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Factors related to improvement of cerebrovascular reserve after superficial temporal artery to middle cerebral artery anastomosis for patients with atherosclerotic steno-occlusive disease

Munehiro Otsuka[1] · Yuichiro Kikkawa[1] · Tomoya Kamide[1] · Kaima Suzuki[1] · Aoto Shibata[1] · Toshiki Ikeda[1] · Hiroki Kurita[1]

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Abstract

Background This study aimed to investigate factors related to improvement of hemodynamics and evaluated the usefulness of intraoperative Doppler for predicting postoperative hemodynamics in patients with cerebrovascular atherosclerotic steno-occlusive disease (CASD) of the internal carotid artery (ICA) or middle cerebral artery (MCA) who were treated with extracranial–intracranial (EC–IC) bypass surgery.

Method Forty-eight patients with CASD of the ICA or MCA who were treated by superficial temporal artery to middle cerebral artery bypass with a follow-up longer than 12 months were enrolled. Repeated transient ischemic attack or completed ischemic stroke was observed under optimal medical therapy in all patients. Intraoperative blood flow velocity of the MCA was evaluated by a Doppler flowmeter. Cerebral blood flow and cerebrovascular reserve (CVR) were evaluated using N-isopropyl-[^{123}I] p-iodoamphetamine (IMP) single photon emission computed tomography (SPECT) preoperatively and 3 months after surgery. Imaging and clinical data were retrospectively reviewed.

Results CVR was significantly increased postoperatively ($p = 0.03$). One year after the operation, two (4.2%) patients developed cerebral infarction. The change in MCA flow velocity just after anastomosis compared with pre-anastomosis proximal and distal of the anastomosis site was a median of 3.0 and 2.6 times, respectively. However, there was no significant association between changes in intraoperative MCA flow velocity and postoperative CVR. Multivariate analysis showed that the presence of a lower estimated glomerular filtration rate (eGFR) was an independent risk factor for a decrease in CVR ($p = 0.036$).

Conclusions A higher eGFR might have prognostic value for improvement in CVR after EC–IC bypass surgery in patients with CASD and misery perfusion.

Keywords Atherosclerotic steno-occlusive disease · Cerebrovascular reserve · Extracranial–intracranial bypass · Glomerular filtration rate

Introduction

Symptomatic intracranial arterial stenosis has one of the highest rates of recurrent stroke, with an annual rate of 12.2–25%, despite intensive medical therapy [6]. Direct cerebral revascularizations involving superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis have been performed under rigorous selection of patients for preventing recurrent ischemic stroke [20]. Bypass surgery in patients with severe hemodynamic insufficiency was reported to have a 54% reduction in the risk of stroke compared with the natural history [8].

Several reports have shown that cerebrovascular reserve (CVR) improves after extracranial–intracranial (EC–IC) bypass surgery in patients with reduced CVR [13]. Some studies on cerebral blood flow (CBF) in EC–IC bypass surgery showed that EC–IC bypass surgery restored CVR [3, 27]. However, little is known about which clinical factors affect improvement of CVR after EC–IC bypass.

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✉ Yuichiro Kikkawa
ykikkawa@saitama-med.ac.jp

[1] Department of Cerebrovascular Surgery, Saitama Medical University International Medical Center, 1397-1 Yamane, Hidaka, Saitama 350-1298, Japan

Intraoperative measurement of arterial blood flow using a Doppler flowmeter is useful for confirming bypass patency just after anastomosis during surgery. However, there are no intraoperative estimating devices to predict postoperative changes in CBF and CVR. If intraoperative changes in arterial blood flow reflect postoperative hemodynamic changes, intraoperative measurement using a Doppler flowmeter has the potential to provide important information about postoperative hemodynamics, such as hyperperfusion.

