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ORIGINAL ARTICLE - VASCULAR NEUROSURGERY - OTHER

# Angiographic and clinical outcomes of non-patent anastomosis after bypass surgery in adult moyamoya disease

Seung Hwan Kim[1,2] · Hyungon Lee[2] · Minwook Yoo[2] · Seongjin Jin[3] · Sungjoon Lee[2] · Byeong Sam Choi[2] · Hae Yu Kim[2] · Sung-Chul Jin[2]

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## Abstract
**Background** The clinical and radiologic outcomes of symptomatic adult moyamoya disease (MMD) patients who have an occluded anastomosis immediately after bypass surgery are poorly studied. The clinical and angiographic outcomes of non-patent anastomosis in symptomatic adult MMD patients were retrospectively reviewed.
**Methods** From August 2011 to November 2016, 31 revascularization surgeries, consisting of direct and indirect bypass, were performed on 29 adult MMD patients. Primary outcomes were evaluated based on the frequency of transient ischaemic attack (TIA) incidence and the recurrence of cerebral infarction and were assessed as improvement or worsening.
**Results** Among 31 cases, computed tomography angiography (CTA) on the first day after surgery showed patent anastomosis in 20 hemispheres and non-patent anastomosis in 11 hemispheres. Follow-up conventional angiographies showed spontaneous recanalization of non-patent anastomosis in all occlusion cases. The incidence of TIA decreased in both the non-patent and the patent groups. Two newly developed cerebral infarctions were observed, which occurred in the patent group. Patients in the non-patent group also showed clinical improvement after surgery ($p = 0.04$), and no significant relationship was found between immediate postoperative patency and the primary outcome ($p = 0.53$).
**Conclusions** In our series, regardless of patency immediately after bypass surgery, delayed recanalization and clinical improvement can be expected after bypass surgery for adult MMD.

**Keywords** Moyamoya disease · Bypass surgery · Recanalization · Adult

## Introduction

Moyamoya disease (MMD) is a chronic, progressive disease characterized by stenosis or occlusion of the bilateral distal internal carotid arteries (ICA), leading to recurrent stroke [6, 9].

Seung Hwan Kim and Hyungon Lee contributed equally to this article as first authors.

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✉ Sung-Chul Jin
kusmaljin@gmail.com

1 Draft Physical Department, Changwon Military Manpower Administration, Changwon, Republic of Korea

2 Department of Neurosurgery, Inje University, Haeundae Paik Hospital, 875, Haeun-daero, Haeundae-gu, Busan 612-896, Republic of Korea

3 Department of Neurosurgery, Gamma Knife Surgery, Inje University, Haeundae Paik Hospital, Busan, Republic of Korea

Revascularization surgery for symptomatic MMD is considered the treatment of choice for preventing recurrent stroke [6, 9]. Numerous studies have examined the outcomes of revascularization status after superficial temporal artery (STA)-middle cerebral artery (MCA) bypass surgery [1, 5, 11, 13]. However, no research has been performed to monitor radiological and clinical outcomes when the anastomotic site is occluded immediately after STA-MCA bypass surgery in adult MMD. We performed a retrospective investigation of the clinical and angiographic outcomes of an immediately occluded anastomosis after bypass surgery in symptomatic adult MMD patients.

## Methods and materials

### Patient selection

From August 2011 to November 2016, 29 MMD patients received 31 revascularization surgeries at our hospital.

Medical data were collected and reviewed retrospectively with the approval of the institutional review board. The inclusion criteria were as follows: (1) patients aged ≥ 18 years treated by combined (combination of direct and indirect) revascularization surgery; (2) compatibility with the diagnostic criteria for MMD; (3) symptomatic patients with MMD; and (4) significant reduction of basal perfusion and reservoir capacity by brain single-photon emission computed tomography (SPECT). The baseline characteristics are summarized in Table 1. There were 10 male and 19 female patients, and the mean age was 46.4 years (range, 21–73 years). The initial symptoms were transient ischaemic attack (TIA) in 18 cases, cerebral infarction in 8 cases, and intracerebral haemorrhage in 5 cases. The Suzuki grades of the operation site were grade 2 in 3 cases, grade 3 in 15 cases, and grade 4 in 13 cases.

