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Chapter

Surgical Treatment of Moyamoya Disease

Vicente Vanaclocha, Nieves Saiz-Sapena and Leyre Vanaclocha

Abstract

Moyamoya disease is a rare cerebrovascular disease most prevalent in East Asian Countries. Thanks to the new diagnostic capabilities, the number of cases discovered has been rising steadily in the latest years, including many asymptomatic patients. But asymptomatic from the clinical point of view does not necessarily mean that there are no subjacent problems and that there will be no disease progression. Indeed, many patients harbour cognitive decline long before they start with clinical or even radiological manifestations. The only effective treatment is surgical revascularization, with all its possibilities: direct, indirect, and combined. While direct techniques are more useful in adult moyamoya patients, children seem to benefit most from indirect techniques. Additionally, indirect or combined procedures can be used as salvage procedures in case of unsatisfactory outcomes. Thus, many surgeons posit that surgical treatment should be considered in moyamoya patients, even if asymptomatic, particularly in the paediatric age group.

Keywords: moyamoya disease, surgical revascularization, bypass surgery, asymptomatic moyamoya disease, cerebral revascularization, treatments modalities

1. Introduction

1

Takeuchi and Shimizu first described Moyamoya disease (MMD) in 1957 [1]. It is an idiopathic cerebral vasculopathy characterised by progressive stenosis of the terminal internal carotid artery and its branches, usually on both sides, and the development of a compensatory network of abnormal collateral vessels [2]. Unilateral involvement does not rule out this disease [3]. It affects mainly the middle (MCA) and anterior cerebral (ACA) arteries, less commonly the posterior cerebral or the middle meningeal arteries, and in a few cases the arteries that supply other organs [4], like the lungs or kidneys [5]. Some MMD patients suffer from pulmonary artery hypertension, which usually starts in adolescence or young adulthood and progresses slowly [5].

The collateral vessels that develop as the disease progresses [6] have a thin and weak non-elastic wall with aneurysm formation prone to haemorrhages [7–9]. These aneurysms' prevalence varies in the different series between 1.9 [10], 2.8% [11], 3.9 [12], 8.3 [6] and 14% [13]. They are usually located in deep areas [11], small in size and with very fragile walls, making their treatment, endovascular or surgical, extremely challenging [11, 12, 14]. They can also be found at the circle of Willis [9, 11, 15, 16], where they usually have a fusiform shape [11, 17] and can lead to a subarachnoid haemorrhage [11]. The prognosis in the case of this type of haemorrhage is poor [11].

Their recommended treatment is brain revascularization (BR) [12, 18, 19] as many regress spontaneously after their haemodynamic stress is reduced [11, 20–24].

MMD can be associated with other diseases like Down syndrome (trisomy 21) [25], sickle cell disease [26], neurofibromatosis type 1 [27], thalassemia [28], Graves' disease [29] and after head- and neck-radiotherapy [30]. In this case, it is known as moyamoya syndrome [3].

MMD patients have impaired cerebral haemodynamics with a low cerebral blood flow (CBF) or a poor brain vasodilatory capacity, making them prone to cerebrovascular events [31], particularly at the frontal lobe [32]. The CBF and the cerebral vascular reserve (CVR) capacity are used to evaluate the need for surgical treatment [33–36].

Although it is a rare disease, it is the leading cause of ischemic stroke in the paediatric population in Korea and Japan [37–39].

Digital subtraction angiography (DSA) is the gold standard for diagnosis, but Magnetic Resonance Angiography (MRA) is also helpful [40, 41]. More specific methods but not currently used because of the costs and equipment involved are xenon-enhanced CT, DSC, MRI, H_2 [[15]O]-PET and [42] I aromatic amines SPECT [43–48]. These diagnostic techniques are used for preoperative evaluation to decide the best surgical approach. Their drawbacks are that they require contrast agents' intravenous injection and entail radiation exposure that can be harmful to patients, particularly in the paediatric age group. Preoperative transcranial colour-duplex sonography is a non-invasive method used to evaluate the degree of vascular impairment in MMD and monitor the results after surgical BR [49–51].

The patients' mean age at diagnosis peaks at ten and 30–50 years [9, 12, 52] with a ratio of women-to-men 1.00:1.03 [12].

