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Comparison of Outcomes After Direct Extracranial-to-Intracranial Bypass for Moyamoya Disease and Non-Moyamoya Pathology: A Systematic Review and Meta-Analysis

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Additional Declarations: Competing interest reported. Author N.R.K. authors of one of the studies included in this systematic review/meta-analysis. To mitigate potential bias, study selection, data extraction, and risk-of-bias assessment for that study were performed independently by reviewers who were not authors of the included study, with discrepancies resolved by consensus/third reviewer. No other conflicts of interest are declared.

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Abstract

Background

Extracranial-intracranial (EC-IC) bypass is an established technique to augment intracranial flow in patients with moyamoya disease (MMD) and other steno-occlusive diseases. The outcomes after direct EC-IC bypass for MMD compared to non-MMD pathologies (N-MMD) have not been systematically reviewed or compared in a meta-analysis.

Methods

We performed a systematic review and meta-analysis of studies reporting on outcomes in adults undergoing EC-IC bypass stratified by indication. Patients were assigned to either MMD or N-MMD pathologies with the latter primarily consisting of intracranial atherosclerotic disease (ICAD) and extracranial carotid occlusion (CO). Outcomes included graft patency, postoperative stroke or intracranial hemorrhage (ICH), and hyperperfusion syndrome (HPS). Random effects models were used to obtain pooled estimates for each outcome.

Results

Seventeen studies met inclusion criteria comprising 1,354 patients and 1,451 hemispheres. The weighted mean age was 49.1 years and 56.7% of patients were female. The indications for bypass included MMD or MMS in 52.6% of patients. ICAD and CO comprised 46.3% and 3.1% of patients, respectively. There was no difference in graft patency rates for the MMD and N-MMD groups (OR 0.81, 95% CI 0.54–1.21; I^2 = 0%). There was also no difference in postoperative stroke (OR 0.68, 95% CI 0.33–1.41; I^2 = 23%) or ICH (OR 1.46, 95% CI 0.34–6.26; I^2 = 61.4%). There was no significant difference in the rate of HPS between the N-MMD and MMD groups (OR 1.69, 95% CI 0.67–4.26; I^2 = 0).

Conclusion

This meta-analysis suggests that technical and postoperative outcomes are similar whether direct EC-IC bypass is performed for moyamoya or non-moyamoya steno-occlusive diseases. Further research with large multicenter cohorts, standardized techniques, and consistent outcome reporting is required to confirm these results.

Registration

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Introduction

Extracranial-intracranial (EC-IC) direct bypass is a neurosurgical procedure consisting of microsurgical anastomosis between an extracranial donor and an intracranial recipient artery. In the setting of steno-occlusive disease (SOD), EC-IC bypass is performed to achieve flow augmentation. SODs can broadly be categorized into Moyamoya disease (MMD) and non-MMD (N-MMD) pathologies. MMD involves stenosis or occlusion of the terminal internal carotid arteries and is often bilateral.[1] It is characterized by formation of moyamoya collaterals and can present as stroke or transient ischemic attack (TIA) due to hypoperfusion or intracranial hemorrhage. Moyamoya syndrome (MMS) describes MMD in the presence of a coexisting syndrome such as Down syndrome, sickle cell disease, neurofibromatosis type 1, or history of cranial radiation. N-MMD pathologies include intracranial atherosclerotic disease (ICAD), which is an age-related and typically unilateral buildup of atherosclerotic plaque leading to stenosis or occlusion of major intracranial arteries. It usually involves the intracranial internal carotid or proximal middle cerebral arteries.[2] Extracranial carotid occlusion (CO) is an additional N-MMD cause of cerebral hypoperfusion that can be treated with EC-IC bypass.

EC-IC bypass is an established treatment for symptomatic and progressive MMD, with the Japanese Adult Moyamoya (JAM) Trial showing lower rates of intracranial hemorrhage after bypass[3], and cases series reporting low rates of recurrent ischemia with long term follow-up.[4,5] The role of EC-IC bypass for N-MMD pathologies remains controversial given the publication of the EC-IC Bypass Study, Carotid Occlusion Surgery Study (COSS), and Carotid and Middle Cerebral Artery Occlusion Surgery Study (CMOSS), which did not report a benefit compared to medical management.[6–8] However, long term results from CMOSS suggest a potential delayed benefit of EC-IC bypass,[9] and it remains an important treatment option for patients with symptomatic hypoperfusion refractory to medical management.

