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Title:

Postoperative intracerebral hemorrhage after combined revascularization surgery in moyamoya disease: profiles and clinical associations

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Running title:

Postoperative ICH after combined revascularization surgery in MMD

Abbreviations list:

APD: anti-platelet drugs

BP: blood pressure

CBF: cerebral blood flow

CHP: cerebral hyperperfusion

CI: confidence interval

CT: computed tomography

dBP: diastolic blood pressure

FLAIR: fluid attenuation inversion recovery

ICH: intracerebral hemorrhage

IVH: intraventricular hemorrhage

JAM: Japan Adult Moyamoya

MBs: micro-bleeds

MCA: middle cerebral artery

MMD: moyamoya disease

MRI: magnetic resonance imaging

MRA: magnetic resonance angiography

mRS: modified Rankin Scale

OR: odds ratio

PET: positron emission tomography

POD: postoperative day

SAH: subarachnoid hemorrhage

sBP: systolic blood pressure

SPECT: single photon emission computed tomography

STA: superior temporal artery

TIA: transient ischemic attack

TNDs: transient neurological deficits

T2-WI: T2-weighted image

Title:

Postoperative intracerebral hemorrhage after combined revascularization surgery in moyamoya disease: profiles and clinical associations

Abstract

Objective: In combined revascularization surgery for patients with moyamoya disease (MMD), intracerebral hemorrhage (ICH) during the postoperative acute phase is a rarely observed but severe complication. Its clinical features remain unclear due to its low incidence rate. The aim of this study was to clarify the clinical characteristics of immediate postoperative ICH.

Methods: The frequency, onset timing, and hematoma location of patients who demonstrated immediate postoperative ICH were investigated in 201 consecutive surgeries performed in 134 patients. Associations between immediate postoperative ICH and demographics, clinical presentation type, perioperative blood pressure (BP), and neuroimaging data were analyzed.

Results: Postoperative ICH was observed in six cases (2.99%, mean age = 46.0 ± 7.6 years). The onset timing of ICH was within 24 hours after surgery in most patients (83.3%). Hematomas were located at the subcortical lesion beneath the anastomosed cortex (n = 5) and caudate head (n = 1). Three cases (50.0%) required hematoma evacuation. A higher age at surgery was associated with postoperative ICH (P = 0.046). In adult cases (132 surgeries, 65.7%), hemorrhagic presentation at onset (P = 0.0027) and an increase in BP from pre- to postoperative stage (systolic BP increase: P = 0.0058, diastolic BP increase: P = 0.0274) were significantly associated with postoperative ICH.

Conclusions: The results suggest that older patients, with hemorrhagic presentation and greater postoperative BP increase should be carefully managed to avoid postoperative ICH. Immediate

hematoma evacuation may be effective in preventing devastating outcomes following postoperative ICH.

Introduction

Moyamoya disease (MMD) is a rare cerebrovascular disease characterized by steno-occlusive changes in the cerebral arteries at the base of the brain, especially in the terminal portion of the bilateral internal carotid arteries. The pathognomonic finding on angiography in MMD is abnormal fragile collateral vessels, which resemble “puffs of smoke” arising from the bottom of the brain.[1, 2] The progression of the steno-occlusive changes in cerebral arteries causes cerebral hemodynamic impairments, which are occasionally followed by cerebral ischemia or intracranial hemorrhage. The most effective treatment for MMD is revascularization surgery.

Recent reports have described complications after revascularization for MMD, such as postoperative ischemic/hemorrhagic stroke or cerebral hyperperfusion (CHP) syndrome, during the post-surgical acute phase.[3, 4] Hemorrhagic stroke can be classified as subarachnoid hemorrhage (SAH), intraventricular hemorrhage (IVH), or intracerebral hemorrhage (ICH). Although SAH and IVH do not usually cause parenchymal damage and recovery occurs without neurological deficits, ICH causes destructive and irreversible changes in brain structure, followed by severe neurological symptoms. The purpose of surgical treatment for MMD is prevention of stroke in future; therefore, postoperative ICH is a devastating complication.

