



Original Research

Clinical and CT perfusion outcomes after direct STA–MCA bypass in moyamoya and non-moyamoya steno-occlusive disease: an Indonesian single-center cohort

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ABSTRACT

Background: Direct superficial temporal artery-to-middle cerebral artery (STA–MCA) bypass is used for selected haemodynamic cerebrovascular disorders, but comparative data between moyamoya and non-moyamoya disease remain limited in Indonesia.

Methods: Consecutive patients undergoing direct STA–MCA bypass from 2021 to 2025 were retrospectively analysed. Clinical and operative outcomes were assessed in 68 patients; paired CT perfusion data were available in 41.

Results: The cohort included 40 patients with moyamoya disease and 28 with non-moyamoya disease, predominantly intracranial atherosclerotic disease [27/28 (96%)]. Patients with moyamoya were younger [41 (29–49) vs 48 (38–59) years; $p = 0.003$] and had lower rates of diabetes mellitus [7% vs 29%; $p = 0.041$] and hypertension [42% vs 86%; $p < 0.001$]. Bypass patency was documented in 90% versus 100% ($p = 0.226$). Paired modified Rankin Scale scores improved in both cohorts: from 2.08 ± 1.51 to 1.38 ± 1.39 in moyamoya (mean difference 0.70; $p < 0.001$) and from 2.82 ± 1.19 to 1.86 ± 1.33 in non-moyamoya disease (mean difference 0.96; $p < 0.001$). M4 frontal clipping time was longer in moyamoya [33 (31–37) vs 26 (24–32) minutes; $p = 0.002$]. Postoperative seizure occurred in 15% versus 7% ($p = 0.455$), and ischaemic stroke in 0% versus 11% ($p = 0.065$). In the CT perfusion cohort, pre-bypass Tmax was higher in non-moyamoya disease [2.17 (1.25–3.34) vs 1.31 (1.10–1.92); $p = 0.048$], while infarct volume was higher in moyamoya [8.65 (1.41–17.23) vs 5.63 (3.35–7.32) mL; $p = 0.034$]. No follow-up CT perfusion parameter differed significantly.

Conclusion: Direct STA–MCA bypass was followed by functional improvement in both cohorts and comparable follow-up CT perfusion profiles.

1. Introduction

Direct superficial temporal artery-middle cerebral artery (STA–MCA) bypass provides immediate flow augmentation to hypoperfused cortex and is a cornerstone revascularisation strategy for symptomatic moyamoya angiopathy (progressive terminal internal carotid stenosis with

fragile basal collaterals) and selected non-moyamoya patients with haemodynamic insufficiency [1,2]. As non-moyamoya steno-occlusive disease often reflects atherosclerosis or occlusion with heterogeneous collateral reserve, earlier randomised trials reported no overall benefit, emphasising refined haemodynamic selection [3,4].

Computed tomography perfusion (CTP) can quantify relative

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perfusion deficits and infarct–penumbra volumes, enabling objective assessment of revascularisation and surveillance for cerebral hyperperfusion syndrome, a recognised complication after direct bypass particularly in adult moyamoya [5–7]. In Indonesia, where stroke burden is high and advanced neurovascular services remain concentrated in few centres, comparative perfusion-based bypass data are scarce [8]. We therefore compared early clinical events and follow-up CTP profiles after direct STA–MCA bypass in Indonesian patients with moyamoya versus non-moyamoya disease to inform perioperative haemodynamic management and service planning.

2. Methods

2.1. Study design and setting

This retrospective single-center single-surgeon cohort study was conducted at Prof. Dr. Mahar Mardjono National Brain Center Hospital, Indonesia, to evaluate early clinical outcomes and follow-up computed tomography (CT) perfusion findings after direct superficial temporal artery-to-middle cerebral artery (STA–MCA) bypass. Consecutive patients who underwent direct STA–MCA bypass between 2021 and 2025 were identified from the institutional cerebrovascular surgery database and operative records. Patients were classified into moyamoya and non-moyamoya cohorts according to the underlying cerebrovascular diagnosis established from the clinical record and preoperative imaging. Because moyamoya and non-moyamoya steno-occlusive disease differ in underlying biology, collateral architecture, and expected perioperative risk profile, the comparison between cohorts was interpreted as an exploratory clinical comparison rather than as a definitive pathophysiological equivalence analysis. The study was therefore framed as an early institutional experience evaluating the feasibility of standardized direct STA–MCA bypass and perioperative CT perfusion monitoring in an Indonesian cerebrovascular center.

2.2. Patient selection

Preoperative diagnosis and staging were established using digital subtraction angiography and CT or Magnetic Resonance Angiography (MRA) according to institutional protocols. Patients were classified as having moyamoya disease when preoperative angiography demonstrated stenosis or occlusion of the terminal internal carotid artery and/or proximal anterior or middle cerebral arteries with abnormal basal or leptomeningeal collateral networks, according to established angiographic criteria. Patients were classified as non-moyamoya steno-occlusive disease when the treating cerebrovascular team identified symptomatic anterior-circulation steno-occlusive disease without angiographic features sufficient for moyamoya disease. The non-moyamoya cohort was further categorized by etiology as intracranial atherosclerotic disease, dissection, radiation vasculopathy, or other steno-occlusive vasculopathy. RNF213 genetic testing was not routinely available and was therefore not used for diagnostic classification.

Eligible patients were those who underwent direct STA–MCA bypass and had sufficient demographic, operative, and perioperative imaging data for analysis. Inclusion required availability of baseline clinical characteristics, operative parameters, and at least one perioperative clinical outcome assessment. For perfusion analyses, paired CT perfusion studies were required, including a preoperative study obtained before surgery and a postoperative study obtained during routine follow-up after revascularization. Surgical candidacy was determined by a multidisciplinary cerebrovascular team based on recurrent or clinically significant ischemic symptoms, anterior-circulation steno-occlusive disease, surgically accessible donor and recipient vessels, and baseline CT perfusion evidence of haemodynamic compromise. CT perfusion supported surgical selection when territorial hypoperfusion, infarct–penumbra mismatch, or delayed contrast transit was present in the symptomatic hemisphere. The thresholds of time to maximum

(Tmax) > 6 s and relative cerebral blood flow (CBF) < 30% were used to define tissue compartments on CT perfusion rather than as standalone surgical-candidacy thresholds. No acetazolamide challenge, positron emission tomography oxygen extraction fraction measurement, or standardized vasodilatory cerebrovascular reserve protocol was performed; therefore, formal distinction between compensated hypoperfusion and stage II haemodynamic failure could not be established. A total of 68 patients met the study criteria, including 40 with moyamoya disease and 28 with non-moyamoya disease. All 68 patients were included in the clinical and operative analyses. Patients with available paired preoperative and follow-up CT perfusion studies were included in the perfusion analysis, comprising 29 patients with moyamoya disease and 12 patients with non-moyamoya disease.