MMD two basic clinical manifestation types are ischemic (30.4%) and haemorrhagic (70.9%) stroke [12]. The ischemic type is more common in children and the haemorrhagic in adults [13, 53]. Other clinical symptoms are headache [54], epilepsy [55], chorea movements [56] and cognitive decline [53, 57]. In comparison, haemorrhages are more frequent in the adult MMD population [58] and ischemic events in the paediatric age group [59–62]. Patients starting with ischemic symptoms like transitory ischemic attack (TIA) are more prone to develop an ischemic than a haemorrhagic stroke [63, 64]. In the paediatric population, multiple ischemic strokes, significantly if both hemispheres are affected, can lead to severe cognitive impairment and developmental delay [65–67]. Brain infarcts present in the ACA and MCA territories and less commonly in the posterior cerebral artery (PCA) covered area and vertebrobasilar system [68]. Posterior circulation involvement leads to more severe symptomatology and worse outcomes [69]. Haemorrhagic strokes are often followed by rebleeding and infarction in short to medium follow-up [70].

Unless surgical BR is undertaken, the stroke rate is 18% for the first year and 3.2–5% for the following years [71–73]. Once patients suffer an ischemic or haemorrhagic stroke, the risk of a new cerebrovascular insult in the following five years is 65% [74, 75].

In MMD, the PCA provides the collateral flow to the anterior circulation [32, 76–79] with choroidal anastomosis and hypertrophic collateral vessel formation [76, 80]. This increased blood flow through the PCA creates haemodynamic stress on the vertebrobasilar system and facilitates aneurysm formation [76, 81]. The choroidal collateral vessels are potential sources of haemorrhages and rebleeding [82]. A common complication is a brain haemorrhage [80, 83, 84], usually intraventricular [80, 85], particularly in the rear brain areas [80]. Moreover, MMD patients with haemorrhages in the posterior part of the brain have a higher risk of rebleeding than those with haemorrhages located in the anterior part [85]. PCA stenosis is typical of juvenile-onset MMD [86].

Microbleeds' are more common in MMD than in the general population [87] and usually in the periventricular areas, followed by the basal ganglia and thalamus [87–89]. The asymptomatic microbleeds are related to hypertrophy, dilatation and aneurysm formation of the posterior communicating and anterior choroidal arteries [90–92]. Those areas are where the MMD related haemorrhagic strokes typically happen, and these microbleeds are an excellent prognosticator of future haemorrhages [83, 93, 94].

Asymptomatic MMD patients have a 3.2% annual stroke risk [95], more often haemorrhagic than ischemic, showing an evolving situation that is usually is not silent nor stable [72, 96], particularly in those with a compromised CVR capacity [97]. Moreover, cognitive decline over time is the rule [98]. Thus, asymptomatic MMD patients should be monitored closely and submitted to surgical BR at the slightest sign of deterioration [99].

Although there might be a subgroup of children with a benign course [100], most have a relentless and progressive worsening [99], and unilateral disease often evolves to bilateral [99]. Predictors of unfavourable outcome are onset at a younger age, a long time before BR, brain infarcts, and PCA involvement [86]. Children under nine years of age with minor changes in the contralateral brain hemisphere are most likely to undergo disease progression [101, 102].

This disease, particularly if untreated, can induce severe disability and even death [3]. White matter involvement, particularly in adults, correlates with cognitive impairment [57].

2. Treatment modalities in moyamoya disease

Without a known aetiology, the only treatment is symptomatic. The medical treatment does not affect this disease's relentless progression [103, 104], and patients under drug treatment alone have a 5-year 65% stroke risk [72, 105–107] which climbs up to a dismal 82% in case of bilateral involvement [105]. In children, it has been reported that under conservative treatment, 37% will present clinical symptoms of neurological damage, and 3% will eventually die [108]. It can be helpful, though, to alleviate some symptoms like headache or epileptic seizures [109]. Endovascular treatment has been attempted in some cases with unsatisfactory results [110–112]. The surgical treatment with BR offloads the haemodynamic stress [113] and reduces the risk of subsequent ischemic and haemorrhagic cerebrovascular events [104, 114–122], providing symptom improvement to 87% of patients [104].

