



# Combined Direct and Indirect Revascularization for Adults with Moyamoya Disease: A Single-Center Retrospective Study

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## Abstract

**Background** Moyamoya vasculopathy is a rare neurological disease characterized by the progressive constriction of major intracranial vessels and secondary collateral formation. In the past decade, the popularity of combined bypass surgery has increased. They take advantage of the quick perfusion of direct bypass and collaterals ingrowth from indirect bypass.

**Objective** This study aimed to describe a single-center experience with surgical management of moyamoya disease (MMD) and moyamoya syndrome (MMS) over 7 years.

**Materials and Methods** In this retrospective medical records review, we enrolled patients diagnosed with MMD and MMS who were treated with combined surgical revascularization at the Hamad Medical Corporation center between 2015 and 2022. SPSS 26.0 was used to analyze the data.

**Results** A total of 20 patients were included, with 15% having MMS. The mean age was  $37.4 \pm 10.26$  years, and 60% of them were males. The mean follow-up period was 13.6 months. The modified Rankin score was significantly decreased by  $1.9 \pm 2.1$ ,  $p = 0.0001$ . Following surgery, no deficits were observed in 16 cases, whereas three were not improved, and one died. Following up on the stroke status, one patient developed a hemorrhagic stroke, and another showed right-side numbness. The postoperative status was substantially linked with the initial clinical presentation ( $p = 0.004$ ).

**Conclusion** Combined direct and indirect surgical revascularization procedures have favorable outcomes in MMD and MMS patients. Additional rigorous, prospective, controlled, high-quality trials with large-sample are needed to support our results.

## Keywords

- ▶ moyamoya
- ▶ direct bypass
- ▶ indirect bypass
- ▶ combined
- ▶ revascularization

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## Introduction

Moyamoya vasculopathy is a rare cerebrovascular disease with a prevalence ranging from 3.92 to 16.1 cases per 100,000 individuals and an incidence of 0.09 to 2.3 cases per 100,000 individuals per year.<sup>1</sup> It is characterized by the progressive steno-occlusion of large intracranial arteries along with the secondary development of small vascular collaterals with a characteristic smoky appearance on angiography.<sup>2–4</sup> According to the latest guidelines from the Research Committee on Moyamoya Disease (RCMD),<sup>5</sup> moyamoya disease (MMD) is idiopathic moyamoya vasculopathy in the absence of any other risk factors for the arterial stenosis or occlusion, while moyamoya syndrome (MMS) represents the same diagnostic criteria of MMD but linked with other comorbidities that are associated with the vasculopathy, such as autoimmune disease, meningitis, brain tumors including meningioma, craniopharyngioma, hemangioblastoma, and glioma, head irradiation, neurofibromatosis type 1, Down syndrome, and sickle cell disease.<sup>6</sup> MMD or syndrome might present with a wide variety of heterogeneous manifestations such as ischemic stroke, intracranial hemorrhage (ICH), seizures, and cognitive deterioration.<sup>7</sup> Neither neurointerventional approaches nor medications showed promising therapeutic effects. Medical therapy and supportive treatment might help reducing the risk of complications. Still, surgery is required in the vast majority of patients, especially those with a high risk of future vascular events.<sup>7</sup> Neurosurgeons acknowledged the advantages of surgical revascularization. Currently, studies suggest that combined bypass (direct and indirect) is better for moyamoya patients as it increases blood flow from direct anastomosis and collaterals ingrowth from indirect bypass.<sup>7–9</sup> However, postoperative complications, such as ischemia, infarction, hemorrhage, and seizures, are frequent.<sup>10–13</sup> This article describes our experience in Hamad Medical Corporation center with combined surgical revascularization of moyamoya cases over the past 7 years.

## Materials and Methods

### Study Design, Settings, and Eligibility Criteria

This was a retrospective record review study involving all adult patients with MMD or MMS who were operated in Hamad Medical Corporation center in Qatar between 2015 and 2022. The Hamad Medical Corporation center is the largest and only neurosurgery center in the Middle East and North Africa region that operates this disease on regular patients. The inclusion criteria included adult patients, a definite diagnosis of MMD or MMS, surgically operated cases, and who had follow-up data in their medical records. Patients were candidates for surgery depending on the presence of symptoms and radiological findings of magnetic resonance imaging/magnetic resonance angiography, computed tomography (CT) angiography, and digital subtraction angiography (DSA) according to the diagnostic criteria for MMD<sup>5</sup> (► **Supplementary Table S1** [available in the online version]). Patients who were managed conservatively (i.e., medical therapy only) and those with incomplete data or lost to follow-up were not included in the study.