2.3. Data collection

Clinical and perioperative data were extracted from medical records, operative notes, anesthesia records, and imaging archives using a pre-defined data collection form. Baseline variables included age, sex, diabetes mellitus, hypertension, presenting symptoms, and operated side. Operative variables included STA donor pressure, MCA recipient pressure before and after bypass, bypass pressure after anastomosis, recipient-vessel location, and recipient-vessel temporary clipping time. Recipient vessels were categorized as M4 temporal, M4 frontal, anterior cerebral artery, or angular branch according to operative documentation.

2.4. Surgical procedure

All patients underwent direct extracranial-to-intracranial revascularization with STA–MCA bypass performed by the cerebrovascular surgery team. Briefly, the STA donor branch was harvested and prepared microscurgically, followed by end-to-side anastomosis to a cortical recipient artery selected intraoperatively on the basis of vessel caliber and accessibility. When anatomy permitted, at least two recipient were used, on the frontal and temporal side, with the aim of distributing donor flow across more than one cortical territory (Fig. 1). A representative operative video demonstrating the standardized direct STA–MCA bypass technique used in this cohort is provided as [Supplementary Video 1](#). Intraoperative arterial line pressure on the donor and recipient were recorded routinely, as was recipient vessel temporary clipping time. Only direct STA–MCA bypass procedures were included in the analysis.

Perioperative management followed institutional cerebrovascular protocols. Aspirin 80 mg was initiated at least 6 days before surgery in all patients and continued postoperatively. The antiplatelet agent was standardized across cohorts; however, the intended duration differed according to the underlying disease mechanism. In moyamoya disease, aspirin was continued for at least 2 weeks after surgery and could be discontinued thereafter according to postoperative clinical and angiographic assessment. In patients with intracranial atherosclerotic disease, aspirin was intended for lifelong secondary stroke prevention unless contraindicated. Intraoperative management consisted of normocapnic anesthesia, continuous neurophysiologic monitoring, and strict blood pressure control based on individualized targets. All patients were admitted to the intensive care unit postoperatively for close hemodynamic monitoring, with tight blood pressure control and prophylactic antiepileptic therapy administered at the discretion of the treating neurosurgeon.

2.5. CT perfusion assessment

Perioperative cerebral perfusion was evaluated using CT perfusion performed before and after bypass surgery according to institutional practice. CT perfusion maps were generated using syngo.via VB80H software (Siemens Healthineers, Erlangen, Germany) with

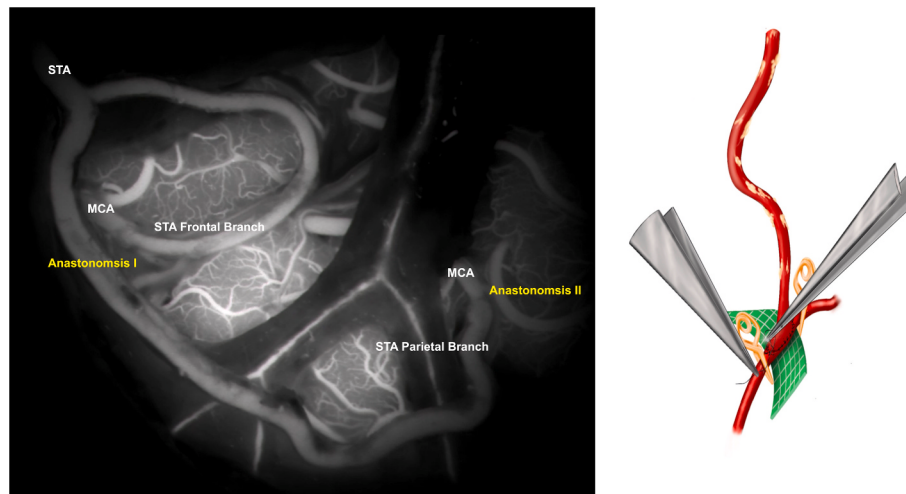


Fig. 1. Intraoperative indocyanine green videoangiography after double-barrel STA-MCA bypass. Intraoperative indocyanine green (ICG) videoangiographic image obtained after completion of a double-barrel superficial temporal artery-to-middle cerebral artery (STA-MCA) bypass. The superior donor limb, corresponding to the frontal branch of the STA, is anastomosed to a cortical MCA branch (Anastomosis I), whereas the inferior donor limb, corresponding to the parietal branch of the STA, is anastomosed to a second cortical MCA branch (Anastomosis II). This configuration reflects the surgical technique, which uses two cortical recipient anastomoses to distribute donor flow more broadly, augment revascularization, and potentially reduce focal postoperative hyperperfusion. The ICG image confirms patency of both bypasses and donor-to-recipient flow. Abbreviations: ICG, indocyanine green; STA, superficial temporal artery; MCA, middle cerebral artery.

deconvolution-based post-processing and automatic segmentation. Extracted parameters included maximum intensity projection (MIP), CBF, cerebral blood volume (CBV), mean transit time (MTT), Tmax, hypoperfusion volume, infarct volume, penumbra volume, mismatch ratio, and penumbra rescue ratio (PRR).

For hemispheric perfusion parameters, regions of interest were assessed across the operated or symptomatic hemisphere and compared with the corresponding contralateral hemisphere. Therefore, MIP, CBF, CBV, MTT, and Tmax are reported as software-derived relative hemispheric values rather than absolute quantitative perfusion units or absolute seconds. Tissue-based volumetric parameters were derived using standardized thresholds across cases. Hypoperfusion volume was defined as tissue with Tmax > 6 s, infarct core as tissue with relative CBF < 30%, and penumbra volume as hypoperfusion volume minus infarct core. Mismatch ratio was calculated from the relationship between hypoperfusion and infarct core volumes, while PRR was expressed as a percentage.

Standardized CT perfusion obtained before surgery and repeated during routine follow-up after revascularization was required for inclusion in the perfusion analysis. Quality control and region-of-interest delineation were performed by a radiologist blinded to clinical outcomes. Preoperative and postoperative perfusion data were analyzed separately to compare perfusion status between cohorts and to explore associations with postoperative complications. For descriptive temporal analysis, follow-up CT perfusion assessments were categorized as early or late according to a 30-day postoperative cutoff.