To date, there are limited reports describing ICH after revascularization surgery in MMD. Fujimura et al. and Ito et al. have reported cases of postoperative ICH after surgery, involving a 47-year-old woman and 35-year-old man, respectively.[5, 6] In both the patients, hematoma had

developed at the subcortical lesion beneath the operative field, and did not require evacuation.[5, 6] Several reviews have discussed postoperative complications, including ICH; however, to the best of our knowledge, a sufficient number of detailed case studies or reviews describing postoperative ICH is lacking.[4, 7] Furthermore, the clinical features, including appropriate management and prognosis, are still unclear. This is mainly due to the low incidence rate. Nevertheless, publication bias may exist with severe complications, which may lead to under-representation of the true incidence of postoperative ICH. Thus, the aim of the present study was to clarify the clinical profiles and factors associated with postoperative ICH.

Materials and methods

Patient population

This study was approved by the institutional review board of the local research ethics committee. Due to the retrospective nature of the assessment, this study was deemed exempt from the requirement for individual informed consent. A prospective database of MMD cases was created in March 1980, and 390 consecutive patients with MMD were registered in the database until November 2017. Data of surgically treated patients from January 2003 to November 2017 were extracted from the database, and 201 revascularization procedures in 134 patients were included in this study. A retrospective review was performed to analyze the demographics and neuroimaging data from the patients' medical records. In this study, the postoperative acute phase was defined as within 14 days of surgery. The diagnosis of MMD was based on guidelines established by the Research Committee on the Pathology and Treatment of

Spontaneous Occlusion of the Circle of Willis, from the Ministry of Health and Welfare of Japan.[8, 9]

Surgical procedures and perioperative management

Surgical procedures were characterized by the universal application of combined revascularization, including both direct and indirect methods, regardless of the patient's age. A superior temporal artery to middle cerebral artery (STA-MCA) double anastomosis was performed. The temporal muscle (and pericranial flap in some cases) was laid on the brain surface, with the dura mater inverted out of the craniotomy field.[10, 11] We primarily selected the MCA as the recipient artery distributed in the frontal region, but the middle temporal artery was occasionally selected.

Anti-platelet drugs (APD) were administered preoperatively for patients with symptomatic cerebral ischemia, discontinued at least 7 days prior to the operation, and not resumed during the postoperative acute phase. Patients with hypertension had their blood pressure (BP) controlled before surgery with anti-hypertensive drugs. Patients with hemodynamic compromise received an intravenous infusion of extracellular fluid (500–1000 mL/day). After the induction of general anesthesia, the partial pressure of CO_2 was maintained at 35–40 mmHg throughout the surgery. Sufficient intravenous administration of extracellular fluid was performed postoperatively, depending on the ability of the patients to orally ingest fluids. Continuous elevated systolic BP (sBP) above 140 mmHg was treated by continuous intravenous infusion of diltiazem hydrochloride.

Neuroimaging-based assessment

Magnetic resonance imaging (MRI) and MR angiography (MRA) were performed before surgery. MRI included T2-weighted imaging (T2-WI), T2*-WI, and fluid attenuation inversion recovery (FLAIR) sequences to confirm lesions from past infarctions or hemorrhage. Suzuki's stage, which indicates disease severity and advancement of MMD, was evaluated using catheter angiography or 3 T time-of-flight MRA, based on a past report on the correlation of Suzuki's stage-related findings between MRA and conventional angiography.[12] Cerebral micro-bleeds (MBs) were evaluated using T2*-WI and judged using previously established parameters.[13, 14] Cerebral hemodynamic assessment was performed via [^{123}I] *N*-isopropyl-iodo-amphetamine single photon emission computed tomography (SPECT) or ^{15}O-gas positron emission tomography (PET). Preoperative hemodynamic compromise was judged qualitatively as regional cerebral blood flow (CBF) reduction in the focal lobe or hemisphere. Postoperative radiological assessment was performed as follows: computed tomography (CT) scans were acquired immediately after and the day following surgery (postoperative day 1 [POD 1]); MRI, MRA, and SPECT were performed 2–3 times before POD 7.

Data analysis

Clinical presentation was classified as cerebral infarction, transient ischemic attack (TIA), intracranial hemorrhage, and other symptoms, such as headaches, seizures, or as asymptomatic. The data of all the patients who developed postoperative ICH were collected, and the timings of hemorrhage and hematoma volume were documented. Clinical parameters, such as demographics, neuroimaging data, and perioperative BP were compared between groups with or without ICH. Increases in sBP/diastolic BP (dBP), calculated as postoperative sBP/dBP minus preoperative sBP/dBP (mmHg), were compared between the two groups. Patients were stratified

according to their age: pediatric (< 18 years old) and adult (≥ 18 years old). The outcome was measured using the modified Rankin Scale (mRS) at 90 days post-surgery or at discharge.

