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Management of Moyamoya disease. A systematic review and meta-analysis on surgical revascularization, outcomes and clinical manifestations

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ABSTRACT

Background: Moyamoya disease (MDD), defined by a chronic, progressive stenosis of the terminal portion of the internal carotid arteries (ICA) on both sides, carries the anomalous vascular information network, which functions as a collateral pathway to the brain. The aim is to understand the management of moyamoya disease (MMD) in terms of the approaches and different types of arterial revascularisations (direct, indirect, and combined), regardless of the pathological mechanism of origin to be investigated.

Materials and methods: A review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The review focused on moyamoya disease, outcomes before and after revascularisation, and related treatment modalities (STA-MCA) in various databases, including ScienceDirect and PubMed/MEDLINE, using the PRISMA guidelines, R, and Excel. Only studies published in English up to August 2025 were included.

Results: Our systematic review included 4800 patients, comprising (N=2866, 60%), patients, (N=2024,42%), surgical interventions, and (N=2112,44%,), revascularisations. See Table 1. (N=1199, 25%), patients included (N=977, 20%), surgical approaches (N=615, 13%), and revascularisations.

Conclusion: This study has shown that moyamoya disease (MMD) is a vascular concern that, regardless of ethnicity, is very rare; cases have been reported in Europe and the United States, as well as in the Hispanic population, but none have been reported in African regions. Therefore, encountering this pathology cannot be ruled out, and one should be up-to-date on the types of revascularisations, whether STA-MCA, ACA-PCA.

Keywords
Moyamoya disease, internal carotid arteries (ICA), direct bypass, indirect bypass, artery temporal superficial, middle cerebral artery, revascularisation

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Introduction

Moyamoya disease (MDD), defined by a chronic, progressive stenosis of the terminal portion of the internal carotid arteries (ICA) on both sides, carries the anomalous vascular information network, which functions as a collateral pathway to the brain stem. is understood from its appearance as a smoke-like vascular network on cerebral angiography, which was termed "moyamoya." Angiography for this disease was described in mid-1957, for both carotid arteries or bilaterally, and designated as a pathological entity in the 1960s. [1]. MMD, we proceed with a bypass of the superficial artery to the middle cerebral artery. (STA-MCA); this is the surgical method of choice for moyamoya disease (MMD); at the time of ischemic onset, it will improve cerebral blood flow. This method, by increasing flow, is also essential in preventing rebleeding in patients with moyamoya without early hemorrhagic disease. When they undergo bypass surgery, perioperative catheterization will be included, which will be essential in assessing postoperative complications. [2].

New studies indicate that RNF213 can modify the E3 ubiquitin ligase associated with the East Asian gene. Another variant of this gene is the non-Arg4810Lys variant of RNF213, which is associated with moyamoya disease in European countries, etc. This Arg4810Lys variant is said to be the most strongly genetically associated and is generally associated with moyamoya disease. [3]. MMD: There are factors that influence stenosis, its vascularization, and angiogenesis. The pathophysiology includes surgical and nonsurgical approaches that influence the pathogenesis so much that they tend to halt and slow its progression. Therefore, the intervention is surgical revascularization through direct and indirect bypass techniques, leading to the restoration of cerebral hypoperfusion. [4]. Moyamoya disease can develop in both children and adults, although its characteristics manifest differently. In children, ischemia is a common manifestation, presenting with an irreversible and progressive deterioration of nerve function with an unknown pathogenesis, unlike in adults, who begin with bleeding and require early intervention. It should precede treatment of the disease, which can be classified as direct and indirect bypass surgeries with orifice trepanation with anastomosis of the superficial temporal artery (STA), encephalomyosynangiosis (EMS), and encephaloduroarteriosynangiosis (EDAS), direct surgery tends to reconstruct intra-extracranial vessels with anastomosis of the superficial temporal artery and/or the middle cerebral artery (STA-MCA). Indirect surgery in children with moyamoya has been shown to be effective. Although both direct and indirect surgery are recommended, they tend to have a better response in children. [5].

Material and Methods

A review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The review focused on moyamoya disease, outcomes before and after revascularization, and related treatment modalities (STA-MCA). A comprehensive search was conducted in various databases, including ScienceDirect and PubMed/MEDLINE, using the PRISMA guidelines, R, and Excel. Search terms included "Moyamoya disease, MMD" in children and adults, along with terms specifying surgical therapies and techniques, different rehabilitation methods, and pathologies associated with the disease. Only studies published in English up to August 2025 were included.

The PICO (Population, Intervention, Comparison, Outcome) framework was used to define the study population, focusing on patients aged 1 to 75 years with moyamoya disease (Figure 1). Search Strategy and MeSH Terms

The search strategy incorporated MeSH terms (Medical Subject Headings) related to revascularization, both direct and indirect, in Moyamoya disease (MMD), with a focus on disease management.