### Surgical Management

A single surgeon and the same surgical techniques operated on all the patients. Prior to surgery, all patients underwent DSA to document occlusion of the internal carotid artery (► **Fig. 1**). During the surgical procedure, both direct (external carotid internal carotid) and indirect (encephaloduroarteriosynangiosis via placing the temporalis muscle over the brain surface) revascularization techniques were used (► **Fig. 2**). CT with volume rendering technique was conducted postoperatively to assess the surgical results (► **Fig. 3**).

### Surgical Technique

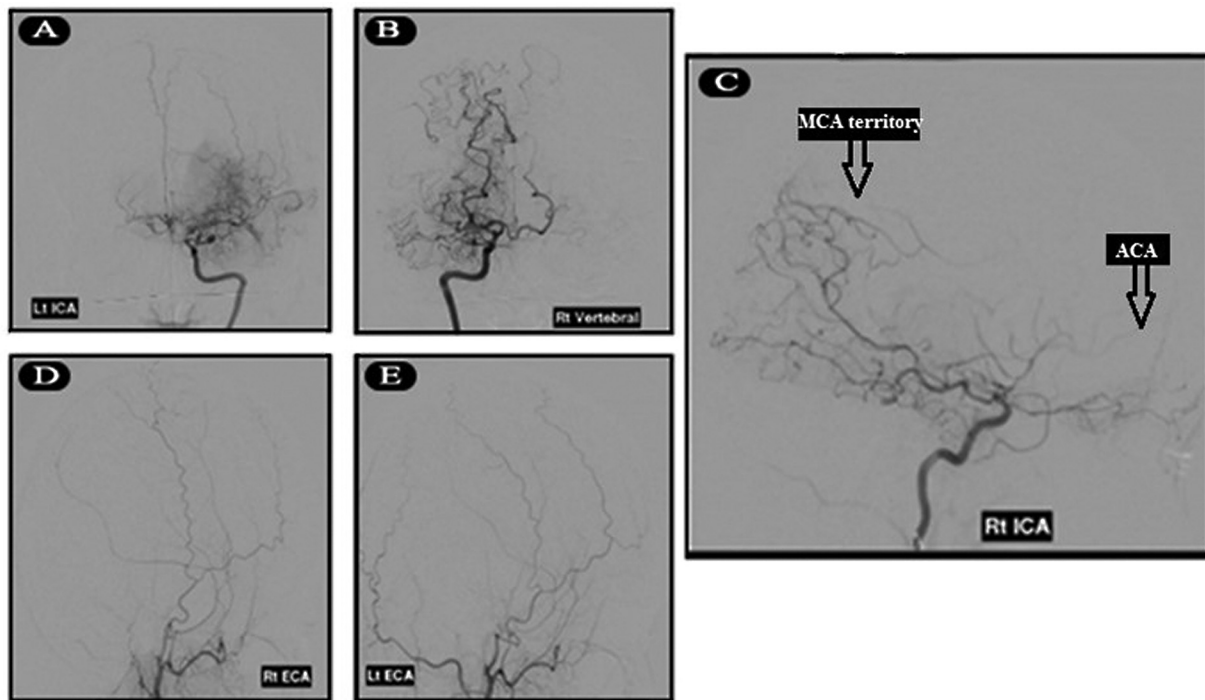
The surgical technique that was used involves a combined bypass using the frontal and parietal branches of the superficial temporal artery. After patient intubation and shaving the surgical site, Doppler ultrasound is used to track the course of the artery branches. A curvilinear incision is made to harvest maximum length, with considerations for anatomical variations. Blunt and sharp dissection techniques are employed, and early identification of the main artery stem is crucial. The parietal branch is dissected first to prevent stretching, followed by the frontal branch. Coagulation is used for tiny branches. A 2 mm galeoadventitial cuff is harvested with donor vessels, followed by dissection and flushing. The temporalis muscle is split, and a small craniotomy exposes the M4 branches while protecting the middle meningeal artery. Suitable branches are identified, and arachnoid dissection is performed, sacrificing limited branches. The donor vessel is prepared, and an anastomosis is performed using sutures (► **Fig. 2B**). Doppler ultrasound and indocyanine green (ICG) confirm blood flow through the bypass (► **Fig. 2A**). The procedure is repeated for the second anastomosis, followed by the application of fibrin glue. After completing the direct bypass, the dura is addressed by inverting the proximal leaflets over the brain surface and obtaining two flaps from the temporalis muscle. The distal dural leaflets are approximated and stay sutures are used to secure the muscle in place, ensuring good hemostasis. The bone flap is cut in half to avoid pressure on the donor artery and fixed with miniplates.

