). *A*, CT at onset shows intraventricular hemorrhage. *B*, Preoperative left internal carotid angiography shows choroidal anastomosis (*dotted circle*), which corresponds to the hemorrhage site. *C*, Quantitative measurement of the revascularization area in the left hemisphere. The revascularization areas anterior and posterior to the CS are 3.4% and 16.1%, respectively. The *dotted line* indicates the CS. *D*, Postoperative left internal carotid angiography shows reduction of choroidal anastomosis.

Table 2: Multiple adjusted ORs for reduction of choroidal anastomosis

	Crude		Multivariate Adjustment	
	OR	(95% CI)	OR	(95% CI)
Revascularization area posterior to CS[a]	1.53	(1.20–1.95)	1.57	(1.21–2.03)
Female	3.44	(0.94–12.59)	3.96	(0.66–23.86)
Hemorrhagic presentation	0.3	(0.08–1.11)	0.97	(0.16–6.07)

[a] Every 1% increase.

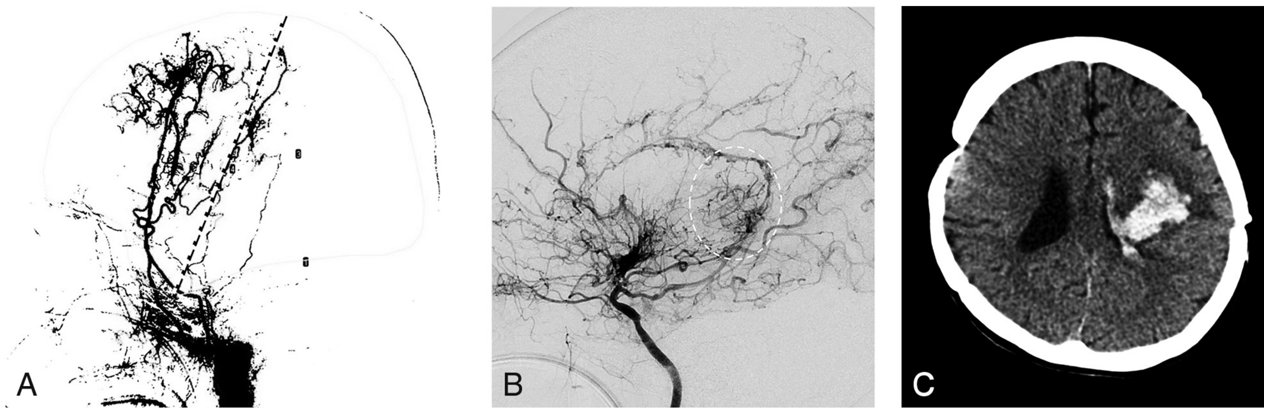

FIG 6. Case 2. The patient had initially manifested seizure at 43 years of age and had undergone direct bypass. *A*, Quantitative measurement of the revascularization area in the left hemisphere. The revascularization areas anterior and posterior to the CS were 12.3% and 1.5%, respectively. The *dotted line* indicates the CS. *B*, Postoperative left ICA shows persistence of choroidal anastomosis (*dotted circle*). *C*, CT obtained at the onset of de novo intracranial hemorrhage, which occurred 13 years after the operation.

Supplemental Data

We performed a supplemental analysis to identify factors associated with the overall revascularization area (the area comprising both anterior and posterior revascularization areas). As shown in the Online Supplemental Data, female sex (P = .02), PCA involvement ($P <$ .001), and SPECT stage 2 in the MCA territory ($P <$ .001) were univariate factors positively associated with the overall revascularization area.

DISCUSSION

There were 3 major observations from our study: First, 85% of the patients had reduction of choroidal anastomosis after bypass surgery. Second, the revascularization area posterior to the CS was significantly associated with the reduction, whereas that anterior to the CS was not. Third, a posterior revascularization area of <10.7% increased the risk of choroidal anastomosis persistence.

The reduction rate of choroidal anastomosis in our series seems comparable with that in the literature (62%–70%).[15,28,29] Our results are also in line with the seminal work by Yamamoto et al,[15] one of the first to identify the factors associated with this change. They revealed that a revascularized area exceeding two-thirds of the MCA territory was associated with reduction of choroidal anastomosis. Our study might add novel information to theirs because the posterior extent of revascularization might be an underlying mechanism for the reduction.