Differences in dichotomous variables were analyzed using Pearson's chi-square or Fisher's exact tests. Continuous variables are shown as mean ± standard deviation. Comparisons of continuous variables between the two groups were performed using unpaired *t*-tests. A simple logistic regression analysis was conducted to examine the factors associated with postoperative ICH. Data were considered statistically significant if $P < 0.05$. Statistical analysis was performed using JMP software (version 12; SAS Institute, Inc., Cary, NC, USA).

Results

Patient characteristics

Of the 134 patients treated with combined revascularization, 67 patients each received treatment in bilateral and unilateral hemispheres. Of the 201 procedures, 132 (65.7%) and 69 (34.3%) involved adult and pediatric cases, respectively. The mean age was 31.1 ± 18.7 (range, 1–71; median, 34) years. Table 1 shows the characteristics of the patients included in this study.

Profiles of postoperative ICH

Of the 201 revascularization procedures, six surgeries in six patients demonstrated postoperative ICH (2.99%; 95% confidence interval [CI], 1.38–6.36%). All six surgeries involved adult cases (mean age = 46.0 ± 7.6 years).

None of the cases showed new ICH on the CT scans acquired immediately after the surgery. The timing of postoperative ICH onset from surgery ranged from POD 0–3. Five out of six cases

(83.3%) exhibited ICH within 24 hours post-surgery. Postoperative SPECT was performed in four cases (66.7%) before the onset of ICH. Two out of four cases (50%) showed CBF increases when compared with preoperative CBF; however, there were no neurological symptoms in either case.

The CT scans acquired at the onset of postoperative ICH showed hematoma in the cerebral hemisphere ipsilateral to revascularization in all cases (Figure 1). Hematoma was observed as a subcortical lesion beneath the anastomosed area in five cases. One case (Case 6) presented with caudate head hemorrhage with IVH. The location of the hematoma differed from the primary hemorrhagic site in five cases. There were no low-intensity lesions, which would have presented as an old minor hemorrhage in T2*WI or micro-aneurysm in preoperative catheter angiography or MRA performed at the diagnosis of postoperative ICH. Mean hematoma volume was 34.2 ± 26.2 (range, 1.3–71.0; median, 39.4) mL.

Three cases (50.0%) with larger hematoma volumes (≥42.8 mL) underwent emergent hematoma evacuation surgery immediately after ICH diagnosis. None of the operated cases exhibited re-bleeding. The three non-surgical cases (without hematoma evacuation) were observed closely, including strict BP control and fluid administration; no worsening of the hemorrhage was detected. Intraoperative findings showed occlusion of the STA-MCA anastomosis with clot in two (Cases 2 and 5) out of the three operated cases. In Cases 3, 4, and 6, the patency of STA-MCA anastomosis was confirmed via operative findings or MRA. There was no patency in Case 1 after ICH, as confirmed using MRA. We did not perform STA ligation in any case, and there was no worsening of hemorrhage in any case.

No case demonstrated ischemic complications following ICH during the acute phase. There was no difference in pre- and postoperative mRS scores in five cases (83.3%), including cases with

hematoma evacuation. One patient (16.7%), who did not receive hematoma evacuation, exhibited worsened postoperative neurological status. This was due to a worsening of preexisting hemiparesis and motor aphasia. Follow-up MRA showed recanalization of STA-MCA anastomosis after hematoma evacuation in Cases 2 and 5, which had shown bypass occlusion in intraoperative findings. Table 2 shows the characteristics of the postoperative ICH cases.

Factors associated with immediate postoperative ICH

Unpaired *t*-test revealed that the ICH group had a significantly higher mean age than the non-ICH group (P = 0.046). The adult cases underwent 132 revascularization procedures. A simple logistic regression analysis showed that postoperative ICH was significantly more frequent when patients presented with intracranial hemorrhage than with other MMD types (odds ratio [OR], 16.0; 95% CI, 2.46–312.8; P = 0.0027). Increases in sBP and dBP were significantly greater in the ICH group (sBP increase: OR, 1.69; 95% CI, 1.17–2.58; P = 0.0058; dBP increase: OR, 2.02; 95% CI, 1.08–4.03; P = 0.0274; OR and 95% CI were calculated based on a change of 10 mmHg). Other preoperative factors, such as hypertension, APD usage, MBs, Suzuki's stage (≥4), and hemodynamic compromise, were not significantly associated with postoperative ICH. The comparison of the clinical factors between the two groups and statistical analysis results are shown in Table 3.