### Surgical procedures

In our hospital, combined revascularization surgery consisting of direct (anastomosis between the STA and cortical branch of the MCA) and indirect (encephalodurogaleosynangiosis) surgery is performed. After harvesting the STA with the surrounding galea from the scalp, craniotomy including Charter's point is performed [6]. The cortical branches of the MCA are recipient vessels, excluding the arteries to the eloquent area. The donor artery is fish mouthed, and the anastomosis is completed in an end-to-side manner. After anastomosis, the galea flap is sutured with incised dura margins to cover the brain [6]. After anastomosis, blood flow through the bypass pedicle is examined using Doppler ultrasound. The blood flow of the bypass is assessed several times using Doppler ultrasound until the skin is closed. Diagnostic tools such as intraoperative angiography, indocyanine green (ICG) angiography, or a Charbel flow probe that are generally used as quantitative tools of Doppler ultrasound were not available in our hospital during the study period. Brain computed tomography (CT) is performed to detect postoperative haemorrhaging immediately after surgery. On the first day after surgery, all patients underwent brain computed tomography angiography (CTA) to evaluate the patency of anastomosis and postoperative haemorrhage. Patients without postoperative haemorrhage began taking aspirin (100 mg/day) to prevent thromboembolism of the anastomosis site. Cilostazol (200 mg/day) was empirically added to aspirin when CTA showed no patency at the anastomosis site.

**Table 1** Baseline characteristics of 29 patients with moyamoya disease

| Variable | No. (%) |
|---|---|
| Hemispheres/patients | 31/29 |
| Age (mean) | 46.4 ± 13.3 (21~73) |
| Gender | |
| Female | 19 (66%) |
| Male | 10 (34%) |
| Location | |
| Rt. | 9 (29%) |
| Lt. | 22 (71%) |
| Preoperative Symptom | |
| TIA | 18 (58%) |
| Ischaemic stroke | 8 (26%) |
| Haemorrhage | 5 (16%) |
| Suzuki grade | |
| 2 | 3 (10%) |
| 3 | 15 (48%) |
| 4 | 13 (42%) |
| Recipient artery | |
| Pre-frontal artery | 1 (3%) |
| Pre-central artery | 1 (3%) |
| Ant. temporal artery | 8 (26%) |
| Middle temporal artery | 6 (19%) |
| Post. temporal artery | 3 (10%) |
| Angular artery | 12 (39%) |

*TIA*, transient ischaemic attack

### Evaluation of angiographic patency

Follow-up angiographies were performed with CTA or transfemoral cerebral angiography (TFCA) at 1–2 weeks and 6–15 months after surgery to evaluate the patency of the anastomosis. Based on the 1-day postoperative CTA results, patients who underwent bypass surgeries were divided into non-patent anastomosis and patent anastomosis groups.

### Evaluation of clinical outcomes

The patients were evaluated using the modified Rankin Scale (mRS) score before and following surgery. The mRS is an ordinal scale: 0 (no symptoms), 1 (no significant disability), 2 (slight disability), 3 (moderate disability), 4 (moderately severe disability), 5 (severe disability), and 6 (dead) [12]. Primary outcomes included the frequency of TIA incidence and the recurrence of cerebral infarction after bypass surgery. Primary outcomes were assessed as improvement or worsening. "Improvement" was defined as a reduction in TIA incidence or no recurrence of cerebral infarction, and "worsening" was defined as an increase in TIA incidence or newly developed cerebral infarction.