Our results are highly consistent with those of recent studies focusing on the posterior half of the brain in hemorrhagic Moyamoya disease. The prespecified analysis of the Japan Adult Moyamoya Trial has revealed that patients with posterior hemorrhage, who are at higher risk of rebleeding, accrue greater benefit in preventing rebleeding from an operation.[30] The angiographic analysis of the trial has also revealed that choroidal anastomosis, which is most likely to be distributed posteriorly, is responsible for posterior hemorrhage.[1] PCA involvement is another significant factor associated with posterior hemorrhage.[1] All these findings, together with ours, suggest the significance of the revascularization site for preventing hemorrhage.

The periventricular vascular morphology typical of Moyamoya disease might explain the reduction of choroidal anastomosis depending on the revascularization site. Periventricular anastomosis is a term defining anastomotic collaterals between the perforating or choroidal artery and the medullary artery in the periventricular area.[2,3] It is classified into 3 types: lenticulostriate, thalamic, and choroidal anastomosis. Choroidal anastomosis outflows to the cortex posterior to the CS, whereas lenticulostriate anastomosis outflows anterior to the CS.[16] Because a revascularization overlapping the outflow is more likely to normalize the medullary artery flow and promote successful reduction of the anastomosis,[6,31] a larger revascularization area posterior to the CS might increase the probability of the reduction of choroidal anastomosis.

We identified, however, some hemispheres exhibiting reduction of choroidal anastomosis despite relatively small posterior revascularization. This finding might be explained by 2 possible reasons: First, some of the choroidal anastomoses might outflow exactly into the CS[16]; in such cases, the revascularization could overlap the outflow even with a limited revascularization area posterior to the CS. Second, augmentation of CBF in the cortex posterior to the CS, which could not be assessed with angiography alone, might account for the reduction of choroidal anastomosis.

Our results do not conflict with various excellent modifications of direct bypass,[32-39] most of which target the frontal lobe. Targeting the frontal lobe, including the motor cortex, seems a reasonable approach for ischemic Moyamoya disease. However, our results suggest that hemorrhagic Moyamoya disease requires a different strategy in terms of the revascularization site, especially for those with both choroidal anastomosis and mild hemodynamic failure. According to a recent study, a substantial number of patients with hemorrhagic Moyamoya disease have only mild hemodynamic failure.[26] Given that the overall width of revascularization depends on the preoperative hemodynamic status as suggested in our Online Supplemental Data, bypass directly targeting the outflow might be reasonable for those with mild hemodynamic failure.[31]

Our results suggest that severe hemodynamic compromise in the posterior half of the MCA territory, which might partly lead to a larger posterior revascularization area, is not a direct factor for reducing choroidal anastomosis. This finding is supported by the previous report, in which development of choroidal anastomosis showed no relation to the hemodynamic stage.[26] Reduction of choroidal anastomosis might depend more directly on the surgical procedure, including selection of the recipient artery, than on the hemodynamic status in the parietal lobe. This speculation, however, should be validated in further studies.

The present study has several limitations. First, the study excluded 8 hemispheres in which postoperative angiography was not performed. The possible selection bias caused by this exclusion seems minimal, however, because exclusions should occur randomly according to the reasons for not performing postoperative angiography. Second, the present results were obtained at a single institution, and this might limit generalization, especially to indirect bypass. Third, it remains unknown whether reduction of periventricular anastomosis, including choroidal anastomosis, is associated with subsequent bleeding. Answering this question might require long-term follow-up, considering late-onset hemorrhage shown in Fig 6. Further prospective studies are required.

CONCLUSIONS

The present results support our hypothesis that a larger angiographic extent of revascularization posterior to the CS is associated with postoperative reduction of choroidal anastomosis. A small revascularization in this area might result in persistence of choroidal anastomosis regardless of the revascularization extent anterior to the CS. The present study might facilitate optimization of a direct bypass strategy focusing on hemorrhage prevention through selection of the revascularization site. Further studies are required.

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Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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