Discussion

The present study reports that the incidence of immediate postoperative ICH after revascularization for MMD was 2.99%, and all the cases involved adult patients. We found that

the change in BP between pre- and post-surgery, but not pre- or postoperative BP alone, was significantly associated with immediate postoperative ICH. This indicates that patients with normal preoperative BP should be carefully managed if they have a higher BP after surgery.

The location of ICH was typically a subcortical lesion beneath the anastomosed cortex, suggesting a detrimental effect of direct anastomosis. Nevertheless, the prognosis of postoperative ICH was better than expected, probably because the patients underwent hematoma evacuation at an optimal time.

Incidence of postoperative ICH

In past reports describing complications after direct or combined revascularization for MMD, including ICH and other hemorrhagic complications, the incidence rate of postoperative ICH was 0–5.2%.[4, 7, 15-18] Only one case of postoperative ICH in a pediatric population after direct revascularization has been reported.[7] The present study observed an incidence rate of 2.99%, including only adult cases, which is consistent with previous reports. We observed that patients of older age were more likely to exhibit bleeding during the postoperative acute phase following revascularization surgery.

The Japan Adult Moyamoya (JAM) Trial showed the effectiveness of surgery for the prevention of future intracranial hemorrhage in adult patients with hemorrhage.[19] The present study suggests that revascularization for preventing recurrent hemorrhage may not be beneficial for older adults. Indeed, although Williamson et al. reported the effectiveness of revascularization in older adults with MMD (>50 years old), the group reported two cases (6.1%) of postoperative ICH due to CHP.[20] Thus, further studies in older adults are required to investigate the surgical indication for this population.

Pathogenesis of postoperative ICH

Long-term hemodynamic stress induces the development of fragile collateral vessels in MMD. An immediate increase of internal pressure in cerebral arteries, including these fragile vessels, occurs following direct revascularization. The hemorrhagic site at the onset of MMD is typically in the periventricular area, and is occasionally accompanied by IVH. This spatial characteristic is described in a previous report as the development of fragile collateral vessels around the periventricular area.[21, 22] Conversely, the location of postoperative ICH in the present study was different from the typical primary hemorrhagic site. We speculate that drastic blood flow conversion beneath the anastomosed site may have triggered hemorrhaging in the cases reported here. Nevertheless, it is difficult to predict postoperative ICH using current preoperative neuroimaging information, such as hemodynamic compromise, MBs, or micro-aneurysm.

Involvement of cerebral blood flow

Postoperative ICH has been linked with CHP in past reports.[3, 5, 6, 16] We considered postoperative ICH as a phenomenon that is caused by CHP. However, the typical course of symptomatic CHP shows transient neurological deficits (TNDs), such as aphasia, limb paresis, or sensory disturbance, that arise several days after surgery and persist or worsen at approximately POD 7. Therefore, postoperative ICH can be described as a malignant complication that arises at an earlier phase than do TNDs in CHP.[3, 23, 24]

The discrepancy between typical CHP and ICH, as observed in this study, with respect to onset timing and location, can be explained by the findings of a past study that reported a topographic change in regional CBF in the first 2 weeks after surgery.[25] This report demonstrated that direct

revascularization provides additional CBF to the basal ganglia and subcortical lesions in the frontotemporal lobes immediately after surgery. Moreover, the area of increased regional CBF shifted to the lateral prefrontal cortex approximately one week after the surgery.[25] This phenomenon matches with the ICH pattern in this study because of the onset timing and hematoma location at an earlier phase, such as POD 0–2; and the typical TNDs due to CHP occurring around POD 7–8. Importantly, the present study shows that some of the cases developed ICH before the standard postoperative CBF assessment or exhibited ICH despite reduced increase in CBF after surgery. This may be due to the rupture of fragile vessels resulting from increase in internal pressure that is not detected as an increase in CBF.

