

Factors Associated with Functional Decline After Direct Bypass Surgery for Moyamoya Disease: A Nationwide Multicenter Retrospective Cohort Study

Research Article

Eiichi Baba

Nippon Medical School

Fumihiko Matano

s00-078@nms.ac.jp

Nippon Medical School

Katsuya Umeoka

Nippon Medical School

Asami Kubota

Nippon Medical School

Yohei Nounaka

Nippon Medical School

yasuo murai

Nippon Medical School

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Abstract

Background

Direct bypass surgery is an established treatment for moyamoya disease, but factors associated with short-term postoperative functional decline remain incompletely defined. We evaluated factors associated with decline in activities of daily living after elective direct bypass surgery using a large Japanese multicenter administrative database.

Methods

We conducted a nationwide multicenter retrospective cohort study using the Japanese Diagnosis Procedure Combination database. Patients with moyamoya disease who underwent elective direct bypass surgery between April 2019 and December 2023 and had valid Barthel Index scores at admission and discharge were included. Functional decline was defined as a decrease in Barthel Index from admission to discharge. Multivariable logistic regression was used to estimate adjusted associations.

Results

Among 2,011 patients from 292 institutions, 139 (6.9%) had functional decline. Pediatric age (< 15 years) was associated with higher odds of decline (odds ratio [OR] 1.88, 95% confidence interval [CI] 1.03–3.41), as was anemia or postoperative transfusion (OR 1.99, 95% CI 1.18–3.36). Preoperative antithrombotic therapy was associated with lower odds of decline (OR 0.68, 95% CI 0.46–1.00). Hospital surgical volume was not significantly associated with the outcome.

Conclusions

In this large real-world cohort, pediatric age and anemia or postoperative transfusion were associated with short-term functional decline after direct bypass surgery, whereas preoperative antithrombotic therapy showed an inverse association. These findings may support perioperative risk assessment, but the observational design and administrative nature of the data preclude causal interpretation.

INTRODUCTION

Moyamoya disease is a chronic progressive cerebrovascular disorder characterized by steno-occlusive changes at the terminal internal carotid arteries and development of abnormal collateral vessels at the base of the brain [8, 9]. The disease is more common in East Asian populations and has a bimodal age distribution, with clinically important pediatric and adult presentations [2].

Direct revascularization, most commonly superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis, is an established surgical strategy for improving cerebral perfusion and reducing recurrent ischemic events in appropriately selected patients [3, 6, 14]. Despite technical advances, perioperative neurological and functional outcomes remain heterogeneous. Prior studies have identified clinical and angiographic factors associated with stroke or unfavorable outcome after revascularization, but many reports are single-center series or focus on selected age groups [1, 14, 15].

Preservation of activities of daily living is a central goal of treatment. Large administrative datasets can complement detailed institutional series by providing real-world information across many hospitals. The Japanese Diagnosis Procedure Combination (DPC) database contains discharge abstracts and claims-based information, including diagnoses, procedures, medication records, and functional measures, and has been widely used for nationwide clinical epidemiology research [5, 13]. We therefore aimed to identify factors associated with short-term functional decline after direct bypass surgery for moyamoya disease in a large multicenter cohort derived from the DPC database.

MATERIALS AND METHODS

Study design and data source

This nationwide multicenter retrospective cohort study used the Japanese Diagnosis Procedure Combination (DPC) database and was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. The DPC database contains discharge abstracts and administrative claims data from acute-care hospitals in Japan, including demographic characteristics, diagnoses, procedures, medication records, and selected functional-status measures [5, 13].

Study population

We identified patients with moyamoya disease (International Classification of Diseases, 10th Revision [ICD-10] code I675) who underwent direct bypass surgery (procedure code K6101) between April 2019 and December 2023. Only elective admissions (DPC admission type 100) were included. For patients with multiple procedures during the same hospitalization, only the initial procedure was retained. Patients with missing or invalid Barthel Index values at admission or discharge were excluded. The final analytic cohort included 2,011 patients. Patient selection is shown in Fig. 1.