2.6. Outcomes

The primary analysis compared baseline characteristics, operative variables, early postoperative complications, functional outcomes, and preoperative and follow-up CT perfusion parameters between the moyamoya and non-moyamoya cohorts. Functional status was assessed using the modified Rankin Scale (mRS) before and after bypass. Early postoperative complications of interest were postoperative seizure and postoperative ischemic stroke, as documented during the early postoperative course. Patient-level adverse event summaries were reported descriptively. Given the limited number of outcome events, complication-focused analyses were considered hypothesis-generating. Bypass patency was assessed from postoperative vascular imaging

when available, supplemented by intraoperative indocyanine green videoangiography and Doppler assessment. A bypass was considered patent when donor-to-recipient flow was documented; patency was classified as unknown when postoperative documentation was insufficient.

2.7. Statistical analysis

Continuous variables were assessed for distributional characteristics using visual inspection and normality testing, as appropriate. Normally distributed variables were summarized as mean $\pm$ standard deviation, whereas skewed variables were summarized as median with inter-quartile range. Categorical variables were summarized as counts and percentages. Between-group comparisons were performed using the independent-samples *t*-test or Mann-Whitney *U* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Within-group preoperative and postoperative mRS scores were compared using the paired-samples *t*-test. Because the study was retrospective, modest in size, and involved multiple exploratory comparisons, no multiplicity correction was applied; therefore, *p*-values were interpreted descriptively rather than as confirmatory evidence. Complication-focused analyses were constrained by sparse event counts, including 6 postoperative seizures in the moyamoya cohort and 3 postoperative ischemic strokes in the non-moyamoya cohort. Accordingly, no multivariable model was constructed, and adverse event findings were interpreted descriptively. All tests were two-sided, and *p* < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 31 (IBM Corp., Armonk, NY, USA).

2.8. Ethics

The study was approved by the Research Ethics Committee of Prof. Dr. Mahar Mardjono National Brain Center Hospital, Jakarta, Indonesia (DP.04.03/D.XXIII.9/271/2025). Given the retrospective observational design and use of de-identified data, the requirement for individual informed consent was waived in accordance with institutional policy and the Declaration of Helsinki.

3. Results

3.1. Patient characteristics

A total of 68 patients underwent direct STA–MCA bypass, comprising 40 patients with moyamoya disease and 28 patients with non-moyamoya steno-occlusive disease (Table 1). The non-moyamoya cohort consisted predominantly of intracranial atherosclerotic disease [27/28 (96%)], with one patient [1/28 (4%)] classified as other non-moyamoya steno-occlusive vasculopathy; no cases were classified as dissection or radiation vasculopathy. Compared with the non-moyamoya cohort, patients with moyamoya were significantly younger [41 years (IQR, 29–49) vs 48 years (IQR, 38–59); $p = 0.003$]

Table 1

Baseline demographic and preoperative clinical characteristics of patients undergoing direct STA–MCA bypass, stratified by moyamoya status.

Characteristic	Moyamoya (n = 40)	Non-moyamoya (n = 28)	p-Value
Age, median (IQR)	41 (29–49)	48 (38–59)	0.003
Sex, n (%)			0.421
Male	30 (75%)	18 (64%)	
Female	10 (25%)	10 (36%)	
Comorbidities, n (%)			
Diabetes mellitus	3 (7%)	8 (29%)	0.041
Hypertension	17 (42%)	24 (86%)	<0.001
Presenting symptoms, n (%)			
Seizure	5 (12%)	0 (0%)	0.073
Hemiparesis	36 (90%)	26 (93%)	1
Dysphagia	1 (2%)	1 (4%)	1
Dysarthria	14 (35%)	15 (54%)	0.144
Headache	8 (20%)	4 (14%)	0.748
Aphasia	13 (32%)	5 (18%)	0.265
Monoparesis	6 (15%)	9 (32%)	0.137
Hemihypesthesia	4 (10%)	2 (7%)	1
Numbness	10 (25%)	7 (25%)	1
Operated side, n (%)			0.33
Left	19 (47%)	17 (61%)	
Right	21 (52%)	11 (39%)	
Etiology, n (%)			
Intracranial atherosclerotic disease		27 (96%)	
Dissection		0 (0%)	
Radiation vasculopathy		0 (0%)	
Other steno-occlusive vasculopathy		1 (4%)	
Patency, n (%)			0.226
Patent	36 (90%)	28 (100%)	
Not Patent	1 (2.5%)	0 (0%)	
Unknown	3 (7.5%)	0 (0%)	
mRS Pre Bypass, n (%)			0.017
0	2 (5%)	0 (0%)	
1	19 (47%)	5 (18%)	
2	7 (17%)	6 (21%)	
3	2 (5%)	7 (25%)	
4	6 (15%)	9 (32%)	
5	4 (10%)	1 (4%)	
6	0 (0%)	0 (0%)	
mRS Post Bypass, n (%)			0.123
0	11 (27%)	5 (18%)	
1	17 (42%)	7 (25%)	
2	5 (12%)	7 (25%)	
3	1 (2%)	5 (18%)	
4	5 (12%)	4 (14%)	
5	1 (2%)	0 (0%)	
6	0 (0%)	0 (0%)	

Values are presented as median (interquartile range) or n (%), unless otherwise specified. p-values were calculated using the Mann–Whitney *U* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Etiology is shown only for the non-moyamoya cohort; p-values were not applicable for this descriptive breakdown.

Abbreviations: IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin Scale; SD, standard deviation; STA, superficial temporal artery.

and had lower rates of diabetes mellitus [3 (7%) vs 8 (29%); $p = 0.041$] and hypertension [17 (42%) vs 24 (86%); $p < 0.001$]. Pre-bypass mRS distribution differed significantly between groups ($p = 0.017$), whereas post-bypass mRS distribution did not ($p = 0.123$).

Documented bypass patency did not differ significantly between groups ($p = 0.226$). Patency was confirmed in 36 patients (90%) with moyamoya and 28 patients (100%) with non-moyamoya disease; one moyamoya patient had a non-patent bypass and three had unknown patency status. No perioperative death occurred in either cohort.

3.2. Functional outcome after bypass

Both cohorts demonstrated significant improvement in paired pre-operative and postoperative mRS scores (Table 2). In the moyamoya cohort, mean mRS improved from 2.08 ± 1.51 to 1.38 ± 1.39 , with a mean paired difference of 0.70 points (95% CI, 0.40–1.00; $p < 0.001$). In the non-moyamoya cohort, mean mRS improved from 2.82 ± 1.19 to 1.86 ± 1.33 , with a mean paired difference of 0.96 points (95% CI, 0.55–1.38; $p < 0.001$).