BR techniques can be classified into two main groups: direct and indirect. The first involves artery-to-artery bypasses between an external carotid artery branch and a brain arterial vessel, usually between the superficial temporal (STA) and MCA [42, 115, 123]. Other donor vessels are the occipital [69, 124], deep temporal, and middle meningeal [125] arteries. The STA can be connected to a branch of the middle cerebral [126] or anterior cerebral [127] arteries. Meanwhile, the occipital artery is sutured to the PCA [128] but can also be used to revascularize the MCA territory [129]. The size of the donor artery should be > 0.8 mm to allow the surgical manoeuvres [130]. In children under four years of age, both the STA and the possible recipient brain arteries usually have an insufficient diameter to enable a bypass [131]. Its most significant advantage is that it provides immediate brain haemodynamic improvement. This fast improvement in the brain blood flow reduces the risk of ischemic and haemorrhagic strokes faster than the indirect techniques, which require 3-4 months to achieve the same result [132]. Its main risk is a hyperperfusion-reperfusion syndrome, which can induce haemorrhages with neurological deterioration and worsening [115, 133, 134]. This risk can be minimised with strict

postoperative blood pressure control and mild hypotension in symptomatic cerebral hyperperfusion [135]. Direct BR is mainly used to increase the perfusion of the MCA territory [99]. Direct BR of the anterior or PCA branches is challenging as the donor's vessels are further away, a severe problem when those vascular territories are affected [99]. Under experienced hands, the patency rates are over 90% [136]. As the cortical arteries atrophy, it is increasingly difficult to find a suitable recipient vessel to perform a direct bypass [137]. The ideal is an M₃ branch, but micro-anastomoses with these vessels are technically very difficult [138].

In the indirect BR, no arterial anastomoses are performed. Instead, a pedicle graft vascularized by the external carotid artery is placed over the brain's surface and rely on the new collateral vessel formation between the donor tissue and the ischemic underlying brain [139]. For a successful result, three elements are needed—first, a well-vascularized donor tissue. Second, intimate contact between donor tissue and recipient brain vascularization. And third, a good selection of the hypoperfused recipient brain areas [140]. Indirect BR requires forming a fibrous scar at the donor tissue-brain interface with new collateral vessel formation between the donor and recipient vascular beds [141]. The possibilities of indirect BR techniques are broad [104]. Depending on the donor tissue used, the options are encephalo-myo-synangiosis (EMS) [142] when a muscle is used, encephaloduro-synangiosis (EDS) [143] with dural graft, split-duro-encephalo-synangiosis (DES) [144, 145] with a split dura graft, encephalo-duro-myo-synangiosis (EDMS) [146] with dural and muscle graft, encephalo-duro-arterio-synangiosis (EDAS) [147–150] with dura and external carotid artery branch, encephalo-duro-arteriomyo-synagiosis (EDAMS) [151] with dura, an external carotid artery branch and muscle, encephalo-galeo-synangiosis (EGS) [152, 153] with galea, encephalopericranium-synangiosis (EPS) [140, 154, 155] with pericranium, omentum transplantation [156, 157] and multiple burr-hole (MBH) [158, 159]. This last surgical technique consists of performing numerous burr holes (10 to 24) through the frontal, parietal and occipital bones, opening the dura and arachnoid and introducing a pericranium flap inside each burr-hole [160]. It can be used isolated, as part of other BR techniques or as a rescue procedure when other surgical approaches have failed or proved insufficient [160–162]. Not only is it technically effortless and straightforward, but it can be performed under local anaesthesia, which is an advantage in patients in a seriously compromised status [161]. As the dura is also an essential source of collateral vessel formation, a small craniotomy (3–3.5 cm in diameter) placing the pericranium directly over the brain surface provides better results than MBH [140]. Contrarywise, extensive craniotomies are not recommended because they disrupt the already spontaneously formed collateral vascularization increasing the risk of postoperative brain ischemic events [140]. The EPS is particularly helpful to provide collateral circulation to the anterior and PCA territories, areas not easily covered by the STA [140]. Duropexy is crucial in all indirect BR techniques [140].

Direct BR is preferred whenever possible because the haemodynamically compromised hemisphere gets an immediate increase in blood flow, reducing sooner the ischemic and haemorrhagic stroke risk [113, 163]. In contrast, with the indirect techniques, the new collateral vascularization takes 3 to 4 months to develop [53, 164, 165], but long-term, the blood–brain supply is better than with the direct BR [141]. In this period in which the collateral vessel formation is taking place, may persist brain hypoperfusion symptoms, and at times the final result may require an additional surgical BR procedure [128, 166–168].

