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Moyamoya Disease Worldwide-Global Burden East and West

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Abstract

The Moyamoya disease [MMD] is a cerebrovascular disorder characterized by progressive stenosis of intracranial internal carotid arteries and compensatory collateral formation at the base of the brain, mainly around the circle of Willis. When no particular associated risk factors can be identified, it is termed as Moyamoya disease. However, it may be associated with other neurological and extra-neurological disorders where it is termed as Moyamoya syndrome [MMS]. The condition is predominantly seen in East Asia and has bimodal age of distribution. The clinical manifestations are also age dependant with ischemia predominating in childhood and hemorrhagic manifestations being more common in adults. The pathogenesis is not entirely known, but genetic susceptibility is believed to be an important predisposing factor. The Suzuki staging system is most widely used for evaluation and staging of Moyamoya disease. The gold standard diagnostic modality is cerebral angiography but magnetic resonance imaging [MRA] has also been employed for diagnosis. Treatment is primarily surgical revascularization which is of 3 types: direct, indirect or combined revascularization. Although the role of revascularization surgery has been well established for ischemic MMD, the ideal surgical approach and the role of surgery in hemorrhagic MMD remains controversial.

Keywords: moyamoya disease, moyamoya syndrome, stroke, cerebral angiography, revascularization

1. Introduction

Moyamoya disease [MMD] is a form of chronic cerebrovascular occlusion characterized by occlusion of terminal internal carotid artery [ICA] along with a network of collateral vessels at the base of the brain. The disease was first brought to light by Takeuchi and Shimizu, where they described a young man with bilateral occlusion of ICA which was found to be due to congenital hypoplasia rather than atherosclerotic lesion [1]. Similar cases have been described in Japanese literature. After that, the condition came to be known by various names and the term 'spontaneous occlusion of the circle of Willis' by Kudo gained popularity [2]. The disease was finally coined '*moyamoya*' by Suzuki and Takaku based on the abnormal vascular network at the base of the brain that resembles 'vague or hazy puff of smoke' which is called *moyamoya* in Japanese [3].

This cerebral angiopathy is broadly termed ‘moyamoya phenomenon’ comprising of two nosological entities. The cerebrovascular syndrome is called ‘Moyamoya syndrome’ [MMS] when it is associated with neurological and extra neurological diseases like Neurofibromatosis 1 [NF1], Down syndrome, thyroid disease, cranial irradiation, sickle cell anemia, among other pathological conditions [4]. The Guidelines of the Research Committee on the Pathology and Treatment of Spontaneous Occlusion of Circle of Willis defined isolated moyamoya angiopathy as being idiopathic and called it ‘Moyamoya disease’ [5].

MMD is more common in Asian ethnicities as compared to the Western population [6]. The increased prevalence in Japan, Korea and other East Asian countries raised genetic predisposition to this condition. Subsequently, Kamada *et al.* identified a susceptibility gene, Ringin Protein 213 [RNF 213], and it was seen that this gene was positively associated with familial MMD [7]. Symptomatology of MMD varies according to the age group. Cerebral ischemia is more common in the pediatric than in the adult age group, whereas, the hemorrhagic type is more common in >40 years of age. Only one type predominates in a particular patient, but the symptoms are often recurrent. The disease diagnosis often rests upon angiography, and revascularization procedures are performed to avoid recurrence of symptoms. The lack of understanding of the exact pathophysiologic mechanism of MMD limits the development of treatments to prevent vascular damage.

2. Methods used

A literature search was conducted using PubMed. The keywords used were Moyamoya disease, Moyamoya syndrome, ‘puff of smoke’, Suzuki classification, angiography, revascularization procedures etc. Relevant articles were reviewed in detail. The search was filtered to include as many recent publications as possible. An effort was made to compile and highlight the key differences in the disease’s clinical profile from East to West.

3. Epidemiology

For a very long time, Moyamoya disease was thought to be a disease of Asian lineage, but now it has been observed to be prevalent across the world in people with many ethnic backgrounds. MMD has been most extensively studied in Japan, where it is the most common pediatric cerebrovascular disease [8]. It shows a prominent East–West gradient, with a in East Asian countries ten times higher than the Western countries [9]. MMD is most frequently seen in Japan, with an incidence of 0.35–1.13/1,00,000/year and a prevalence of 3.16–10.5/1,00,000 [10]. In a study done in Hokkaido, Japan, 267 new cases were diagnosed between 2002–2006 [8]. The incidence and prevalence were also found to be high in other Asian countries like Korea, China and Taiwan [11]. The incidence in all these countries is found to be increasing over the years, most likely due to advancements in diagnostic modalities and a better understanding of the genetic factors linked to the disease [12]. Studies from outside Asia are very few. The incidence in Washington state and California was 0.086/1,00,000, but in them the incidence in Asian Americans was 4.6 times that of White [9]. In Europe, the incidence of MMD was 1/10th of that in Japan. North America’s incidence was as low as 0.09/1,00,000 individuals, although an increasing trend is now being noted [13].

A similar bimodal age distribution is seen across the world, with the first peak occurring at 5–14 years in the pediatric population and around 4th decade in

adulthood [5]. In Japan, family history is present in 10–15% of cases, and the risk of the disease in a family member is about 30–40 times higher than the general population. A familial predisposition was less commonly seen in European countries. In most countries, the disease was more frequently seen in females, with male to female ratio ranging from 1:1.8 to 1:2.2 [10, 14]. These epidemiological parameters remained constant from East to West as evident in the literature review from across the world by Kim et al. [6].

4. Pathology

The pathological features have been described based on autopsy findings of cases of MMD. The most common lesion is intracranial hemorrhage, which occurs in basal ganglia, thalamus, hypothalamus and brain stem. The intracranial hemorrhage may show intraventricular extension. Other findings are subarachnoid hemorrhage and small infarcts in the capsule- ganglionic area [14]. The main pathological findings according to the vessels involved are mentioned below.

