Turk Neurosurg 36(1):64-73, 2026
DOI: 10.5137/1019-5149.JTN.47854-24.2

Original Investigation
Cerebrovascular-Endovascular

Received: 18.11.2024
Accepted: 12.01.2025
Published Online: 16.01.2026

Revascularization in Pediatric Patients with Moyamoya Disease

Emre DURDAG[1], Baran BABAYIGIT[2], Mustafa MAZICAN[3], Sibel CATALCA[4], Ben Ali OMARI[1], Soner CIVI[1], Cagatay ANDIC[3], Halil Ibrahim SUNER[1], Ozgur KARDES[1], Ilknur EROL[5], Kadir TUFAN[1], Cem YILMAZ[2]

[1]Baskent University Adana Dr. Turgut Noyan Training and Research Hospital, Department of Neurosurgery, Adana, Türkiye
[2]Baskent University Ankara Hospital, Department of Neurosurgery, Ankara, Türkiye
[3]Baskent University Adana Dr. Turgut Noyan Training and Research Hospital, Department of Interventional Radiology, Adana, Türkiye
[4]Baskent University Adana Dr. Turgut Noyan Training and Research Hospital, Department of Anesthesiology, Adana, Türkiye
[5]Baskent University Adana Dr. Turgut Noyan Training and Research Hospital, Department of Pediatric Neurology, Adana, Türkiye

This study has been presented at the Turkish Neurosurgical Society 36th Scientific Congress between 27 and 30 April 2023, Antalya, Türkiye

Corresponding author: Emre DURDAG ✉ emredurdag@yahoo.com

To watch the surgical videoclip, please visit https://youtu.be/cToaxjztGrA?si=R4zkd3SOrS5DVbbI.

ABSTRACT

AIM: To evaluate the patients who underwent surgery with a diagnosis of Moyamoya disease (MMD), and to contribute to the literature from a single-center in Türkiye.

MATERIAL and METHODS: Patients were evaluated retrospectively based on age, symptoms, history of cerebrovascular events (CVE), genetic disorders, pre-operative (pre-op) radiological stage, surgical technique, post-operative (post-op) improvement, and post-op radiological staging. The absence of new CVEs and reduced seizure frequency were considered indicators of clinical improvement.

RESULTS: A total of 7 patients, 4 of whom had bilateral MMD, underwent surgery. The average age was 11.8 ± 5 years. 4 patients (57%) presented with cerebrovascular events as symptoms, and the remaining 3 patients (43%) presented with headaches. Cranial digital subtraction angiography (DSA) revealed that the patients were in advanced stages (Suzuki Stage 4.9 ± 1.1). Encephalo Duro Arterio Myo Synangiosis (EDAMS) surgical technique was performed on 10 hemispheres, and a combined bypass (EDAMS + direct) was performed on 1 hemisphere. Clinical improvement was observed approximately 6 months postoperatively. During follow-up, disease progression in the contralateral hemisphere with associated symptoms was noted in 4 patients, and these patients subsequently underwent surgery on the contralateral hemisphere. The average time between the first and second surgeries was 15 ± 7.7 months. Post-operative follow-up was conducted with DSA, and radiological success was defined as Lucia Stage 2 ± 0.85. No clinical difference was observed between craniotomy and craniectomy as surgical techniques. No differences were found between vessel selection and clinical outcomes.

CONCLUSION: The EDAMS protocol has proven to be an effective treatment method for pediatric patients with MMD. Post-operative clinical improvements are rapidly observed, followed by radiological improvements. Patients may experience progression from unilateral to bilateral disease, which can progress quickly.

KEYWORDS: Moyamoya, EDAMS, Incision technique, Craniotomy, Türkiye

Emre DURDAG : 0000-0001-6939-5491
Baran BABAYIGIT : 0009-0002-1283-841X
Mustafa MAZICAN : 0000-0003-1142-213X
Sibel CATALCA : 0000-0002-8899-1106
Ben Ali OMARI : 0009-0006-4242-5922
Soner CIVI : 0000-0002-1055-5152
Cagatay ANDIC : 0000-0001-8581-8685
Halil Ibrahim SUNER : 0000-0002-5957-8611
Ozgur KARDES : 0000-0003-2854-941X
İlknur EROL : 0000-0002-3530-0463
Kadir TUFAN : 0000-0003-1509-4575
Cem YILMAZ : 0000-0002-2353-8044

INTRODUCTION

Moyamoya disease (MMD), which was first reported in 1957, is an idiopathic condition characterized by nonatherosclerotic progressive stenosis of intracranial arteries, and it typically involves the distal internal carotid artery (ICA), the proximal branches of the anterior cerebral artery (ACA), and the middle cerebral artery (MCA). This stenosis results in irregular neovascularization and elevates the risk of infarction and hemorrhage (3,43). Cerebrovascular events (CVE), including transient ischemic attacks (TIA), stroke, and hemorrhage, are the most frequent symptoms reported by these patients (23). Ischemic CVEs are more prevalent in pediatric patients, whereas hemorrhagic CVEs are more common in adults (10). It is not uncommon for MMD to progress from unilateral to bilateral involvement, and the brain parenchyma can be affected unilaterally or bilaterally (27).

The diseased prevalence is 0.086 per 100,000 individuals, with the highest prevalence among Japanese children (6.03 per 100,000) (36). MMD exhibits a bimodal age distribution, with peaks at ages 5–9 and 35–50 years, and it predominantly affects females (8).

Although medical and endovascular techniques have been employed in treatment, their long-term efficacy is restricted (16,17,33). Currently, surgical revascularization techniques including direct and indirect bypass are considered as the most effective treatment modality for MMD (33).

This study aimed to contribute to Turkish literature by sharing our surgical experiences and clinical outcomes related to this disease.

MATERIAL and METHODS

The Institutional Review Board approved the study (Baskent University Clinical Research Ethics Board, KA24/348, 09/10/2024).

The data of seven patients who underwent surgical treatment for MMD in our clinic between January 2019 and January 2024 were retrospectively evaluated. During the postoperative follow-up, progression in the contralateral hemisphere was noted in 4 of these patients who underwent surgery on the contralateral hemisphere, resulting in a total of 11 hemispheres that were operated on. The symptoms, radiological findings, and surgical techniques employed during the second surgery in the bilaterally operated patients were also documented. Antiepileptic drug (AED) treatments and acetylsalicylic acid (ASA) were either maintained at an appropriate dosage or introduced in the drug regimen of all patients.

Cerebral digital subtraction angiography (DSA) and brain magnetic resonance imaging (MRI) were employed for preoperative and postoperative follow-up imaging. DSA follow ups were performed every six months for the first year and annually thereafter. Interventional radiologists, blinded to the patient data, conducted the radiological staging. The Suzuki staging system was utilized for preoperative staging, while the radiological staging system described by Lucia et al. was employed for postoperative follow-up (30,42).