This study aimed to evaluate factors affecting improvement in CVR after surgery. Moreover, we evaluated intraoperative changes in blood flow velocity of the middle cerebral artery (MCA) using a Doppler flowmeter. We also assessed the associations between an increase in intraoperative MCA velocity and postoperative changes in regional CBF (rCBF) and CVR in patients who underwent STA-MCA anastomosis for cerebrovascular atherosclerotic steno-occlusive disease (CASD).

Methods

Patients

Medical chart of 128 consecutive patients who underwent EC–IC bypass at Saitama Medical University International Medical Center between April 2012 and December 2016 were retrospectively reviewed. Among them, 62 EC–IC bypass surgeries were performed for patients with CASD, while 66 were performed for patients with moyamoya disease. Among the 62 patients with CASD, those with bilateral steno-occlusive lesions and those who were lost to radiological follow-up were excluded. Finally, 48 patients who underwent EC–IC bypass for CASD were enrolled in the study. All of these patients underwent STA-MCA single-bypass procedures on one side approximately 3 months after the last ischemic event. All study protocols were approved by the Institutional Review Board at Saitama Medical University International Medical Center (IRB No. 18-079).

Hypertension was defined as blood pressure higher than 140/90 mmHg or current use of anti-hypertensive agents. Diabetes mellitus was defined as a hemoglobin A1C value of higher than 6.5% or current use of anti-glycemic medications. Patients with serum low-density lipoprotein cholesterol levels higher than 140 mg/dL or current use of lipid-lowering agents were considered as having hyperlipidemia. Current smoking was defined as having a smoking habit on a daily basis within 3 months before admission. Other cardiac and vascular disorders were carefully investigated in our hospital on the basis of a past history, physical examinations, chest X-ray, electrocardiography, and ambulatory 24-h electrocardiography.

Single-photon emission computed tomography and surgical indications

Indications for the use of STA-MCA anastomosis for cerebral atherosclerotic disease in our study were decided on the basis of those detailed in the Japan Extracranial-Intracranial Bypass Trial (JET) protocol [15]. A preoperative CBF study was performed using N-isopropyl-[^{123}I] p-iodoamphetamine (IMP) single-photon emission computed tomography (SPECT) in all of the patients. The SPECT study was evaluated by autoradiography [11].

The CBF image set was quantified using autoradiography with 222 MBq of ^{123}I-IMP, which was administered intravenously at a constant rate over 1 min. SPECT data were acquired 2 min after the injection, and blood samples were taken from the antecubital or the radial artery 10 min after administration of ^{123}I-IMP. The SPECT system had a full-width, half-maximum resolution of 10.0 mm. This system had a two-headed gamma camera (Millennium MG; GE Healthcare, Hino, Japan) equipped with low-energy, general-purpose collimators, and a GEniE Xeleris processing computer (GE Healthcare). A paired CBF study with an acetazolamide challenge was conducted according to the JET study protocol. The three-dimensional stereotactic surface projection method provided quantitative information and three-dimensional displays of CBF at rest and after an acetazolamide challenge. This method also provided information regarding CVR and the severity of hemodynamic impairment. CVR was classified into three stages (stages 0–2) on the basis of CVR, which was calculated from rCBF values at rest and during the acetazolamide challenge [24]. CVR was calculated as follows: ([CBF under acetazolamide–rCBF]/rCBF) × 100 (%). The severity of hemodynamic brain ischemia was classified into the following three stages: stage 0 (resting CBF < 15 mL/100 g/min and CVR > 30%), stage 1 (resting rCBF > 15 and < 34 mL/100 g/min [80% or normal rCBF] and CVR > 10% and < 30%), and stage 2 (resting rCBF > 15 and < 34 mL/100 g/min and CVR > − 30% and < 10%) [14, 18]. We investigated CBF at rest, CBF with an acetazolamide challenge test, and acetazolamide reactivity at the normal and affected sides of the cerebral hemisphere. Postoperative improvement of CVR was defined as postoperative CVR/preoperative CVR > 1 in the affected MCA territory.