3.3. Operative characteristics and early postoperative complications

Operative characteristics are summarized in Table 3. Intraoperative STA, MCA, and bypass pressures were comparable between groups. Among recipient-vessel clipping times, only M4 frontal clipping time differed significantly, being longer in the moyamoya cohort than in the non-moyamoya cohort [33 min (IQR, 31–37) vs 26 min (IQR, 24–32); $p = 0.002$]. The number of anastomoses, recipient-vessel distribution, and M4 temporal clipping time did not differ significantly between groups.

Early postoperative seizure occurred in 6 patients (15%) with moyamoya and 2 patients (7%) with non-moyamoya disease ($p = 0.455$). Postoperative ischemic stroke occurred only in the non-moyamoya cohort [0 (0%) vs 3 (11%)], although this difference did not reach statistical significance ($p = 0.065$).

3.4. Perioperative CT perfusion findings

Perioperative CT perfusion findings are presented in Table 4. CT perfusion data were available for 29 patients with moyamoya and 12 patients with non-moyamoya disease. Before bypass, the non-moyamoya cohort had significantly higher Tmax than the moyamoya cohort [2.17 (IQR, 1.25–3.34) vs 1.31 (IQR, 1.10–1.92); $p = 0.048$]. Conversely, pre-bypass infarct volume was significantly higher in the moyamoya cohort [8.65 mL (IQR, 1.41–17.23) vs 5.63 mL (IQR, 3.35–7.32); $p = 0.034$]. No other overall pre-bypass CT perfusion parameter differed significantly between groups.

In the descriptive early versus late follow-up subgroup analysis, moyamoya patients assessed at later follow-up had higher pre-bypass hypoperfusion volume [54.65 mL (IQR, 25.74–92.57) vs 23.66 mL (IQR, 4.30–36.25); $p = 0.011$] and penumbra volume [45.51 mL (IQR, 18.48–70.92) vs 16.02 mL (IQR, 2.73–26.03); $p = 0.032$]. At follow-up CT perfusion assessment, no statistically significant between-group differences were observed in MIP, CBF, CBV, MTT, Tmax, hypoperfusion volume, infarct volume, penumbra volume, mismatch ratio, PRR, or timing of follow-up imaging. These findings suggest that measured follow-up CT perfusion profiles were comparable between groups within the observed postoperative interval.

3.5. Patient-level adverse event findings

Patient-level details of postoperative seizure and ischemic stroke are shown in Table 5 and Table 6. Among patients with postoperative seizure, no new persistent neurological deficit was documented at final outcome assessment. Postoperative hyperperfusion and edema were not documented in cases with available imaging information, whereas postoperative haemorrhage was recorded in the two non-moyamoya

Table 2
Paired-samples *t*-test of preoperative and postoperative mRS scores.

Group	n	Preoperative mRS, mean ± SD	Postoperative mRS, mean ± SD	Mean difference, mean ± SD	95% CI of difference	t	df	p-value
Moyamoya	40	2.08 ± 1.51	1.38 ± 1.39	0.70 ± 0.94	0.40 to 1.00	4.714	39	<0.001
Non-moyamoya	28	2.82 ± 1.19	1.86 ± 1.33	0.96 ± 1.07	0.55 to 1.38	4.765	27	<0.001

Values are presented as mean ± standard deviation, unless otherwise specified. Mean difference was calculated as preoperative mRS minus postoperative mRS; therefore, a positive value indicates postoperative functional improvement. Abbreviations: CI, confidence interval; df, degrees of freedom; mRS, modified Rankin Scale; SD, standard deviation.

Table 3
Operative characteristics and early postoperative complications after direct STA–MCA bypass, stratified by moyamoya status.

Characteristic	Moyamoya (n = 40)	Non-moyamoya (n = 28)	P-Value
Number of anastomoses, n (%)			
Single	6 (15%)	3 (11%)	0.179
Double	30 (75%)	25 (89%)	0.179
Triple	4 (10%)	0 (0%)	0.179
Intraoperative pressure measurements, median (IQR)			
STA Pressure, mmHg	74.00 (70.25–78)	75.50 (67.50–82)	0.798
MCA Pressure, mmHg	42.50 (37.25–47)	48.50 (37.25–64)	0.28
Bypass Pressure, mmHg	72 (63–77)	74 (64.75–81.25)	0.502
Recipient vessel, n (%)			
M4 temporal	39 (97%)	26 (96%)	0.776
M4 frontal	35 (87%)	26 (100%)	0.061
ACA	3 (7%)	1 (4%)	0.543
Angular	1 (2%)	0 (0%)	0.426
Vessel clipping time, median (IQR)			
M4 temporal, minutes	34 (30.75–37)	30 (26–37.50)	0.321
M4 frontal, minutes	33 (31–37)	26 (24–32)	0.002
ACA, minutes	34 (28–34.50)	28	0.806
Angular, minutes	40.00	–	
Early postoperative complications, n (%)			
Seizure	6 (15%)	2 (7%)	0.455
Ischemic Stroke	0 (0%)	3 (11%)	0.065

Values are presented as median (interquartile range) or n (%), unless otherwise specified. p-values were calculated using the Mann–Whitney *U* test for continuous variables and the chi-square test or Fisher’s exact test for categorical variables, as appropriate. A dash indicates that no value was available because no patient in that group had the corresponding recipient vessel. Abbreviations: ACA, anterior cerebral artery; IQR, interquartile range; MCA, middle cerebral artery; M4, cortical segment of the middle cerebral artery; STA, superficial temporal artery.

patients who developed seizure. All postoperative ischemic strokes occurred in the non-moyamoya cohort, involved the left MCA/anterior-circulation territory according to available postoperative documentation, and occurred 8, 16, and 9 days after surgery. All three patients had documented graft patency, and no graft thrombosis or *peri*-event hypotension was recorded. However, infarct-pattern classification, including whether the events represented watershed infarction, could not be determined because routine postoperative MRI with diffusion-weighted imaging was not performed. Given the small number of events, these observations were interpreted descriptively and were not considered sufficient to infer mechanism or independent predictors.

3.6. Exploratory supplementary analyses

As postoperative adverse events were infrequent, all complication-focused analyses were considered descriptive and hypothesis-generating (Supplementary File). Supplementary subgroup tables are provided to show the distribution of selected clinical and perfusion variables according to complication status. These findings should be

interpreted cautiously because of sparse event counts and limited statistical power, and they should not be considered definitive prognostic models.