Suzuki staging is based on conventional angiographic findings and classifies the MMD progression into six stages (Table I) (42). The staging system described by Lucia et al. is also angiography-based, and assesses distal perfusion following a superficial temporal artery (STA)-MCA anastomosis (Table II) (30).

Surgical Technique

Direct by-pass in one patient and indirect by-pass (encephaloduroarteriomyosynangiosis (EDAMS protocol) in the other surgical procedures were performed**.** The primary aim of the EDAMS protocol is to establish anastomosis between the STA and MCA to enhance perfusion. All patients were placed in a supine position with the head completely turned to the contralateral side. Mild hypertension and hypercapnia were

Table I: Suzuki Grading System (42)

Stage I	Narrowing of Terminal ICA
Stage II	Initiation of moyamoya vessels in basal carotid circulation, dilation of intracerebral arteries
Stage III	Intensification of moyamoya vessels, severe carotid stenosis, defection of ACA and MCA
Stage IV	Minimization of moyamoya vessels, defection of PCA
Stage V	Further reduction of moyamoya, disappearance of major cerebral arteries
Stage VI	Disappearance of moyamoya collaterals and ICA, cerebral blood supply comes from external carotid arteries via leptomeningeal anastomoses

Table II: Angiographic Staging System Proposed by Lucia et al. (30)

Stage	Definition	Findings
I	Poor	No filling of the MCA territory
II	Moderate	Antegrade filling of one or two MCA branches
III	High	Complete filling of the MCA territory

preferred for preventing perfusion disruption and facilitating technical ease via vasodilation. A skin Doppler was employed to trace the STA and its branches, and these were evaluated along with DSA imaging. A question mark-shaped incision was utilized to increase arterial mobilization in patients with an increased distance between the artery and the Sylvian fissure. For patients with a reduced distance, a linear incision was implemented. The STA was employed as the donor artery in all surgeries. After performing an appropriate skin incision, the STA was dissected in accordance with microvascular surgical principles, ensuring 360-degree isolation, and it was suspended. The temporal muscle was then incised in a cruciate shape and suspended. After two burr holes were made, a circular craniotomy was performed. Subsequently, a cruciate opening was created in the dura mater, preserving the middle meningeal artery as much as possible, and the edges were folded inward. Following the opening of the Sylvian fissure, the STA was sutured to the pia near the MCA using microvascular surgical techniques (Figure 1). The tissue adhesive was applied without suturing the dura mater, and standard closure procedures were performed.

Craniectomy was preferred to craniotomy in cases where the selected STA branch's thickness was deemed insufficient to ensure adequate perfusion to maximize the contact between the temporal muscle and the brain parenchyma without replacing the bone. In other cases, the craniotomy flap was affixed to the intact bone.

The presenting symptom, age at initial symptom onset, sex, preoperative ischemic events, presence of syndromes, consanguinity, and a history of genetic diseases in the patient or their family were analyzed. Furthermore, data regarding the surgical technique, skin incision type, donor artery, preference for craniotomy or craniectomy, perioperative complications, symptoms during follow-up, and the interval between the first and second surgeries were obtained. The absence of new ischemic events or hemorrhage, reduced seizure frequency, improved ischemic findings, and the absence of new ischemic events or hemorrhage were regarded as indicators of clinical improvement during the postoperative period.

RESULTS

The average age of the patients at initial presentation was 11.8±5 years. Only one patient was male, while the remaining six were female (M/F ratio: 1/6). At initial presentation, two patients (28%) exhibited hemiplegia/paresis, two (28%) presented with monoplegia/paresis, and three (43%) experienced headaches. One of the patients with hemiplegia also reported a history of focal seizures (14%). Vomiting was noted as an additional symptom in two patients. Upon reviewing the patients' medical histories, it was observed that one patient had been previously diagnosed with migraines, while another had been experiencing headaches and nausea/vomiting attacks for four years.

Regarding genetic predisposition, one patient had Down syndrome, another had Poland syndrome, while a third was being monitored for NF-1. Genetic screening for MTHFR, factor V, prothrombin, and prothrombin activator inhibitor (PAI) mutations was performed in four out of seven patients. A heterozygous MTHFR mutation was present in one patient, while a homozygous mutation was present in the other. The patient with the homozygous mutation had a history of consanguinity. Genetic screening data for the remaining three patients could not be retrieved due to follow-up at other centers. DSA performed preoperatively revealed that the patients were predominantly in the advanced stages of the disease (Suzuki stage 4.9 ± 1.1).

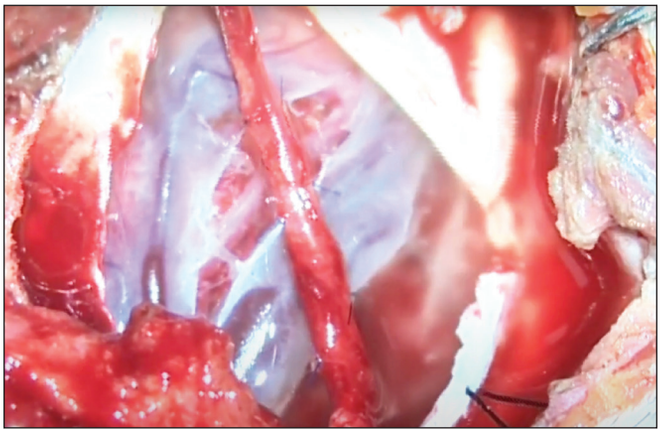


Figure 1: Intraoperative imaging during the EDAMS procedure. Please check "Surgical Technique" and/or "Surgical Videoclip" for attention in details.

Antiepileptic drugs (AEDs) were administered by a pediatric neurologist following the initial diagnosis in four patients (one on carbamazepine, three on levetiracetam). Levetiracetam was administered perioperatively as AED prophylaxis to the remaining three patients. The treatment doses for patients who were already receiving AEDs preoperatively were not modified. AEDs prescribed prophylactically were altered or tapered based on clinical and EEG-based monitoring under the guidance of the pediatric neurologist. The prophylactically prescribed AEDs were discontinued within three months postoperatively. All patients were administered aspirin (ASA) at an appropriate dose (100 mg) based on their body weight, which was Continued postoperatively.