## Results

### Surgical complications

In all except one patient, blood flow through the bypass pedicle was adequate by Doppler ultrasound. In the one case of anastomosis failure, blood flow was not detected by Doppler ultrasound after anastomosis. We applied an intravenous, 3000-unit, heparin loading dose and used the milking method for the donor artery several times. We could not explore the suture sites of the anastomosis because we were concerned about failure of re-sutures of the anastomosis site due to the fragile conditions of the moyamoya vessels. The patient showed no patency of anastomosis on CTA at 1 day after bypass surgery or on TFCA at 2 weeks after bypass surgery. Additionally, the patient showed no neurological deterioration, such as cerebral infarction, after bypass surgery. Surgical site infection and intracerebral haematoma after surgery did not occur in any cases. Postoperative epidural haematoma occurred in one patient without clinical symptoms, and CTA 1 day after surgery showed good blood flow at the bypass site.

## Angiographic outcomes

Postoperative CTA showed a patent anastomosis in 20 hemispheres and a non-patent anastomosis in 11 hemispheres. Delayed recanalization was observed in all 11 non-patent cases, including one case of anastomosis failure. One case of anastomosis recanalization was observed at 1 week after bypass surgery, and ten cases of anastomosis recanalization were observed at more than 6 months after bypass surgery. In the patent group, delayed occlusion was not observed in follow-up angiographies. The recanalization time of each patient is shown in Table 2. Figure 1 shows a non-patent anastomosis immediately post-surgery and delayed recanalization at 1 week and 2 weeks after bypass surgery. Figure 2 shows a non-patent anastomosis immediately post-surgery and 2 weeks after bypass surgery and delayed recanalization at 38 months after bypass surgery.

## Clinical outcomes

The mean clinical follow-up duration was 47.7 months (range, 29–75 months). In all cases, regardless of patency, the mRS score remained the same or decreased in the period following surgery compared to before surgery. In the patent group, the mean mRS score before surgery was 1.25 (range, 1–3), and the mean mRS score in the period following bypass surgery was 0.6 (range, 0–2). In the non-patent group, the mean mRS score before surgery was 1.90 (range 1–5), and the mean mRS score in the period following bypass surgery was 1.18 (range 0–3). The Wilcoxon signed-rank test demonstrated that patients in both the patent and non-patent groups clinically improved after surgery ($p = 0.01$ for the patent group, $p = 0.04$ for the non-patent group). The clinical characteristics and changes in the mRS score of the non-patent group are shown in Table 2.

After surgery, all patients with TIA symptoms showed a decreased TIA incidence. Newly developed cerebral infarctions occurred in two patients of the patent group at 10 months and 13 months after surgery. Both patients underwent bypass surgery on the left side and experienced new infarction in the left MCA–posterior cerebral artery (PCA) border zone. One patient experienced right arm weakness, which has improved, while the other patient showed incomplete global aphasia, which has improved. Both patients had stopped their antiplatelet medication temporally for endoscopic gastroduodenoscopy, and this may be the cause of the new cerebral infarction.

Among 31 patients, 29 showed improvement, and 2 showed worsening. No patient in the non-patent group showed worsening, while 2 patients in the patent group showed worsening. Fisher's exact test demonstrated no significant relationship between immediate postoperative patency and the primary outcome ($p = 0.53$).

**Table 2** Clinical characteristics and outcomes of the non-patent group

| Patient | Gender/Age | Location | Presentation | mRS before OP | Suzuki grade | mRS during F/U | Clinical outcome | Recanalization time |
|---|---|---|---|---|---|---|---|---|
| 1 | F/32 | Rt. | Motor TIA | 1 | 4 | 0 | Improvement | 12 months |
| 2 | F/39 | Lt. | Haemorrhage | 1 | 4 | 1 | Improvement | 12 months |
| 3 | F/21 | Lt. | Motor TIA | 1 | 4 | 1 | Improvement | 6 months |
| 4 | F/53 | Lt. | Motor TIA | 1 | 3 | 1 | Improvement | 7 months |
| 5 | M/45 | Lt. | Infarction | 3 | 3 | 3 | Improvement | 8 months |
| 6 | F/58 | Lt. | Haemorrhage | 5 | 4 | 2 | Improvement | 15 months |
| 7 | F/52 | Rt. | Motor TIA | 1 | 4 | 0 | Improvement | 7 months |
| 8 | M/57 | Lt. | Verbal TIA | 1 | 4 | 1 | Improvement | 38 months |
| 9 | F/57 | Lt. | Haemorrhage | 5 | 4 | 3 | Improvement | 1 week |
| 10 | F/25 | Lt. | Motor TIA | 1 | 4 | 1 | Improvement | 8 months |
| 11 | F/28 | Lt. | Motor TIA | 1 | 4 | 0 | Improvement | 8 months |