### Data Collection

The patients' sociodemographic and clinical characteristics were obtained from the medical records. Preoperative modified Rankin score (mRS) was also obtained. The intraoperative indocyanine green (ICG) fluorescence, Doppler findings, postoperative mRS, and complications were collected.

### Statistical Analysis

All data obtained were fed into a computer and analyzed using International Business Machines Statistical Package for the Social Sciences software version 26.0. Mean and standard deviation were utilized to describe quantitative parametric variables. Frequency and percentage were utilized to describe qualitative variables. The association between initial clinical presentation and different outcome variables was studied using Fisher's exact test. The change between pre- and postoperative mRS was assessed using Wilcoxon signed rank test.



**Fig. 1** Diagnostic cerebral angiogram of the bilateral internal carotid, superficial temporal, and external carotid arteries (ECAs). (A) Left internal carotid artery (ICA) occlusion; (B) fetal circulation from the right (Rt) vertebral artery; (C) total occlusion of the Rt ICA immediately distal to the posterior communicating artery (PCOM) with an adequate filling of the Rt posterior cerebral artery (PCA) through PCOM artery. Multiple hairline collaterals at the skull base that are filling the Rt middle cerebral artery (MCA). Pial collaterals are seen contributing to the Rt MCA territories from the Rt PCA branches. The per-callosal anastomosis refilling of the Rt anterior cerebral artery (ACA) is noted from the PCA territories. There is also markedly narrowing, and irregularity of the left supraclinoid left ICA as well as the origin of both the MCA and ACA, mounting to occlusion at the later. There is total occlusion of Rt A1/A2 segments with pial collateral refilling noted during the left PCA territories; (D and E) average caliber and smooth outline of both superficial temporal arteries during ECA injections.

*p*-values less than 0.05 were considered statistically significant.

## Results

### Demographics and Clinical Characteristics of the Included Patients

Twenty adults with moyamoya were operated in this study. Their mean age was  $37.4 \pm 10.26$  years and the mean follow-up period was 13.6 months. Almost two-thirds were males (60%), and most cases (85%) were Asian. None of the patients had a positive family history of MMD, but a single patient had a family history of subarachnoid hemorrhage. Transient ischemic attack (TIA) was the main presentation occurring in approximately 55% of the cases. Headache and ICH were the next two most common presentations occurring in 25 and 20% of patients, respectively. The disease involved both hemispheres in the vast majority of the cases (80%). Of all patients, 85% ( $n=17$ ) had MMD, and only 15% ( $n=3$ ) patients were diagnosed with MMS. The mean preoperative mRS score of the patients was  $2.9 \pm 1.119$ . ► **Table 1** summarizes the demographics and clinical characteristics of the patients.

