Article

Innovations in Diagnostic and Surgical Treatment Approaches for Moyamoya Disease

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Abstract: Moyamoya disease, characterized by progressive stenosis of the internal carotid arteries, necessitates advanced diagnostic and therapeutic strategies for optimal management. This scientific review explores the latest innovations in both diagnostic modalities and treatment approaches for Moyamoya disease. Through an exhaustive analysis of recent literature, this work aims to elucidate novel techniques in imaging and surgical interventions, providing valuable insights for clinicians and researchers involved in the care of Moyamoya patients.

Keywords: Moyamoya disease, MRI, MRA, CT, angiography, EEG, cerebral blood flow, surgical revascularization, treatment.

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1. Introduction

Moyamoya is an uncommon cerebrovascular condition characterized by progressive narrowing of large intracranial arteries and the secondary development of prominent small vessel collaterals. These collateral vessels produce a characteristic smoky appearance on angiography, which was first called "moyamoya," the Japanese word for something hazy like a "puff of cigarette smoke" (which it fancifully resembles on angiography) (first described in 1957 [1], and named in 1969) [2].

Moyamoya, or moyamoya vasculopathy, refers to the characteristic vascular findings. The term moyamoya disease (MMD) is used when the condition is idiopathic and not associated with another disease or due to a genetic susceptibility; moyamoya syndrome (MMS) is used when vascular findings occur in the presence of an associated condition, such as sickle cell disease. MMD or MMS may lead to ischemic stroke or intracranial hemorrhage in children and adults. With progression, involvement includes the proximal. MCAs and ACAs and on rare occasion the vertebrobasilar system. Associated aneurysms and rarely AVMs may be observed. Eventually the dilated capillary (moyamoya) vessels disappear with the development of collaterals from the ECA (meningeal collaterals are called "rete mirabile") [3,4].

2. Pathophysiology

2.1. Primary moyamoya disease.

The most common pathology is stenosis of the proximal anterior and middle cerebral arteries that is neither atherosclerotic nor inflammatory in origin. Exact etiology is unknown but some studies show elevated basic fibroblast growth factor in the dura and scalp arteries in patients with moyamoya [7]. The internal elastic lamina of affected vessels may be thinned or duplicated. Similar vascular changes may also occur in the heart, kidney, and other organs, suggesting it may be a systemic vascular disease.

2.2. Secondary moyamoya disease.

AKA "quasi-moyamoya disease" or "moyamoya syndrome." Angiographic findings of moyamoya associated with e.g.:

1. graves' disease/thyrotoxicosis
2. history of cerebral inflammatory disease, including meningitis (especially tubercular (TB) meningitis and leptospirosis)
3. retinitis pigmentosa
4. vascular disorders: atherosclerosis, fibromuscular dysplasia, pseudoxanthoma elasticum

5. congenital disorders: Down syndrome, Marfan syndrome, Turner syndrome, neurofibromatosis type 1, tuberous sclerosis, Apert syndrome
6. hematologic disorders: Fanconi anemia, sickle cell disease (in the U.S. one of the more common associations) and sickle cell trait
7. following radiation therapy for skull base glioma in children [5]
8. head trauma
9. systemic lupus erythematosus (SLE)

2.3. Associated aneurysms.

Intracranial aneurysms are frequently associated with moyamoya disease (MMD). This may be a result of the increased flow through dilated collaterals, or it may be that patients with moyamoya may also have a congenital defect in the arterial wall that predisposes them to aneurysms. 3 types:

1) usual sites of aneurysms in the Circle of Willis
2) in peripheral portions of cerebral arteries, e.g., posterior/anterior choroidal, Heubner's
3) within moyamoya vessels

The frequency of aneurysms in the vertebrobasilar system is ≈ 62%, which is much higher than in the general population [6]. Aneurysmal SAH may be the actual cause of some hemorrhages that were erroneously attributed to moyamoya vessels.

3. Evaluation and diagnosis

3.1. Diagnostic criteria.

Diagnosis of moyamoya requires bilateral symmetrical stenosis or occlusion of the terminal portion of the ICAs as well as the presence of dilated collateral vessels at the base of the brain [7]. (If unilateral, the diagnosis is considered questionable, and these cases may progress to bilateral involvement) [8].