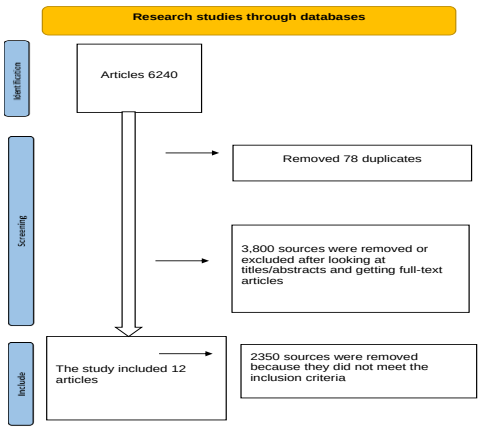

Figure 1. Flowchart of the articles selected according to the PRISMA protocol base of Moyamoya disease, (MMD).

Comprehensive Search Strategy Keywords

The comprehensive search strategy incorporated the following MeSH terms:

Moyamoya disease/inmmunotherapy"[Mesh]
Moyamoya disease/nanotechnology"[Mesh]
Moyamoya disease/cerebrospinal fluid"[Mesh]
Moyamoya disease/chemically induced"[Mesh]
Moyamoya disease/complications"[Mesh]
Moyamoya disease/congenital"[Mesh]
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Moyamoya disease/diagnostic imaging"[Mesh]
Moyamoya disease/diet therapy"[Mesh]
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Moyamoya disease/epidemiology"[Mesh]
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Moyamoya disease/genetics"[Mesh]
Moyamoya disease/history"[Mesh]
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Moyamoya disease/radiotherapy"[Mesh]
Moyamoya disease/rehabilitation"[Mesh]
Moyamoya disease/surgery"[Mesh]
Moyamoya disease/therapy"[Mesh]

Keywords

Additional keywords included "Revascularization of Moyamoya disease," "anastomosis" "Carotid arteries" "Direct bypass," "Indirect bypass," "Artery temporal superficial," "Middle cerebral artery" and "Surgical Approaches.

Data Collection

We collected data from the included studies covering various aspects of the manifestations of Moyamoya disease (MMD). We also included diagnosis, clinical and surgical management, and treatment. Factors influencing the genetics of the RNF213 Arg4810Lys variant were examined, along with details on surgical or conservative techniques, as well as revascularization as the treatment for patients with MMD. Novel therapies for anastomosis, which induce recovery and regeneration of arterial circulation, were also reviewed.

Data Extraction

Data extraction from studies that met the inclusion criteria was performed using a standard, generalized search for the study of Moyamoya disease (MMD). Relevant information related to therapy or immunotherapy for MMD was extracted from manuscripts that met the search methods. We focused on relevant studies on MDD, population demographics, details of the intervention and control, and the methodology used in each study.

Risk of Bias in Individual Studies

In each study, we assessed risk of bias and applicability issues using different Kaplan survival methodologies, along with revascularization of the affected arteries, both the superficial temporal arteries and the middle cerebral artery, restoring their flow and anatomy in MMD. The datasets analyzed focused on various current and modern treatments for Moyamoya disease in children and adults, as we searched and focused on MMD and its genetic, molecular, and cellular factors. This review included standard protocols for conventional and surgical therapeutic removal and treatment.

Statistical Analysis

For each data point and relevant event, the odds ratio (OR) with the mean difference as the summary statistic was used to analyze MMD. The outcomes of interest were defined using the 95% confidence interval (CI) and the weighted mean difference (OR). A random-effects model was used to estimate outcome measures using data from MMD patients from the included studies to date. R software 5.3 and Excel were used for all primary and subgroup analyses, and a P value of 0.05 was considered statistically significant.

RESULTS

Our systematic review included 4800 patients, comprising (N=2866, 60%) patients, (N=2024,42%), surgical interventions, and (N=2112,44%,) revascularizations. See Table 1. (N=1199, 25%), patients included (N=977, 20%), surgical approaches, and (N=615, 13%), patients included revascularizations. See Table 2. (N=735, 15%), patients from three studies were also included.

(N=297, 6%), direct bypass procedures are the most common, (N=1702, 35%), and indirect bypass studies. See Table 3. A 2023 analysis of a randomized controlled trial in adult moyamoya patients that included bilateral direct revascularization versus therapy for hemorrhagic MMD demonstrated a reduction in revascularization with surgery (2.7%/year vs. 7.6%/year; P = .04). This study demonstrated that hemorrhages originating posteriorly from the cerebral or posterior choroidal arteries could rebleed and would therefore benefit from reintervention. Nearly all studies strongly support revascularization as beneficial for patients with MMD symptoms. Therefore, the positive findings were limited to patients with hemorrhagic MMD who underwent surgery. While in patients with ischemic MMD it has been seen in class 2a, its limitation was found with type C evidence, according to the AHA/American Stroke Association GUIDE, 2021, established as beneficial revascularization for the same prevention of ischemic stroke and/or transient ischemic stroke, TIA [6].