Seven patients underwent surgery, with 11 hemispheres being operated on, including bilateral operations in four patients. The EDAMS protocol was implemented in ten hemispheres (91%), while the combined bypass technique [direct + indirect (EDAMS)] was performed in one hemisphere (9%). A longitudinal linear incision anterior to the tragus was used in seven hemispheres (63%), while a question mark-shaped incision was utilized in four hemispheres (36%). The frontal branch of the STA was used in three hemispheres (27%), the parietal branch in four hemispheres (36%), and both the major branches of the STA in four hemispheres (36%). Craniotomy was performed to access three hemispheres (27%), while craniectomy was performed for acessing the remaining eight hemispheres (63%).

In the early postoperative phase, one patient developed an epidural hematoma, requiring reoperation. The remaining

patients did not experience any additional early postoperative complications. One patient experienced a focal seizure on the fifth postoperative day. In terms of surgical success, no clinical difference was observed between craniotomy and craniectomy. The question mark incision technique was implemented in four surgeries, while linear incisions were used in seven surgeries. Two patients with question mark-shaped incisions experienced wound dehiscence following suture removal; these wounds were allowed to heal through secondary intention. No wound complications were observed in patients with linear incisions. No clinically significant difference in outcomes was observed based on the choice of donor artery.

The follow-up period was 30.57 ± 14.48 months. No lateralizing symptoms were idenified on the side of the body innervated by the operated hemisphere during the follow-up period. Two patients reported persistent headaches, the intensity of which decreased following the initial surgery and did not continue to affect their quality of life (18%). Unrelated to the surgery, one patient developed stage 2 essential hypertension and was initiated on antihypertensive therapy.

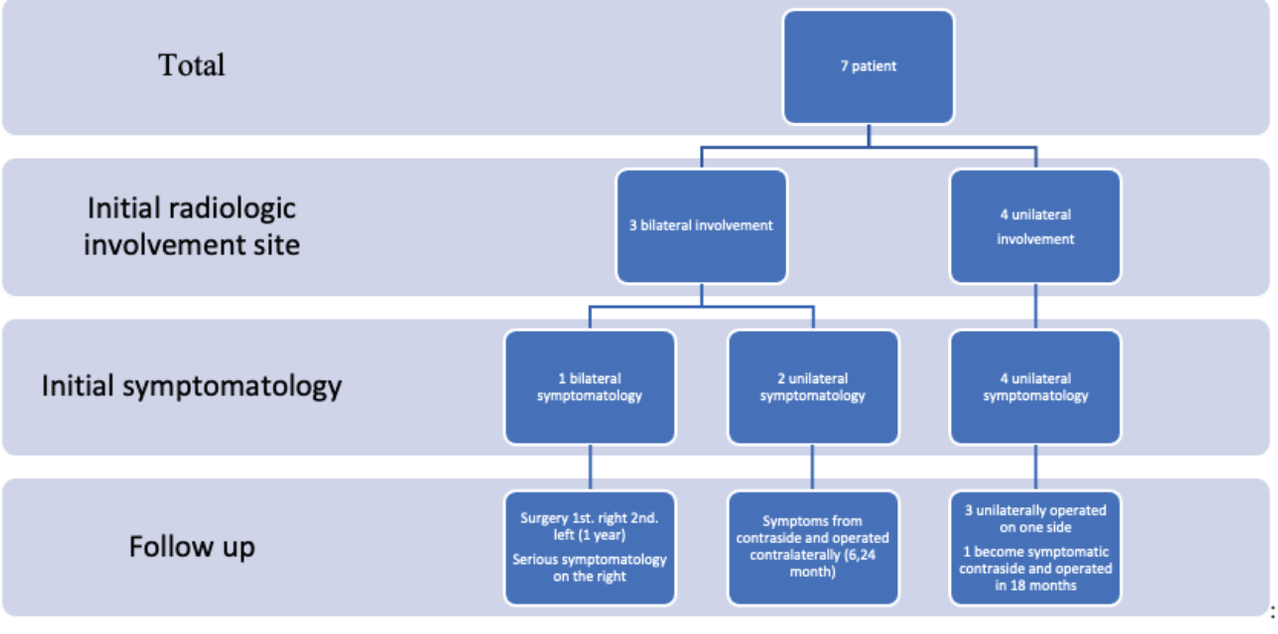
Based on the radiological findings, bilateral involvement was observed in three patients at the time of diagnosis. One of these patients experienced stroke-like symptoms on both sides of the body, including left upper limb plegia and right upper limb paresis (power: 4/5). The right hemisphere, which was the more symptomatic side, was operated on first. The left hemisphere was operated one year later, as planned. The other two patients were symptomatic on only one side of the body; therefore, the symptomatic hemisphere was operated on first. These patients were monitored for contralateral symptoms, and a second surgery was scheduled when the symptoms manifested. However, in one patient, the second surgery was postponed for more than 24 months due to insurance coverage issues. In another patient, the unilateral disease was diagnosed initially; however, subsequent DSA revealed the involvement of the contralateral hemisphere. Therefore, contralateral surgery was performed after the patient became symptomatic. Hypesthesia was the most prevalent symptom in all patients who underwent bilateral surgery. None of the patients developed early postoperative complications. The average duration between the first and second surgeries was 15 ± 6 months (Table III).

According to the first post-operative DSA performed at 6 months Lucia stage was 1.81 ± 0.87. Last radiological stage based on last DSA was identified as 2 ± 0.85 (Figure 2, 3) (Table IV). Although there were insufficient data to make a statistical assessment, there was no significant difference between early and late results.

DISCUSSION

Moyamoya disease is a cerebrovascular condition characterized due to ischemic and hemorrhagic stroke caused by stenosis or occlusion at the terminal ICA and ACA-MCA proximal regions, although its pathophysiology remains incompletely understood. Moyamoya syndrome refers to similar clinical and vascular manifestations observed in patients with underlying conditions such as autoimmune diseases, meningitis, cranial tumors, Down syndrome, NF-1, or cranial radiation exposure (27). Although it does not meet the diagnostic criteria for Moyamoya disease, it has been linked to sickle cell anemia, renal artery stenosis, antiphospholipid syndrome, and intracranial atherosclerotic disease (39). The diagnostic criteria most recently revised by the Moyamoya Disease Research Committee in 2021 (27). The definitive diagnosis is determined based on angiography. Historically, DSA was essential for a definitive

Table III: Involved Side, Symptomatology, Surgery, and Follow-Up Chart of Study Participants



diagnosis; however, current diagnostic protocols may utilize MR angiography. DSA may still be implemented in the event of diagnostic uncertainty or for temporal imaging (27,33). Surgical revascularization is recognized as the most effective treatment for the disease (34).

In our case series, we noted that most patients were female (F:M = 6:1). Epidemiological studies in the literature have also suggested a higher disease prevalence among females, with a general female predominance ratio of 1–2:1 (37,48). The female-to-male ratio was 4.25:1 in a case series conducted by Kraemer and colleagues in Germany (25).