### Outcomes

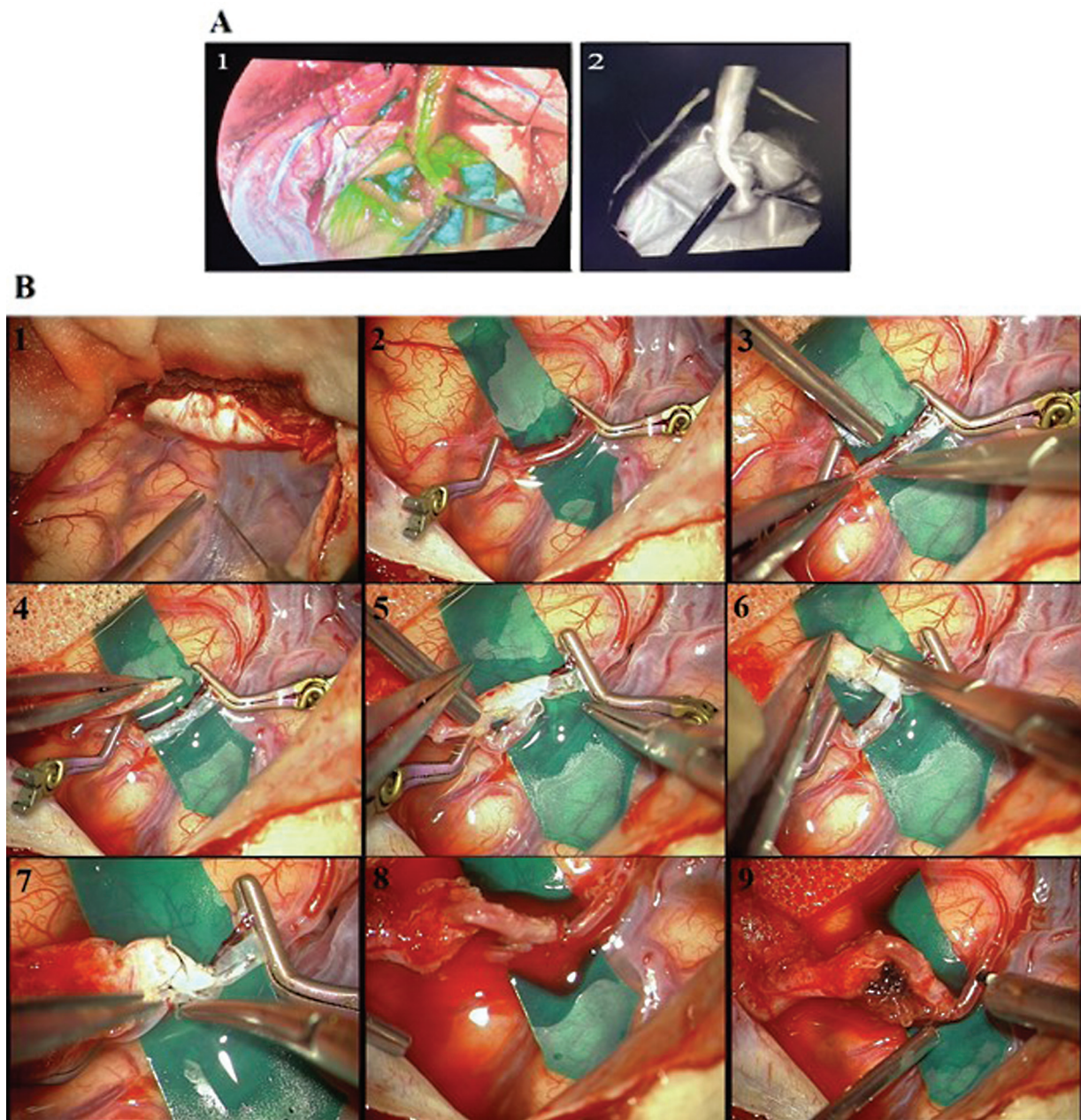
Intraoperatively, all the patients (100%) had a patent artery on ICG fluorescence and intraoperative Doppler. The mRS

improved postoperatively to a mean of  $1 \pm 1.78$  with a significant mean change of  $-1.9 \pm 2.1$ , *p*-value = 0.001. Around 80% ( $n=16$ ) of the patients had no deficits postoperatively. While three patients (15%) had left-sided weakness (same as preoperative), and one patient developed ICH during surgery and died. After a mean of 13.6 months of follow-up, one patient developed a hemorrhagic stroke, and another showed right-side numbness (► **Table 2**).

On analyzing the potential impact of patients' characteristics on outcomes, it was noted that the initial clinical presentation was the only variable significantly correlated with the postoperative status (*p* = 0.004). No significant difference was found between MMD and MMS patients (*p* = 1; ► **Table 3**).

## Discussion

Surgical revascularization is the mainstay treatment in MMD to enhance cerebral perfusion, prevent ischemic stroke, reduce blood pressure in the small vascular collaterals, and prevent hemorrhage.<sup>7</sup> Both direct and indirect surgical techniques are used to connect the external carotid artery with the cerebral hemispheres.<sup>7</sup> In the past decade, the popularity of the combined bypass has increased. They take advantage of the quick perfusion of direct bypass and collaterals ingrowth from indirect bypass.<sup>14</sup> In this research, we described our experience with implementing a combined surgical