A 2024 retrospective, multicenter cohort comparative investigation aimed to determine the differences in stroke onset between moyamoya disease and moyamoya syndrome. Both surgical and conservative therapies were assessed by multivariate Cox regression analysis. Out of 2,565 patients, 2,349 diagnosed with MMD were included. No significant difference was observed between the two groups; nevertheless, it was demonstrated that individuals undergoing surgical treatment had a reduced incidence compared to those receiving conservative treatment. Hazard ratio (HR): 0.487; 95% confidence interval (CI): 0.334-0.711; $p < 0.001$. The modified Rankin scale prior to admission was > 2 (HR: 3.139; 95% CI: 1.254-7.857; $p = 0.015$), and perioperative problems were noted (HR: 8.666; 95% CI: 3.476-21.604; $p < 0.001$). The difference is that stroke implications rose in patients with moyamoya syndrome, although both groups benefited from revascularization, therefore it was indicated to urge and minimize perioperative problems as a way of preventive [40].

A supplementary retrospective investigation with 65 individuals aimed to elucidate the distinctions in clinical symptoms between moyamoya illness and moyamoya syndrome. Eighteen percent of patients were classified as asymptomatic with an underlying illness, compared with 82% of patients with moyamoya disease. Evaluating neurological signs, 66% of both groups had cerebrovascular manifestations, with ischemic stroke present or not, and 32%–42% without hemorrhagic strokes. Headache was prevalent in 18% of patients, and only 26% had phenotypes. Patients with ≥2 presented with stroke, TIA, headache, and seizures. Imaging studies demonstrated ≥1 ischemic lesion, while posterior circulation lesions were impacted in 51%. Forty-seven patients underwent surgical procedures, and 45 patients were administered aspirin. Subsequently, following diagnosis, 12 patients suffered additional strokes. From symptom onset and stroke incidence to follow-up, only 5 instances were seen per year, 26%; 19 patients presented with intellectual disability, 8 of whom had epilepsy, while 7 had behavioral difficulties. Therefore, in patients with MMD vs. MMS, the difference was more complex in patients with external circumstances for an incMMS ($p = 0.021$). It should be mentioned that studies of stroke patients detected within 4 years had a lower incidence of intellectual or cognitive damage. [41].

Monitoring has two intraoperative approaches: first, fluorescence phenomena, and second, oscillatory neural activity. Some unique techniques have been developed under real-time blood flow conditions employing indocyanine green videography, while others focused on electrophysiological characteristics of high gamma activity (HGA). Indocyanine green videography (ICG-VG) was employed in four patients with moyamoya plus two patients with AVM, while DEHGA was used in four patients with brain tumors via craniotomy techniques in the conscious patients. Perfusion imaging parameters were also used, as was the case with perfusion imaging techniques that revealed shortening and increased hyperfusion when connected to the surgical microscope after moyamoya revascularization and flow visualization techniques, providing key anatomical and functional information for the removal of AVMs under the microscope. [42, 43, 44]

Discussion

MMD: Its origins, pathogenesis, and relationship between diagnosis and clinical symptoms are still under controversy, especially in other ethnic groups than in Asians. Susceptibility to the RNF213 p.R4810K mutation is regarded uncommon in Asians than in

Caucasian Europeans. Therefore, MMD should be treated in various ethnic groups [45].

Etiology

We are reminded that the genetics of moyamoya disease is of interest. However, chromosome 17 has been discovered as a carrier of the gene that may be sensitive to MMD in East Asian individuals. However, it was discovered that women were more likely to be impacted by familial MMD. Another study suggested that it was due to autosomal dominant inheritance with incomplete familial penetrance. Additionally, another study studying the genome and the specific locus discovered that the RNF213 gene was the first susceptible gene, but the biggest number of carriers were of the p.R4859K gene for MMD in Japan, which would explain its frequency compared to Western countries. p.R4859K is associated to autoimmune quasi-MMD and arteriosclerotic MMD [46].