With the direct bypass, the brain perfusion improvement is limited to the area where it is undertaken and is not helpful to perfuse extensive ischemic areas [169].

Contrarywise indirect brain vascularization can cover vast vascular territories, mainly if different techniques are employed, like the EDAS combined with MBH [5, 159]. This combination can provide new blood supply to the whole brain, including the interhemispheric frontal areas and occipital lobe [68].

MMD related aneurysms were treated with embolization or surgical clipping [11], and many improved with BR alone [11, 12].

3. Historical development of surgical BR for MMD

Yaşargil performed the first superficial-temporal artery bypass procedure for an MMD patient in 1972 [170]. In Japan, the first case was completed in 1973 by Kikuchi and Karasawa [171]. In the following years, Karasawa and colleagues in Japan refined this surgical procedure and reported their results in 1978 [123].

The first indirect MMD BR was reported by Karasawa in 1977 and was called encephalo-myo-synangiosis (EMS) [142]. Several researchers confirmed that placement of the temporalis muscle directly over the brain induced collateral vessel formation [172-174]. In 1980 Matsushima et al. introduced a new indirect BR technique, the EDAS [175]. The STA with a strip of its surrounding galea was placed directly over the brain through a linear dural incision [176]. The galea was sutured to the dural edges, and the STA left over the brain without interrupting its flow, waiting for collateral vessel formation between the dura, the galea, the STA and the brain. It became widely accepted [149, 153, 177–180]. The EMS was the ground stone for other indirect BR techniques introduced in the following years that used different donor tissues, including other scalp arteries [177], split dura [145], neck [181] or distant [182–184] muscles and the omentum [156]. Others reported using the pericranium introduced though multiple burr-holes [185]. These techniques revascularized the MCA territory but not those of the anterior and posterior cerebral arteries. In 1992, Inoue et al. [186] introduced the frontal EDAMS to selectively revascularize the anterior cerebral bed to overcome this drawback. Kinugasa et al. [187] two years later reported the ribbon EDAMS, in which a strip of galea and pericranium were placed over the frontal lobes, including the interhemispheric areas. Tenjin et al. [177] published in 1997 the occipital artery's use to revascularize the PCA territory. Ever since a combination of direct and indirect BR techniques is recommended to achieve a good collateral flow in all three brain arterial territories (anterior, middle, and posterior cerebral arteries).

4. Indication of surgical techniques for cerebral revascularization in moyamoya disease

The hemisphere with the worse vascularization is operated first [12]. If both hemispheres are equally affected, the recommendation is to start with the dominant one and revascularize the other six months latter [178].

In unilateral involvement, if the patients' symptoms disappear with the unilateral BR and an asymptomatic contralateral hemisphere, no further brain vascularization is advised for the time being [12] as contralateral hemisphere surgical BR in patients with unilateral involvement is controversial [99]. In an ischemic or haemorrhagic stroke, surgical BR is delayed for at least six weeks [188], and ideally, three months [12] and the BR of the contralateral cerebral hemisphere postponed at least 4–6 weeks [148]. Nevertheless, delaying surgical treatment is not advisable in late Suzuki stages [2], as BR improves brain collateral vascularization but not the stroke

rate [178]. So, once the diagnosis is made, it is better to avoid unnecessary delays, particularly in children [178].

Direct BR is particularly indicated in adult and adolescent MMD patients [189, 190] but not recommended before ten years of age [191]. An STA to MCA bypass is strongly advised as it corrects the MMD related hemodynamic insufficiency [71, 121]. For a successful result, both the donor and recipient arteries must be at least 0.8 mm in outer diameter [192].

Indirect techniques are much less demanding [193] but are not as valuable for adults as for children [99, 149, 150, 152, 159, 179, 194, 195]. Its main drawback is that BR takes time, on average 3–4 months [196], during which there is a continued risk of cerebrovascular events [140]. In the paediatric age group, these indirect surgical techniques are preferred because the vessels are often of insufficient size and maturity to safely allow a direct arterial bypass [197], significantly below ten years of age [198]. One of the main advantages of indirect BR is the possibility of improving the anterior and PAC territories' blood perfusion apart from the area covered by the MCA [146, 199]. This possibility of a wider area covered by the BR is crucial in children [99, 152, 158] as they often develop long-term symptoms secondary to hypoperfusion of the whole hemisphere [99]. The BR that use the temporalis muscle is not recommended in children [200] because it thickens with time, compressing the brain and inducing ischemia [201] and because it adheres to the brain and when it contracts can cause long-term neurological damage [202]. Additionally, it generates an unsightly cosmetic head [200].