4. Discussion

In this Indonesian single-center cohort of direct STA–MCA bypass, moyamoya and non-moyamoya steno-occlusive disease showed distinct baseline clinical and preoperative perfusion profiles, while measured follow-up CT perfusion parameters did not differ significantly between groups among patients with paired perfusion imaging. Both cohorts demonstrated significant postoperative improvement in paired mRS analysis. These findings should be interpreted as an early institutional experience with standardized direct bypass and CT perfusion monitoring rather than as evidence of equivalent haemodynamic biology between disease categories. The absence of statistically significant postoperative perfusion differences may reflect limited sample size, heterogeneous disease mechanisms, variable timing of follow-up imaging, and selection of patients with available paired CT perfusion studies.

For intracranial atherosclerotic disease (ICAD)-related steno-occlusion, these findings must be interpreted within the historical trial signal that perioperative hazard can erase haemodynamic benefit. The EC/IC Bypass Study (n = 1377) demonstrated no advantage of STA–MCA bypass over best medical management for atherosclerotic carotid/MCA disease, and even suggested harm in certain angiographic subgroups [4]. The Carotid Occlusion Surgery Study (COSS) advanced selection by targeting positron emission tomography oxygen extraction fraction (PET OEF)-defined haemodynamic failure in symptomatic internal carotid artery (ICA) occlusion but was terminated for futility; critically, 30-day ipsilateral ischaemic stroke was far higher after surgery (14.4% vs 2.0%) [3]. The Carotid and Middle Cerebral Artery Occlusion Surgery Study (CMOSS), using CTP-based selection and refined operator and centre criteria across 13 Chinese centres (n = 324), showed no significant benefit in the composite primary endpoint but fewer late ipsilateral strokes beyond 30 days in the surgical arm, supporting an “early hazard, late protection” pattern that depends on low perioperative event rates [9]. In contrast, the Japanese Extracranial–Intracranial Bypass Trial 2 applied more stringent haemodynamic thresholds, enrolling patients with only mild to moderate haemodynamic compromise rather than advanced misery perfusion, and demonstrated a low incidence of ipsilateral stroke under contemporary medical therapy, thereby questioning the necessity of surgical revascularization in this subgroup and underscoring the importance of avoiding operative exposure in patients without critical haemodynamic failure [10]. Contemporary observational cohorts likewise suggest that carefully selected patients with haemodynamic insufficiency, particularly prophylactic anterior circulation pedicle graft cases, can achieve high patency and acceptable morbidity in expert hands [11].

The present cohort is most directly comparable with the high-volume experience reported by Golub et al. [12], which evaluated direct STA–MCA bypass across moyamoya and non-moyamoya steno-occlusive disease subtypes. Their cohort similarly suggested that direct bypass can be performed with comparable perioperative safety across disease categories in carefully selected patients, although graft occlusion and adjunct dural synangiosis were important modifiers of outcome. In contrast, the present study was smaller and had shorter and more

Table 4

Perioperative CT perfusion parameters before and after direct STA–MCA bypass, stratified by moyamoya status.

Parameter	Moyamoya (n = 29)		p-Value	Non-moyamoya (n = 12)		p-Value	Moyamoya (n = 29)	Non-moyamoya (n = 12)	p-Value
	Early Post-Op Follow-Up (n = 13)	Late Post-Op Follow-Up (n = 16)		Early Post-Op Follow-Up (n = 3)	Late Post-Op Follow-Up (n = 9)				
Pre-bypass CT perfusion, median (IQR)									
MIP	0.98 (0.83–1.03)	0.98 (0.90–1.04)	0.622		0.92 (0.87–0.97)		0.96 (0.87–1.03)	0.92 (0.87–0.98)	0.992
CBF	0.79 (0.31–1.06)	0.83 (0.61–1.05)	0.622		0.45 (0.35–0.72)		0.72 (0.35–1.04)	0.56 (0.35–0.91)	0.514
CBV	1.06 (0.51–1.24)	1.07 (0.74–1.18)	0.622		0.84 (0.68–1.02)		0.96 (0.69–1.139)	0.84 (0.68–1.07)	0.868
MTT	1.46 (1.06–2.70)	1.24 (1.09–1.67)	0.526		1.68 (1.2–2.47)		1.36 (1.1–1.87)	1.66 (1.03–2.37)	0.896
Tmax	1.41 (1.04–1.93)	1.2 (1.12–2.35)	0.569		1.85 (1.12–3.16)		1.31 (1.1–1.92)	2.17 (1.25–3.34)	0.048
Hypoperfusion volume, mL	23.66 (4.30–36.25)	54.65 (25.74–92.57)	0.011		17.11 (5.3–56.49)		34.93 (18.42–61.28)	27.54 (11.74–43.84)	0.568
Infarct volume, mL	5.02 (1.08–9.61)	16.48 (4.95–17.6)	0.110		4.65 (2.84–8.67)		8.65 (1.41–17.23)	5.63 (3.35–7.32)	0.034
Penumbra volume, mL	16.02 (2.73–26.03)	45.51 (18.48–70.92)	0.032		13.5 (1.23–47.83)		25.5 (13.63–60.49)	19.65 (4.55–31.5)	0.314
Mismatch ratio	3.32 (1.66–4.07)	4.38 (2.76–6.7)	0.183		3.49 (1.55–8.82)		4.22 (2.77–6.73)	4.78 (1.9–8.33)	0.551
PRR, %	71.84 (58.91–74.36)	77.76 (63.92–81.37)	0.329		63.95 (33.7–88.6)		76.48 (66.76–85.6)	79.05 (47.44–88)	0.437
Timing of preoperative CT perfusion assessment, days	52 (15.5–115.25)	34 (19–76)	0.778		60 (37.5–106.5)		39.5 (19–92.5)	73 (32–140)	0.062
Post-bypass CT perfusion, median (IQR)									
MIP	0.96 (0.84–1.06)	0.97 (0.89–1.01)	0.565		0.95 (0.87–1.02)		0.97 (0.9–1.04)	0.98 (0.9–1.03)	0.790
CBF	0.61 (0.42–1)	0.84 (0.6–1.03)	0.539		0.41 (0.29–1.01)		0.68 (0.48–1.02)	0.46 (0.34–0.98)	0.546
CBV	1.14 (0.52–1.2)	0.83 (0.62–1.04)	0.662		0.9 (0.58–1.23)		0.84 (0.6–1.16)	0.98 (0.59–1.28)	0.247
MTT	1.4 (0.94–1.8)	1.1 (0.93–1.32)	0.420		1.21 (0.94–3.11)		1.13 (0.93–1.64)	1.21 (0.96–3.72)	0.089
Tmax	1.74 (1–2.23)	1.18 (0.99–1.53)	0.099		1.12 (0.63–1.85)		1.40 (0.99–1.82)	1.03(0.56–2.02)	0.456
Hypoperfusion volume, mL	20.16 (2.27–61.02)	20.88 (0.09–46.76)	0.956		17.61 (7.93–25.28)		20.16 (7.32–50.29)	13.70 (6.05–22.36)	0.215
Infarct volume, mL	7.94 (2.09–17.23)	3.45 (2.29–10.8)	0.434		3.31 (2.05–10)		4.34 (2.25–16.49)	4.61 (1.43–7.96)	0.401
Penumbra volume, mL	22.73 (7.35–44.76)	14.05 (7.18–29.13)	0.483		16.14 (3.64–16.6)		18.9 (7.76–32)	11.64 (0.14–16.39)	0.114
Mismatch ratio	2.77 (1.7–5.43)	2.99 (1.93–8.5)	0.713		3.68 (1.62–9.1)		2.88 (2.12–6.45)	2.95 (1.02–7.49)	0.720
PRR, %	73.75 (58.25–73.75)	68.59 (58.02–89.01)	0.943		72.86 (28.5–87.43)		70.62 (58.25–84.78)	63.78 (2.31–85.21)	0.189
Timing of follow-up CT perfusion assessment, days	24 (19.5–26.5)	57.5 (44.25–111.75)	<0.001		59 (47–260.5)		36 (24–62)	56 (22.75–239.25)	0.722