Epidemiology of Moyamoya Disease (MMD)

Its incidence is relatively high geographically in East Asia, and according to some research, the prevalence of MMD is 10 per 100,000 individuals, while the incidence rate is 1 per 100,000 in Japan. Moving to South Korea, the incidence is 2 per 100,000, and its prevalence is 16 per 100,000, whereas in the West it is less than 1 per 100,000. In regions of North America, but in the United States, the trend is increasing. In the Chinese city of Nanjing, the prevalence of moyamoya was 3 per 100,000 as of 2000. Thus, in the latest investigations, 2,430 cases of moyamoya have been reported since 1976. A peak rate worldwide was identified in young people with moyamoya disease (MMD), between 20 and 30 years of age. The difference has increased according to geography and sex, and in foreign cases, the growth has been more prevalent in women than in men. [47].

Pathology of Moyamoya Disease (MMD)

Based on spontaneous progressive occlusions with bilateral inclinations to the terminal branches of the internal carotid arteries, the pathological vasculature of the intracranial vessels in individuals with MMD has been examined. Thickening of the intimal layer of fibrocellular origin, an increase in smooth muscle cells, irregular undulation of the internal elastic laminae, and attenuation of the medial layer without atherosclerotic or inflammatory alterations have been reported. Previous findings have indicated caspase-3 apoptosis in the middle cerebral arteries, which is related with histological abnormalities. The collateral branches in MMD are the so-called dilated perforating arteries, a constant mix of vessels and their growth. According to pathological investigation, the elastic laminae are weakened with the creation of microaneurysms and previously collapsed or thrombotic arteries. Additionally, a light microscope examination of the superficial temporal artery revealed enlarged inner membranes, with disturbed and absent elastic layers. This study indicated that the smooth muscle cells in the inner membrane of the superficial temporal artery were filled with a basement membrane material. Therefore, it was considered that these histological abnormalities must have been a consequence of ischemic and hemorrhagic strokes in patients with moyamoya disease [48].

Moyamoya disease with Down syndrome

The relation between Moyamoya disease with Down syndrome has been noticed as a higher-than-expected frequency, but it is co-occurring in patients with Down syndrome. Existing data in the US national database suggested that 3.8% of patients admitted with MMD were affected. These patients, among Hispanics and Caucasians, represented 15% with ischemic strokes. Although Down syndrome has not been specifically represented in Asian countries, its clinical presentation is more widespread, and although most treated patients presented with symptoms or local deficits with bilateral involvement, the pathological mechanism of MMD in patients with Down syndrome is also not fully understood. Cardiac problems have been documented in 40% to 50% of patients with Down syndrome, impacting the body's circulatory system. There is also an increase in retinal veins flowing into the optic disc in Down syndrome. There are further symptoms from diabetic retinopathy through diabetes mellitus, such as the low incidence of malignancy in these patients. Therefore, reduced levels of systemic angiogenesis and high amounts of endostatin minimize diabetic retinopathy in people with Down syndrome. Although this angiogenesis potential may be linked to Down syndrome with moyamoya, people with moyamoya tend to have thyroid dysfunction, and the immunological dysregulation in Down syndrome could lead to MMD in some cases [49].

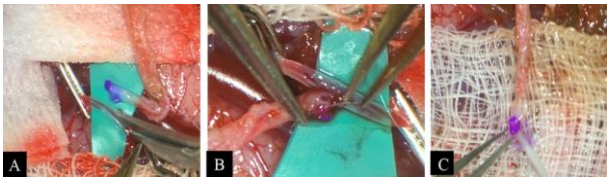

Figure 5. Moyamoya MMD procedure a,b,c) Revascularization STA-MCA.

Conservative Treatment of MMD

According to a review of a global survey, just 31% explored long-term aspirin use. Antiplatelet therapy has been utilized for stroke prevention in people with MMD. According to some research, antiplatelet medication is sufficient, however its usefulness in preventing stroke is currently being investigated. However, it cannot prevent recurrent cerebral infarction in people with MMD. Ischemic damage in persons with MMD is not considered embolic damage, but rather a hemodynamic infarction. Pathological changes in the vasculature of individuals with MMD, toward the ICA bifurcation, are not considered endothelial damage, which is more prone to platelet adhesion. In this circumstance, ischemic stroke prevention will not be helpful in people with MMD. However, persons getting antiplatelet therapy likely to develop issues with bleeding; the therapy is not connected with cerebral hemorrhage. In symptomatic MMD, its alternative use should not be considered. Ischemic stroke can impact posterior circulation, which is considered a risk factor for ischemic stroke [50].