The present study showed early onset of postoperative ICH. Although a SPECT/PET study is useful for monitoring alterations in postoperative regional CBF, SPECT/PET is not always applicable immediately after surgery in most cases in the clinical setting. Thus, intraoperative measurements, such as blood flow velocity and mean transit time, may contribute to the earlier detection of CHP syndrome.[26] Recently, noninvasive monitoring, involving the measurement of flow velocity, has been used to monitor cerebral perfusion immediately after the revascularization procedure, which may allow for the early detection of excessive regional CBF increase.[27, 28]

Clinical factors associated with postoperative ICH

Our study shows that a greater increase in pre- and post-operative BP is one of the factors associated with postoperative ICH. The increase in sBP was more significant than that in dBP (sBP: $P = 0.0058$, dBP: $P = 0.0274$). These results suggest that a difference between pre- and postoperative BP, particularly sBP, may cause greater hemodynamic stress in abnormal collateral

vessels. The autoregulation of BP for drastic blood flow conversion is thought to be impaired in cases of greater BP increases. The cerebral vascular structure may not be able to tolerate a sharp increase in BP. The importance of postoperative BP control after revascularization for MMD has been mentioned in past reports.[29, 30] In line with this, our study indicates that a thorough BP control and patient monitoring should be performed, even in the absence of CHP, when a large BP increase is observed at the early postoperative stage.

An additional factor associated with postoperative ICH is hemorrhagic presentation. This may be due to changes in abnormal vessel structure in the periventricular area, where primary hemorrhaging typically occurs; and the area where the collateral vessels pass through the subcortical to the cortical medullary artery.

Hematoma evacuation and prognosis

It is difficult to select the appropriate indication and timing of hematoma evacuation in cases of ICH after revascularization for MMD. Hematoma evacuation was performed in this study in cases with a large hematoma volume. This is because without hematoma evacuation, extension or high intracranial pressure may occur, followed by a large cerebral infarction in other regions or brain herniation, resulting in devastating neurological deficits or even death.

Another consideration is whether to occlude the STA to reduce additional blood flow and prevent any worsening of the hemorrhage. Bypass occlusion in the present cases (Cases 2 and 5) was suggested because they exhibited compression due to the hematoma mass. The occluded STA was recanalized following recovery, and no recurrence of ICH was detected. These results suggest that occlusion of STA may not be necessary in cases of postoperative ICH; however, the STA should be occluded if a massive or growing hematoma is threatening the patient's life with

a patent STA. All three cases of hematoma evacuation in this study underwent revision of indirect revascularization at the end of hematoma evacuation surgery, which was successful in obtaining the desired outcome. Therefore, we consider that revision of indirect revascularization may be effective during hematoma evacuation surgery.

The outcome of hematoma evacuation was favorable in this study as there was no difference in the final mRS scores of the patients. In addition, the condition of the patients who did not receive hematoma evacuation was also improved. This may be because the subcortical lesion where the destructive change occurred was functionally less extensive. Nonetheless, it is important to perform emergent hematoma evacuation surgery when the hematoma volume is large and neurological condition is poor, even immediately after the revascularization for MMD.

Study limitations

This study has some limitations. First, the low incidence rate of postoperative ICH should be considered when discussing the correlation between factors. This is because a low incidence rate is an unstable factor in statistical analysis. Since this study involves a rare complication in a rare disease, it is difficult to collect a sufficient number of postoperative ICH cases from a single institute. Second, this study was conducted in a single institute, which may affect the generalizability of the results. The surgical procedures and perioperative patient management differ depending on institutional policies. For example, indirect revascularization was not evaluated in this study. Third, preoperative CBF data was analyzed qualitatively to ascertain the hemodynamic compromise.

Taking these limitations into consideration, a multicenter trial on postoperative ICH involving a large number of surgical cases is warranted for further verification of the results from this study.

Conclusions

This study observed an incidence rate of 2.99% for postoperative ICH in patients with MMD who underwent combined revascularization surgery. Postoperative ICH occurred at subcortical lesions immediately beneath the anastomosed area within 24 hours after surgery in most cases. Emergent hematoma evacuation surgery was performed in three cases that displayed a larger hematoma volume, and the overall outcome was better than expected. Furthermore, patients with older age at the time of surgery, hemorrhagic presentation, and a greater BP increase from pre- to post-surgery should be carefully managed to avoid postoperative ICH, as these factors were significantly associated with postoperative ICH.

Ethical considerations:

Ethical approval for the study protocol was obtained from the Institutional Review Board of Hokkaido University Hospital (reference no.: 015-0086).