- a. *The Circle of Willis*: The distal ends of the internal carotid artery, Circle of Willis and its major branches are narrowed, tapered and often occluded. The occlusion is because of intimal thickening with marked attenuation of media. The intimal thickening is composed of smooth muscle cell proliferation rather than lipid and lipid-laden macrophages deposition, as seen in atherosclerosis [15].
- b. *Perforating vessels*: The branches of Circle of Willis, anterior choroidal arteries, posterior cerebral arteries become dilated. Numerous dilated and tortuous vessels then originate from these arteries to penetrate the base of the brain. Aneurysm formation can also be seen. These small arteries can be enlarged with thin-walled or thick-walled with luminal stenosis [16].
- c. *Leptomeningeal Vessels*: Angiographic findings in MMD reveal leptomeningeal anastomosis between the three main cerebral arteries and transdural anastomosis from external carotid arteries. These form the abnormal collateral circulation seen as the ‘puff of smoke’ [17].
- d. *Other features*: Intracranial aneurysms, stenosis in extracranial arteries like carotid, renal, pulmonary arteries, etc.

Thus, the pathology of the disease can be viewed as ICA [Internal carotid artery] to ECA [External carotid artery] prism, where the contribution of ICA to cerebral blood supply gradually decreases, and the compensatory vascular network is formed which is predominantly fed by ECA.

5. Pathogenesis

The mechanisms leading to the above-mentioned pathology are not entirely known. It is not clear what leads to migration and proliferation of smooth muscle cells in the intima and leads to its thickening. Moreover, why this thickening happens only in the circle of Willis is unknown. Many features of the disease point towards a hereditary predisposition- high incidence in Japanese people, familial occurrence, association with other congenital disorders like sickle cell anemia,

neurofibromatosis, Down syndrome, etc. A multifactorial mode of inheritance has been suggested. A possible linkage of the disease with markers located on chromosome 6, chromosome 17, chromosome 8q23 has been suggested [18–20]. Recently, a genetic locus in the Ring Finger Protein [RNF] 213 gene was also associated with MMD [7]. A higher carrier rate in Eastern Asia probably explains the higher prevalence of the disorder in Japan and other eastern Asian countries as compared to the Western world [21].

Moyamoya angiopathy has been identified with many genetic disorders like Neurofibromatosis 1, Noonan syndrome, Costello syndrome, Sickle cell disease, GUCY1A3 mutations, BRCC3/MTCP1 gene mutation, Down syndrome, Turner syndrome, etc. [19] Moyamoya disease associated with other familial or acquired conditions has also been termed as ‘quasi-MMD’. It was noted that unilateral presentation was more common than bilateral and hemorrhagic manifestations were less common in quasi- MMD [21].

Although genetic predisposition to the disease exists, the majority of cases are sporadic. Certain acquired factors have been suggested for disease progression. These include vasculitis [3], infections [20], cranial trauma [22], post-irradiation state [23] to name a few.

6. Clinical features

The pathological changes in cerebral arteries lead to cerebrovascular events in Moyamoya disease. Two peaks have been identified, at around ten years and 30–40 years. The peak occurs later in women than in men [24].

The symptoms can be classified in the following four main heads (Figure 1) [13].

Transient ischemic attacks [TIA] and infarct may present as a variety of symptoms- motor paresis, sensory disturbance, speech disturbances, alteration of consciousness [25]. Whereas these symptoms present acutely, mental decline, dyskinesias tend to progress over the years. Dilated collateral vessels in basal ganglia have been implicated in the development of choreiform movements [26]. Bilateral disease is associated with cognitive deficits. Hemorrhagic type is more common in adults >40 years of age and most commonly present with impaired consciousness. Irrespective of the primary pathology [ischemic/hemorrhagic], the symptoms tend to be recurrent and usually a single pathology predominates in each individual. Headache is another common symptom generally seen in children <14 years old [27]. Dilated transdural collaterals stimulate dural nociceptors precipitating migraine-like headaches. Headache may also be a manifestation of chronic hypoxemia.

The symptoms are triggered by hyperventilation, such as blowing/crying due to decreased cerebral blood flow secondary to CO₂ washout. Worsening is also seen

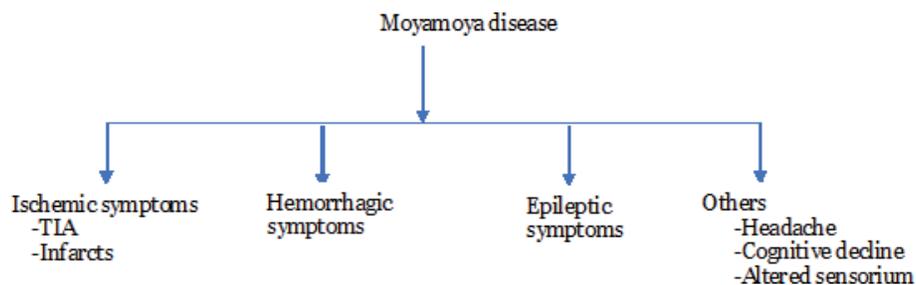


Figure 1.
Clinical symptoms of Moyamoya disease.

with infection of the upper respiratory tract. Hypertension and aging often contribute to hemorrhage, which may occur at repetitive intervals. Massive bleeding may even lead to death. Epilepsy, as a manifestation of the disease, is usually seen in children less than ten years of age [28].

The clinical features also tend to vary from East to West. The ischemic manifestations are more predominant in the US [United States] than in other eastern countries. The rate of hemorrhagic disease in adults in Asian countries is higher [42%] than in those of Asian descent residing in the US [29]. The disorder's overall spectrum remains constant worldwide, with ischemic manifestations as the main presenting feature in children and both ischemia and hemorrhage in adults.