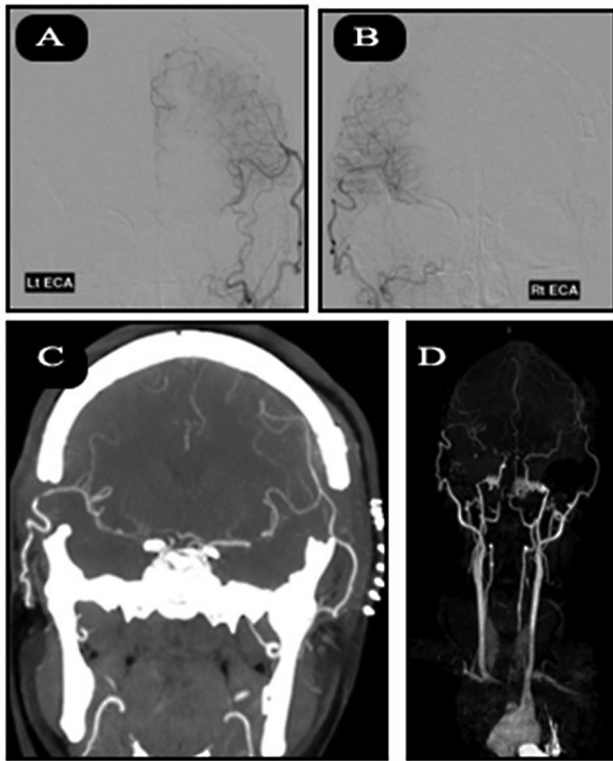
**Fig. 2** (A) Intraoperative indocyanine green image showing the patency of the anastomosis. (B) Intraoperative image showing the revascularization technique.

revascularization technique in a sample of 20 patients in our center. We found that combined bypass improved the mRS score, and most patients showed no deficits. On follow-up, 5% had hemorrhagic stroke, and 5% had right-side numbness. There was a significant association between the preoperative presentation and postoperative status.

A recent large meta-analysis based on 143 articles, with a total of 11,454 patients, showed that combined bypass was significantly associated with more favorable outcomes than indirect bypass. Furthermore, combined and direct bypasses are favored over indirect bypass in lowering the risk of late stroke and hemorrhage.<sup>15</sup> Moreover, a meta-analysis of 18 trials proved that combined and direct bypasses reduced the recurrence stroke rate.<sup>11</sup> Further studies showed that MMD patients who underwent combined bypass had considerable

functional and angiographic outcomes.<sup>16–19</sup> These results are consistent with our results that revealed that combined bypass was effective in MMD patients by reducing the mRS score. In comparison to conservative management, multiple meta-analyses have demonstrated that bypass surgery is favored in patients with MMD.<sup>20–22</sup> On the other hand, when Zhao et al compared direct to combined bypass, they revealed that there was no statistically significant difference between the two surgical groups in the effect of revascularization for MMD.<sup>23</sup>

In this study, 16 patients (80%) had favorable outcomes, three patients (15%) showed no improvement, and one patient (5%) developed ICH during surgery and died. On the last follow-up, one patient (5%) developed a hemorrhagic stroke, and another (5%) showed right-side numbness. In a



**Fig. 3** (A and B) Postoperative angiogram of external carotid artery demonstrating bilateral superficial temporal artery to middle cerebral artery (STA-MCA) bypass with moderate focal stenosis at the right (Rt) STA-MCA anastomosis. The left STA-MCA bypass appears patent. (C) No internal carotid artery (ICA) contribution from the radiotherapy or left ICA is seen. (D) Postoperative computed tomography and a volume rendering technique showing opacification of the left superficial temporal artery with anastomosis with the left MCA branches, well opacification of the Rt superficial temporal artery and Rt MCA branches, significant narrowing of the intracavernous and intracranial part bilateral ICAs.

prior prospective study, Cho et al have reported that, out of 60 patients who underwent combined bypass, 96.6% improved, 1.7% remained the same, and 1.7% worsened. Post-operative complications included symptomatic cerebral hyper-perfusion syndrome (29.9%), hemorrhage (5.2%), infarction (13%), seizures (2.6%), and wound infection (1.3%). However, their mortality rate was zero compared with 5% in our study, and the permanent residual deficits were seen in 6.7% of cases in comparison to 20% of our cases.<sup>24</sup> Sum et al reported no mortality and 9.8% with deficit in 61 patients who underwent direct/combined bypass.<sup>19</sup> Moreover, a study of 13 adult patients undergoing combined surgery for MMD has suggested that combined bypass can provide temporally complementary revascularization, resulting in no mortality; one case (7.7%) suffered from minor stroke with transient symptoms, two cases (15.3%) showed transient symptoms consistent with seizure, and one case (7.7%) developed TIA.<sup>25</sup> In Zhao et al study, of the 71 moyamoya patients, 54 underwent combined bypass. The noted complications in the combined bypass group were ischemic events (4.4%), hemorrhage (4.2%), TIA (2.8%), and wound infection (1.4%).<sup>23</sup>