Direct Revascularization

This is a proven effective procedure, the first employed between the superficial temporal artery and middle cerebral artery (SMA-MCA) bypass. The first surgical report was performed by Yasargil in 1967. Considered one of the most exact surgical treatments to date, however, modern technology breakthroughs have modified it over time. The STA is employed as a primary donor channel for the anastomosis of a distal branch to the middle cerebral artery. STA has both parietal and frontal branches, which can both be donors, and is followed using surface Doppler and neuronavigation, citing an angiographic diameter of 1 mm or more. Although the angiographic STA may be reduced, it can be enhanced during dissection with surgical measurement and appropriate flow following the anastomosis. When dissecting the STA, care must be given to avoid any form of vasospasm or damage by leaving any soft tissue remnants of the galea. When irrigating with heparinized solution after clipping the proximal STA to make the anastomosis, care must be given to protect the STA branches to avoid scalp necrosis. Remember that combined bypasses should be performed with a bigger incision than direct bypasses, which can be associated with 3-15% skin scarring. The linear incision will be even more essential, with less healing issues (1.6%), while curved incisions will be made in 3.8% and Y-type incisions in 17%. STA-MCA is conducted less frequently than those performed in the anterior cerebral artery and posterior cerebral artery. [51]. For ACA revascularization, a substantial piece of the STA, no less than 10 cm, must be dissected, with the craniotomy directed into the anterior cerebral artery. If revascularization affects the ACA and MCA, then both STAs are dissected bilaterally.

Therefore, two distinct craniotomies must be performed, one toward the Sylvian fissure and the other toward the ACA section. [52]. After passing the donor vessel of the STA, more toward the bone bridge between both craniotomies, thereby producing the medial anastomosis. Therefore, both STAs must be removed to minimize any damage of the scalp. We can also use the occipital artery for revascularization of the MCA or PCA area. However, direct revascularization of the posterior quadrant is more complex, particularly for the smaller recipient arteries if the occipital artery is employed. The average diameter of the recipient vessels should be 1 mm, although 0.8–0.9 mm can be considered. after performing a normal craniotomy, the middle meningeal branches should be preserved after exposing the dura, and after opening the dura, its collaterals should be preserved around it for a distal cortical anastomosis, which can be confirmed by preoperative angiography [53, 54].

Indirect revascularization

This is a technique for developing new vessels through the blood flow of vascularized tissue, stimulating the formation of new vessels. Unlike direct bypass, indirect bypass does not usually use vascular anastomosis. Other revascularization types, such as encephaloduroarteriosynangiosis (EDAS) and encephalomyosynangiosis, are considered, depending on the presence of several burr holes, such as synangiosis, followed by

encephaloduromyoarteriopericranial and omental transplantation. This method of indirect revascularization is advised for patients with recipient vessels of inadequate size for direct anastomosis, in pediatric and adult cases of MMD, which is regarded rare. The postoperative time will be shorter, and hypoperfusion syndrome does not develop postoperatively. If we employ the collateral branches of the distal pulmonary artery, we will confine direct bypass to the posterior temporoparietal-occipital regions, making direct bypass a good alternative for stroke revascularization in the PCA areas. The occipital artery can be used for indirect bypass compared to EDAS. Indirect bypass has shown beneficial in youngsters compared to adults. The increased indirect rate in children is attributable to cerebrovascular plasticity at very early ages. [55].

Combined revascularization

This is simply the combined use of direct and indirect revascularization for the treatment of MMD. Its objective is to obtain the cerebrovascular hemodynamic improvement of direct bypass, together with the benefits of indirect bypass. Direct bypass assists with revascularization as a backup method to direct anastomosis. Quantitative results vary depending on the patient. Although some suggest that direct bypass has advantages over indirect bypass in patients with MMD, adult patients with symptomatic MCA and ACA territories should be treated with combined revascularization instead of direct bypass, and combined bypass will be more effective or beneficial in pediatric patients. One restriction of combined revascularization is its increased use in dissection and surgical exposure. [56, 57].

Moyamoya disease (MMD) in pediatric patients usually presents with ischemic events, with intracranial hemorrhage occurring in only 10% of cases, compared to 60% in adults. [58, 59]. Spontaneous acute subdural hematoma in MMD is very rare; 1 to 6 cases have been reported. Acute subdural hematoma presents as a complication of MMD, as it is due to the rupture of transdural vessels. [60]. Some patients temporarily lose consciousness and develop lower limb weakness. For example, an SDH can be identified on a brain CT scan by noting a sudden increase in intracranial pressure, which is the cause of the symptoms. [61]. However, the location of the SDH, around the parasagittal area, could explain the lower limb weakness. An acute subdural hematoma results from a tear of the bridging veins due to head trauma. [62]. In contrast, spontaneous acute subdural hemorrhage can be caused by bleeding from the cortical artery, arteriovenous malformations, coagulopathies, or neoplasms like meningiomas, metastases, spontaneous intracranial hypotension, cocaine use, and arachnoid cysts. [63, 64].