We sought to compare outcomes following direct EC-IC bypass for MMD and N-MMD indications to provide further insight into the unique challenges of treating each population. Given the younger population and pro-angiogenic environment of MMD compared to the older population of N-MMD patients with greater comorbidity burden, we hypothesized the latter would be associated with worse postoperative outcomes.

Methods

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO; crd.york.ac.uk).

Eligibility Criteria and Search Strategy

The literature search was conducted by three authors (N.F.M., T.R.B., K.S.) using PubMed, Scopus, Ovid Embase (Elsevier), and the Web of Science. The search was performed on September 9th, 2025, and

included all available records from January 1995 to August 2025. The applied search strategy can be found in Supplementary Table 1.

Study Selection and Data Extraction

Three reviewers (N.F.M., K.S., T.R.B.) screened titles and abstracts to determine study eligibility. Studies deemed irrelevant were excluded at this initial stage. All remaining studies underwent full-text review. The bibliographies of included studies were examined to identify any missed articles, consistent with PRISMA recommendations. Studies authored by the same investigators or originating from the same collaborative research group were excluded to avoid duplicated patient cohorts. Any disagreements were resolved through discussion with the senior author (H.H.).

Original studies reporting outcomes after direct EC-IC bypass for patients with MMD or MMS and indications other than MMD such as ICAD or CO were included. The latter were assigned to the N-MMD group. All study types including retrospective cohort or case control studies and randomized controlled trials were considered. There had to be at least 5 patients in both the MMD and N-MMD groups. At least one outcome had to be reported and stratified by bypass indication (MMD vs. N-MMD). All donors, recipients, and bypass configurations were included. Exclusion criteria included bypass for flow replacement (i.e. for aneurysms or tumors), pediatric cohorts, and inclusion of patients who underwent indirect bypass. Abstracts, conference proceedings, and technical reports were also excluded.

For data extraction, a standardized Excel sheet was used to record data in duplicate. Any discrepancies that remained were resolved by the senior author. The extracted datapoints included mean age, sex, race, comorbidities, indication for bypass, location of vessel occlusion or stenosis requiring bypass, preoperative symptom status, donor vessels, bypass configurations, and follow-up duration. Outcomes included graft patency, which was recorded according to the imaging modality used in each study. The incidence of postoperative stroke (including the perioperative period and beyond) and intracranial hemorrhage were also recorded. The incidence of postoperative hyperperfusion syndrome (HPS) was also recorded according to the study's own definition. The risk of bias, overall study quality, and certainty of evidence were determined by a single author using the JBI critical appraisal tool for case series.

Statistical Analysis

Continuous variables were summarized as weighted means, and categorical variables were reported as proportions. Pooled estimates for each outcome were calculated using random effects models and represented with forest plots. Logit-transformed proportions were calculated for each outcome. The I-square (I^2) statistic was used to describe heterogeneity. Publication bias was determined for each outcome by evaluating the funnel plot for asymmetry and using Egger's test. For the latter, $p > 0.05$ indicated the absence of publication bias. R version 4.2.1 with the "metafor" package was used.

Results

The literature search yielded a total of 3,025 articles, including 556 from PubMed, 1,116 from Embase, 762 from Scopus, and 591 from the Web of Science. After screening, seventeen studies met inclusion criteria comprising 1,354 patients and 1,451 hemispheres.[10–26] The search strategy and selection process are summarized in the PRISMA flowchart (Fig. 1).

Demographic and Clinical Characteristics of Studies

The weighted mean age was 49.1 years and 56.7% of patients were female. The indications for bypass included MMD or MMS in 52.6% of patients. ICAD and CO comprised 46.3% and 3.1% of patients, respectively. The weighted mean follow-up duration was 498 days. Additional study characteristics are shown in Table 1, and the risk of bias assessment is provided in Table 2. Only one study had a moderate risk of bias, and the remainder had low risk.