Surgical treatment and MCA flow measurement

All of the patients were treated with single anti-platelet therapy before surgery, which was continued during the perioperative period. We performed single bypass anastomosis. One branch of the STA was anastomosed to the M4 portion of the MCA in an end-to-side fashion with 10–0 PROLENE thread (Ethicon Inc., Somerville, NJ, USA). The recipient M4 was decided on the basis of preoperative SPECT evaluation and the intraoperative finding of the M4 caliber compared with the donor. A Doppler flowmeter (DVM-4500; Nihon Kohden, Tokyo, Japan) was used to measure blood flow velocity of M4 at the proximal and distal sides of anastomosis just before and after performing anastomosis. We measured the vessel diameter before Doppler evaluation to quantitatively evaluate flow velocity as accurately as possible. The probe was then applied to the vessel with an insonation angle of 30 to 60° to confirm the flow spectrum with a typical "systolic window." For evaluation at post-anastomosis, the measurement site was 2 to 5 mm distal or proximal to the anastomosis site to avoid detecting turbulent flow. The ratio of an increase in MCA blood flow velocity between the distal and proximal MCA after anastomosis (Δdistal MCA/Δproximal MCA) was calculated using the absolute value of flow velocity.

Statistical analysis

The association between the rate of increase in MCA blood flow velocity (%) and the resting CBF ratio of the stenotic/normal side or the CVR ratio (%) was calculated using linear regression models. Pearson's chi-square test, Wilcoxon signed-rank test, Mann–Whitney *U* test, and the unpaired Student's *t* test were used to determine statistical differences between the two groups. A value of $p < 0.05$ was considered to be statistically significant. All statistical analyses were performed using SPSS (Version 24.0; Armonk, NY, USA).

Table 1 Characteristics of 48 patients with STA-MCA bypass

Factors	
Age (yr), mean ± SD	59.7 ± 11
Male gender, *n* (%)	31 (65)
Onset	
TIA, *n* (%)	15 (31)
Ischemic stroke, *n* (%)	33 (69)
Diabetes, *n* (%)	19 (40)
Hypertension, *n* (%)	31 (65)
Dyslipidemia, *n* (%)	17 (35)
Renal dysfunction, *n* (%)	12 (25)
Obesity, *n* (%)	15 (31)
Smoking, *n* (%)	26 (54)
Coronary disease, *n* (%)	6 (13)
SAPT, *n* (%)	42 (88)
DAPT, *n* (%)	5 (10)
Postoperative hyperperfusion, *n* (%)	7 (17)
Bypass patency at POD1, *n* (%)	48 (100)
Bypass patency at 3 months, *n* (%)	42 (88)

TIA transient ischemic attack, *SAPT* single anti-platelet therapy, *DAPT* double anti-platelet therapy, *POD* postoperative day

Results

Of the 48 patients with CASD, impaired CVR corresponding to stage 2 in the acetazolamide challenge, as shown by ^{123}I-IMP-SPECT, was detected in all patients preoperatively. The demographics of the enrolled patients are shown in Table 1. Thirty-three (69%) patients presented with completed ischemic stroke, while 15 (31%) patients presented with transient ischemic attack. The mean age was 59.7 years (range: 36–79 years) and 31 (65%) patients were men. Preoperatively, the modified Rankin scale (mRS) score was 0–1 in 96% of the patients (Table 2). Follow-up three-dimensional computed tomography angiography was performed at day 1 after surgery in all patients, and bypass patency was confirmed in all of the patients. Follow-up magnetic resonance angiography 3 months after surgery showed a good bypass patency in 42 (88%) patients, whereas in three (6%) patients, a reduction in signal was observed in the donor artery. In three (6%) patients, follow-up magnetic resonance angiography at 3 months was not performed.