Variables and definitions

Demographic variables included sex and age, categorized as < 15 years, 15–73 years, and ≥ 74 years. Preoperative functional status was assessed using the Barthel Index and categorized as 100 versus 0–95. Smoking history was defined as a smoking index > 0. Comorbidities identified from admission

diagnoses included diabetes mellitus, hypertension, dyslipidemia, prior cerebral hemorrhage, prior cerebral infarction, epilepsy, thyroid dysfunction, and anemia. For diabetes mellitus, hypertension, dyslipidemia, and epilepsy, diagnoses were additionally confirmed by concurrent medication use.

Hospital and perioperative variables

Annual institutional surgical volume was categorized as high volume (≥ 5 cases/year; 19 centers) or low volume (< 5 cases/year; 273 centers). Preoperative variables included cerebral blood flow (CBF) studies and antithrombotic medication use. CBF studies included single-photon emission computed tomography, positron emission tomography with 150-labeled gas, nonradioactive xenon CBF studies, or scintigraphy. Antithrombotic medications included aspirin, cilostazol, clopidogrel, ethyl eicosapentaenoate, rivaroxaban, apixaban, dabigatran, and warfarin. Intraoperative variables included CBF monitoring (procedure code K939-2) and extended anesthesia time (≥ 9 hours). Postoperative variables included CBF studies, magnetic resonance imaging, edaravone use, minocycline use, and blood transfusion. For the multivariable analysis, the anemia/transfusion variable was defined as anemia recorded at admission or postoperative blood transfusion.

Outcome measures

The primary outcome was functional decline, defined as any decrease in Barthel Index from admission to discharge. Postoperative hemorrhagic and ischemic complications, prolonged intensive care unit stay (≥ 7 days), and 30-day readmission were summarized descriptively.

Statistical analysis

Categorical variables are presented as frequencies and percentages. Associations with functional decline were first examined using the chi-square test or Fisher exact test, as appropriate. A multivariable logistic regression model was then fitted using the covariates shown in Table 2. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Multicollinearity was assessed using the variance inflation factor, with values > 5 considered indicative of relevant multicollinearity. Missing data were handled by complete-case analysis for the variables included in each analysis. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Analyses were performed using Stata/MP version 17.0 (StataCorp, College Station, TX, USA).

Table 2
Multivariable logistic regression analysis of factors associated with functional decline

Variable	Odds ratio	95% CI	P value
Age (reference: 15–73 years)			
<15 years	1.88	1.03–3.41	0.039
≥74 years	3.48	0.98–12.40	0.054
Anemia or postoperative transfusion	1.99	1.18–3.36	0.010
Preoperative antithrombotic therapy	0.68	0.46–1.00	0.049
Low-volume center (< 5 cases/year)	0.83	0.56–1.22	0.339
Diabetes mellitus	0.97	0.46–2.06	0.944
Postoperative CBF study within 2 days	0.91	0.62–1.33	0.621
Postoperative minocycline use	0.97	0.62–1.51	0.880
CI, confidence interval; CBF, cerebral blood flow.			

Ethics

The study used fully anonymized secondary DPC data and did not involve personally identifiable information. The protocol was approved by the Institutional Review Board of Nippon Medical School (Approval No. B-2025-1056), which waived the requirement for informed consent. The study was conducted in accordance with the Declaration of Helsinki and applicable guidelines.

RESULTS

Cohort characteristics

The final cohort comprised 2,011 patients treated at 292 institutions (Table 1). Overall, 1,409 patients (70.1%) were female, 114 (5.7%) were aged < 15 years, 1,880 (93.5%) were aged 15–73 years, and 17 (0.8%) were aged ≥ 74 years. A Barthel Index of 100 at admission was recorded in 1,872 patients (93.1%). Hypertension was present in 1,112 patients (55.3%), epilepsy as defined by diagnosis plus medication use in 933 (46.4%), diabetes mellitus in 129 (6.4%), and prior cerebral infarction in 348 (17.3%). Preoperative antithrombotic therapy was recorded in 771 patients (38.3%), and intraoperative CBF monitoring was performed in 1,729 (86.0%).