Outcome comparison

There were 13 studies that reported graft patency rates.[10–22] The pooled overall graft patency rate was 94.4% (95% CI 87–98; I^2 = 93.5%). Compared to the N-MMD group there was no significant difference in graft patency for the MMD group (OR 0.81, 95% CI 0.54–1.21; I^2 = 0% [Figure 2]). The funnel plot did not reveal publication bias (p = 0.41 [Supplemental Fig. 1]).

There were 10 studies that reported the incidence of postoperative stroke or TIA[12–15,17,18,20,21,26] with a pooled overall rate of 5.7% (95% CI 3.6–8.9; I^2 = 51.4%). As shown in Fig. 3 there was no significant difference in the postoperative stroke or TIA rates for the N-MMD group compared to the MMD group (OR 0.68, 95% CI 0.33–1.41; I^2 = 23%). There was no funnel plot asymmetry (p = 0.28).

A total of 6 studies reported postoperative ICH rates.[12,14,17,18,20,26] The pooled overall rate of postoperative ICH was 5.3% (95% CI 2.8–9.8; I^2 = 59.9%). Compared to the N-MMD group, there was no significant difference in the postoperative ICH rate for the MMD group (OR 1.46, 95% CI 0.34–6.26; I^2 = 61.4%). There was no funnel plot asymmetry (p = 0.54).

There were 5 studies that reported the incidence of postoperative HPS with a pooled overall rate of 16.2% (95% CI = 5.9–37.2; I^2 = 88.1%).[11,20,23–25] There was no significant difference in the rate of HPS between the N-MMD and MMD groups (OR 1.69, 95% CI 0.67–4.26; I^2 = 0 [Figure 4]) and there was no funnel plot asymmetry (p = 0.15).

Discussion

Direct EC-IC bypass was first performed by Yasargil[27] and has been used for flow replacement in the setting of aneurysms and tumors as well as flow augmentation for SODs. This systematic review and meta-analysis compared outcomes of direct EC-IC bypass based on indication for flow augmentation.

Bypass for flow augmentation often involves a single anastomosis between a parietal superficial temporal artery (STA) donor and an M4 middle cerebral artery (MCA) recipient, but variations such as use of the frontal STA or other donor, double barrel, and one donor two recipient configurations also exist. Although surgical technique for direct STA-MCA bypass is similar between MMD and N-MMD cases, there are major differences in the underlying pathologies that could affect perioperative complications. MMD is a progressive idiopathic, non-atherosclerotic, non-inflammatory angiopathy that predominantly involves the terminal ICAs and is characterized by intracranial collateral formation.[1] It has been associated with increased angiogenesis through growth factors such as vascular endothelial growth factor.[28] In this study the N-MMD group mostly consisted of patients with ICAD, which is characterized by formation of plaque that can become symptomatic through hypoperfusion or emboli. Distinguishing between these mechanisms is important given patients with hypoperfusion are more likely to benefit from bypass. Patients with ICAD are older and more likely to have poorer baseline functional status as well as comorbidities such as hypertension, hyperlipidemia, and diabetes, which could place them at higher risk for complications.[29–31] Furthermore, ICAD is often associated with decreased angiogensis through the inhibitor endostatin.[32] However, we found no differences in graft patency, postoperative ischemia, ICH, and hyperperfusion between MMD and N-MMD groups. This is the first meta-analysis to directly compare outcomes between these two pathologies.

The overall graft patency rate was high and did not differ between groups, suggesting that EC-IC bypass has similar technical feasibility regardless of indication. Graft patency is influenced by multiple factors including technical performance of the anastomosis, bypass configuration, number of anastomoses, quality of the donor and recipient vessels, cut flow index, as well as demand in the revascularized territory. High graft patency rates have been reported in multiple large cohorts. Both the EC-IC and COSS trials found long term graft patency rates to be 96%[7,8] and the CMOSS trial reported 94% graft patency.[6] Yoon et al. reported a patency rate of 97% among 430 revascularization procedures comprising all indications.[33] All occlusions were discovered within one week of surgery and were more likely to occur with high flow bypasses and those with multiple anastomotic sites.[3] The overall graft patency rate of 94% in this meta-analysis is similar to the rest of the literature, but it should be interpreted with caution given patency was assessed at different time points between studies with varying imaging modalities.