7. Diagnosis

7.1 Angiography

Angiography is the gold standard for diagnosis and assessing disease progression. The hallmark findings of cerebral angiography are occlusion of intracranial internal carotid arteries (**Figure 2**) and abnormal smog-like arteriolar network [moyamoya vessels] at the base of the brain (**Figure 3**). The Circle of Willis and its main branches, leptomeningeal vessels and transdural anastomosis between ophthalmic artery, external carotid artery and vertebral artery are frequently seen. Involvement of posterior circulation is less commonly observed.

Suzuki et al. staged the disease progression into the following stages based on the angiographic findings [3, 22, 27].

1. Narrowing of the carotid forks
2. Initiation of moyamoya [dilated major cerebral artery and a slight network of collaterals]
3. Intensification of moyamoya with the disappearance of middle and anterior cerebral arteries
4. Minimization of moyamoya [disappearance of posterior cerebral artery and narrowing of individual moyamoya vessels]
5. Reduction of moyamoya [disappearance of main cerebral arteries, further minimization of moyamoya, increase in collaterals from external carotid arteries]
6. Disappearance of moyamoya [complete disappearance of moyamoya with blood flow derived only from the external carotid artery and vertebrobasilar system]

Apart from these changes, aneurysm formation can also be seen in angiography. A revised version of Suzuki staging system was given by Mugikura et al. (**Table 1**), where staging is done based on angiographic severity of stenosis of the middle cerebral artery and anterior cerebral artery [30].

Both the staging systems highlight that with the progression of the disease, the contribution of blood supply from ICA decreases and an intricate collateral network is formed which derives its blood flow from vessels outside the cerebral circulation.

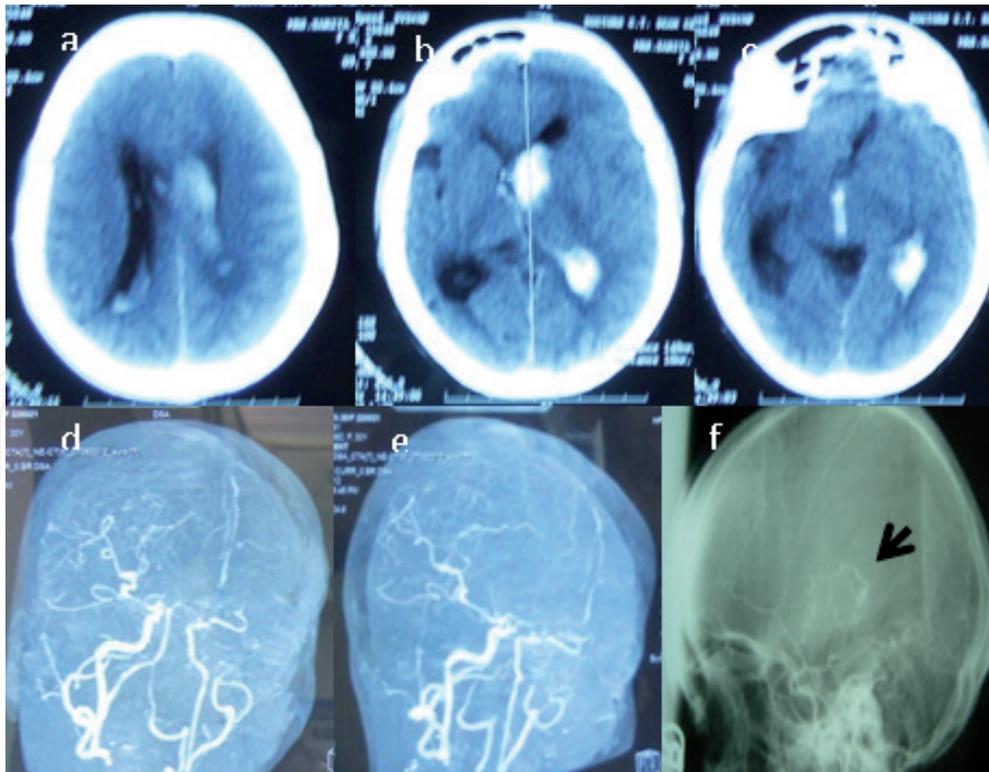


Figure 2. Neuroimaging of a 40 years old lady who presented with ICH. Non-contrast CT axial sections of brain (a, b, c) show intraventricular hemorrhage involving bilateral lateral ventricles (L > R), third and fourth ventricle. Angiographic images (d, e) show occlusion of the supraclinoid segment of the left internal carotid artery and attenuation on the right side with lenticulostriate collaterals showing a “puff of smoke” appearance (f).