**Table 1** Demographics and baseline characteristics of included patients

Variables	Total (N=20)
Age (mean ± SD)	37.4 ± 10.262
Gender (n, %)	
Male	12 (60%)
Female	8 (40%)
Region (n, %)	
Asia	17 (85%)
Africa	3 (15%)
Family history (n, %)	
No	19 (95%)
SAH	1 (5%)
Presentation (n, %)	
TIA	11 (55%)
ICH	4 (20%)
IVH	3 (15%)
SAH	2 (10%)
Stroke	2 (10%)
Headache	5 (25%)
Dysphasia	2 (10%)
Confusion	2 (10%)
Dizziness	2 (10%)
Unsteadiness	1 (5%)
Dysarthria	2 (10%)
Vomiting	1 (5%)
Comorbidities (n, %)	
No	13 (65%)
HTN	6 (30%)
HTN/DM	1 (5%)
D/S (n, %)	
Disease	17 (85%)
Syndrome	3 (15%)
Preoperative mRS (n, %)	2.9 ± 1.119
Bilaterality (n, %)	
Rt/Lt	16 (80%)
Rt	2 (10%)
Lt	2 (10%)

Abbreviations: D/S, disease/syndrome; DM, diabetes mellitus; HTN, hypertension; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; Lt, left; mRS, modified Rankin Scale; Rt, right; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

This was in agreement with several reports in the literature, especially in the pediatric population.<sup>10,26</sup> Further 518 direct and combined procedures were conducted by Chen et al, of which 11 (2.1%) cases have developed ICH or ICH with intraventricular hemorrhage. They reported that preoperative hypertension, posterior circulation involvement, and CT

**Table 2** Surgical outcomes of the included patients

Variables	Total (N = 20)
Intraoperative ICG (n, %)	
Patent	20 (100%)
Intraoperative Doppler (n, %)	
Patent	20 (100%)
Postoperative status (n, %)	
Improved	16 (80%)
Not improved	3 (15%)
Died	1 (5%)
Postoperative mRS, (mean ± SD)	1 ± 1.777
Follow-up stroke/TIA (n, %)	
Hemorrhagic stroke	1 (5%)
Rt-side numbness	1 (5%)

Abbreviations: ICG, indocyanine green fluorescence; mRS, modified Rankin Scale; Rt, right; SD, standard deviation; TIA, transient ischemic attack.

**Table 3** Associations between postoperative status and baseline data using Fisher's exact test

Variables	Postoperative status
Gender	0.462
Region	1
Family history	1
Presentation	0.004 <sup>a</sup>
Comorbidities	0.09
D/S	1
Bilaterality	0.393

Abbreviation: D/S, disease/syndrome.

<sup>a</sup>Statistically significant.

perfusion stage more than III were risk factors for developing ICH after direct/combined bypass,<sup>13</sup> while the only factor in our records that was significantly correlated with the postoperative status was the initial clinical presentation. Previous studies suggested that other factors were found to significantly impact the postoperative outcome of moyamoya patients, such as age, history of diabetes mellitus or infarction, the preoperative Karnofsky performance scale score, and higher Suzuki stage.<sup>14,26,27</sup>

Our study's limitations include the limited sample size and the variation in follow-up periods among the included patients, in addition to the retrospective nature of our research and the data obtained over 7 years. However, the consistency of evaluation and surgical approach by single-surgeon may mitigate such point. Another limitation is the lack of comparison to alternative therapy options. Therefore, prospective comparative studies with a larger sample size are required.

## Conclusion

Combined direct and indirect surgical revascularization methods had favorable outcomes in patients with MMD with low risk of postoperative complications and good long-term follow-up.

### Authors' Contributions

All the authors have contributed equally to writing, editing, and reviewing the manuscript. All authors read and approved the final version of the manuscript.

### Funding

None.

### Conflict of Interest

None declared.

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