Other characteristic findings include:

1. stenosis/occlusion starting at termination of ICA and at origins of ACA and MCA
2. abnormal vascular network in region of BG (intraparenchymal anastamosis)
3. transdural anastomosis (rete mirabile), AKA "vault moyamoya." Contributing arteries: anterior facial, middle meningeal, ethmoidal, occipital, tentorial, STA
4. moyamoya collaterals may also form from internal maxillary artery via ethmoid sinus to forebrain in frontobasal region

3.2. MRI and MRA.

MRA usually discloses the stenosis or occlusion of the ICA. Moyamoya vessels appear as flow voids on MRI (especially in basal ganglia) and a fine network of vessels on MRA, and are demonstrated better in children than adults. Parenchymal ischemic changes are commonly shown, usually in watershed areas.

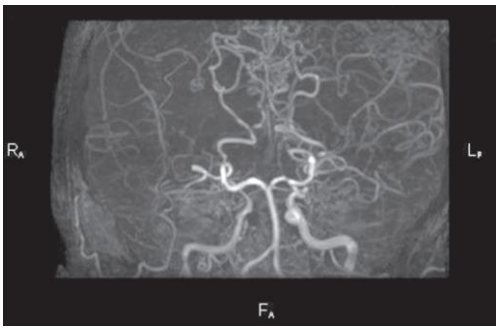

Figure 1. MR-angiogram of a patient with moyamoya disease. Bilateral stenosis of the intracranial internal carotid artery and developed collateral network at the base of the brain.

3.3. CT.

Work-up in suspected cases typically begins with a non-enhanced head CT. Up to 40% of ischemic cases have normal CT. Low-density areas (LDAs) may be seen, usually confined to cortical and subcortical areas (unlike atherosclerotic disease or acute infantile hemiplegia which tend to have LDAs in basal ganglia as well). LDAs tend to be multiple and bilateral, especially in the PCA distribution (poor collaterals), and are more common in children.

3.4. Angiography.

In addition to helping to establish the diagnosis, angiography also identifies suitable vessels for revascularization procedures and unearths associated aneurysms. The angiography-related complication rate is higher than with atherosclerotic occlusive disease. Avoid dehydration prior to and hypotension during the procedure. Six angiographic stages of MMD that tend to progress up until adolescence and stabilize by age 20 are described in the Figure 2 [2].

Stage	Finding
1	stenosis of suprasellar ICA, usually bilateral
2	development of moyamoya vessels at base of brain. ACA, MCA, & PCA dilated
3	increasing ICA stenosis & prominence of moyamoya vessels (most cases diagnosed at this stage). Maximal basal moyamoya
4	entire circle of Willis and PCAs occluded, extracranial collaterals start to appear, moyamoya vessels begin to diminish
5	further progression of stage 4 with intensification of ECA collaterals & reduction of moyamoya associated vessels
6	total occlusion of ICA & major cerebral arteries and complete absence of moyamoya vessels

Figure 2. Six angiographic stages of MMD (Suzuki stages).

3.5. EEG.

Non-specific in the adult. Juvenile cases: high-voltage slow waves may be seen at rest, predominantly in the occipital and frontal lobes. Hyperventilation produces a normal buildup of monophasic slow waves (delta-bursts) that return to normal 20–60 seconds after hyperventilation. In > 50% of cases, after or sometimes continuous with buildup is a second phase of slow waves (this characteristic finding is called "rebuildup"), which are more irregular and slower than the earlier waves, and usually normalize in ≤ 10 minutes [9].

3.6. Cerebral blood flow (CBF) studies.

CBF is decreased in children with MMD, but relatively normal in adults. There is a shift of CBF from the frontal to the occipital lobes [18] probably reflecting the increasing dependency of CBF on the posterior circulation. Children with MMD have impaired autoregulation of CBF to blood pressure and CO2 (with more impairment of vasodilatation in response to hypercapnia or hypotension than vasoconstriction in response to hypocapnia or hypertension).

Xenon (Xe-133) CT can identify areas of low perfusion. Repeating the study after an acetazolamide challenge (which causes vasodilatation) evaluates reserve capacity of CBF and can identify areas of "steal" which are at high risk of future infarction.