Patients with MMD may experience complications such as hemorrhage, hydrocephalus, and cerebral palsy. [65]. Patients with MMD may be instructed to undergo encephaloduro-arteriosynangiosis (EDAS) to improve blood perfusion, with a risk of stroke. The outcome can be unpredictable due to the MMD condition. Intraventricular hemorrhage with hydrocephalus—this could progress to a complicated neurological prognosis. [66]. Also, the duration or persistence of these complications. An external ventricular drain (EVD) should be placed; therefore, a peritoneal shunt. VP shunt. Imaging studies will reveal the accuracy of placement versus a decrease in ventricular size, as well as a reduction in IVH and hydrocephalus; therefore, drainage is a positive indication. [67]. and effective optimization of CSF decompression. Verbal impairment may limit baseline functions, leading to failure to notice decompensation. A critical sign present in MMD in a patient with cerebral palsy may be seizure activity, which can be detected through urgent neuroimaging. [68]. Moyamoya disease (MMD) and multiple sclerosis have distinct pathogenesis. The clinical presentation and radiological presentations are similar, which has led to misdiagnosis of MMD. [69].

Limitations and future directions

Several investigations have raised the disadvantage of MMD in the context of stroke: it is more prevalent, and bleeding assessment is class C evidence. According to the AHA/American Stroke Association (2021) guidelines, revascularization was identified as effective for the prevention of ischemic stroke and/or transient ischemic attack (TIA). The difference is that the incidence of stroke rose in patients with moyamoya syndrome, while both groups benefited from revascularization, so urging and minimizing perioperative problems was indicated as a

preventive approach. When dissecting the superficial temporal artery (STA), care must be taken to avoid any vasospasm or damage, leaving any soft tissue remnants of the galea. When irrigating with heparinized solution after cutting the proximal STA to conduct the anastomosis, care must be given to protect the STA branches to avoid scalp necrosis. However, direct revascularization of the posterior quadrant is more complex, particularly for smaller recipient arteries if the occipital artery is employed. A mixture of combined revascularization may be employed in the future, although laboratory samples should be gathered for further evaluation. [70].

Conclusion

This study has proven that moyamoya disease (MMD) is a vascular problem that, regardless of ethnicity, cannot be ignored, as very rare cases have been documented in Europe and the United States, as well as in the Hispanic population, but none have been identified in African locations. Therefore, encountering this pathology cannot be ruled out, and one should be up-to-date on the types of revascularizations, whether STA-MCA, ACA-PCA, since their effectiveness in blood return after performing the procedure has been demonstrated, taking into account direct revascularization or direct bypass and indirect revascularization and indirect bypass as advantages and disadvantages that help us further with this type of pathology.

Table 1. Patients with Moyamoya disease treated with anatomical revascularization of both the superficial temporal artery and the middle meningeal artery and some variants.

Author	Kind of study	Patients No.	Range of age	Surgical intervention	Revascularization	Bypass	Follow up	Mortality	P= value
Yoshida Y. et al. 1999[7].	Retrospective	28	7 to 69 years (mean 39.2 years)	19	10	EDA, EMS, STA-MCA	14.2 years	5	P>0.05
Kawaguchi S. et al.2000 [8].	CT	22	43 years	11	6	STA-MCA bypass	0.8 to 15.1 years	N/A	p<0.05
Duan L. et al. 2012[9].	Retrospective	802	28 (range, 0.5-77) years.	500	773	EDAS	26.3 months (range, 6.0-101.9 months).	3	*P*<0.01)
Choi et al. 2013[10].	Retrospective	44	44.9 years (range: 17-65 years)	29	35	STA-MCA	12 to 105 months (mean of 55.4 months)	N/A	*p* > 0.05
Liu X. et al. 2013[11].	Retrospective	97	(mean age 31±10 years; range 5–56 years)	54	97	STA-MCA/EDAS	N/A	6	p<0.001
Miyamoto S. et al. 2014[12].	RCT	160	+18	80	42	STA-MCA Direct+indirect	5 years		*P*=0.048)
Han C. et al. 2015[13].	Retrospective	6	(range, 1-23 years)	6	5	N/A	18-108 month	N/A	N/A
Huang Z. et al. 2015[14].	Retrospective	154	33.95 years.	126	124	EDAS	36.12 months	N/A	P < 0.001
Jang DK. et al. 2017[15].	Retrospective /Comparative study	249	N/A	158	91	STA-MCA Direct+indirect	6-year	N/A	p = 0.014
Liu X. et al. 2015[16].	Case series	528	2-67 years	406	406	EMAS	39.5 months)	N/A	p<0.001