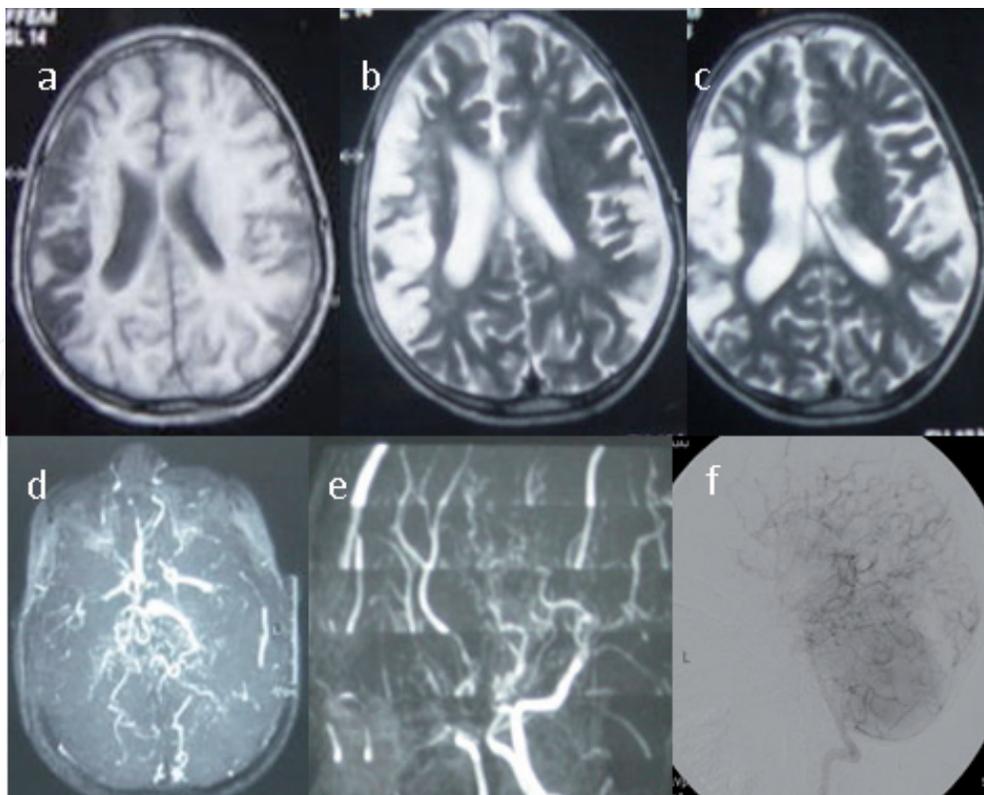


Figure 3. Neuroimaging of a young boy of 6 years of age who presented with recurrent ischemic strokes. MRI brain axial sections show altered signal intensity areas hypointense on T1 (a) and hyperintense on T2 (b, c) in bilateral frontoparietal cortex involving the MCA territory. Angiographic images show multiple tortuous collaterals involving both anterior (d) and posterior circulation (d, e, f) giving the typical “puff of smoke” appearance on cerebral DSA (f).

ICA Stage	Angiographic findings
I	Mild to moderate stenosis around carotid bifurcation, absent/slightly developed moyamoya, ACA/MCA branches opacified in anterograde fashion
II	Severe stenosis around carotid bifurcation, well developed moyamoya, several of ACA/MCA branches opacified in anterograde fashion
III	Occlusion of proximal ACA/MCA, well developed moyamoya, only a few of ACA/MCA branches are faintly opacified in anterograde fashion through the mesh work of ICA moyamoya
IV	Complete occlusion of proximal ACA and MCA, small amount of moyamoya, no opacification of either ACA/MCA branches in anterograde fashion

ACA- anterior cerebral artery, MCA- middle cerebral artery, ICA- internal cerebral artery.

Table 1.
 The angiographic ICA staging system modified by Mugikura et al.

7.2 Computed tomography [CT]

CT scan shows hyperdensities in basal ganglia, thalamus, ventricular system and subarachnoid spaces in the hemorrhagic type of MMD. In the ischemic type of the disease, lacunar infarcts can be seen as the areas of hypodensities. When contrast-enhanced, tortuous and curvilinear vessels in basal ganglia can be visualized which represent the moyamoya vessels.

Magnetic Resonance Imaging and Angiography [MRI and MRA].

MRI and MRA provide visualization of the arterial tree without being invasive as conventional angiography. In addition to this, MRI also helps demonstrate small

Score for each artery	MRA finding
<i>Internal cerebral artery</i>	
0	Normal
1	Stenosis of C1
2	Discontinuity of the C1 signal
3	Invisible
<i>Middle cerebral artery</i>	
0	Normal
1	Stenosis of M1
2	Discontinuity of the M1 signal
3	Invisible
<i>Anterior cerebral artery</i>	
0	Normal A2 and blood vessels distal to A2
1	Signal decrease A2 and its distal blood vessels
2	Invisible
<i>Posterior cerebral arteries</i>	
0	Normal P2 and blood vessels distal to P2
1	Signal decrease P2 and its distal blood vessels
2	Invisible

Table 2.
 The classification and scoring based on the MRA findings- Score of each artery.

MRA total score	MRA stage
0-1	1
2-4	2
5-7	3
8-10	4

MRA: Magnetic Resonance Imaging.

Table 3.
The classification and scoring based on the MRA findings – MRA total Score.

subcortical lesions that are difficult to identify on the CT scan. MRA helps to identify the stenotic distal end of the internal carotid artery, small moyamoya vessels and dural anastomosis between external carotid arteries and vessels of the posterior circulation.

The classification and scoring based on the MRA findings are given above in **Tables 2** and **3**. This MRA scoring system also finds its place in the 2012 Guidelines for the Diagnosis and Treatment of MMD in Japan [5].

7.3 Ultrasonography

In patients with moyamoya disease, the involvement of many extracranial arteries like external carotid arteries, aorta, pulmonary artery, celiac artery, and renal artery has been described. Characteristic signs like ‘champagne bottleneck sign’ seen due to reduction in the diameter of proximal ICA and ‘diamond reversal sign’ due to smaller ICA diameter compared to external carotid artery have been demonstrated [31].

Though all the diagnostic modalities contribute to identifying and staging abnormal vasculature, angiography remains the mainstay of diagnosis. It is also helpful in documenting the postoperative resolution of moyamoya.

Electroencephalography [EEG].

The following EEG findings have been seen in moyamoya disease [32]:

1. Diffuse, bilateral, low voltage, slow spike and wave
2. ‘Buildup’ phenomenon- a diffuse pattern of slow waves
3. ‘Rebuildup’ phenomenon- diffuse slow waves during hyperventilation. This rebuild up phenomenon is seen due to decreased pCO₂ on hyperventilation leading to cerebral ischemia and vasoconstriction.

8. Diagnostic guidelines

The advancements in various diagnostic modalities lead to the formulation of diagnostic guidelines for Moyamoya disease shown in **Table 4** [5].