Table 3 shows the results of the SPECT study and intraoperative evaluation of MCA blood flow velocity using a Doppler flowmeter. There were no significant changes in CBF at rest between before and after surgery. However, CVR 3 months after surgery was significantly increased compared with before surgery ($p = 0.03$). Intraoperative MCA blood flow velocity was increased by 304.8% ± 37.4% at the proximal anastomosis site and by 259.4% ± 32.9% at the distal site compared with before anastomosis. Although MCA blood flow velocity was increased immediately after anastomosis in all patients, there was no significant association between intraoperative changes in MCA flow velocity just after anastomosis and changes in CVR at 3 months after surgery.

Postoperative hyperperfusion syndrome, including aphasia, perioral or upper limb sensory disturbance, and seizures, was observed in seven of 48 (15%) patients. However, no patients developed intracranial hemorrhage and all of the patients recovered with induction of hypotension therapy and medication of anti-convulsants. One year after the operation, two (4.2%) patients developed cerebral infarction. The

Table 2 Pre- and postoperative functional status

	Preoperative mRS	Postoperative mRS
0	40	40
1	6	5
2	1	3
3	1	0
4	0	0
5	0	0

mRS modified Rankin scale

Table 3 Changes in the SPECT study and intraoperative Doppler study

	Mean ± SD	*p* value
SPECT study		
Preoperative CBF, ml/100 g/min	29.71 ± 5.62	*p* = 0.237
Postoperative CBF, ml/100 g/min	30.43 ± 5.25	
Preoperative CVR, %	7.96 ± 3.98	*p* = 0.03
Postoperative CVR, %	18.98 ± 3.31	
Doppler study (% increase of MCA velocity after anastomosis)		
Proximal of anastomosis site, %	304.8 ± 37.4	*p* = 0.280
Distal of anastomosis site, %	259.4 ± 32.9	

CBF cerebral blood flow, *CVR*, cerebrovascular reserve, *MCA* middle cerebral artery

postoperative modified Rankin scale (mRS) score at 1 year after surgery was 0–1 in 94% of the patients.

Table 4 shows univariate analysis of clinical factors that affected improvement in CVR. CVR tend to improve in male patients. The ratio of an increase in MCA blood flow velocity between the distal and proximal MCA after anastomosis (Δdistal MCA/Δproximal MCA) was significantly higher in patients without improvement in CVR than in those with improvement in CVR ($p = 0.043$). The estimated glomerular filtration rate (eGFR) was significantly different between the two groups ($p = 0.017$).

A favorable outcome (mRS: 0–1) was achieved in 28 (93%) patients with improvement of CVR and in 12 (100%) patients without improvement of CVR (Table 4). There was no significant difference in the rate of patients who achieved a favorable outcome between these two groups ($p = 0.51$). Postoperatively, improvement of mRS scores was observed in one (3%) patient with improvement of CVR and in one (3%) patient without improvement of CVR (Table 4). Furthermore, worsening of mRS scores was observed in two (7%) patients with improvement of CVR and in no patients without improvement of CVR (Table 4). There were no significant differences in improvement and worsening of mRS scores between the two groups ($p = 0.50$ and $p = 0.51$, respectively). Postoperative infarction occurred in only two patients with improvement of CVR (Table 4). However, there was no significant difference in the occurrence rate of postoperative infarction between the two groups ($p = 0.51$). The occurrence of hyperperfusion syndrome was observed in five (17%) patients with improvement of CVR and in two (17%) patients without improvement of CVR (Table 4). There was no significant difference in the occurrence rate of hyperperfusion syndrome between the two groups ($p = 0.44$).

Multivariate analysis was performed using three factors (Table 5) with a *p* value < 0.1 on univariate analysis. A higher eGFR ($p = 0.036$; odds ratio, 1.057; 95% confidence interval, 1.004–1.113) was significantly associated with good recovery of CVR. There was no significant difference in eGFR values between patients with a favorable (mRS: 0–1; 68.9 ± 19.3) and unfavorable (mRS: 2–3; 90.4 ± 31.6) outcome ($p = 0.08$). Five patients had postoperative complications, including two patients with postoperative cerebral infarction and three patients with postoperative bypass occlusion. There was no significant difference in eGFR values between patients with (77.2 ± 15.9 mL/min/1.73 m2) and those without complications (69.4 ± 20.6 mL/min/1.73 m2, $p = 0.43$).