The absence of adult patients in our study cohort is inconsistent with Moyamoya's bimodal age distribution (mean age 11.8 ± 5 years) (37,48). This could be attributed to the fact that our center has only recently begun administering Moyamoya treatments within the past four years as well as a result of our collaboration with the pediatric neurology department, leading to a predominance of pediatric patients in our study population.

Table IV: DSA Results of Procedures

Number of Procedures	Patient Number	Side	Pre-operative Suzuki stage	Post-operative Lucia stage on 6th month DSA	Lucia stage on last DSA (Follow-Up)
1	1	Right	6	2	3 (3th year)
2	1	Left	4	1	1 (2nd year)
3	2	Right	5	2	2 (6th month)
4	2	Left	5	1	1 (2nd year)
5	3	Right	2	1	1 (6th month)
6	3	Left	5	2	2 (2nd year)
7	4	Right	5	1	2 (2nd year)
8	5	Right	5	3	3 (2nd year)
9	6	Right	6	3	3 (2nd year)
10	6	Left	5	3	3 (12th month)
11	7	Left	6	1	1 (6th month)

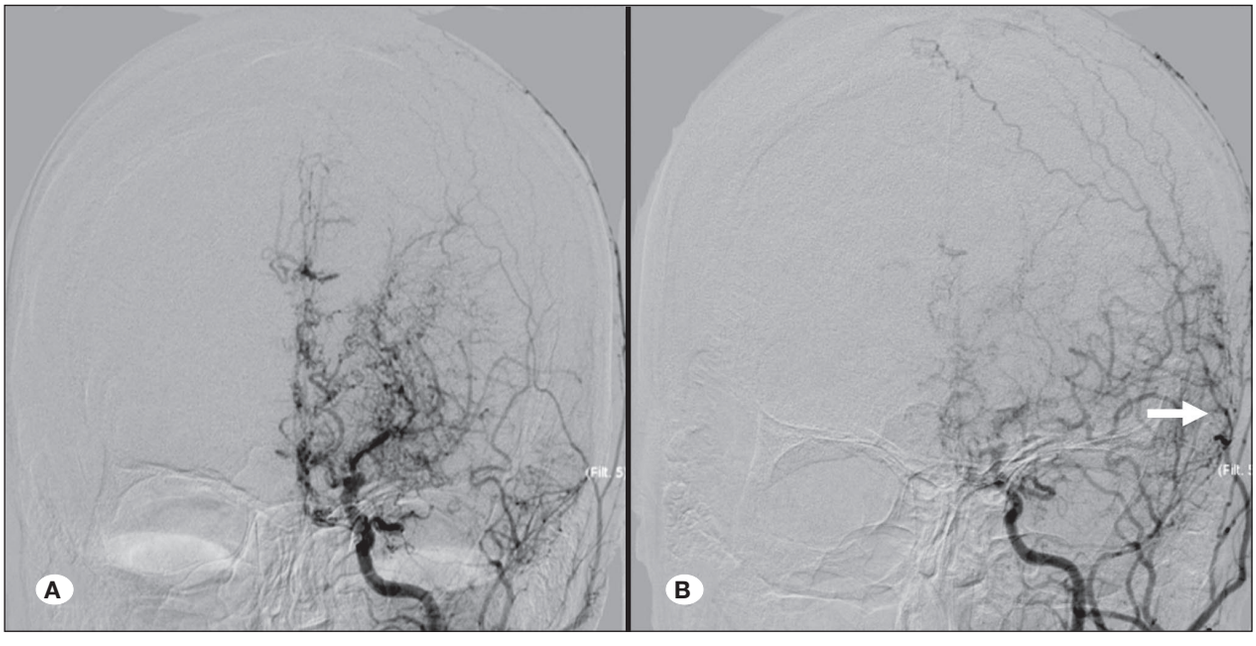


Figure 2: A) Classic "puff of smoke" sign observed on pre-operative DSA imaging of the patient, **B)** In the fourth year of postoperative follow-up, white arrow mentioned anastomosis site. The Moyamoya disease-involved arteries have disappeared and the MCA filling now occurs through the ECA.