Values are presented as median (interquartile range), unless otherwise specified. CT perfusion maps were generated using syngo.via VB80H software (Siemens Healthineers) with deconvolution-based post-processing and automatic segmentation. MIP, CBF, CBV, MTT, and Tmax are software-derived relative hemispheric values obtained from the operated or symptomatic hemisphere relative to the contralateral hemisphere, and therefore do not represent absolute perfusion units or absolute seconds. Hypoperfusion volume was defined using Tmax > 6 s, infarct volume using relative CBF < 30%, and penumbra volume as hypoperfusion volume minus infarct volume. Hypoperfusion volume, infarct volume, and penumbra volume are reported in milliliters. Mismatch ratio is unitless, and PRR is reported as a percentage. Timing variables are reported in days. Early and late follow-up subgroups are presented descriptively according to postoperative CT perfusion timing using a 30-day cutoff.

Abbreviations: CBF, cerebral blood flow; CBV, cerebral blood volume; CT, computed tomography; IQR, interquartile range; MCA, middle cerebral artery; MIP, maximum intensity projection; MTT, mean transit time; PRR, penumbra rescue ratio; STA, superficial temporal artery; Tmax, time to maximum.

variable follow-up, but it contributes a Southeast Asian institutional experience and incorporates perioperative CT perfusion monitoring. Therefore, our findings should be viewed as complementary feasibility data rather than as validation of disease-specific haemodynamic equivalence or long-term stroke protection.

The evidence base for bypass in moyamoya disease and moyamoya syndrome (MMD/MMS) is comparatively stronger and supports guideline-level revascularisation in appropriately selected symptomatic patients. The Japan Adult Moyamoya Trial (JAM) showed that bilateral direct bypass reduced rebleeding in haemorrhagic adult MMD over 5

years [13], and subsequent analyses suggested that cortical haemodynamic failure may stratify haemorrhage risk and identify hemispheres deriving greater preventive benefit from bypass [14]. Consistent with this, updated meta-analytic evidence in adult MMD favours direct or combined bypass over indirect procedures for late stroke and intracerebral haemorrhage, although indirect revascularisation may reduce early post-treatment haemorrhage, supporting a tailored rather than uniform approach [15]. A large contemporary cohort study (n = 19,700) further associated bypass with lower long-term risks of death and stroke according to onset type, reinforcing the plausibility of population-level

Table 5

Patient-level characteristics of seizure patients.

Age	Sex	Group	Patency	Pre-Op mRS	Post-Op mRS	Post-Op Hyperperfusion	Post-Op Haemorrhage	Post-Op Edema	Seizure Treatment	Final Outcome
53	Male	Moyamoya	Yes	1	0	No	No	No	Phenytoin	No new neurological deficits
51	Male	Moyamoya	Yes	1	0	No	No	No	Phenytoin	No new neurological deficits
42	Male	Moyamoya	Yes	5	5	No	No	No	Phenytoin	No new neurological deficits
58	Male	Moyamoya	Yes	2	2	No	No	No	Phenytoin	No new neurological deficits
41	Male	Moyamoya	Unknown	4	4	Unknown	Unknown	Unknown	Phenytoin	No new neurological deficits
54	Female	Moyamoya	Yes	1	0	No	No	No	Phenytoin	No new neurological deficits
70	Male	Non-moyamoya	Yes	4	0	No	Yes	No	Diazepam	No new neurological deficits
52	Male	Non-moyamoya	Yes	4	3	No	Yes	No	Phenytoin	No new neurological deficits

Data are presented at the individual-patient level for patients who developed postoperative seizure. Postoperative hyperperfusion, haemorrhage, and edema refer to imaging findings documented after surgery. "Unknown" indicates unavailable or undocumented information.

Abbreviations: mRS, modified Rankin Scale; Post-Op, postoperative; Pre-Op, preoperative.

Table 6

Patient-level characteristics of ischemic stroke patients.

Age	Sex	Group	Patency	Pre-Op mRS	Post-Op mRS	Ischemic Time (days)	Ischemic Territory	Graft Thrombosis	Ischemic Blood Pressure	Hypotension
76	Male	Non-moyamoya	Yes	3	3	8	Left MCA	No	115/68	No
38	Female	Non-moyamoya	Yes	3	2	16	Left MCA	No	118/70	No
66	Female	Non-moyamoya	Yes	1	1	9	Left MCA	No	186/101	No

Data are presented at the individual-patient level for patients who developed postoperative ischemic stroke. Ischemic time indicates the interval from surgery to the diagnosis or documentation of ischemic stroke. Ischemic blood pressure refers to the recorded blood pressure at or near the ischemic event. Hypotension refers to clinically documented *peri*-event hypotension.