Table 4 Univariate analysis of factors related to improvement in CVR (six patients were excluded without bypass patency or follow-up imaging at 3 months)

	CVR improvement		*p* value
	Yes	No	
Male, *n* (%)	21 (70)	5 (41)	0.088
Age, year ± SD	61.3 ± 11.4	55.4 ± 12.3	0.168
Onset (symptomatic CI), *n* (%)	19 (63)	10 (83)	0.187
Hypertension, *n* (%)	20 (67)	8 (67)	0.647
Diabetes mellitus, *n* (%)	10 (33)	6 (50)	0.255
Hyperlipidemia, *n* (%)	10 (33)	5 (42)	0.434
eGFR, 100 ml/min/1.73m^2 ± SD	73.0 ± 17.3	57.0 ± 21.9	0.017
Hyperperfusion syndrome, *n* (%)	5 (17)	2 (17)	0.439
Δproximal MCA, % ± SD	300.8 ± 46.0	267.1 ± 46.8	0.676
Δdistal MCA, % ± SD	297.0 ± 45.0	232.2 ± 72.6	0.393
Δdistal/Δproximal MCA, % ± SD	1.61 ± 2.14	0.70 ± 0.32	0.043
Postoperative infarction, *n* (%)	2 (7)	0 (0)	0.505
Preoperative mRS 0–1	29 (97)	12 (100)	0.714
Postoperative mRS 0–1	28 (93)	12 (100)	0.505
Improvement of mRS, *n* (%)	1 (3)	1 (8)	0.495
Worsening of mRS, *n* (%)	2 (7)	0 (0)	0.505

CVR cerebrovascular reserve, *MCA* middle cerebral artery, *eGFR* estimated glomerular filtration rate, *proximal MCA* proximal MCA Doppler flow velocity, *distal MCA* distal MCA Doppler flow velocity, *Δdistal/Δproximal MCA* change in distal/change in proximal Doppler flow velocity

Table 5 Multivariate analysis of factors related to improvement in CVR

			EXP(B) 95%CI	
	p value	Exp(B)	Lower limit	Upper limit
Male gender	0.157	3.582	0.612	20.949
Δdis/Δpro MCA	0.256	3.466	0.405	29.635
eGFR	0.036	1.057	1.004	1.113

CVR cerebrovascular reserve, *MCA* middle cerebral artery, *eGFR* estimated glomerular filtration rate

Discussion

The present study showed that STA-MCA bypass was effective for improving CVR in patients with hemodynamic insufficiency caused by CASD. Additionally, a preoperative lower eGFR was associated with worse improvement of CVR at 3 months after surgery. Furthermore, the amount of increase in intraoperative MCA flow velocity was not associated with the level of improvement in CVR 3 months after surgery.

In our study, CVR was significantly improved 3 months after STA-MCA bypass, with a 4.6% annual rate of cerebral infarction. With regard to inclusion criteria for EC–IC bypass, only patients in whom transient ischemic attack or ischemic stroke attack was observed during maximal medical treatment were included in our series. Additionally, all of the included patients had a severely impaired hemodynamic state with stage 2 classification by the JET study protocol using ^{123}I-IMP-SPECT with an acetazolamide challenge test. Many studies that showed the effectiveness of EC–IC bypass for preventing recurrent stroke emphasized the importance of selecting patients for EC–IC bypass. In our study, strict selection criteria enabled observation of improvement in CVR and achievement of a low risk of recurrent stroke. However, in the current study, resting CBF remained unchanged after surgery. These results are consistent with findings from previous studies. Several studies reported that resting CBF was unchanged, while CVR was significantly improved after EC–IC bypass surgery in patients with severe hemodynamic insufficiency [5, 13, 22, 27]. Vorstrup et al. speculated that resting CBF will increase after EC–IC bypass only in patients with severely decreased CBF below the lower limit of autoregulation [31]. Ishikawa et al. also reported that patients with reduced resting CBF are at greater risk for further ischemic stroke, even though resting CBF was unchanged after EC–IC bypass surgery.