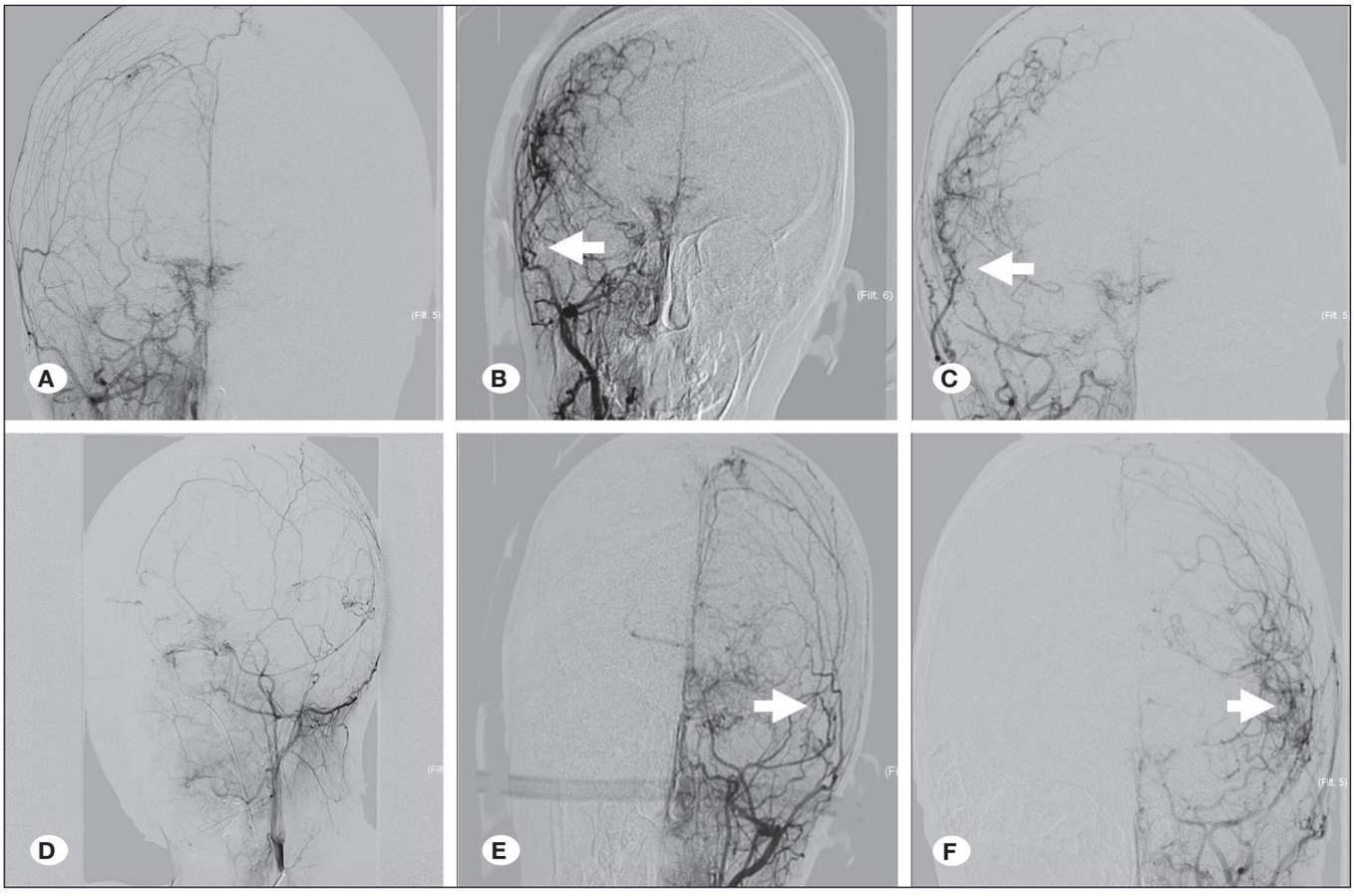


Figure 3: DSA images of another patient who underwent bilateral EDAMS protocol: **A)** preoperative, **B, C)** patient's 6th month and 18th follow-up (right), **D)** preoperative, **E, F)** patient's 6th month and 18th follow-up (left). White arrow mentioned anastomosis sites.

There are two principal methods for managing patients with bilateral disease: simultaneous bilateral surgery or a two-stage approach, in which the more symptomatic hemisphere is operated initially. Xu et al. demonstrated that patients who underwent simultaneous bilateral surgery had longer hospital stays, a greater incidence of postoperative ischemic stroke, and a shorter stroke-free survival compared to those who underwent staged surgeries (47). Deckers et al. have shown that unilateral surgery in patients with bilateral involvement also enhances perfusion in the contralateral hemisphere (7). Given that our patient population was pediatric and considering the higher risks associated with bilateral surgery, we selected a two-stage surgical approach. Our objective in monitoring patients during asymptomatic periods was to gain a more comprehensive understanding of the natural progression of the disease. The interval between operations was 15 ± 6 months in the four patients who underwent bilateral surgery.

During the second year of DSA-based monitoring, one patient initially exhibited unilateral involvement; however, progression to the contralateral hemisphere was observed. Existing literature indicates that patients with unilateral involvement can progress to develop bilateral disease; thus, the 2021 revision of the Moyamoya Diagnostic Criteria now includes patients with unilateral MMD (27). Lee and colleagues found that 29% of patients progressed from unilateral to bilateral disease in their investigation of young adults (29). Conversely, Church et al. reported a lower rate of 8.3% (5). Kelly et al. found a 38% progression rate, with an average time of 12.7 months (20). A mean progression time of 43.7 months was reported in another study (28). We recommend close monitoring of the diagnosed patients for potential disease progression. Bilateral progression in one of our four patients with initial unilateral involvement by the second postoperative year is consistent with the literature.

In pediatric patients with CVE, genetic and metabolic disorders should be considered. We conducted a differential diagnosis by assessing the homocysteine levels, factor V, prothrombin, prothrombin activator inhibitor (PAI), and MTHFR mutations in our patients. Unlike MMD patients, those with homocystinuria exhibit significant clinical improvement by normalizing homocysteine levels through vitamin B12 and folate supplementation (9). In two patients, the homocysteine levels were marginally elevated. Due to the absence of the characteristic phenotypes associated with homocystinuria (mental retardation, atypical facies, lens subluxation), MMD was considered the primary diagnosis, with the MTHFR polymorphism identified as a risk factor. Although all of our patients underwent MTHFR gene screening, the current

literature suggests that MTHFR analysis without homocysteine level assessment is unnecessary (35). Nevertheless, due to the increased risk of thrombosis associated with elevated homocysteine levels, vitamin B12 and folate supplementation were administered, and homocysteine levels were regularly monitored.

In 3 of our 7 patients, syndromic diseases were noted. One patient had Down syndrome, and another was diagnosed with NF-1. The association of these conditions with MMD has been documented in literature. Therefore, in patients with these syndromes, the presence of neurological symptoms should prompt the consideration of MMD as a differential diagnosis (44). One of our patients had Poland syndrome, and to our knowledge, this is the first reported case of the coexistence of MMD and Poland syndrome. Although there is insufficient data to ascertain whether this is incidental, this association may offer a novel insight into the pathogenesis of MMD. The high number of patients with syndromes in our study could be attributed to the fact that our patient population was predominantly from the Eastern and Southeastern Anatolia regions of Turkey, which are known for their high ethnic diversity (45).

It was observed that most patients experienced prodromal symptoms prior to their initial presentation. These nonparetic symptoms may result in a delayed diagnosis, as MMD is a rare disease and does not always manifest with the typical symptoms of CVE (14). Non-paretic symptoms in these patients can be misinterpreted as epileptic seizures, and similarly, epileptic seizures may be confounded with stroke or transient ischemic attack (TIA) (14,46). These scenarios underscore the significance of EEG and perfusion imaging in such cases (46). At the initial presentation, four patients (57%) presented with ischemic stroke, while three patients (43%) reported headaches. One of the patients with ischemic stroke also experienced focal seizures (14%). These findings are consistent with previous studies, indicating that MMD presents differently from other ischemic strokes (4,18,19,35).

In terms of revascularization, both direct bypass (STA-MCA) and indirect bypass techniques are accessible. In direct bypass, a patent artery is connected to the affected artery's distal segment. Conversely, indirect revascularization involves the placement of a patent artery or tissue supplied by an artery in contact with the brain parenchyma to facilitate spontaneous vascularization (12). Indirect techniques, including encephaloduroarteriosynangiosis (EDAS), encephalomyosynangiosis (EMS), encephalomyoarteriosynangiosis (EMAS), encephaloduroaortic synangiosis (EDAMS), and omental transplantation, have been developed (12). These techniques are frequently preferred in patients possessing a cortical artery that is suitable for anastomosis. However, there are concerns that indirect methods alone may be inadequate to prevent ischemia (4). Fujimura et al. reported that direct STA-MCA anastomosis is safe and effective for all age groups (11). Certain studies indicate that the direct bypass technique is more effective for achieving radiological improvement, as it rapidly resolves hypoperfusion (22,32). However, direct bypass surgery also carries risks, primarily due to the fragility of the vascular walls in these patients, necessitating the use of precise surgical techniques. Another potential complication of the direct bypass technique is postoperative hyperperfusion injury (26). The current literature is divided on the advantages of direct versus indirect bypass techniques.