8.1 Treatment

Moyamoya disease is a chronic progressive disease described earlier, leading to recurrent strokes due to internal carotid artery occlusion and ischemia due to narrow, low caliber collaterals. The illness’s mainstay is revascularization surgery

A. Cerebral angiography should present at least the following findings:
1. Stenosis/occlusion at the terminal portion of ICA and/or at the proximal portion of ACA and/or MCA
2. Abnormal vascular network in the vicinity of stenotic/occluded vessels
3. Bilateral findings
B. Conventional angiogram not required when MRI/MRA demonstrate following findings:1.
1. Stenosis/occlusion at the terminal portion of ICA and/or at the proximal portion of ACA and/or MCA on MRA
2. Abnormal vascular network in the basal ganglia on MRA[>2 flow voids in basal ganglia in MRI].
3. Bilateral findings
C. Absence of arteriosclerosis, autoimmune disease, meningitis, brain neoplasm, down syndrome, Recklinghausen's disease, head trauma, irradiation to head, others.
D. Pathological findings:
1. Stenosis/occlusion due to intimal thickening at the terminal ICA, usually on both sides
2. Arteries of Circle of Willis show varying degree of stenosis/occlusion of intima, attenuation of media and waving of internal elastic lamina
3. Numerous small vascular channels around the Circle of Willis
4. Reticular conglomerates of small vessels in pia matter.
Definitive case: A/B + C [In children, a case that fulfills A1 and A2 or B1 and B2 on one side and remarkable stenosis of terminal ICA on opposite side is also included.]
Probable case: A1 and A2 [or B1 and B2] and C [unilateral]

Table 4.
Diagnostic guidelines for Moyamoya disease.

to increase the intracranial blood flow using extracerebral blood vessels by direct bypass or pialsynangiosis. The decision for surgical intervention is based on the patient's age, symptomatic/asymptomatic disease, ischemic/hemorrhagic manifestations, presence/absence of aneurysm and risk of recurrence.

The indication of surgery can be briefly summarized as follows in **Figure 4** [33].

8.2 Risk factors for disease recurrence

Moyamoya disease is known to progress over the years. The disease progression rate was reported to be approximately 20% over six years in those managed conservatively [34]. The risk factors of disease progression and subsequent ischemic stroke were identified as follows:

1. Female gender
2. Graves' disease
3. RNF213 variant
4. Family history positive [35]
5. Posterior circulation was also recognized as a decisive risk factor for ischemic stroke [36].

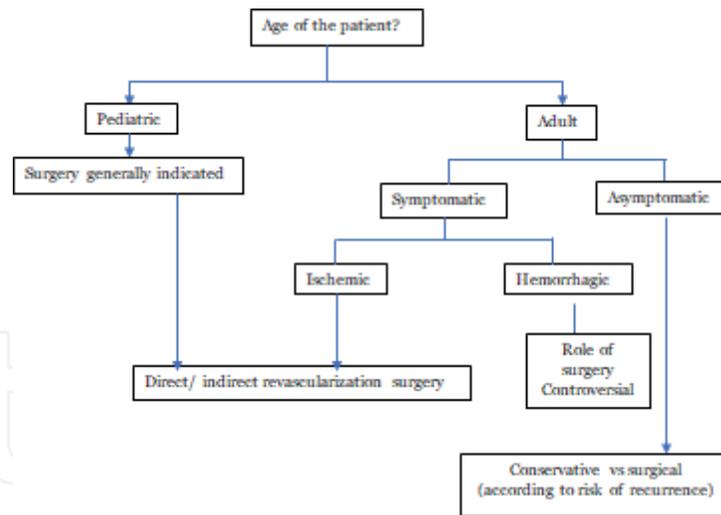


Figure 4.
Overview of the management of Moyamoya disease.

Moyamoya disease is a progressive disease, and symptomatic progression is seen in approximately two-thirds of patients. [29] In a large meta-analysis, where 1,156 people were studied, it was seen that 87% of those who underwent surgical revascularization showed partial or complete resolution of symptomatic cerebral ischemia [37].

A careful choice of treatment, that is, conservative vs. surgical should thus be made keeping in mind the above-mentioned risk factors.

8.3 Conservative treatment of mmd

The predominant manifestation of MMD is ischemic stroke. However, antiplatelet therapy is ineffective to prevent recurrent cerebral infarction in ischemic MMD. The ischemic insult in MMD patients is a consequence of hemodynamic instability. There is no evidence of endothelial dysfunction at the site of internal carotid artery bifurcation. Therefore, increased platelet adhesion is not seen in MMD. Hence, theoretically, antiplatelet drugs are ineffective for preventing ischemic stroke in MMD. Moreover, increased risk of hemorrhage remains with antiplatelets in patients with MMD [38]. The annual stroke rate in patients managed conservatively is between 3.2%–15% [35].

8.4 Indication of surgical revascularization

Surgical revascularization is done to increase the cerebral blood flow and restore reserve capacity. The increase in cerebral blood flow prevents recurrent cerebral infarction. The indications for surgical revascularization are:

1. Recurrent clinical symptoms due to cerebral ischemia
2. Pediatric MMD because pediatric MMD is more progressive than adult MMD. Early diagnosis and intervention are of paramount importance to prevent irreversible damage. In a recent study, Rosi et al. confirmed a high benefit/risk ratio, with better postoperative functional status and low rates for the need of surgical retreatment in the pediatric population undergoing surgical revascularization [39].
3. Role of revascularization surgery in asymptomatic MMD with stable hemodynamics is not well established but preferred by neurosurgeons given the disease

being a progressive disorder. Risk–benefit ratio determines the feasibility of the surgical intervention in such patients.

4. Role of revascularization surgery in hemorrhagic stroke is controversial.

With increased understanding of MMD being familial in at least some of the world's regions, it is being suggested that asymptomatic siblings and family members should be screened for moyamoya pathology. Whenever such a condition is detected, it should be managed surgically, keeping in mind the illness's progressive nature.