Perioperative stroke or TIA is a known complication of EC-IC bypass and can occur due to temporary clipping of recipient arteries, graft occlusion, or due to intraoperative hemodynamic fluctuations in the setting of impaired cerebral autoregulation. Patients with numerous preoperative strokes or TIAs are at greater risk.[34] Rates of perioperative stroke are higher in trials for N-MMD than MMD. Across the EC-IC bypass study, COSS, and CMOSS, perioperative ischemic events occurred between 12–14.4%, and these comprised most of the strokes in the follow-up period.[6–8] Conversely, some cohort studies have reported lower perioperative stroke rates in N-MMD patients, ranging around 4%.[35,36] In the JAM trial, the postoperative stroke rate was only 2.4% in the surgical group.[3] These rates are closer to the pooled overall stroke and TIA rate of 5.7% in this meta-analysis. We did not find any differences in postoperative stroke or TIA between MMD and N-MMD groups. While N-MMD patients are older and have more

comorbidities, MMD patients are particularly sensitive to perioperative changes in hemoglobin, blood pressure, volume status, or CO_2.[37] Anatomical factors such as donor and recipient artery sizes as well as physiologic factors such as the pressure gradient between the donor and recipient could also influence outcomes.

ICH is a rare complication of EC-IC bypass. It may occur due to the sudden increase in intracranial perfusion when autoregulation is impaired, mismatch between the donor and recipient arteries, bleeding at an anastomotic site, or hemorrhagic conversion of an ischemic stroke.[38,39] Patients with MMD are further at risk for ICH due to MMD-associated aneurysms and the presence of fragile moyamoya collaterals, which could be susceptible to perioperative blood pressure variability. However, a large cohort of direct and indirect bypass procedures for MMD patients reported a 1.8% ICH rate.[40] Postoperative ICH rates have ranged from 2% in the COSS trial to 11.1% in individual cohorts of EC-IC bypass patients that did not distinguish between type of SOD,[7,39] which is in line with our pooled rate of 5.3%. We did not find any difference in ICH rates between the N-MMD and MMD groups.

HPS is believed to be rare in N-MMD patients but has been reported to occur after up to 27.5% of bypasses for MMD.[41] Symptoms of HPS include focal neurologic deficits such as hemiparesis and aphasia or seizure. However, many studies have diagnosed HPS purely radiographically based on a focal increase in cerebral blood flow with advanced imaging such as single-photon emission computed tomography.[42] Risk factors for HPS have been described, including increase in cerebral blood volume, increased age, larger volume with Tmax > 6 seconds, higher preoperative hematocrit, and lower preoperative protein level.[43–45] The flow in the donor vessel as well as size mismatch between the donor and recipient also may be contributing factors. In this meta-analysis there were no differences in ICH or HPS rates between MMD and N-MMD groups, suggesting it may be more common in N-MMD pathologies than previously thought. Alternatively, increased awareness of HPS and improvements in anesthesia as well as critical care management of perioperative blood pressure could have equalized any differences between the groups. Only a small subset of studies reported on HPS, which could make the results less generalizable.

This meta-analysis has several limitations. All studies were retrospective with self-reported outcomes, which could have introduced selection bias, confounding, and the possibility for inconsistent data quality. Furthermore, indications for EC-IC bypass could have differed between cohorts, and detailed preoperative radiographic data such as Suzuki grade or locations of intracranial occlusions were not specified in many studies. Only seventeen studies were included, and many outcomes were limited to a smaller number of studies, limiting statistical power and generalizability. The smaller number of studies was likely due to the fact that we only included studies with both MMD and N-MMD patients to reduce confounding from surgical experience, technique, and indications. Follow-up durations were variable, and certain outcomes were defined differently between studies. Several studies failed to specify the exact EC-IC bypass configuration, such as double-barrel or single-donor/single-recipient which can confound

the results. Finally, the study period (2005–2025) spanned the publication of COSS and CMOSS, which could have led to changing indications for bypass in N-MMD patients.

This is the first systematic review and meta-analysis to compare outcomes for direct EC-IC bypass between different types of SODs. Despite differences in patient populations and pathologies, similar postoperative outcomes were identified. This likely reflects a combination of careful preoperative planning, judicious patient selection, technical excellence, and optimized postoperative care.