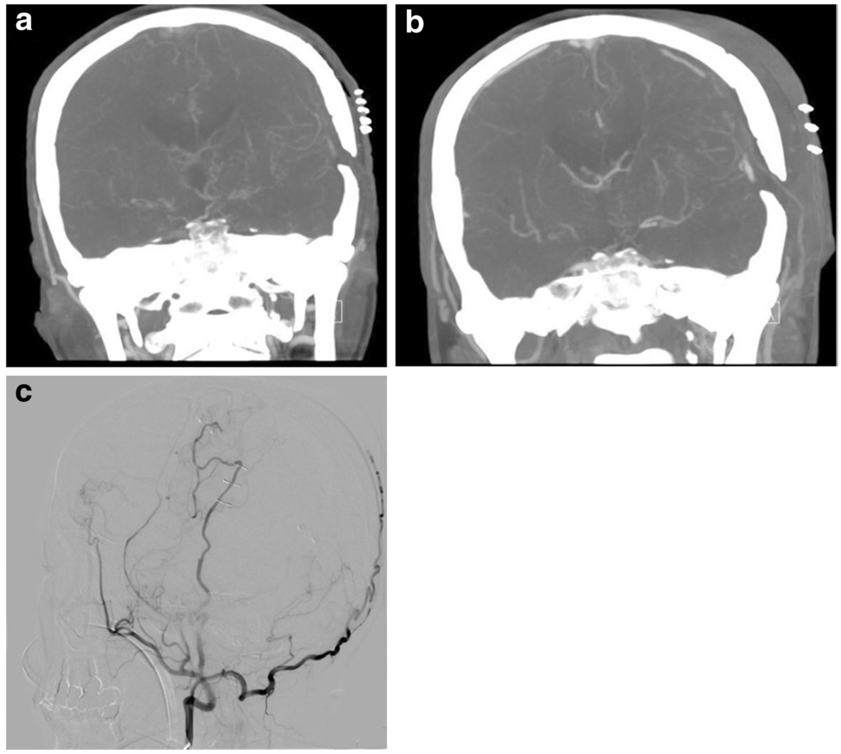


**Fig. 1** **a** Non-patent anastomosis immediately post-surgery. **b** Delayed recanalization at 1 week after bypass surgery. **c** Delayed recanalization at 2 weeks after bypass surgery