Disclosures:

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Author contributions:

Conception and design: Tokairin, Kazumata. Acquisition of data: Tokairin, Kazumata, Tatezawa, Shindo. Analysis and interpretation of data: Tokairin, Kazumata, Uchino. Drafting the article: Tokairin. Critically revising the article: Tokairin, Kazumata. Approval of the final version of the manuscript on behalf of all authors: Tokairin, Kazumata. Statistical analysis: Tokairin, Ono. Final approval of the version to be submitted: Houkin, Kazumata, Tokairin.

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Figure caption:

Figure 1. Computed tomography images showing representative slices of postoperative intracerebral hemorrhage at onset for each of the six cases. A: Case 1; B: Case 2; C: Case 3; D: Case 4; E: Case 5; F: Case 6

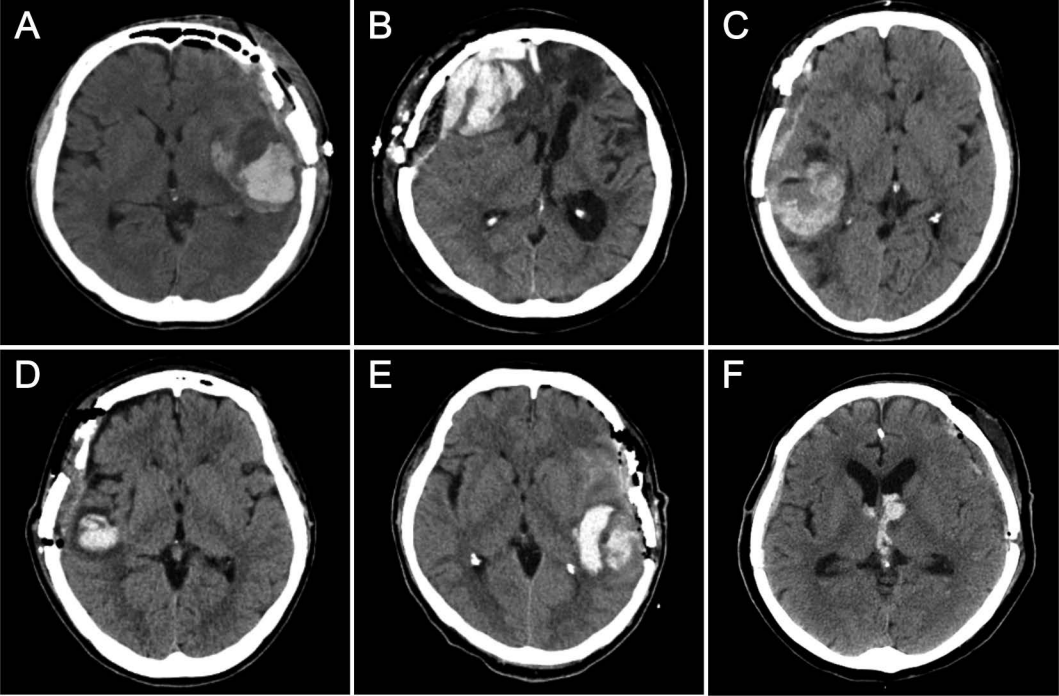
A
B
C
D
E
F

Table 1. Demographic Data of the Adult and Pediatric Cases of Moyamoya Disease

	Total	Adult Cases	Pediatric Cases
Patients	134	91	43
Surgeries	201	132	69
Age (years)	31.1 ± 18.7*	42.7 ± 11.3*	8.9 ± 4.1*
Female sex	140 (69.7)	97 (73.5)	43 (62.3)
Left side	100 (49.8)	67 (50.8)	33 (47.8)
Hypertension	55 (27.4)	54 (40.9)	1 (1.4)
APD usage	45 (22.4)	41 (31.1)	4 (5.8)
MBs	15 (7.5)	13 (9.8)	2 (2.9)
Clinical presentation			
Hemorrhage	37 (18.4)	35 (26.5)	2 (2.9)
Cerebral infarction	49 (24.4)	30 (22.7)	19 (27.5)
TIA	84 (41.8)	47 (35.6)	37 (53.6)
Others	31 (15.4)	20 (15.1)	11 (15.9)
Suzuki's stage ≥ 4	103 (51.2)	84 (63.6)	19 (27.5)
Hemodynamic compromise	157 (78.1)	108 (81.8)	49 (71.0)

APD, Anti-platelet drugs; MBs, microbleeds; TIA, transient ischemic attack

The values given in parentheses are percentage of the surgeries performed in each group (%).