Conclusions

This systematic review and meta-analysis identified high rates of graft patency and low rates of complication after direct EC-IC bypass. Our results suggest that technical and perioperative outcomes such as graft patency, postoperative ischemia, ICH, and HPS after direct EC-IC bypass are comparable between patients with MMD and N-MMD steno-occlusive diseases. These results should be interpreted with caution given the small number of studies with inconsistent outcome reporting.

Declarations

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Tables

Tables are available in the Supplementary Files section.

Figures

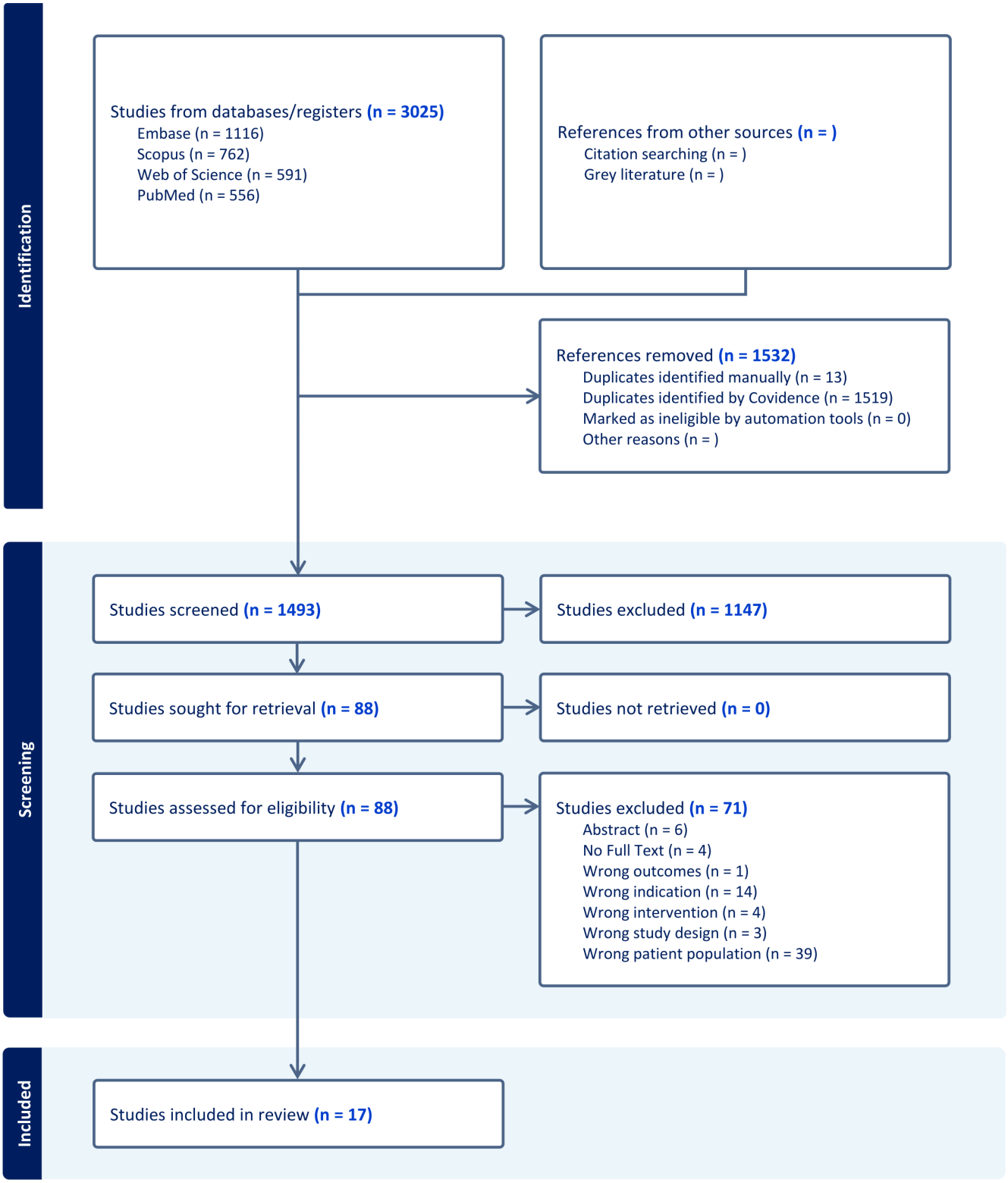


Figure 1

PRISMA flow diagram demonstrating inclusion and exclusion of studies.