Abbreviations: MCA, middle cerebral artery; mRS, modified Rankin Scale; Post-Op, postoperative; Pre-Op, preoperative.

benefit in mature practice settings [16]. Differences in technique, patient selection, and perioperative care likely explain why similar haemodynamic gains do not produce identical complication profiles across pathologies. Direct STA-MCA bypass provides immediate flow augmentation, but in adult MMD/MMS this may increase the risk of cerebral hyperperfusion syndrome, seizure, or transient deficits because of impaired autoregulation [17]. In ICAD, the perioperative focus shifts toward preserving graft patency and preventing hypoperfusion-related perioperative ischemia, supporting careful haemodynamic selection, optimisation of intensive medical therapy, and strict avoidance of postoperative hypotension and hypovolaemia [18]. Accordingly, contemporary ICAD guidance supports bypass primarily as a rescue option for recurrent symptoms with documented haemodynamic compromise in centres able to minimise perioperative stroke and death [19]. As summarized in Table 7, the evidence supporting bypass is substantially stronger in moyamoya than in non-moyamoya steno-occlusive disease, with more consistent long term benefit in selected moyamoya populations, whereas ICAD studies remain limited by perioperative risk and less consistent net clinical benefit.

The longer M4 frontal temporary clipping time observed in the moyamoya cohort may reflect greater technical complexity related to smaller or more fragile cortical recipient arteries, altered collateral networks, and recipient-vessel selection in chronically hypoperfused territories [20]. However, this finding should be interpreted cautiously. In the exploratory complication analyses, M4 frontal clipping time was not clearly associated with postoperative seizure or ischemic stroke, and the sparse number of adverse events precluded reliable inference regarding a clinically meaningful clipping-time threshold. Similarly,

postoperative seizure and ischemic stroke mechanisms could not be definitively inferred from the available data. Seizures were not accompanied by documented persistent neurological deterioration, and postoperative ischemic strokes occurred despite documented graft patency and absence of recorded *peri*-event hypotension; however, routine postoperative diffusion-weighted MRI was not performed, preventing reliable infarct-pattern classification.

From a health-system perspective, these data are best viewed as an early experience from an emerging neurovascular bypass program in Indonesia. The value of the present cohort lies in demonstrating that standardized direct STA-MCA bypass, structured perioperative monitoring, and longitudinal CT perfusion assessment can be implemented in this setting. However, the study was not designed to establish institutional superiority, population-level effectiveness, or definitive disease-specific treatment thresholds.

Several limitations temper inference. Diagnostic classification was based on clinical and angiographic documentation, without routine RNF213 testing or uniform vessel-wall imaging. Therefore, imperfect separation between moyamoya disease, moyamoya syndrome, intracranial atherosclerotic disease, and other vasculopathies remains possible. Surgical candidacy was based on clinical symptoms, angiographic anatomy, donor-recipient suitability, and baseline CT perfusion evidence of haemodynamic compromise, but acetazolamide challenge, PET oxygen extraction fraction, and standardized vasodilatory reserve testing were unavailable. Consequently, compensated hypoperfusion could not be reliably distinguished from stage II haemodynamic failure. Paired CT perfusion was available only in 41 of 68 patients, follow-up timing was variable despite early versus late stratification, and MIP,

Table 7

Key studies evaluating extracranial to intracranial bypass in moyamoya disease or moyamoya syndrome and non-moyamoya steno occlusive disease.

Study	Setting	Study design	n (Moyamoya)	n (non-moyamoya)	Bypass type(s)	Perioperative 30 day stroke/death	Other major complications	Main conclusion/interpretation
EC/IC Bypass Study Group, 1985 [4]	Multinational (71 centres)	RCT	0	1377	Direct STA to MCA	0.6% 30 day mortality; 2.5% 30 day major stroke morbidity	Earlier and more frequent strokes in surgical arm (reported qualitatively)	EC IC bypass did not prevent ischaemic stroke in atherosclerotic carotid/MCA disease; perioperative hazard and lack of subgroup benefit dominated outcomes
Kawaguchi et al., 2000 [21]	Japan (single centre)	Comparative cohort (reported as clinical trial)	22	0	Direct STA to MCA (n = 6) vs EDAS (n = 5) vs conservative (n = 11)	Not reported	Not reported	Direct STA to MCA was associated with fewer future stroke events than indirect bypass or conservative management in haemorrhagic MMD
Tsai et al., 2009 [22]	Taiwan (single centre)	Case series	0	11	Direct STA to MCA	Not reported	Not reported	STA to MCA bypass improved perfusion and CVR and was associated with no recurrent stroke during follow up in a small, selected atherosclerotic MCA cohort
Powers et al., 2011 [3]	United States multicentre	RCT (COSS)	0	195	Direct STA to MCA plus best medical therapy vs best medical therapy	30 day ipsilateral ischaemic stroke: 14.4% (surgery) vs 2.0% (medical)	Perioperative stroke burden dominated outcomes (detailed in surgical report)	No reduction in ipsilateral stroke at 2 years; high perioperative stroke rate offset potential haemodynamic benefit
Miyamoto et al., 2014 [13]	Japan (22 institutes)	Multicentre RCT (JAM)	80	0	Bilateral direct EC IC bypass vs conservative care	Not reported as 30 day; morbidity causing significant disability reported	Significant morbidity: 14.3% surgery vs 34.2% non-surgery; rebleeding 11.9% vs 31.6%	Direct bypass reduced rebleeding and serious adverse events over 5 years; effect described as statistically marginal in Cox model but significant in Kaplan Meier analyses
Low et al., 2015 [11]	Singapore (tertiary centre)	Comparative observational cohort	0	112	Direct STA to MCA vs best medical therapy	Not reported	Not reported in abstract	In selected intracranial ICA/MCA steno occlusive disease with impaired CVR, bypass improved haemodynamics and was associated with fewer subsequent ischaemic events than medical therapy
Gunawardena et al., 2019 [23]	Australia (single surgeon group; long period cohort)	Retrospective cohort	0	112	Predominantly arterial pedicle graft (80%); venous interposition graft (20%)	Not reported	Higher risk for acute procedures, posterior circulation pathology, and venous interposition grafting	Carefully selected prophylactic anterior circulation arterial pedicle bypass was associated with high patency and low complication rates; higher risk subsets require caution
Gonzalez et al., 2021 [24]	United States (phase II trial; single arm with external benchmark)	Phase II objective performance criterion trial (ERSIAS)	0	52	Indirect EDAS plus intensive medical management	Not reported separately; overall primary endpoint events 9.6% during follow up	Two (3.8%) surgical complications; no intracranial haemorrhages; neovascularisation in 89%	EDAS plus intensive medical management showed safety and a non futility efficacy signal, supporting progression to phase IIb/III evaluation