The EDAMS technique was employed at 91% of the cerebral bypass surgeries in our clinic. The donor arteries were chosen based on the distance of the STA branches from the Sylvian fissure and their diameter. A combined direct-indirect bypass technique was performed in one patient, as the STA and MCA branches were considered appropriate for anastomosis due to their larger diameter. In other cases, the risk of anastomosis was deemed excessive due to the small size of the STA branches. Rapid clinical improvement was observed postoperatively, and no new neurological findings were noted on the affected side. Our clinical experience suggests that indirect bypass can yield favorable results in pediatric MMD patients. However, given our limited experience with direct bypass, assessing the superiority of different surgical techniques is beyond the scope of this study.

Although data are insufficient for establishing statistical significance, we observed that epithelialization was completed by postoperative day 14 in patients with linear skin incisions, and scabs were fully resolved. Conversely, wound healing did not progress as quickly in patients with question mark-shaped incisions, and two patients experienced wound dehiscence. Linear incisions seem superior as they preserve skin perfusion and facilitate easier suturing. This observation is consistent with the results of previous studies (1).

In terms of complications, one patient (14%) experienced early postoperative epidural hemorrhage, while another experienced focal seizure during the first postoperative week (14%). No new ischemic stroke occurred in the operated hemispheres of any patient. In a 2024 review conducted by Batista et al., hemorrhagic, ischemic, and epileptic complications were reported at rates of 4%, 6%, and 3%, respectively, with no significant difference in the complication rates between the pediatric and adult populations (2).

In 3 of the 11 surgeries that were performed, a craniectomy was conducted, while the other 8 entailed a craniotomy. In all cases, the bone flap was removed employing a single-burr keyhole technique with an average diameter of 4 cm. The objective was to reduce the surgical field and mitigate the risk of potential hemorrhage or parenchymal injury. Shimizu et al. have reported that larger craniotomies elevate the risk of surgical complications (38). Nevertheless, there is no consensus on the optimal craniotomy size, as larger craniotomies may expand the area of indirect revascularization, a critical factor in postoperative progression (26). Considering that potential complications in pediatric patients could be more severe, we opted for a craniotomy size of approximately 4 cm^2 in all patients.

While the Suzuki staging system is the standard for the radiological classification of MMD, multiple classifications have been proposed for evaluating vascular structures postoperatively, and no consensus has been reached in the

literature (6,31). For the radiological follow-up of our patients, we employed the classification described by Lucia et al., which is simple to understand and practical to implement. This classification also demonstrated positive surgical outcomes (30).

Our clinical experience indicates that clinical symptoms are likely to develop after a significant occlusion is detected radiologically. Clinical improvement typically manifests within the first six months of the postoperative period, followed by radiological improvement. However, clinical improvement was also noted in three patients without the evidence of angiographic improvement. This could be attributed to an increase in perfusion, even if there was no morphological evidence of new vessel formation. So et al. observed that MR perfusion SPECT results significantly correlated with clinical outcomes, although SPECT and angiographic findings were not always correlated (40,41). We believe that digital subtraction angiography (DSA) is essential for bypass patency assessment. Clinical follow-up and angiography alone may not always be sufficient. The growing availability of 3 Tesla MR and perfusion imaging provides more comprehensive information and can serve as a supplementary follow-up method in managing MMD in addition to direct angiography (21).

Study Limitations

The study's results were consistent with the literature, and certain relationships could be established. However, the small sample size undermines the ability to conduct statistical analyses. A more extensive, multi-center study is required. Another study limitation is the absence of genetic studies on the patients. Han et al. demonstrated that the prevalence of asymptomatic familial Moyamoya disease (MMH) is higher than anticipated through family screening using transcranial Doppler ultrasonography (18). In our study, the absence of family screening resulted in the scarcity of information regarding the familial background of our patients. Investigating genes associated with MMD and performing family screenings may provide valuable insights for future research, particularly given our patient population's high rate of consanguineous marriages. Transcranial Doppler ultrasonography could be a cost-effective and noninvasive screening procedure for family members in our country.

Although the surgery demonstrated symptomatic benefits, no follow-up was conducted to assess the status of patients' social reintegration or participation in daily life. Tools such as the Modified Rankin Scale or Pediatric Stroke Outcome Measure could be employed in this regard (15,24). Because the patients in our study were from the pediatric population, it is crucial to determine the extent to which they benefit from surgery and how they cope with such a condition and adapt to social life (13). The absence of psychological, mental, and social participation assessments during preoperative and postoperative follow-up restricts our understanding in this area.

From a radiological standpoint, the lack of perfusion imaging in the patients implies that, while increased vascular filling could be demonstrated via DSA, it is insufficient in providing quantitative data when compared to MRI or CT perfusion imaging (40). Additionally, the fact that all surgeries were conducted by a single surgeon in a single clinic setup introduces potential bias, further limiting the data reliability.

CONCLUSION

The EDAMS protocol is an effective surgical technique for treating Moyamoya disease. Although the global literature on the disease has advanced significantly, the absence of sufficient studies in our country renders this research important in contributing to the literature. Future studies and long-term follow-ups should assess the epidemiology and genetic background of Moyamoya disease in Turkey, as well as the comparison of various surgical techniques.

Declarations

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: ED
Data collection: BB, MM
Analysis and interpretation of results: CA, SC
Draft manuscript preparation: BAO, IE
Critical revision of the article: SC, IS
Other (study supervision, fundings, materials, etc...): CY, OK, KT
All authors (ED, BB, MM, SC, BAO, SC, CA, HIS, OK, IE, KT, CY) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Acker G, Schlinkmann N, Fekonja L, Grünwald L, Hardt J, Czabanka M, Vajkoczy P: Wound healing complications after revascularization for Moyamoya vasculopathy with reference to different skin incisions. Neurosurg Focus 46:E12, 2019. https://doi.org/10.3171/2018.11.FOCUS18512
2. Batista S, Koester S, Bishay AE, Bertani R, Oberman DZ, de Abreu LV, Bocanegra-Becerra JE, Amaral D, Isaacs AM, Dewan M, Figueiredo EG: Complications associated with combined direct and indirect bypass in moyamoya disease: a meta-analysis. Neurosurg Rev 47:58, 2024. https://doi.org/10.1007/s10143-024-02285-4
3. Berry JA, Cortez V, Toor H, Saini H, Siddiqi J: Moyamoya: An update and review. Cureus 12:e10994, 2020. https://doi.org/10.7759/cureus.10994
4. Burke GM, Burke AM, Sherma AK, Hurley MC, Batjer HH, Bendok BR: Moyamoya disease: A summary. Neurosurg Focus 26:E11, 2009. https://doi.org/10.3171/2009.1.FOCUS08310
5. Church EW, Bell-Stephens TE, Bigder MG, Gummidipundi S, Han SS, Steinberg GK: Clinical course of unilateral Moyamoya disease. Neurosurgery 87:1262-1268, 2020. https://doi.org/10.1093/neuros/nyaa284