A combination of direct and indirect BR procedures is often used to profit from the advantages of each of them [34, 114, 136, 150, 160, 203], because the reported results are better than isolated direct or indirect techniques [204–207]. The treatment strategy has to be tailored to the specific needs of each patient [136, 160, 208]. Combining more than one indirect BR techniques has similar mortality and morbidity as any of them isolated [136].

During the surgical procedure, it is essential to avoid hypotension, hyperthermia, hypocarbia, hypercarbia, and epileptic seizures as they all increase the brain metabolism and thus the chance of an ischemic event [148, 149, 188, 200, 209–211] and perioperative morbidity [212]. It is vital to control the pain and cry in the postoperative period to avoid hyperventilation as this will produce hypocarbia and an increased risk of ischemia [149, 213]. It is recommended to provide intravenous fluids at 1.5 times the regular maintenance rate for 48–72 hours [3, 149]. Platelet counts and prothrombin time must be monitored and controlled with transfusions if needed [148]. The blood haemoglobin must be kept above the 12–13 g/dL range [148].

Some improvements in the surgical technique have eased the surgical manoeuvres and improved the clinical results. Among them is placing 10-0 Proline sutures to the arachnoid membrane in both sides of the brain sulcus. When some retraction is applied, the recipient artery is brought to the surface, and the STA to MCA bypass is made more easily [192].

While it seems intuitive that arachnoid removal will improve the collateral vessel formation between the donor artery or tissue and the brain [153], it is no longer recommended in indirect BR because it is associated with a significantly higher complication risk with no improvement in the final clinical outcome [148]. Among these complications are the postoperative ischemic strokes secondary to the vasospasm induced by the arachnoid dissection [148]. Preserving the arachnoid membrane reduces the operating time at an average of 30 minutes [148].

The middle meningeal artery provides a vital source of collateral circulation, so during the surgical procedure, this artery and its main branches should be preserved as much as possible [191]. Preservation of this crucial source of collateral

vessel formation requires gentle dura handling and careful planning of any dural incisions.

Some have recommended medical treatment for asymptomatic MMD because it is associated with a 5.3% rate of clinical progression [97] unless they have reduced cerebral vascular reserve [97, 103, 214] or smoke [97, 215]. Most of these asymptomatic patients will undergo disease progression [103, 216]. When that happens, surgical BR is advisable [95, 103, 215].

In case of failure to initial BR, a new procedure, direct, indirect or combined, should be attempted, as good outcomes are common [166, 217].

5. Results surgical techniques of cerebral revascularization in moyamoya disease

BR decreased both the haemorrhagic [115] and the ischemic stroke [164, 218], but it is more effective in the first than in the second [219–221]. On one-year follow-up, haemorrhagic stroke was 4.6% for those who underwent BR versus 18.6% for those managed conservatively [115, 116, 164, 219]. The mortality rate due to haemorrhagic stroke is four times higher in the conservative than in the BR group [116, 164, 220]. The medical treatment had even worse results in the paediatric than in the adult MMD age group [107, 222].

Younger age at BR surgery correlates with better results and long-term prognosis [62, 164, 205]. In children, indirect BR is associated with a 0.4%/year symptomatic haemorrhage and 0.2%/year infarction rates, with cumulative incidences of 1.8% at ten, 7.3% at 20 and 7.3% at 30 years [223, 224]. There are no statistically significative differences in clinical outcome between direct, indirect and combined BR procedures [99, 205]. The average good clinical outcome is 84.8–88% [143, 205] with a 6.4% 5-year risk of ischemic or haemorrhagic stroke [143]. Children seem to improve more than adults (93% versus 82.7%) [205].