8.5 Surgical modalities for revascularization

8.5.1 Direct revascularization

Anastomosis is formed between the superficial temporal artery and cortical branches of middle cerebral arteries in this procedure. For posterior circulation, the occipital artery is used as a donor for anteroposterior cerebral arteries' cortical branches. The transdural or transcalvarial collateral channels should be preserved during the surgery.

The advantage of this procedure is an immediate improvement in the cerebral blood flow after surgery. However, the successful restoration of cerebral blood flow is operator dependant as it is challenging to perform. Moreover, postoperative hyperperfusion syndrome may develop after surgery leading to neurological deterioration. Patency and amount of bypass flow may be assessed postoperatively by digital subtraction angiography or quantitative magnetic resonance angiography.

The annual stroke rate after direct revascularization was reportedly 0–1.6% [40].

8.5.2 Indirect revascularization

The various surgical procedures are

1. Encephalomyosynangiosis[EMS] where deep temporal artery supplying the temporalis muscle is the vessel for neovascularization
2. Encephalo-duro-arteriosynangiosis[EDAS]: Here, superficial temporal artery[STA] is harvested with surrounding galea and periosteum; STA flap is placed with a galea cuff. The dura and galea are then sutured to cover the brain with arterial flap.
3. Encephalo-myo-arteriosynangiosis[EDAMS]
4. Encephalo-galeo-synangiosis[EGS]
5. Omental flap surgery
6. Multiple burr hole surgery

The last two surgeries are performed as primary or after failed revascularization by other techniques.

Indirect revascularization is relatively easier to perform than direct surgeries, and the incidence of hyperperfusion is also less. However, the improvement in cerebral revascularization takes longer than the direct surgeries where the effect is immediate.

After indirect revascularization, patients experienced 0–14.3% postoperative annual stroke rate [41].

Thus either of the indirect and direct revascularization procedures can be performed to rectify the underlying pathology, but the risk of recurrence is much less with the direct revascularization surgeries without any delay to the benefit.

8.6 Peri/postoperative complications

The following complications have been noted in the peri/postoperative period in MMD:

1. The risk of postoperative stroke has been estimated to be 1.6%- 16% [42].
2. The risk of perioperative ischemic complications is more in patients with unstable hemodynamics and advanced Suzuki stage with a lower cerebral blood flow.
3. Hemorrhagic stroke develops in 0.7%–8% [42].
4. Hyperperfusion syndrome- due to the chronic changes in cerebral blood vessels, the auto-regulatory function is lost, and the vascular reserve is decreased. The excessive blood flow immediately after the surgery is sometimes not well tolerated, leading to cerebral hemorrhage. Another factor that may predispose to intracranial hemorrhage is increased vascular permeability secondary to chronic ischemia.
5. Epidural hematoma mainly in the pediatric population.
6. Skin problems due to scalp ischemia after revascularization.

9. Conclusion

Moyamoya disease is a chronic progressive vasculopathy seen in children and adults, characterized by occlusion/stenosis at the terminal portions of the internal carotid artery and abnormal collateral network formation at the base of the brain. It is predominantly seen in Asian countries. It may be idiopathic [moyamoya disease] or associated with other disorders when it is called moyamoya syndrome. Various angiographic and magnetic resonance angiographic findings have been described which form the basis of the diagnostic guidelines for MMD. It may present as an ischemic/hemorrhagic stroke. It is generally managed with direct/indirect revascularization surgical techniques that aim to restore the cerebral blood flow and prevent strokes that restore the cerebral blood flow and prevent strokes' recurrence.

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References

- [1] Smith JL. Understanding and treating moyamoya disease in children. *Neurosurg Focus*. 2009 Apr;26(4): E4. doi: 10.3171/2000.01.FOCUS08306. PMID: 19335128.
- [2] Menon G, Hegde A. Moyamoya disease. *Arch Med Health Sci*. 2019;7(2): 224-232
- [3] Suzuki J, Takaku A. Cerebrovascular “moyamoya” disease. Disease showing abnormal net-like vessels in base of brain. *Arch Neurol*. 1969 Mar;20(3):288-99. doi: 10.1001/archneur.1969.00480090076012. PMID: 5775283.
- [4] Phi JH, Wang KC, Lee JY, Kim SK. Moyamoya Syndrome: A Window of Moyamoya Disease. *J Korean Neurosurg Soc*. 2015 Jun;57(6):408-14. doi: 10.3340/jkns.2015.57.6.408. Epub 2015 Jun 30. PMID: 26180607; PMCID: PMC4502236.
- [5] Research Committee on the Pathology and Treatment of Spontaneous Occlusion of the Circle of Willis; Health Labour Sciences Research Grant for Research on Measures for Intractable Diseases. Guidelines for diagnosis and treatment of moyamoya disease (spontaneous occlusion of the circle of Willis). *Neurol Med Chir (Tokyo)*. 2012;52(5):245-66. doi: 10.2176/nmc.52.245. PMID: 22870528.
- [6] Kim JS. Moyamoya Disease: Epidemiology, Clinical Features, and Diagnosis. *J Stroke*. 2016 Jan;18(1):2-11. doi: 10.5853/jos.2015.01627. Epub 2016 Jan 29. PMID: 26846755; PMCID: PMC4747069.
- [7] Kamada F, Aoki Y, Narisawa A, Abe Y, Komatsuzaki S, Kikuchi A, Kanno J, Niihori T, Ono M, Ishii N, Owada Y, Fujimura M, Mashimo Y, Suzuki Y, Hata A, Tsuchiya S, Tominaga T, Matsubara Y, Kure S. A genome-wide association study identifies RNF213 as the first Moyamoya disease gene. *J Hum Genet*. 2011 Jan;56(1):34-40. doi: 10.1038/jhg.2010.132. Epub 2010 Nov 4. PMID: 21048783.
- [8] Baba T, Houkin K, Kuroda S. Novel epidemiological features of moyamoya disease. *J Neurol Neurosurg Psychiatry*. 2008 Aug;79(8):900-4. doi: 10.1136/jnnp.2007.130666. Epub 2007 Dec 12. PMID: 18077479.
- [9] Uchino K, Johnston SC, Becker KJ, Tirschwell DL. Moyamoya disease in Washington State and California. *Neurology*. 2005 Sep 27;65(6):956-8. doi: 10.1212/01.wnl.0000176066.33797.82. PMID: 16186547
- [10] Wakai K, Tamakoshi A, Ikezaki K, Fukui M, Kawamura T, Aoki R, et al. Epidemiological features of Moyamoya disease in Japan: findings from a nationwide survey. *Clinical Neurology and Neurosurgery*. 1997 Oct; 99:S1-5.
- [11] Chen Pei-Chun, Yang Shih-Hung, Chien Kuo-Liong, Tsai I-Ju, Kuo Meng-Fai. Epidemiology of Moyamoya Disease in Taiwan. *Stroke*. 2014 May 1;45(5):1258-63
- [12] Ahn IM, Park DH, Hann HJ, Kim KH, Kim HJ, Ahn HS. Incidence, prevalence, and survival of moyamoya disease in Korea: a nationwide, population-based study. *Stroke*. 2014 Apr;45(4):1090-5. doi: 10.1161/STROKEAHA.113.004273. Epub 2014 Mar 4. PMID: 24595588.
- [13] Zhang H, Zheng L, Feng L. Epidemiology, diagnosis and treatment of moyamoya disease. *Exp Ther Med*. 2019 Mar;17(3):1977-1984. doi: 10.3892/etm.2019.7198. Epub 2019 Jan 25. PMID: 30867689; PMCID: PMC6395994.