CVR is thought to be a marker of cerebral hemodynamic integrity. The underlying physiological process of CVR is cerebral autoregulation, which is defined in terms of changes in vascular resistance or arteriolar caliber in response to fluctuations in perfusion pressure [25]. Therefore, small arteries and arterioles play important roles in determining cerebral autoregulation. Consequently, atherosclerotic changes in small vessels, as well as large artery atherosclerotic steno-occlusion, appear to affect improvement of CVR. Postmortem studies have shown that large artery atherosclerosis commonly coexists with small vessel disease. This could be because small vessel disease shares common risk factors with large artery atherosclerosis in development of pathological processes [4]. Therefore, many patients in our study might have had small vessel disease besides large artery atherosclerosis. Impairment of CVR has been clinically demonstrated in small vessel disease. Transcranial Doppler studies have shown that cerebral autoregulation is globally impaired in patients with small vessel disease [9, 12, 17]. However, there have been few reports describing the degree of improvement in CVR after revascularization in patients with small vessel disease. Ishikawa et al. reported that, in steno-occlusive disease with reduced CVR, EC–IC bypass surgery was successful in restoring CVR, even in patients with advanced arteriosclerosis in small cerebral arteries [13]. We did not evaluate small vessel disease preoperatively. However, our finding that a lower eGFR was an independent risk factor for a decrease in CVR appears to be consistent with recent evidence demonstrating that worse kidney function is associated with cerebral small vessel disease [1]. A reduced eGFR was also reported to be associated with an increased risk of cerebral small vessel disease [30]. Further studies might be required to clarify the relationship between atherosclerotic changes in small vessels and the degree of improvement in CVR.

Preoperative eGFR was associated with an improvement in CVR at 3 months after surgery in our study. Renal dysfunction is closely related to cardiovascular disorders [26]. Vascular endothelial dysfunction is a common cause of renal dysfunction and contributes to the pathogenesis of hypertension, coronary syndrome, and chronic kidney disease, which result from atherosclerosis. [7]. Endothelium-dependent vasodilation is associated with the GFR [23, 28]. Therefore, a decrease of GFR could be attributed to endothelial dysfunction. Atherosclerosis is a systemic disease that affects arteries at multiple sites simultaneously. Therefore, endothelial dysfunction may occur not only in renal arteries, but also in cerebral arteries. Endothelial dysfunction also plays an important role in a decrease in cerebrovascular hemodynamics [29]. Hecht et al. reported that improvement of endothelial function by endothelial progenitor cell treatment restored impairment of CVR in a rat model of chronic cerebral hypoperfusion [10]. The abovementioned findings suggest that postoperative improvement in CVR might be impaired in patients with a decreased GFR caused by severe endothelial dysfunction. Accordingly, medical treatment for atherosclerosis, such as statins, which restore endothelial function, might affect better recovery of CVR after bypass surgery. However, studies with a large sample size are warranted to validate this possibility.