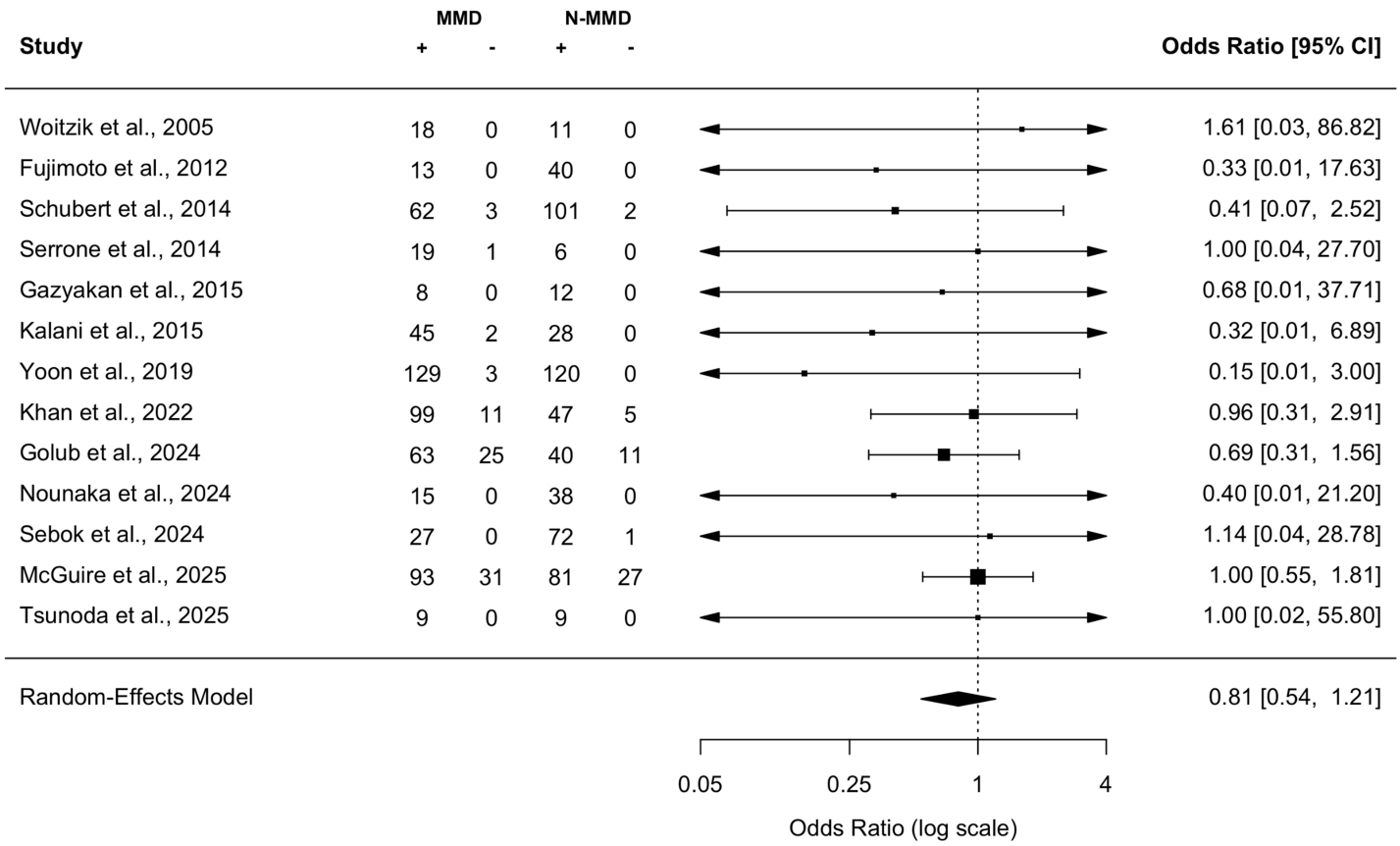


Figure 2

Forest plot comparing graft patency between moyamoya and non-moyamoya disease groups.