Lee SB. et al. 2012[17].	Retors pective	142	N/A	126	124	STA-MCA/EDAS	10 years	N/A	P < 0.05
Kang K. et al. 1996[18].	Retros pective	312	(39.4 ± 9.1 years old)	133	186	STA-MCA	48 (IQR 32–67) months	17	*P* = 0.006
Mizoi K. et al. 1996[19].	TC	23	(mean age, 35; range, 20-59)	23	16	STA-MC	6 months	N/A	p = 0.056
Zhang M. et al. 2020[20].	Retros pective	219	N/A	219	157	STA-MC	18 months (3-69 months	N/A	P = 0.004
Lukshin VA. et al. 2021[21].	Cohort study	80	N/A	134	40	N/A	N/A	N/A	N/A

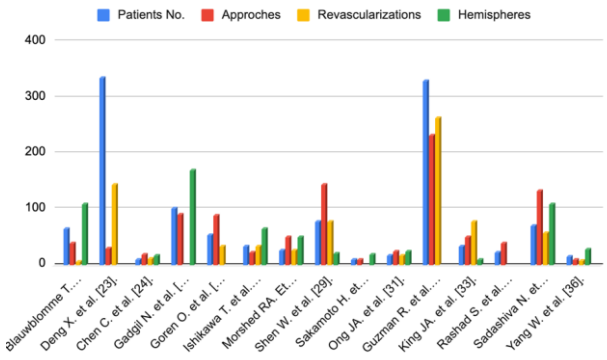

Figure 2. Graphics of patients with Moyamoya disease treated with revascularization.

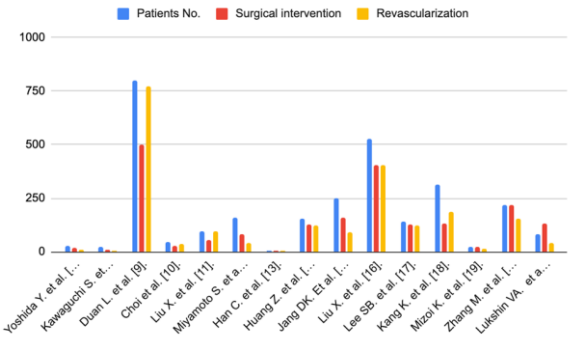

Figure 3. Graphs Patients with Moyamoya disease with revascularization approaches and intervention of the cerebral hemispheres.

Table 2. Patients with Moyamoya disease with different surgical approaches.

Authors	Kind of study	Year	Patients No.	Approaches	Revascularizations	Hemispheres	follow-up
Blauwblomme T. et al. [22].	Retrospective	2017	64	39	5	108	4.2 years
Deng X. et al. [23].	Retrospective	2021	336	30	144	N/A	N/A
Chen C. et al. [24].	Retrospective	2018	10	18	12	16	63.4 months ± 36.0.
Gadgil N. et al. [25].	Retrospetive	2018	102	90	N/A	169	4.3 years
Goren O. et al. [26].	Retrospective	2021	54	88	34	N/A	3-6 years
Ishikawa T. et al. [27].	Cohort study	1997	34	23	34	64	> 5 postoperative years
Morshed RA. Et al. [28].	Retrospective	2020	26	49	26	49	2.6 years
Shen W. et al. [29].	Retrospective	2017	77	143	77	20	28.43 ± 15.31 months
Sakamoto H. et al. [30].	Cohort study	1997	10	10	N/A	19	4 years,
Ong JA. et al. [31].	Retrospective	2020	16	24	16	24	3 months to 12 year
Guzman R. et al. [32].	Cohort study	2009	329	233	264	N/A	4.9 years
King JA. et al. [33].	Cohort study	2010	33	50	78	10	4.1 years.
Rashad S. et al. [34].	retrospectivey	2016	23	38	N/A	N/A	3 and 131 months
Sadashiva N. et al. [35].	Retrospective	2016	70	133	58	108	15.9 months (range 3-62 months)

Yang W. et al. [36].	Retrospective/case reports	2017	15	9	7	28	11.6 years

Table 3. Patients with Moyamoya disease were approached by direct and indirect revascularization.

Author	Kind of study	Year	Patients No.	Direct Vascularization or bypass	%	Indirect Vascularization or bypass	%
Deng X. et al. [23]	Retrospective	2021	336	70	21	447	75
Ha EJ. Et al. [37].	Longitudinal and crossectional analysis	2019	627	N/A	N/A	773	81
Ishikawa T. et al. [27].	Cohort study	1997	34	48	70	16	47
Morshed RA. Et al. [28].	retrospectivo	2020	23	33	69	16	69
Guzman R. et al. [32].	Cohort study	2009	329	96	29	264	80
Sadashiva N. et al. [35].	Retrospective	2016	70	17	21	50	71
Wang Y. et al. [36].	Retrospective/case reports	2022	144	N/A	N/A	37	25
Mizoi K. et al. [19]	TC	1996	23	16	69	7	30
Chou SC. et al. [38].	Retrospective	2022	50	17	34	50	100
Zheng EY. et al [39].	retrospective	2023	58	N/A	N/A	58	100