4. Treatment

4.1. General information.

No medical or surgical treatment has been proven effective in reducing the rate of hemorrhage in the adult with MMD. However, multiple large case series have supported the efficacy of cerebral revascularization for reducing the incidence of ischemic strokes and TIAs [10].

4.2. Asymptomatic moyamoya disease.

Guidelines for management of asymptomatic moyamoya disease have not yet been established. A multicenter, nationwide survey in Japan focusing on asymptomatic moyamoya disease provided the following findings [11]: subtle findings of cerebral infarction and disturbed cerebral hemodynamics were detected in 20% and 40% of the involved hemispheres, respectively. Angiographic stage was more advanced in elderly patients. Of 34 medically-treated patients, 7 experienced TIA, ischemic stroke, or hemorrhage during a mean follow-up period of 43.7 months. Cerebral infarction or hemorrhage did not occur in the 6 patients who underwent surgical revascularization.

4.3. Medical treatment.

Medical treatment with platelet inhibitors, anticoagulants, calcium channel blockers [12], steroids, mannitol, low-molecular-weight dextran, and antibiotics have not proven to be of benefit. Steroids may be considered for involuntary movements and acutely during recurrent TIAs.

4.4. Surgical treatment.

Patients with mass effect from clot may be candidates for urgent decompression. Revascularization procedures, however, should be performed when the patient is stable under nonemergent conditions.

Perioperative management

During any surgical procedure:

1. avoid hyperventilation: due to increased sensitivity of collaterals, keep PaCO2 40–50 mm Hg to avoid ischemic infarction
2. avoid hypotension: maintain BP at normotensive levels
3. avoid alpha-adrenergic agents because of vasoconstrictive effects
4. cerebral protection: mild hypothermia (32–34 °C) and barbiturates are routinely used
5. papaverine helps prevent vascular spasm

Postoperatively following STA-MAC bypass procedures:

1. avoid hypertension: may cause bleeding at anastomotic site and in areas of increased perfusion within the brain
2. avoid hypotension: may result in graft occlusion
3. aspirin is started on the post-op day 1
4. watch for evidence of CSF leak
5. monitor coag studies and correct abnormalities
6. cerebral arteriogram is recommended 2–6 months post-op

Suggested criteria for revascularization procedures:

1. patients presenting with infarction or hemorrhage but are in good neurologic condition
2. infarction < 2 cm maximal diameter on CT, and all previous hemorrhages have completely resolved
3. angiographic stage is II–IV (see Figure 2) [2]
4. timing of operation: ≥ 2 months after most recent attack

Surgical revascularization options:

Various methods to revascularize the ischemic brain, used primarily in children, include:

1. direct revascularization procedures:
    a) results are superior to indirect revascularization procedures if a donor and recipient vessel of sufficient caliber (≥ 1 mm outer dia) can be identified (may be difficult in the pediatric age group who are the most likely to benefit) [13, 14]. Otherwise, indirect revascularization procedures (see below) are options.
    b) Among direct revascularization procedures, STA-MCA bypass [15] is the procedure of choice.
2. indirect revascularization procedures: usually reserved for younger patients (suggested cutoff age ≈ < 15 years). May be combined with STA-MCA bypass. Includes:
    a) encephalomyosynangiosis (EMS): laying the temporalis muscle on the surface of the brain (may cause problems with muscle contractions during talking and chewing, and neural impulses on surface of brain).
    b) encephaloduroarteriosynangiosis (EDAS): suturing the STA with a galeal cuff to a linear defect created in the dura. Variations on this technique include splitting the dura [16].
    c) omental transposition: either as a pedicle graft or as a vascularized free flap. Felt to have higher potential to revascularize ischemic tissue than above procedures, but there is greater risk of mass effect from the thickness of the omentum.
3. the above indirect revascularization procedures improve blood flow in the MCA distribution, but not ACA circulation. This may be rectified by:
    a) simple placement of frontal burr holes with opening of the underlying dura and arachnoid [17].
    b) "ribbon EDAS" where a pedicle of galea is inserted into the interhemispheric fissure on both sides.
4. stellate ganglionectomy and perivascular sympathectomy: unproven that this increases CBF permanently.

5. Outcome with surgical treatment

Neurologic status at time of treatment generally predicts long-term outcome. The mortality rate in adults (≈ 10%) is higher than for juveniles (≈ 4.3%).The cause of death was bleeding in 56% of 9 children and 63% of 30 adults.