Table 1
Patient characteristics and selected perioperative variables

Variable	n (%)
Demographics	
Total patients	2,011 (100)
Female sex	1,409 (70.1)
Age group	
<15 years	114 (5.7)
15–73 years	1,880 (93.5)
≥74 years	17 (0.8)
Preoperative status	
Barthel Index 100	1,872 (93.1)
Smoking history*	525 (28.0)
Comorbidities	
Diabetes mellitus	129 (6.4)
Hypertension	1,112 (55.3)
Dyslipidemia	454 (22.6)
Prior cerebral hemorrhage	50 (2.5)
Prior cerebral infarction	348 (17.3)
Epilepsy (diagnosis plus medication)	933 (46.4)
Thyroid dysfunction	66 (3.3)
Anemia	85 (4.2)
Perioperative variables	
Preoperative CBF study	188 (9.3)
Preoperative antithrombotic therapy	771 (38.3)
Intraoperative CBF monitoring	1,729 (86.0)
Extended anesthesia (≥ 9 h)	561 (27.9)
*Smoking-history data were missing for 138 patients. †Hospital-volume values are numbers and percentages of institutions; all other values are patient-level n (%) unless otherwise indicated. CBF, cerebral blood flow.	

Variable	n (%)
Demographics	
Hospital characteristics†	
High-volume centers (≥ 5 cases/year)	19/292 (6.5)
Low-volume centers (< 5 cases/year)	273/292 (93.5)
*Smoking-history data were missing for 138 patients. †Hospital-volume values are numbers and percentages of institutions; all other values are patient-level n (%) unless otherwise indicated. CBF, cerebral blood flow.	

Functional decline and other outcomes

Functional decline from admission to discharge occurred in 139 patients (6.9%). Hemorrhagic complications occurred in 32 patients (1.6%) and ischemic complications in 119 (5.9%). A prolonged intensive care unit stay of ≥ 7 days occurred in 71 patients (3.5%), and 15 patients (0.7%) were readmitted within 30 days.

Univariable associations

Variables associated with functional decline in univariable analyses included age group ($P = 0.005$), preoperative Barthel Index < 100 ($P < 0.001$), prior cerebral hemorrhage ($P = 0.045$), epilepsy ($P < 0.001$), postoperative magnetic resonance imaging within 2 days ($P < 0.001$), and postoperative transfusion ($P = 0.004$).

Multivariable analysis

In the multivariable model (Table 2), age < 15 years was associated with higher odds of functional decline compared with age 15–73 years (OR 1.88, 95% CI 1.03–3.41; $P = 0.039$). Age ≥ 74 years had a larger point estimate, but the association did not reach conventional statistical significance (OR 3.48, 95% CI 0.98–12.40; $P = 0.054$). Anemia or postoperative transfusion was associated with higher odds of functional decline (OR 1.99, 95% CI 1.18–3.36; $P = 0.010$). Preoperative antithrombotic therapy was associated with lower odds of decline (OR 0.68, 95% CI 0.46–1.00; $P = 0.049$). Low institutional surgical volume, diabetes mellitus, an early postoperative CBF study, and postoperative minocycline use were not significantly associated with functional decline.

DISCUSSION

Principal findings

In this nationwide multicenter retrospective cohort of 2,011 patients undergoing elective direct bypass surgery for moyamoya disease, 6.9% had a decrease in Barthel Index by discharge. Pediatric age and the composite variable of admission anemia or postoperative transfusion were associated with higher

adjusted odds of short-term functional decline. Preoperative antithrombotic therapy showed an inverse association, whereas institutional surgical volume was not associated with the primary outcome. These results should be interpreted as associations rather than causal effects.

Age and functional decline

Pediatric patients had higher adjusted odds of functional decline. Children with moyamoya disease differ from adults in clinical presentation, cerebrovascular physiology, and perioperative management requirements, and specialized perioperative protocols have been emphasized in pediatric practice [7, 10]. However, interpretation of our pediatric finding requires particular caution because the Barthel Index was developed as an activities-of-daily-living measure and may not capture age-dependent function in children as well as pediatric-specific outcome instruments. The association may therefore reflect both biological vulnerability and limitations of outcome measurement. The estimate for patients aged ≥ 74 years was imprecise because only 17 patients were in this category, and the 95% CI included the null.

Anemia and transfusion

The association between admission anemia or postoperative transfusion and functional decline is clinically plausible in a population with impaired cerebrovascular reserve, but the composite variable cannot distinguish the contribution of baseline anemia from perioperative blood loss, surgical complexity, or the indication for transfusion. Transfusion is also a postoperative exposure and may function as a marker of a complicated perioperative course rather than a causal risk factor. Accordingly, these data support attention to perioperative hemoglobin status and blood loss, but they do not establish that a specific transfusion threshold or anemia-correction strategy improves outcome.