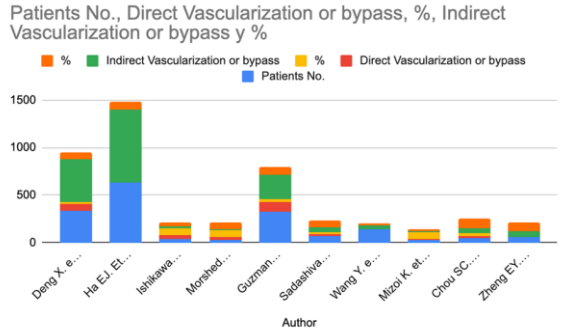

Figure 4. Graphs of patients with Moyamoya disease undergoing direct and indirect bypass.

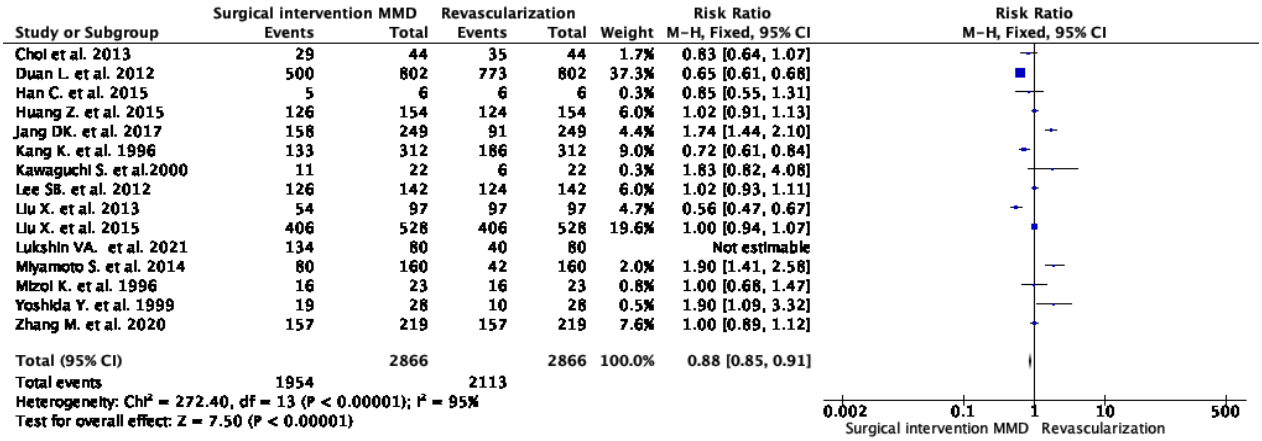

Figure 6. Forest plot Risk-ratio of patients with moyamoya disease MMD.

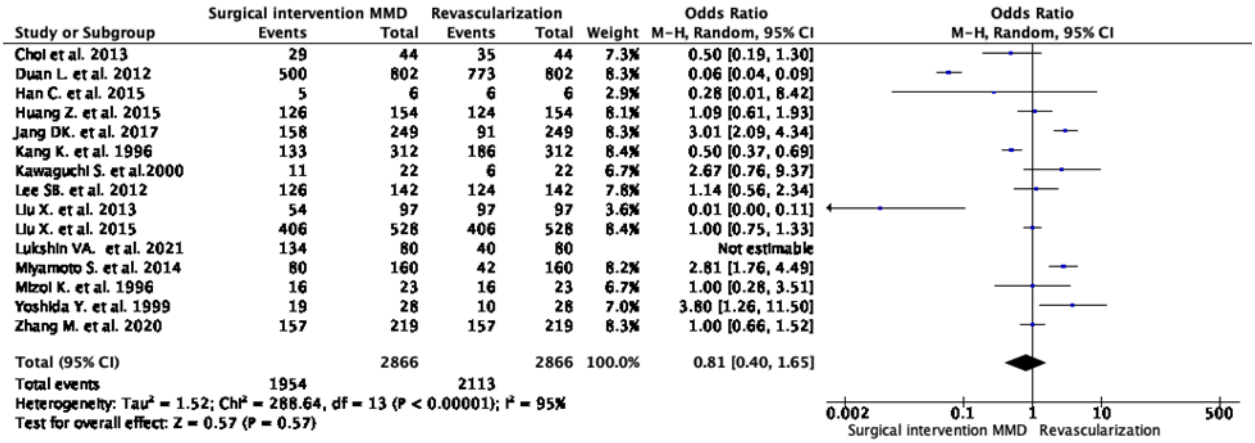

Figure 7. Forest plot Odds ratio of patients with moyamoya disease MMD, surgical intervention vs. revascularization.

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