Intraoperative measurement of arterial blood flow velocity using a Doppler flowmeter is not useful for predicting postoperative improvement in CVR, but is useful for confirming bypass patency during surgery. Several methods, such as Doppler flowmetry, indocyanine green videoangiography, and thermography, are applied for intraoperative measurement of anastomotic flow [2, 16, 21, 32]. These methods are useful for detecting bypass patency, changes in CBF, or postoperative hyperperfusion [2, 16, 21, 32]. In the current study, we evaluated whether there are associations of blood flow with intraoperative changes and long-term changes. We found that the flow statement immediately after anastomosis, such as which direction had a strong blood flow between the distal and proximal sides, did not affect long-term CVR postoperatively. Our observation that Δdistal MCA/Δproximal MCA flow velocity was significantly higher in patients with improvement in CVR suggests that strong bypass flow is required in patients with severely impaired CVR. The ratio of Δdistal MCA/Δproximal flow velocity is elevated when flow velocity at the distal site increases much higher than that in the proximal site after opening the bypass. An important factor for determining whether blood flow via the bypass is well perfused is metabolic demand of the perfusion area. The bypass perfusion area is mainly distal to the anastomosis site. Therefore, if cerebral metabolic demand is large, blood flow at the distal site may greatly increase. Therefore, a higher ratio of Δdistal MCA/Δproximal flow velocity might be caused by a higher metabolic demand of cerebral ischemia. When CVR is severely impaired, EC–IC bypass significantly improves CVR after surgery [13]. Therefore, unsurprisingly, Δdistal MCA/Δproximal MCA flow velocity was significantly higher in patients with improvement in CVR than in those without improvement in our study. However, there is a time lag between the Doppler flowmeter and postoperative SPECT. Therefore, the results from a Doppler flowmeter might not directly represent postoperative improvement in CVR at 3 months after surgery. This is because postoperative improvement in CVR may result from not only bypass flow, but also newly established collateral vessels via leptomeningeal anastomosis [19]. Although the underlying mechanism remains unclear, results from our study suggest that a higher ratio of Δdistal MCA/Δproximal flow velocity may be a predictor of improvement in CVR after bypass.

This study has several limitations. First, the main limitations of this study are its retrospective design and single center-based findings. Therefore, the sample size was too small to determine a definitive cutoff value for the eGFR, and inherent limitations leading to potential ascertainment bias could not be precluded. Future prospective studies including large populations are required to evaluate other factors that are difficult to be assessed retrospectively. Second, positron emission tomography was originally used to evaluate preoperative cerebral metabolism for determining the indication of EC–IC bypass. However, in this study, we used SPECT because positron emission tomography is not widely available in Japan and hemodynamic evaluation of the JET study was based on SPECT findings.

Conclusions

This study shows that STA-MCA bypass is effective for improving CVR with a relatively low recurrence rate of ischemic stroke. Additionally, a higher eGFR value is related to improving CVR in patients with misery perfusion caused by CASD, suggesting that the eGFR may be a good prognostic value for estimating postoperative improvement of CVR after EC–IC bypass. Selecting patients with low CBF and CVR based on a SPECT study and a high eGFR value might be important for performing effective EC–IC bypass. Furthermore, if a definite cutoff value of eGFR is found in further studies with a larger sample size, patients with eGFR values below this cutoff value should be included after careful consideration for candidates for EC–IC bypass.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. This study was approved by the Institutional Review Board at our institutes (IRB No. 18-079).

Informed consent For this type of (i.e., retrospective) study, our institutional review board decided that formal consent was not required from each patient.

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Comments There is evidence regarding the preventive effect of bypass surgery for atherosclerotic lesions of intracranial arteries in Japan. The Japanese authors' retrospective analysis in 48 patients with atherosclerotic steno-occlusive lesions of internal carotid artery or middle cerebral artery (MCA) revealed that improvement of cerebrovascular reserve (CVR) at 3 months after superficial temporal artery-MCA bypass depended on estimated glomerular filtration rate (eGFR). They speculated that endothelial dysfunction was one of possible causes to prevent postoperative CVR from increasing. This indicates that eGFR can be a good indicator of CVR improvement after bypass surgery, and also, that preoperative treatment for renal function may enhance the efficacy for bypass surgery. We reaffirm the significance of collaboration between medical and surgical treatment in patients with atherosclerotic steno-occlusive lesions of intracranial arteries because they are involved in generalized atherosclerosis. We hope that this paper will contribute to further improvement of surgical results of bypass for atherosclerotic lesions.

Tomohito Hishikawa
Kenji Sugiu
Okayama, Japan