Direct BR with extra-intracranial artery bypass significantly decreases the haemorrhagic stroke rate [115, 223], particularly in the patients with haemorrhages in the posterior half of the brain [85]. Compared to indirect procedures, it reduces the stroke risk [116, 205, 219, 221], particularly the haemorrhagic type in adults [225] and adolescents [196]. These differences are not so evident in children as adults due to the technical difficulty in performing a successful arterial bypass in the first group [140]. Both in adults and the paediatric population, direct BR is technically more challenging that indirect BR, demands a longer operating time, and there is always the risk of hyperperfusion syndrome [116]. There no statistically significative difference in the number of perioperative complications between direct and indirect BR techniques [219]. The direct bypass was accompanied by an annual stroke rate of 0–6% for children and 1.4% for adults, while the indirect techniques had a 1.6% stroke rate for the same period of time [196]. Direct BR is recommended whenever it is technically feasible [197, 221].

Indirect BR is easier to perform, but 40–50% of adult MMD patients do not develop an adequate collateral arterial circulation [53, 62, 141, 226]. These results have been improved with changes in the surgical technique and perioperative care [140], but a new surgical procedure with a combined approach will be needed if there is an unsatisfactory outcome [189, 207, 224]. Meanwhile, paediatric patients submitted to indirect BR have low middle and long term haemorrhagic stroke rates [227, 228].

Perioperative complications happen in 9.4–13.6% of BR procedures [116, 149, 194, 205, 219, 221, 226] with a 0–0.5% [188] mortality rate. Indirect BR has a significantly higher postoperative stroke rate than direct techniques [116, 205] but fewer haemorrhages and no hyperperfusion syndrome [140, 229, 230]. The

incidence of postoperative surgical complications is higher in Asian than other racial groups (6.51/100,00 inhabitants/year versus 5.21/100,000/persons/year) [198, 231]. They also show a different response to BR [198]. Patients with MMD associated with other diseases have a higher perioperative complication rate than regular MMD patients [188].

Preoperative infarction is related to a greater risk of postoperative complications [232, 233].

Direct or combined BR is associated with better outcomes than indirect BR, particularly in the ischemic type MMD [140, 190, 205]. Meanwhile, for haemorrhagic strokes, there are no differences between direct, indirect or combined BR, and thus the indirect techniques are recommended because they are more accessible to perform [205].

The best collateral vessel formation results are obtained using a superficial temporal to MCA bypass combined with an EDAMS and lowest with EDAS [140]. Nevertheless, EDAS combined with multiple burr-holes can provide similar outcomes with a less technically demanding procedure and fewer postoperative negative events [159, 177].

Surgical BR in MMD can prevent future cerebrovascular insults and avoid cognitive decline [116, 117, 227]. It is indicated in asymptomatic patients at the slightest sign of disease progression or patient neurological or mental impairment [103, 234, 235], particularly in the paediatric age group [62, 103]. If performed early before irreversible damage, it can improve the neurological status and prevent the cognitive decline [103], stopping or at least slowing the progression of this nasty disease [136, 206, 234]. Ideally, in children, the surgical BR should be performed not later than three months after the first symptoms appear at a young age [190], the best before six years of age [106].

6. Conclusions

MMD is an uncommon cerebrovascular disorder with a higher frequency among people with Asian ancestry. Medical treatment is not helpful to stop the MMD progression and only can control minor symptoms but not ischemic nor haemorrhagic events. BR can improve brain vascularization, providing a collateral blood supply source that contains this nasty disease's progression. Direct BR is more effective in adults and adolescents than in the paediatric population. Children benefit most from indirect BR. Combined BR improves the results from direct and indirect BR and can also be used as a rescue procedure. Although controversial, many surgeons posit that asymptomatic MMD patients should be submitted to preventive BR before irreversible brain damage happens.

Abbreviations

ACA	anterior cerebral artery
BR	brain revascularization
CBF	cerebral blood flow
CVR	cerebral vascular reserve
DES	split-duro-encephalo-synangiosis
EDS	encephalo-duro-synangiosis
EDAMS	encephalo-duro-arterio-myo-synagiosis
EDAS	encephalo-duro-arterio-synangiosis
EDMS	encephalo-duro-myo-synangiosis

EGS	encephalo-galeo-synangiosis
EMS	encephalo-myo-synangiosis

EPS encephalo-pericranium-synangiosis

MBH multiple burr-hole
MCA middle cerebral artery
MMD moyamoya disease
PCA posterior cerebral artery
STA superficial temporal artery
TIA transitory ischemic attack

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