6. Czabanka M, Peña-Tapia P, Scharf J, Schubert GA, Münch E, Horn P, Schmiedek P, Vajkoczy P: Characterization of direct and indirect cerebral revascularization for the treatment of European patients with Moyamoya disease. Cerebrovasc Dis 32:361-369, 2011. https://doi.org/10.1159/000330351
7. Deckers PT, van Hoek W, Kronenburg A, Yaqub M, Siero JCW, Bhogal AA, van Berckel BNM, van der Zwan A, Braun KPJ: Contralateral improvement in cerebrovascular reactivity and TIA frequency after unilateral revascularization surgery in Moyamoya vasculopathy. Neuroimage Clin 30:102684, 2021. https://doi.org/10.1016/j.nicl.2021.102684
8. Duan L, Bao XY, Yang WZ, Shi WC, Li DS, Zhang ZS, Zong R, Han C, Zhao F, Feng J: Moyamoya disease in China: Its clinical features and outcomes. Stroke 43:56-60, 2012. https://doi.org/10.1161/STROKEAHA.111.621300
9. Erol M, Gayret OB, Yigit O, Serefoglu Cabuk K, Toksoz M, Tiras M: A case of homocystinuria misdiagnosed as Moyamoya disease: A case report. Iran Red Crescent Med J 18:e30332, 2016. https://doi.org/10.5812/ircmj.30332
10. Fox BM, Dorschel KB, Lawton MT, Wanebo JE: Pathophysiology of vascular stenosis and remodeling in Moyamoya disease. Front Neurol 12:661578, 2021. https://doi.org/10.3389/fneur.2021.661578
11. Fujimura M, Kaneta T, Tominaga T: Efficacy of superficial temporal artery-middle cerebral artery anastomosis with routine postoperative cerebral blood flow measurement during the acute stage of childhood Moyamoya disease. Childs Nerv Syst 24:827-832, 2008. https://doi.org/10.1007/s00381-007-0551-y
12. Fukui M: Current state of the study on Moyamoya disease in Japan. Surg Neurol 47:138-143, 1997. https://doi.org/10.1016/S0090-3019(96)00358-8
13. Funaki T, Takahashi JC, Miyamoto S: Late cerebrovascular events and social outcome after adolescence: Long-term outcome of pediatric Moyamoya disease. Neurol Med Chir 58:240-246, 2018. https://doi.org/10.2176/nmc.ra.2018-0026
14. Ghosh R, Das S, Roy D, Ray A, Benito-León J: Moyamoya angiopathy in a case of Klinefelter syndrome. Childs Nerv Syst 38:1195-1199, 2022. https://doi.org/10.1007/s00381-021-05371-w
15. Goren O, Hendrix P, Peled A, Kimchi G, Zauberman J, Griessenauer C, Feldman Z: Encephaloduroarteriosynangiosis with dural inversion for Moyamoya disease in a pediatrics and adult population: A single-center 20-year experience. World Neurosurg 149:e16-21, 2021. https://doi.org/10.1016/j.wneu.2021.02.102
16. Gross BA, Thomas AJ, Frerichs KU: Endovascular treatment of symptomatic Moyamoya. Neurosurg Rev 37:579-583, 2014. https://doi.org/10.1007/s10143-014-0542-x
17. Hallemeier CL, Rich KM, Grubb RL Jr, Chicoine MR, Moran CJ, Cross DT 3rd, Zipfel GJ, Dacey RG Jr, Derdeyn CP: Clinical features and outcomes in north American adults with Moyamoya phenomenon. Stroke 37:1490-1496, 2006. https://doi.org/10.1161/01.STR.0000221787.70503.ca
18. Han C, Feng H, Han YQ, Liu WW, Zhang ZS, Yang WZ, Duan L: Prospective screening of family members of Moyamoya disease patients. PLoS One 9:e88765, 2014. https://doi.org/10.1371/journal.pone.0088765
19. Houkin K, Yoshimoto T, Kuroda S, Ishikawa T, Takahashi A, Abe H: Angiographic analysis of moyamoya disease-how does moyamoya disease progress? Neurol Med Chir 36:783-787, 1996. https://doi.org/10.2176/nmc.36.783
20. Kelly ME, Bell-Stephens TE, Marks MP, Do HM, Steinberg GK: Progression of unilateral Moyamoya disease: A clinical series. Cerebrovasc Dis 22:109-115, 2006. https://doi.org/10.1159/000093238
21. Kikuta K: Experiences using 3-tesla magnetic resonance imaging in the treatment of Moyamoya disease. Acta Neurochir Suppl 103:123-126, 2008. https://doi.org/10.1007/978-3-211-76589-0_22
22. Kim H, Jang DK, Han YM, Sung JH, Park IS, Lee KS, Yang JH, Huh PW, Park YS, Kim DS, Han KD: Direct bypass versus indirect bypass in adult Moyamoya angiopathy with symptoms or hemodynamic instability: A meta-analysis of comparative studies. World Neurosurg 94:273-284, 2016. https://doi.org/10.1016/j.wneu.2016.07.009
23. Kim JS: Moyamoya disease: Epidemiology, clinical features, and diagnosis. J Stroke 18:2-11, 2016. https://doi.org/10.5853/jos.2015.01627
24. Kitchen L, Westmacott R, Friefeld S, MacGregor D, Curtis R, Allen A, Yau I, Askalan R, Moharir M, Domi T, deVeber G: The pediatric stroke outcome measure: A validation and reliability study. Stroke 43:1602-1608, 2012. https://doi.org/10.1161/STROKEAHA.111.639583
25. Kraemer M, Heienbrok W, Berlit P: Moyamoya disease in Europeans. Stroke 39:3193-3200, 2008. https://doi.org/10.1161/STROKEAHA.107.513408
26. Kuroda S: Bypass surgery for Moyamoya disease, part 1: Special considerations and techniques. No Shinkei Geka 50:806-818, 2022. https://doi.org/10.11477/mf.1436204624.
27. Kuroda S, Fujimura M, Takahashi J, Kataoka H, Ogasawara K, Iwama T, Tominaga T, Miyamoto S; Research Committee on Moyamoya Disease (Spontaneous Occlusion of Circle of Willis) of the Ministry of Health, Labor, and Welfare, Japan: Diagnostic criteria for Moyamoya disease-2021 revised version. Neurol Med Chir 62:307-312, 2022. https://doi.org/10.2176/jns-nmc.2022-0072
28. Kuroda S, Hashimoto N, Yoshimoto T, Iwasaki Y; Research Committee on Moyamoya Disease in Japan: Radiological findings, clinical course, and outcome in asymptomatic Moyamoya disease: Results of multicenter survey in Japan. Stroke 38:1430-1435, 2007. https://doi.org/10.1161/STROKEAHA.106.478297
29. Lee WJ, Jeong SK, Han KS, Lee SH, Ryu YJ, Sohn CH, Jung KH: Impact of endothelial shear stress on the bilateral progression of unilateral Moyamoya disease. Stroke 51:775-783, 2020. https://doi.org/10.1161/STROKEAHA.119.028117
30. Lucia K, Acker G, Mrosk F, Beyaztas D, Vajkoczy P: Longitudinal angiographic characterization of the efficacy of combined cerebral revascularization using minimally invasive encephalodurosynangiosis in patients with Moyamoya angiopathy. Neurosurg Rev 45:3689-3698, 2022. https://doi.org/10.1007/s10143-022-01862-9