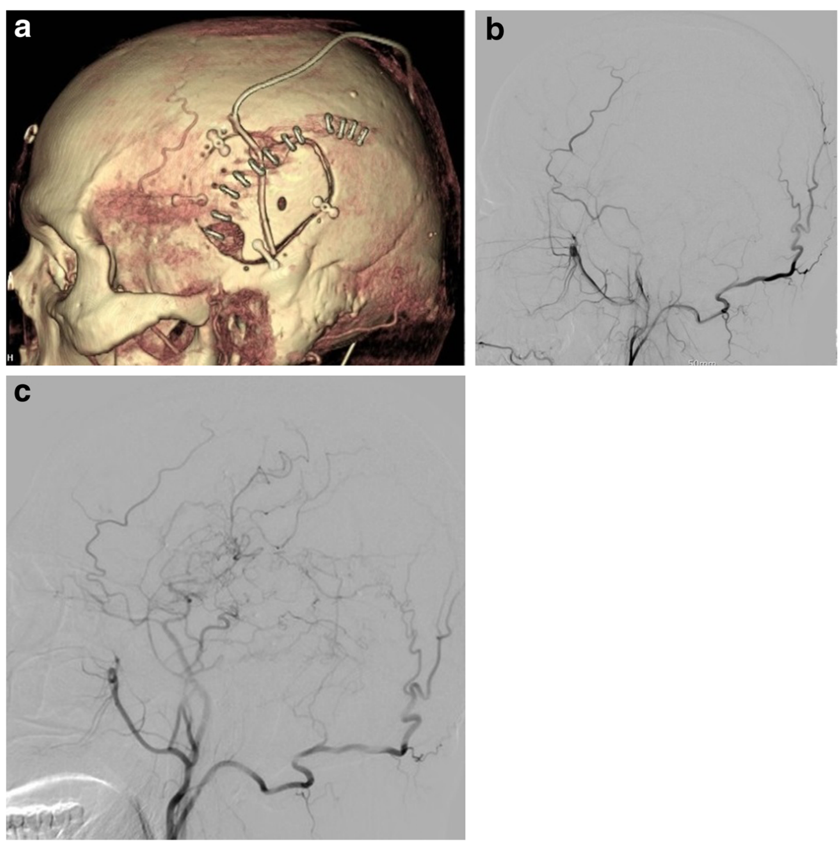


**Fig. 2** **a** Non-patent anastomosis immediately post-surgery. **b** Non-patent anastomosis at 2 weeks after bypass surgery. **c** Delayed recanalization at 38 months after bypass surgery

### Postoperative perfusion abnormalities

In our study, symptomatic postoperative perfusion abnormalities occurred in 4 patients. All four patients were in the patent group. One patient experienced a non-neurologic-specific symptom of dizziness, and the other three patients experienced neurologic symptoms such as aphasia or seizure. The onset time was 3 days to 3 weeks after bypass surgery. After symptoms developed, the patients were evaluated by perfusion CT to check for postoperative perfusion abnormalities. One patient showed postoperative hyperperfusion, and the other three patients showed postoperative hypoperfusion. All of the patients showed clinical improvement over time.

## Discussion

Early bypass failure after extracranial-intracranial arterial bypass is known to occur in 4–10% of cases [10]. The outcomes of a non-patent bypass vessel in adult MMD have not been studied previously. In this study, we presented our results of non-patent anastomosis immediately after bypass surgery. We observed 11 cases of early bypass failure. However, all of these patients showed delayed recanalization and clinical improvement. Therefore, early bypass failure does not always indicate clinical deterioration or permanent angiographic failure of bypass surgery in adult MMD patients.

In our study, 11 patients who underwent 31 surgeries (35%) showed non-patent anastomosis immediately post-surgery, which is a higher early bypass failure rate than that reported in the literature [4]. All bypass surgeries were performed by one surgeon in our hospital, and the experience of the surgeon can influence the success rate of anastomosis. Our series included all cases of early experience of bypass surgery in adult MMD disease. The condition of the patient's vessels, including the donor and recipient artery, can also be considered as a reason for anastomosis failure because the recipient vessel in MMD patients is more fragile and vulnerable to manipulation injury than that in patients with atherosclerotic disease. In particular, the Suzuki grade was high in the non-patent group. A Suzuki grade of 4 was observed in 9 cases in the non-patent group but only in 4 cases in the patent group. For patients with a Suzuki grade of 4, selection of the donor artery was impeded by the existing external carotid artery (ECA)-ICA collateral. Additionally, the recipient artery was nearly occluded in patients with a Suzuki grade of 4, which caused failure of anastomosis.