- [14] Sun SJ, Zhang JJ, Li ZW, Xiong ZW, Wu XL, Wang S, Shu K, Chen JC. Histopathological features of middle cerebral artery and superficial temporal artery from patients with moyamoya disease and enlightenments on clinical treatment. *J Huazhong Univ Sci Technolog Med Sci.* 2016 Dec;36(6):871-875. doi: 10.1007/s11596-016-1677-5. Epub 2016 Dec 7. PMID: 27924520.
- [15] Masuda J, Ogata J, Yutani C. Smooth muscle cell proliferation and localization of macrophages and T cells in the occlusive intracranial major arteries in moyamoya disease. *Stroke.* 1993 Dec;24(12):1960-7. doi: 10.1161/01.str.24.12.1960. PMID: 7902623
- [16] Oka K, Yamashita M, Sadoshima S, Tanaka K. Cerebral haemorrhage in Moyamoya disease at autopsy. *Virchows Arch A Pathol Anat Histol.* 1981;392(3):247-61. doi: 10.1007/BF02155663. PMID: 7269227.
- [17] Kono S, Oka K, Sueishi K. Histopathologic and morphometric studies of leptomenigeal vessels in moyamoya disease. *Stroke.* 1990 Jul;21(7):1044-50. doi: 10.1161/01.str.21.7.1044. PMID: 2368105.
- [18] Ikeda H, Sasaki T, Yoshimoto T, Fukui M, Arinami T. Mapping of a familial moyamoya disease gene to chromosome 3p24.2-p26. *Am J Hum Genet.* 1999;64(2):533-537. doi:10.1086/302243
- [19] Guey S, Tournier-Lasserre E, Hervé D, Kossorotoff M. Moyamoya disease and syndromes: from genetics to clinical management. *Appl Clin Genet.* 2015 Feb 16;8:49-68. doi: 10.2147/TACG.S42772. PMID: 25733922; PMCID: PMC4337618.
- [20] Tanigawara T, Yamada H, Sakai N, Andoh T, Deguchi K, Iwamura M. Studies on cytomegalovirus and Epstein-Barr virus infection in moyamoya disease. *Clin Neurol Neurosurg.* 1997 Oct;99 Suppl 2:S225-8. doi: 10.1016/s0303-8467(97)00049-8. PMID: 9409443.
- [21] Gupta A, Tyagi A, Romo M, Amoroso KC, Sonia F. Moyamoya Disease: A Review of Current Literature. *Cureus.* 2020;12(8):e10141. Published 2020 Aug 30. doi:10.7759/cureus.10141
- [22] Fernandez-Alvarez E, Pineda M, Royo C, Manzanares R. "Moya-moya" disease caused by cranial trauma. *Brain Dev.* 1979;1(2):133-8. doi: 10.1016/s0387-7604(79)80022-4. PMID: 121867.
- [23] Bitzer M, Topka H. Progressive cerebral occlusive disease after radiation therapy. *Stroke.* 1995 Jan;26(1):131-6. doi: 10.1161/01.str.26.1.131. PMID: 7839383.
- [24] Kuriyama S, Kusaka Y, Fujimura M, Wakai K, Tamakoshi A, Hashimoto S, Tsuji I, Inaba Y, Yoshimoto T. Prevalence and clinicoepidemiological features of moyamoya disease in Japan: findings from a nationwide epidemiological survey. *Stroke.* 2008 Jan;39(1):42-7. doi: 10.1161/STROKEAHA.107.490714. Epub 2007 Nov 29. PMID: 18048855.
- [25] Zipfel GJ, Fox DJ Jr, Rivet DJ. Moyamoya disease in adults: the role of cerebral revascularization. *Skull Base.* 2005;15(1):27-41. doi:10.1055/s-2005-868161
- [26] Scott RM, Smith JL, Robertson RL, Madsen JR, Soriano SG, Rockoff MA. Long-term outcome in children with moyamoya syndrome after cranial revascularization by pial synangiosis. *J Neurosurg.* 2004 Feb;100(2 Suppl Pediatrics):142-9. doi: 10.3171/ped.2004.100.2.0142. PMID: 14758941.
- [27] Seol HJ, Wang KC, Kim SK, Hwang YS, Kim KJ, Cho BK. Headache in pediatric moyamoya disease: review of 204 consecutive cases. *J Neurosurg.*

2005 Nov;103(5 Suppl):439-42. doi: 10.3171/ped.2005.103.5.0439. PMID: 16302616.

[28] Kim DS, Ko TS, Ra YS, Choi CG. Postoperative electroencephalogram for follow up of pediatric Moyamoya disease. *J Korean Med Sci.* 2006 Jun;21(3):495-9. doi: 10.3346/jkms.2006.21.3.495. PMID: 16778396; PMCID: PMC2729958.