6. Prognosis and Conclusion

The natural history of Moyamoya disease tends to be progressive in children and adults. In studies with long-term follow-up of untreated patients, progression of neurological deficit and poor outcome were reported in 50-66% of cases. Radiographic progression within five years of diagnosis was noted in 36% of children with moyamoya. Vascular pathology is usually aggravated by extensive occlusion of intracranial large arteries and collateral circulation. Patients often suffer from cognitive and neurological decline due to recurrent ischemic stroke or hemorrhage.

Application of artificial intelligence: The review is written without the use of artificial intelligence technologies.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Takeuchi K, Shimuzi K. Hypogenesis of Bilateral Internal Carotid Arteries. No To Shinkei. 1957; 9:37–37.
2. Suzuki J, Takaku A. Cerebrovascular "moyamoya" disease. Disease showing abnormal netlike vessels in base of brain. Archives of Neurology. 1969; 20:288–299.
3. Kayama T, Suzuki S, Sakurai Y, Nagayama T, Ogawa A, Yoshimoto T. A Case of Moyamoya Disease Accompanied by an Arteriovenous Malformation. Neurosurgery. 1986; 18:465–468
4. Lichtor T, Mullan S. Arteriovenous Malformation in Moyamoya Syndrome: Report of Three Cases. Journal of Neurosurgery. 1987; 67:603–608.
5. Rajakulasingam K, Cerullo LJ, Raimondi AJ. Childhood Moyamoya Syndrome: Postradiation Pathogenesis. Childs Brain. 1979; 5:467–475
6. Kwak R, Ito S, Yamamoto N, Kadoya S. Significance of Intracranial Aneurysms Associated with Moyamoya Disease (Part I): Differences Between Intracranial Aneurysms Associated with Moyamoya Disease and Usual Saccular Aneurysms - Review of the Literature. Neurol Med Chir (Tokyo). 1984; 24:97–103
7. Smith ER, Scott RM. Surgical management of moyamoya syndrome. Skull Base. 2005; 15(1):15–26
8. Nishimoto A. Moyamoya Disease. Neurologia medico-chirurgica (Tokyo). 1979; 19:221–228
9. Kodama N, Aoki Y, Hiraga H, Wada T, Suzuki J. Electroencephalographic Findings in Children with Moyamoya Disease. Archives of Neurology. 1979; 36:16–19
10. Zipfel GJ, Fox DJ,Jr, Rivet DJ. Moyamoya disease in adults: the role of cerebral revascularization. Skull Base. 2005; 15:27–41
11. Kuroda S, Hashimoto N, Yoshimoto T, Iwasaki Y. Radiological findings, clinical course, and outcome in asymptomatic moyamoya disease: results of multicenter survey in Japan. Stroke. 2007; 38:1430–1435
12. Chang SD, Steinberg GK. Surgical Management of Moyamoya Disease. Contemporary Neurosurgery. 2000; 22:1–9
13. Matsushima Y, 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 Vascularization. Journal of Neurosurgery. 1992; 31:401–405
14. Ishikawa T, Houkin K, Kamiyama H, Abe H. Effects of Surgical Revascularization on Outcome of Patients with Pediatric Moyamoya Disease. Stroke. 1997; 28:1170–1173
15. Karasawa J, Kikuchi H, Furuse S, Kawamura J, Sakaki T. Treatment of Moyamoya Disease with STA-MCA Anastomosis. Journal of Neurosurgery. 1978; 49:679–688
16. Kashiwagi S, Kato S, Yasuhara S, Wakuta Y, Yamashita T, Ito H. Use of Split Dura for Revascularization if Ischemic Hemispheres in Moyamoya Disease. Journal of Neurosurgery. 1996; 85:380–383
17. Endo M, Kawano N, Miyaska Y, Yada K. Cranial Burr Hole for Revascularization in Moyamoya Disease. Journal of Neurosurgery. 1989; 71:180–185
18. Ogawa A, Yoshimoto T, Suzuki J, Sakurai Y. Cerebral Blood Flow in Moyamoya Disease. Part 1. Correlation with Age and Regional Distribution. Acta Neurochir (Wien). 1990; 105:30–34