The present study has several limitations. First, the Doppler ultrasound results during bypass surgery did not reflect on the patency of the anastomosis site. Because this is not based on quantitative data, only qualitative data. Additionally, we did not have access to ICG angiography, intraoperative angiography, and a Charbel flow probe during the study period. Second, CTA was typically used to evaluate the patency of anastomosis at 1 day after bypass surgery, but the results were not exactly correlated with those of TFCA. However, recent CTA studies have demonstrated primary or alternative diagnostic modalities for TFCA in several fields of neurovascular diseases, including the patency of bypass surgery [7, 8]. Additionally, if no clinical symptomatic aggravation develops, TFCA can increase the risk of thromboembolic complication without a beneficial gain in confirming the diagnosis. Third, the number of cases was small, and the statistical significance of this study is not considered to be high. However, this study is important because MMD itself is rare, and long-term follow-up is not easy for patients with non-patent anastomosis immediately post-surgery. Randomized controlled trials can provide more significant results, but it is not possible or ethical for adult MMD patients receiving combined bypass surgery to be divided randomly into a patent anastomosis group and a non-patent anastomosis group. Fourth, the study design is retrospective, and a selection bias may exist. However, all patients underwent bypass surgery by one neurosurgeon, and all were followed up. Fifth, clinical outcomes were assessed based on the mRS, the frequency of TIA incidence, and the recurrence of cerebral infarction. Cognitive and behavioural conditions were not considered, but these are also important parameters; therefore, further research including these conditions is necessary.

Our study showed that delayed recanalization can be divided into two groups by image studies; one group was recanalized within 1 week after bypass surgery ($n = 1$), and the other group was recanalized more than 6 months after bypass surgery ($n = 10$). Our hypotheses regarding recanalization during the perioperative period (within 2 weeks after bypass surgery) in non-patent patients are as follows: First, bypass vessels can be occluded by a fresh thrombus that is mainly caused by platelet aggregation at the anastomotic site. Aspirin is considered the first choice of postoperative medication to inhibit platelet aggregation [3], and all patients were prescribed aspirin at 100 mg per day beginning 1 day after bypass surgery. A thrombogenic event might have occurred at the suture sites of the anastomosis, and the occluded anastomosis was subsequently recanalized, potentially due to aspirin therapy or natural thrombolytic activity.

Second, closure of the bone graft, muscle layers, and scalp can cause morphological changes in the initial bypass vessel [14], even though a successful anastomosis between the donor artery and recipient artery has occurred. We performed end-to-side anastomosis, and the folding of the donor artery over the recipient artery could cause acute occlusion of the anastomosis. Additionally, swelling of the temporalis muscles may also cause donor artery compression after surgery [6]. Recanalization may have occurred due to the natural recovery of the bypass pedicle into the unfolded form, which can be recanalized, or due to recovery of temporalis muscle swelling, which generally occurs within 2 weeks after bypass surgery.

Delayed recanalization at more than 6 months after bypass surgery may be caused by the following: neoangiogenesis can induce collateral formation after indirect revascularization, and neoangiogenesis between the donor and recipient artery near the occluded anastomosis may lead to formation of new collateral vessels near the occlusion of the anastomosis, resulting in mimicking delayed recanalization of the occluded anastomosis more than 6 months post-bypass surgery. When we performed bypass surgery, connective tissues around the donor artery were removed, which is known as debanding; in addition, the arachnoid membrane near the recipient artery was sufficiently removed. Therefore, fewer barriers were present to inhibit the generation of new blood vessels at the occluded anastomosis site, and the occluded bypass pedicle itself could induce neoangiogenesis in the neighbouring occluded anastomosis site. Neoangiogenesis from the indirect anastomosis develops gradually several weeks after surgery [1]. Likewise, neoangiogenesis from the occluded bypass pedicle may develop several weeks after surgery, which may lead to delayed recanalization more than 6 months after bypass surgery.

Identifying which type of surgical method is the most effective has been the subject of controversy in adult MMD [6, 13]. Recently, combined revascularization surgery has been considered the standard treatment in symptomatic adult MMD [1, 2, 5, 13]. Lin Wang et al. reported that indirect bypass surgery may be more beneficial due to vascular anastomosis patency, the operation time, and the hospital stay [11]. However, our results show that despite the occurrence of postoperative occlusion following combined revascularization surgery for adult MMD, delayed recanalization and clinical improvement can be expected.