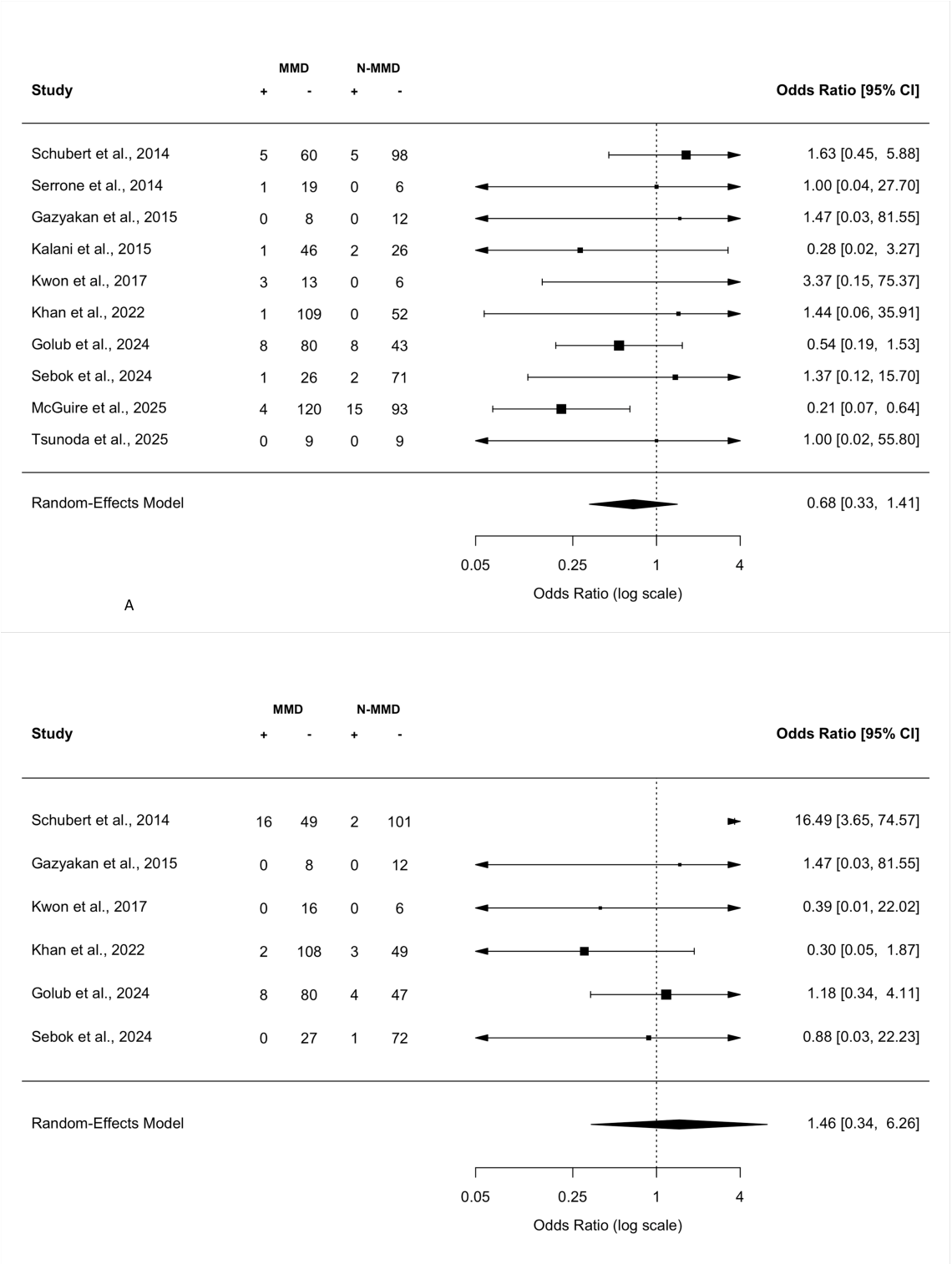


Figure 3

Forest plots comparing incidences of postoperative stroke or transient ischemic attack (A) and intracranial hemorrhage (B).