[*]Data presented as mean ± standard deviation

Table 2. Clinical Features of Postoperative Intracerebral Hemorrhage Cases

Case No.	Age (years)	Sex	Side	Clinical Presentation	Suzuki's Stage	Onset Timing (POD)	Onset Symptoms
	Hematoma Volume (mL)			Hematoma Evacuation		Preoperative mRS	Postoperative mRS*
1	48	M	Lt	Hemorrhage	4	1	Disturbance of consciousness
	36.0			-	2	3	
2	27	F	Rt	Hemorrhage	2	1	Disturbance of consciousness
	71.0			+	4	4	
3	48	F	Rt	Cerebral Infarction	4	3	Agitation, Headache
	42.8			+	0	0	
4	50	F	Rt	Hemorrhage	3	1	Headache
	6.9			-	1	1	
5	51	M	Lt	Hemorrhage	4	0	Disturbance of consciousness, Motor aphasia
	47.1			+	1	1	
6	52	F	Lt	Hemorrhage	4	1	Disturbance of consciousness, Motor aphasia
	1.3			-	1	1	

mRS, modified Rankin Scale; POD, postoperative day; Rt, right; Lt, left; M, male; F, female

*Postoperative mRS was evaluated at 90 days after surgery or discharge

Table 3. Associated Factors for Postoperative Intracerebral Hemorrhage in Adult Moyamoya Disease Cases

	Postoperative ICH		Simple Logistic Regression Analysis		
	Yes	No	OR	95% CI	*P* Value[*]
Surgeries	6	126			
Age (years)	46.0 ± 9.4	42.6 ± 11.4	1.30†	0.63–2.72[†]	0.4750
Female sex	4 (66.7)	93 (73.8)	0.71	0.13–5.28	0.7051
Left side	3 (50.0)	98 (49.7)	0.97	0.17–5.40	0.9697
Hypertension	1 (16.7)	54 (27.7)	0.28	0.014–1.77	0.1908
APD usage	2 (33.3)	43 (22.1)	1.12	0.15–5.96	0.9026
MBs	0	15 (7.7)	[‡]	[‡]	0.2588
Clinical presentation					**0.0100**[§]
Hemorrhage	5 (83.3)	32 (16.4)	16.0[§]	2.46–312.8[§]	**0.0027**[§]
Cerebral infarction	1 (16.7)	48 (24.6)			
TIA	0	84 (43.1)			
Others	0	31 (15.9)			

Suzuki's stage ≥ 4	4 (66.7)	99 (50.8)	1.15	0.22–8.52	0.8738
Hemodynamic compromise	5 (83.3)	152 (77.9)	1.12	0.17–21.9	0.9207
Preoperative sBP (mmHg)	118.5 ± 16.7	123.7 ± 17.6	0.66‖	0.37–1.11‖	0.1273
Preoperative dBP (mmHg)	73.7 ± 8.7	73.9 ± 14.5	0.67‖	0.31–1.34‖	0.2680
Postoperative sBP (mmHg)	150.7 ± 21.6	132.1 ± 18.4	1.42‖	0.94-–2.16‖	0.0917
Postoperative dBP (mmHg)	83.8 ± 12.0	73.6 ± 13.6	1.55‖	0.80–3.20‖	0.1978
ΔsBP (mmHg)¶	32.2 ± 26.7	7.4 ± 19.6	1.69‖	1.17–2.58‖	**0.0058**
Δ dBP (mmHg)¶	10.2 ± 13.9	-2.0 ± 13.1	2.02‖	1.08-4.03‖	**0.0274**

APD, Anti-platelet drugs; CI, confidence interval; dBP, diastolic blood pressure; ICH, intracerebral hemorrhage; MBs, microbleeds; OR, odds ratio; sBP, systolic blood pressure; TIA, transient ischemic attack

The values given in parentheses are the percentage of the surgeries performed in each group (%)

*Bold values indicate statistical significance ($P < 0.05$)

†In the age parameter, OR and 95% CI were calculated by change of 10 years

‡OR and CI not shown because the number of postoperative ICH cases who had MBs = 0

§There was significant difference between four clinical presentation types ($P = 0.0100$); thus, OR, CI, and p values were calculated for "hemorrhage" vs, "cerebral infarction, TIA, and others" in the row below.

‖In the BP parameters, OR and 95% CI were calculated by change of 10 mmHg

¶ Δ BP = increase in BP from pre- to postoperative BP