31. Matsushima T, Inoue T, Suzuki SO, Fujii K, Fukui M, Hasuo K: Surgical treatment of Moyamoya disease in pediatric patients-comparison between the results of indirect and direct revascularization procedures. Neurosurgery 31:401-405, 1992. https://doi.org/10.1227/00006123-199209000-00003
32. Nielsen TH, Abhinav K, Sussman ES, Han SS, Weng Y, Bell-Stephens T; CNRN; Heit JJ, Steinberg GK: Direct versus indirect bypass procedure for the treatment of ischemic Moyamoya disease: Results of an individualized selection strategy. J Neurosurg 134:1578-1589, 2020. https://doi.org/10.3171/2020.3.JNS192847
33. Ott WP, Bellamy S, Onyali CB: A rare case of Moyamoya disease in a Hispanic woman: Unveiling non-Asian ethnicity and atypical risk factors. Am J Case Rep 24:e940353, 2023. https://doi.org/10.12659/AJCR.940353
34. Pang CH, Cho WS, Kang HS, Kim JE: Benefits and risks of antiplatelet medication in hemodynamically stable adult Moyamoya disease. Sci Rep 11:19367, 2021. https://doi.org/10.1038/s41598-021-99009-1
35. Per H, Unal E, Poyrazoglu HG, Ozdemir MA, Donmez H, Gumus H, Uzum K, Canpolat M, Akyildiz BN, Coskun A, Kurtsoy A, Kumandas S: Childhood stroke: Results of 130 children from a reference center in Central Anatolia, Turkey. Pediatr Neurol 50:595-600, 2014. https://doi.org/10.1016/j.pediatrneurol.2013.12.023
36. Said S, Cooper CJ, Alkhateeb H, Galvis JM, Hernandez GT, Salameh HJ: Moyamoya in hispanics: not Only in Japanese. Neurol Int 6:5369, 2014. https://doi.org/10.4081/ni.2014.5369
37. Shang S, Zhou D, Ya J, Li S, Yang Q, Ding Y, Ji X, Meng R: Progress in moyamoya disease. Neurosurg Rev 43:371-382, 2020. https://doi.org/10.1007/s10143-018-0994-5
38. Shimizu T, Aihara M, Yamaguchi R, Sato K, Aishima K, Yoshimoto Y: Large craniotomy increases the risk of minor perioperative complications in revascularization surgery for Moyamoya disease. World Neurosurg 141:e498-507, 2020. https://doi.org/10.1016/j.wneu.2020.05.227
39. Shoukat S, Itrat A, Taqui AM, Zaidi M, Kamal AK: Moyamoya disease: A clinical spectrum, literature review and case series from a tertiary care hospital in Pakistan. BMC Neurol 9:15, 2009. https://doi.org/10.1186/1471-2377-9-15
40. So Y, Lee HY, Kim SK, Lee JS, Wang KC, Cho BK, Kang E, Lee DS: Prediction of the clinical outcome of pediatric Moyamoya disease using postoperative basal/acetazolamide stress brain perfusion SPECT after revascularization surgery. Stroke 36:1485-1489, 2005. https://doi.org/10.1161/01.STR.0000170709.95185.b1
41. Suzuki J, Kodama N: Moyamoya disease-A review. Stroke 14:104-109, 1983. https://doi.org/10.1161/01.STR.14.1.104
42. Suzuki J, Takaku A: Cerebrovascular "Moyamoya" disease. Disease showing abnormal net-like vessels in the base of the brain. Arch Neurol 20:288-299, 1969. https://doi.org/10.1001/archneur.1969.00480090076012
43. Takeuchi K: Hypoplasia of bilateral internal carotid arteries. No To Shinkei 9:37-43, 1957.
44. Tatli B, Ekici B, Sencer A, Sencer S, Aydin K, Aydinli N, Caliskan M, Ozmen M, Kiris T: Clinical features, prothrombotic risk factors, and long-term follow-up of eight pediatric Moyamoya patients. J Clin Neurol 8:100-103, 2012. https://doi.org/10.3988/jcn.2012.8.2.100
45. Türkiye İstatistik Kurumu, Evlenme ve Boşanma İstatistikleri, 2023, Yayım Tarihi :22 Şubat 2024, Saat: 10:00, Sayı: 53707, https://data.tuik.gov.tr/Bulten/Index?p=Evlenme-ve-Bosanma-Istatistikleri-2023-53707
46. Volkan-Salanci B, Lay Ergun E, Genc Sel C, Yalnizoglu D, Turanli G: The role of brain perfusion SPECT in Moyamoya disease. Rev Esp Med Nucl Imagen Mol 31:216-218, 2012. https://doi.org/10.1016/j.remn.2012.02.006
47. Xu R, Xie ME, Kim J, Kothari R, Sun LR, Jackson EM, Tamargo RJ, Huang J, Ahn ES, Cohen AR: Same-day versus staged revascularization of bilateral Moyamoya arteriopathy in pediatric patients. Childs Nerv Syst 39:1207-1213, 2023. https://doi.org/10.1007/s00381-023-05916-1
48. Zhang X, Xiao W, Zhang Q, Xia D, Gao P, Su J, Yang H, Gao X, Ni W, Lei Y, Gu Y: Progression in Moyamoya disease: Clinical features, neuroimaging evaluation, and treatment. Curr Neuropharmacol 20:292-308, 2022. https://doi.org/10.2174/1570159X19666210716114016