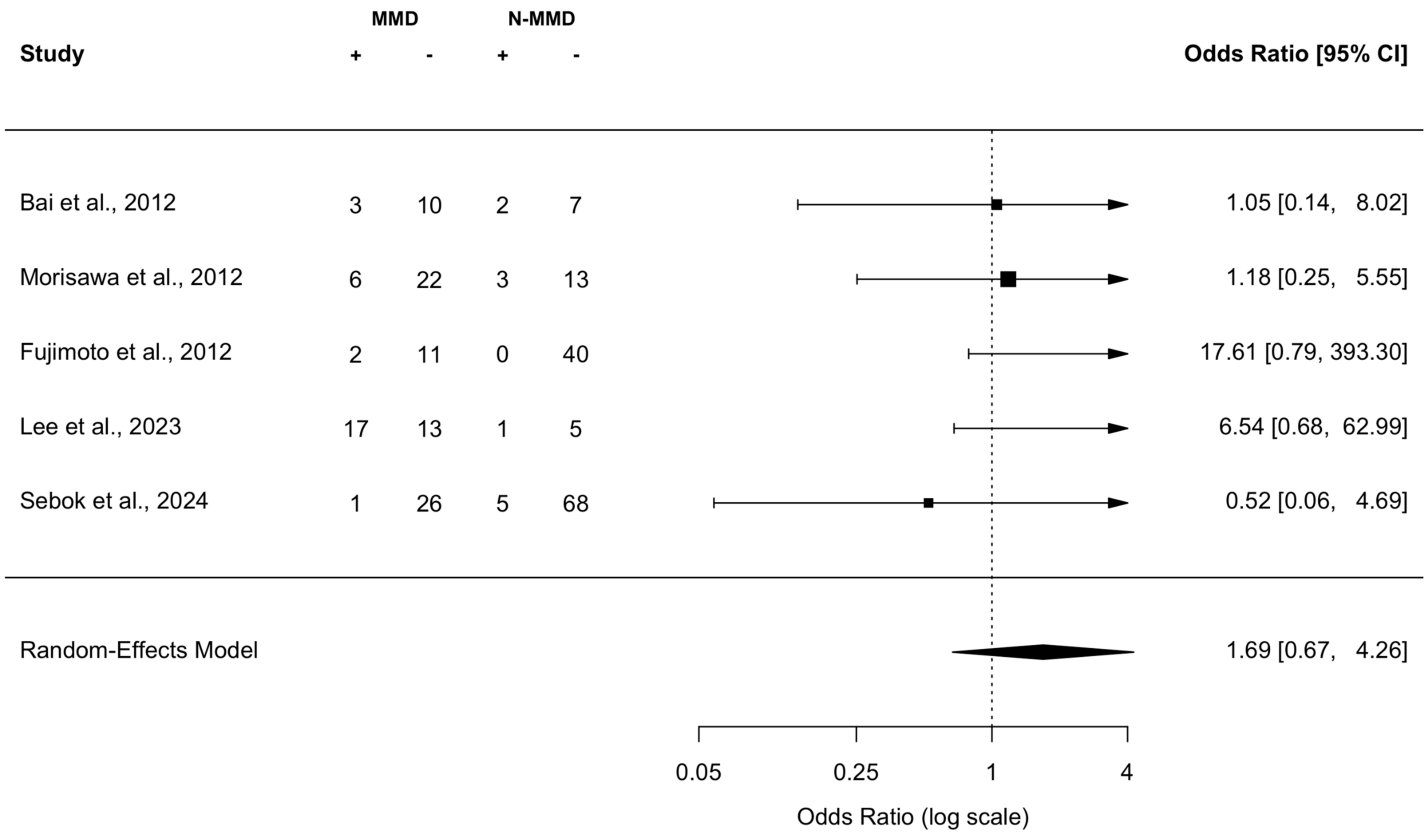


Figure 4

Forest plot comparing hyperfusion syndrome (HPS) between moyamoya and non-moyamoya disease groups across five studies.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.docx
- RiskofBiasJBITable21.docx
- SupplementalTable12.docx
- SFig1.tiff