[29] Smith ER, Scott RM. Moyamoya: epidemiology, presentation, and diagnosis. *Neurosurg Clin N Am.* 2010 Jul;21(3):543-51. doi: 10.1016/j.nec.2010.03.007. PMID: 20561502.

[30] Mugikura S, Takahashi S, Higano S, Shirane R, Sakurai Y, Yamada S. Predominant involvement of ipsilateral anterior and posterior circulations in moyamoya disease. *Stroke.* 2002 Jun;33(6):1497-500. doi: 10.1161/01.str.0000016828.62708.21. PMID: 12052981.

[31] Yasaka M, Ogata T, Yasumori K, Inoue T, Okada Y. Bottle neck sign of the proximal portion of the internal carotid artery in moyamoya disease. *J Ultrasound Med.* 2006 Dec;25(12):1547-52; quiz 1553-4. doi: 10.7863/jum.2006.25.12.1547. PMID: 17121949.

[32] Kodama N, Aoki Y, Hiraga H, Wada T, Suzuki J. Electroencephalographic findings in children with moyamoya disease. *Arch Neurol.* 1979 Jan;36(1):16-9. doi: 10.1001/archneur.1979.00500370046008. PMID: 420596.

[33] Kim T, Oh CW, Bang JS, Kim JE, Cho WS. Moyamoya Disease: Treatment and Outcomes. *J Stroke.* 2016;18(1):21-30. doi:10.5853/jos.2015.01739

[34] Kuroda S, Ishikawa T, Houkin K, Nanba R, Hokari M, Iwasaki Y. Incidence and clinical features of disease progression in adult moyamoya disease.

Stroke. 2005 Oct;36(10):2148-53. doi: 10.1161/01.STR.0000182256.32489.99. Epub 2005 Sep 22. PMID: 16179571.

[35] Cho WS, Chung YS, Kim JE, Jeon JP, Son YJ, Bang JS, Kang HS, Sohn CH, Oh CW. The natural clinical course of hemodynamically stable adult moyamoya disease. *J Neurosurg.* 2015 Jan;122(1):82-9. doi: 10.3171/2014.9.JNS132281. PMID: 25361479.

[36] Kuroda S, Shiga T, Ishikawa T, Houkin K, Narita T, Katoh C, Tamaki N, Iwasaki Y. Reduced blood flow and preserved vasoreactivity characterize oxygen hypometabolism due to incomplete infarction in occlusive carotid artery diseases. *J Nucl Med.* 2004 Jun;45(6):943-9. PMID: 15181128.

[37] Macyszyn L, Attiah M, Ma TS, Ali Z, Faught R, Hossain A, Man K, Patel H, Sobota R, Zager EL, Stein SC. Direct versus indirect revascularization procedures for moyamoya disease: a comparative effectiveness study. *J Neurosurg.* 2017 May;126(5):1523-1529. doi: 10.3171/2015.8.JNS15504. Epub 2016 Jul 29. PMID: 27471892.

[38] Yamada S, Oki K, Itoh Y, Kuroda S, Houkin K, Tominaga T, Miyamoto S, Hashimoto N, Suzuki N; Research Committee on Spontaneous Occlusion of Circle of Willis (Moyamoya Disease). Effects of Surgery and Antiplatelet Therapy in Ten-Year Follow-Up from the Registry Study of Research Committee on Moyamoya Disease in Japan. *J Stroke Cerebrovasc Dis.* 2016 Feb;25(2):340-9. doi: 10.1016/j.jstrokecerebrovasdis.2015.10.003. Epub 2015 Nov 30. PMID: 26654669.

[39] Rosi A, Riordan CP, Smith ER, Scott RM, Orbach DB. Clinical status and evolution in moyamoya: which angiographic findings correlate? *Brain Commun.* 2019 Oct 30;1(1):fcz029. doi: 10.1093/braincomms/fcz029. PMID: 32954269; PMCID: PMC7425301.

[40] Kim T, Oh CW, Kwon OK, Hwang G, Kim JE, Kang HS, Cho WS, Bang JS. Stroke prevention by direct revascularization for patients with adult-onset moyamoya disease presenting with ischemia. *J Neurosurg.* 2016 Jun;124(6):1788-93. doi: 10.3171/2015.6.JNS151105. Epub 2015 Dec 4. Erratum in: *J Neurosurg.* 2016 Jun;124(6):1875. PMID: 26636391.

[41] Noh HJ, Kim SJ, Kim JS, Hong SC, Kim KH, Jun P, Bang OY, Chung CS, Lee KH, Lee KH, Kim GM. Long term outcome and predictors of ischemic stroke recurrence in adult moyamoya disease. *J Neurol Sci.* 2015 Dec 15;359(1-2):381-8. doi: 10.1016/j.jns.2015.11.018. Epub 2015 Nov 10. PMID: 26671146.

[42] Guzman R, Lee M, Achrol A, Bell-Stephens T, Kelly M, Do HM, Marks MP, Steinberg GK. Clinical outcome after 450 revascularization procedures for moyamoya disease. Clinical article. *J Neurosurg.* 2009 Nov;111(5):927-35. doi: 10.3171/2009.4.JNS081649. PMID: 19463046.