Preoperative antithrombotic therapy

Preoperative antithrombotic therapy was associated with lower odds of functional decline, with a 95% CI whose upper bound rounded to 1.00. Antiplatelet management is an important component of perioperative moyamoya care, and expert consensus in pediatric revascularization has supported continuation of aspirin in selected settings [10]. Nevertheless, treatment allocation in this observational dataset was not randomized and may have been influenced by presentation, hemorrhagic risk, surgeon preference, or institutional practice. The observed association therefore should not be interpreted as evidence to initiate or continue antithrombotic therapy in an individual patient without considering the competing ischemic and hemorrhagic risks.

Institutional volume

We did not identify a significant association between the study's institutional volume threshold and functional decline. A prior national analysis of pediatric moyamoya admissions reported volume-outcome relationships for selected outcomes [11]. Differences in population, outcome definition, health-care system, and the relatively low cutoff used to define high volume in the present study may account for the differing findings. Importantly, absence of a statistically significant association does not establish equivalence between high- and low-volume centers.

Comparison with previous literature

The observed ischemic complication rate of 5.9% is within the range reported in prior revascularization series and reviews, although direct comparison is limited by differences in age, surgical technique, indication, and outcome definitions [1, 7, 14]. Detailed angiographic variables such as posterior circulation involvement and specific collateral patterns have been linked to ischemic presentation or postoperative outcomes in prior studies [4, 12, 15], but such information was not available in the DPC dataset. The present study therefore complements, rather than replaces, granular imaging-based cohort studies.

Strengths and limitations

The main strengths of this study are its large sample size, multicenter design, inclusion of 292 institutions, and use of a standardized administrative dataset that reflects real-world practice across Japan. Several limitations are important. First, the retrospective observational design precludes causal inference and residual confounding is likely. Second, administrative coding may be affected by misclassification, and the database lacks detailed angiographic findings, operative technique, bypass configuration, collateral status, intraoperative hemodynamics, and surgeon-level variables. Third, the primary outcome was limited to change in Barthel Index between admission and discharge; it does not measure long-term neurological recovery, stroke-specific disability, cognitive outcome, or quality of life. The very high proportion of patients with an admission Barthel Index of 100 also creates a ceiling-dominated baseline distribution, while pediatric use of the Barthel Index introduces additional measurement limitations. Fourth, the anemia/transfusion variable combines a baseline condition with a postoperative exposure, limiting temporal and mechanistic interpretation. Fifth, the inverse association with antithrombotic therapy is susceptible to confounding by indication and treatment-selection bias. Sixth, the small number of patients aged ≥ 74 years produced imprecise estimates. Finally, the predominantly Japanese cohort may limit generalizability to other health-care systems and populations.

Implications

These findings identify readily observable characteristics associated with short-term functional decline after direct bypass surgery and may help frame perioperative risk discussions. They also generate testable hypotheses regarding age-specific vulnerability, perioperative hemoglobin management, and antithrombotic practice. Prospective studies with standardized neurological and functional outcomes, detailed imaging and operative variables, and longer follow-up are needed before management changes can be recommended.

CONCLUSIONS

In a nationwide multicenter DPC cohort of 2,011 patients undergoing elective direct bypass surgery for moyamoya disease, pediatric age and admission anemia or postoperative transfusion were associated with higher odds of Barthel Index decline by discharge, whereas preoperative antithrombotic therapy was

associated with lower odds. Institutional surgical volume was not significantly associated with the outcome. Because the study is observational and relies on administrative data and a short-term functional endpoint, these associations should be used for hypothesis generation and perioperative risk assessment rather than causal treatment recommendations.

Declarations

Competing interests:

The authors have no relevant financial or non-financial interests to disclose.

Human Ethics and Consent to Participate declarations:

This study was approved by the Institutional Review Board of Nippon Medical School (Approval No. B-2025-1056). The requirement for informed consent was waived by the Institutional Review Board because fully anonymized secondary data were used. The study was conducted in accordance with the Declaration of Helsinki and applicable ethical guidelines.

Consent to publish:

Not applicable. The manuscript contains no identifiable individual participant data.

Clinical trial number

not applicable.