(continued on next page)

Table 7 (continued)

Study	Setting	Study design	n (Moyamoya)	n (non- moyamoya)	Bypass type(s)	Perioperative 30 day stroke/ death	Other major complications	Main conclusion/ interpretation
Ma et al., 2023 [9]	China (13 centres)	Multicentre RCT (CMOSS)	0	324	EC IC bypass plus medical therapy vs medical therapy	30 day stroke or death 6.2% surgery vs 1.8% medical	Fatal stroke within 2 years: 2.0% surgery vs 0% medical (secondary endpoint; not statistically significant)	No statistically significant reduction in the composite primary endpoint; lower late ipsilateral stroke beyond 30 days reported but early hazard persists
Turpin et al., 2023 [25]	USA (single institution, single surgeon)	Retrospective case series	0	30	Direct STA to MCA	Recurrent stroke 3% at 30 days; major perioperative complications 9% (includes one stroke)	Hyperperfusion syndrome (major): 2 cases; seizures (minor): 2 cases; 1 year patency 87.5%	In selected non moyamoya steno occlusive disease, STA to MCA bypass was feasible with favourable functional outcomes; hyperperfusion, while uncommon, remained clinically significant
Golub et al., 2025 [12]	USA (high volume centre)	Retrospective comparative cohort	88	51	Direct STA to MCA for hypoperfusion; adjunct dural synangiosis in some	30 day perioperative stroke 6.5% overall; 5.7% MMD vs 7.8% non MMD (no significant difference)	Graft occlusion at last follow up: 28.4% MMD vs 21.6% non MMD; dural synangiosis associated with improved stroke free survival	In a high volume hypoperfusion selected cohort, direct bypass showed comparable safety profiles across MMD and non MMD disease; imaging based risk stratification may refine selection
Lim et al., 2024 [16]	Republic of Korea (nationwide claims cohort)	Retrospective population based longitudinal cohort	19,700	0	Direct or indirect bypass vs conservative management	Not reported	Increased haemorrhagic stroke risk in asymptomatic MMD associated with bypass; effect modification by age and onset type	Bypass was associated with reduced long term death and stroke outcomes in several onset strata, with heterogeneity and potential harm signals (eg haemorrhagic stroke in asymptomatic MMD), supporting tailored decision making

Data are presented as reported in the original publications and arranged chronologically by publication year. n denotes the number of patients unless otherwise specified. Perioperative outcomes refer to 30 day stroke and or death when these data were explicitly extractable from the source. “Non moyamoya” includes intracranial atherosclerotic disease and other non-moyamoya steno occlusive pathologies. For systematic reviews and meta analyses, the reported sample size may represent pooled patients or bypass procedures rather than unique individuals. “Not reported” indicates that the outcome was not explicitly provided in the cited publication.

Abbreviations: COSS, Carotid Occlusion Surgery Study; CMOSS, Carotid and Middle Cerebral Artery Occlusion Surgery Study; CVR, cerebrovascular reserve; EC IC, extracranial intracranial; EDAS, encephaloduroarteriosynangiosis; ERSIAS, EDAS Revascularization for Symptomatic Intracranial Atherosclerotic Steno Occlusive Disease; ICAD, intracranial atherosclerotic disease; ICA, internal carotid artery; JAM, Japan Adult Moyamoya Trial; MCA, middle cerebral artery; MMD, moyamoya disease; MMS, moyamoya syndrome; PET, positron emission tomography; RCT, randomized controlled trial; STA, superficial temporal artery; TIA, transient ischaemic attack.

CBF, CBV, MTT, and Tmax were relative hemispheric indices rather than absolute perfusion values. Postoperative ischemic stroke mechanisms could not be definitively classified because routine postoperative MRI with diffusion-weighted imaging was not performed.

5. Conclusion

In this Indonesian single-center cohort, direct STA–MCA bypass was followed by significant functional improvement in both moyamoya and non-moyamoya steno-occlusive disease. Although the cohorts differed in baseline clinical profiles and selected pre-bypass CT perfusion parameters, no significant between-group differences were observed in follow-up CT perfusion profiles among patients with paired perfusion imaging. Early adverse events were infrequent; postoperative seizure was

numerically more common in moyamoya disease, whereas post-operative ischemic stroke occurred only in the non-moyamoya cohort, although these differences were not statistically significant and should not be interpreted as disease-specific risk estimates. These findings support the feasibility of direct revascularization in this setting and highlight the need for larger multicenter studies with standardized perfusion timing, angiographic patency assessment, and disease-specific long-term outcome evaluation.

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Ethical approval

The study was approved by the Research Ethics Committee of Prof. Dr. Mahar Mardjono National Brain Center Hospital, Jakarta, Indonesia (approval no. DP.04.03/D.XXIII.9/271/2025). The requirement for individual informed consent was waived because of the retrospective observational design and use of de-identified data, in accordance with institutional policy and the Declaration of Helsinki.

Clinical trial number

Not applicable.

Availability of data and material

Available upon reasonable request.

Declaration of AI usage

During the preparation of this work, the authors used ChatGPT solely for English-language editing, grammar refinement, and improvement of readability. ChatGPT was not used to generate scientific content, formulate the study design, conduct data analysis, interpret the results, create or modify figures, generate references, or draw conclusions. For [Supplementary Video 1](#), the authors wrote and reviewed the voice-over script independently, and ElevenLabs text-to-speech software was used only to generate the audio narration. After using these tools, all authors reviewed and edited the manuscript and [supplementary materials](#) as needed and take full responsibility for the content of the submitted work.

CRedit authorship contribution statement

Muhammad Kusdiansah: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Bryan Gervais de Liyis:** Writing – original draft, Validation, Software, Methodology. **Syifa Aulia Suryani:** Software, Formal analysis, Data curation. **Aisha Lathifa Zahra:** Resources, Project administration, Formal analysis, Data curation. **Abrah Arham:** Writing – original draft, Validation, Supervision, Project administration, Methodology, Conceptualization. **Nakao Ota:** Writing – review & editing, Validation, Supervision, Methodology. **Rokuya Tanikawa:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization. **Rimuljo Hendradi:** Writing – review & editing, Supervision, Software, Project administration, Investigation, Conceptualization. **Asra Al Fauzi:** Visualization, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jocn.2026.112176>.

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