## Conclusion

In our study, follow-up angiographies of anastomosis sites that were not patent immediately after bypass surgery showed satisfactory long-term clinical results with delayed recanalization. Patients in the non-patent group also showed clinical improvement after surgery. No difference in clinical courses was observed between the non-patent and patent groups. After combined revascularization surgery for adult MMD, despite the absence of blood flow after anastomosis, delayed recanalization and clinical improvement can be expected.

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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 this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

**Informed consent** Informed consent was obtained from the study participants prior to their inclusion in the study.

## References

1. Cho WS, Kim JE, Kim CH, Ban SP, Kang HS, Son YJ, Bang JS, Sohn CH, Paeng JC, Oh CW (2014) Long-term outcomes after combined revascularization surgery in adult moyamoya disease. Stroke 45:3025–3031
2. Jin SC, Oh CW, Kwon OK, Hwang G, Bang JS, Kang HS, Kim JE, Lee SH, Chung YS (2011) Epilepsy after bypass surgery in adult moyamoya disease. Neurosurgery 68:1227–1232
3. Jussen D, Horn P, Vajkoczy P (2013) Aspirin resistance in patients with hemodynamic cerebral ischemia undergoing extracranial-intracranial bypass surgery. Cerebrovasc Dis 35:355–362
4. Kim DS, Huh PW, Kim HS, Kim IS, Choi S, Mok JH, Huh CW (2012) Surgical treatment of moyamoya disease in adults: combined direct and indirect vs. indirect bypass surgery. Neurol Med Chir (Tokyo) 52:333–338
5. Kim H, Jang DK, Han YM, Sung JH, Park IS, Lee KS, Yang JH, Huh PW, Park YS, Kim DS, Han KD (2016) Direct bypass versus indirect bypass in adult moyamoya angiopathy with symptoms or hemodynamic instability: a meta-analysis of comparative studies. World Neurosurg 94:273–284
6. Kim T, Oh CW, Bang JS, Kim JE, Cho WS (2016) Moyamoya disease : treatment and outcomes. J Stroke 18:21–30
7. Laurent T, Ronit A, Amir RD, Leodante DC, Christopher W, Karel G, Terbugge MT (2008) Assessment of extracranial-intracranial bypass patency with 64-slice multidetector computerized tomography angiography. Neuroradiology 51:505–515
8. Mehmet T, Alexander M, Charles LT (2004) Multi-slice CT angiography in evaluation of extracranial-intracranial bypass. Eur J Radiol 52:217–220
9. Pandey P, Steinberg GK (2011) Neurosurgical advances in the treatment of moyamoya disease. Stroke 42:3304–3310
10. Scharf J, Schmiedek P, Kemmling A, Gerigk L, Groden C, Horn P (2007) Spontaneous recanalization of occluded standard extracranial-intracranial arterial bypass. Cerebrovasc Dis 23:175–180
11. Wang L, Qian C, Yu X, Fu X, Chen T, Gu C, Chen J, Chen G (2016) Indirect bypass surgery may be more beneficial for symptomatic patients with moyamoya disease at early Suzuki stage. World Neurosurg 95:304–308
12. Wilson JT, Hareendran A, Grant M, Baird T, Schulz UG, Muir KW, Bone I (2002) Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. Stroke 33:2243–2246
13. Xu B, Song DL, Mao Y, Gu YX, Xu H, Liao YJ, Liu CH, Zhou LF (2012) Superficial temporal artery-middle cerebral artery bypass combined with encephalo-duro-myo-synangiosis in treating moyamoya disease: surgical techniques, indications and midterm follow-up results. Chin Med J 125:4398–4405
14. Zhu FP, Zhang Y, Higurashi M, Xu B, Gu YX, Mao Y, Morgan MK, Qian Y (2014) Haemodynamic analysis of vessel remodeling in STA-MCA bypass for Moyamoya disease and its impact on bypass patency. J Biomech 47:1800–1805