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Author Contribution

Eiichi Baba and Fumihiro Matano contributed to the conception and design of the study. Eiichi Baba performed data curation and analysis and drafted the initial manuscript. Fumihiro Matano supervised the study and contributed to data interpretation and manuscript revision. Katsuya Umeoka, Asami Kubota, Yohei Nounaka, and Yasuo Murai contributed to the interpretation of the results and critically revised the manuscript. All authors read and approved the final manuscript.

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Data Availability

The individual-level DPC data analyzed in this study are not publicly available. Information regarding access to the underlying data may be obtained from the corresponding author, subject to the requirements of the data provider and relevant institutional approvals.

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Figures

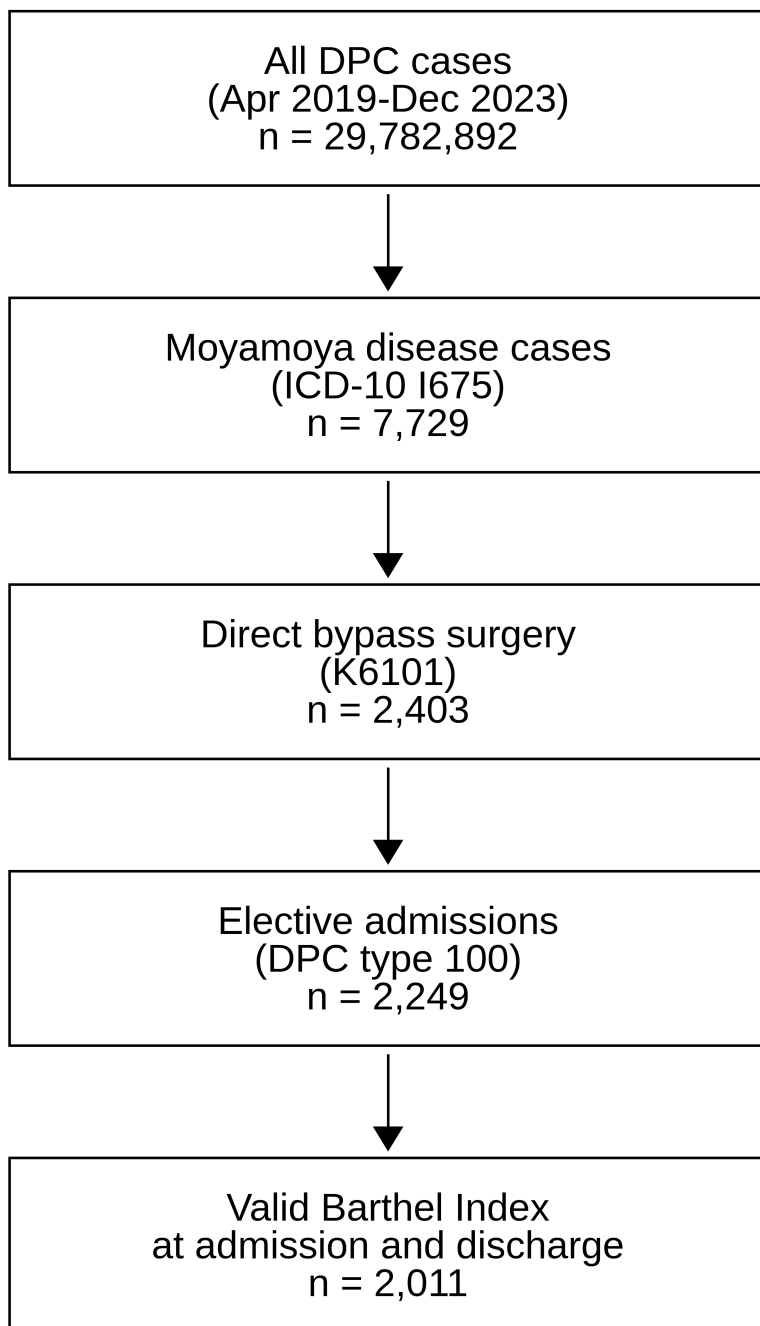


Figure 1

Flow diagram of patient selection. Among all hospitalized patients recorded in the DPC database between April 2019 and December 2023 (n=29,782,892), 7,729 had a diagnosis of moyamoya disease (ICD-10 I675). Of these, 2,403 underwent direct bypass surgery (K6101). After restriction to elective admissions and exclusion of cases without valid Barthel Index data at admission and discharge, 2,011 patients were included in the final analytic cohort.

