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Surgical Treatment of Adult Moyamoya Disease In Saudi Arabia: A Review Article

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Moyamoya disease (MMD) is an isolated chronic, usually bilateral, vasculopathy disease of undetermined etiology. The clinical presentations of MMD include TIA, ischemic stroke, hemorrhagic stroke, seizures, headache, and cognitive impairment. Intra- and extra-cranial revascularization for the prevention of recurrence of bleeding in patients with hemorrhagic MMD is controversial. Surgical revascularization of MMD includes 3 types: Direct revascularization, indirect revascularization and combined revascularization. The surgical goal of cerebral revascularization is to prevent progression of symptomology, alleviate intracranial hemodynamic stress, and reduce the incidence of subsequent ischemic or hemorrhagic stroke. However, surgical treatments pose various complications due to the sudden increase in cerebral blood flow or hemodynamic changes caused by perioperative risk factors and anesthesia, such as HS, cerebral hemorrhage and cerebral infarction, bypass occlusion caused by distal vascular resistance, bypass occlusion caused by compression of the temporalis, and anastomotic aneurysm.

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Keywords: Surgical treatment; moyamoya disease; TIA; ischemic stroke; hemorrhagic stroke; seizures; headache; and cognitive impairment.

1. INTRODUCTION

Moyamoya disease (MMD) is an isolated chronic, usually bilateral, vasculopathy of undetermined etiology characterized by progressive narrowing of the terminal intracranial portion of the internal carotid artery (ICA), middle cerebral artery (MCA) and/or proximal anterior cerebral artery (ACA), which is accompanied by the formation of smoke-like abnormal blood vessels in the base of the skull in digital subtraction angiography (DSA) [1].

MMD is relatively common in people living in East Asian countries such as Korea and Japan, as compared to those in the Western Hemisphere. Age of onset of the symptomatic disease has two peak distributions: 5 to 9 years of age and 45 to 49 years of age. Recently, a study done in East Asian countries found the family history of MMD in 10%-15% of patients from the data of 2000-2011 [2]. The male-to-female ratio is 1:1.8 or 1:2.2, and approximately 10%-15% of patients had a family history. The risk of having MMD in family members is about 30-40 times higher than the general population [3].

The clinical presentations of MMD include TIA, ischemic stroke, hemorrhagic stroke, seizures, headache, and cognitive impairment. Transient ischemic attacks and epilepsy may also happen with the incidence of each symptom varying depending on the age of the patient. MMD has two major symptoms: Cerebral ischemia and cerebral hemorrhage [4]. About half of all adult patients present with intracranial hemorrhage, and the other half with ischemic symptoms. In adult patients aged >40 years, the hemorrhagic type is more common than the ischemic type. The most common symptom for patients with ischemic MMD is dyskinesia, and an impaired consciousness is the most common symptom for those with hemorrhagic MMD [5].

Cerebral angiography is the gold standard for diagnosing MMD and assessing its progression. Brain MR imaging (MRI) is able to display the brain parenchymal lesions associated with MMD, and MRA is able to reveal abnormalities consistent with cerebral angiography. Assessment of cerebral hemodynamics and the brain metabolism level is also an important part of the imaging assessment of patients with MMD which provides a more objective and realistic indicator for the selection and efficacy assessment of surgery regimens for MMD [6].
Intra- and extra-cranial revascularization for the prevention of recurrence of bleeding in patients with hemorrhagic MMD is controversial. Surgical revascularization of MMD includes 3 types: Direct revascularization, indirect revascularization and combined revascularization. The surgical goal of cerebral revascularization is to prevent progression of symptomology, alleviate intracranial hemodynamic stress, and reduce the incidence of subsequent ischemic or hemorrhagic stroke [7].

Surgical revascularization confers upfront peri-procedural risk and costs in exchange for long-term protective benefit against hemorrhagic disease. Main indications for surgical revascularization are apparent cerebral ischemia, reduced regional cerebral blood flow and decreased cerebral vascular reserve in perfusion studies. However, every case is evaluated separately as decisive factors may vary from case to case [8].

Liu et al. conducted a retrospective analysis assessing surgical revascularization in adult Moyamoya patients presenting with hemorrhage and similarly found reduced subsequent hemorrhagic stroke, superior neurologic outcomes, and improved rates of returning to work compared to conservative management [9].

1.1 Direct Revascularization

Direct revascularization by STA-MCA bypass provides the benefit of both immediate and progressive revascularization and the anastomoses are proven to enlarge up to 50% with time [10]. There are also other direct bypass procedures to address ACA or posterior cerebral artery (PCA) territories specifically, such as STA-ACA, STA-PCA, and occipital artery-PCA anastomosis, respectively [11]. Superficial temporal artery is used as the main supply vessel in direct bypass. Direct vascularization is technically more difficult to perform and requires a highly skilled surgeon but the improvement in the cerebral blood flow is noted immediately following the surgery [12]. Some disadvantages of the direct anastomoses are the precipitation of stroke from the embolic event, cross clamping of

recipient vessels, the occurrence of the hyperperfusion syndrome, a prolonged operative time as well as the technical challenges of anastomosing arteries having a submillimeter diameter. In the advanced stage of MMD, most of the cortical arteries have shrunk to a small caliber and the vessel walls of patients with MMD tend to be more fragile. Post-operative hyperperfusion syndrome is another considerable problem leading to neurologic deterioration, which often develops after direct bypass surgery. With experience and skill development, the operative time can be shortened and careful case selection can avoid complications [13].

Lee et al., [14] showed in their study, that the extent of revascularization and decrease in the moyamoya vessels in adult patients was significantly more in patients treated with a direct bypass or a combined procedure when compared to the indirect methods (150 procedures in 106 patients). Guzman et al., [15] in their series of 450 revascularization procedures in children and adults, reported that 91% patients were treated with a direct anastomosis, with the risk of stroke or hemorrhage being only 5.5% over 5 years, and 71% patients had a functional improvement. They reported that symptoms resolved within a month of the direct bypass.

Mizoi et al. showed that a patient's age appears to affect the development of collateral formation from indirect bypass and that the direct bypass procedure should be the first-line surgical treatment option for adult MMD patients [16].

1.2 Indirect Revascularization

Many indirect bypass procedures using various kinds of tissues as blood supply sources have been reported, including encephalo-myo-synangiosis (EMS), encephalo-duro-arterio-synangiosis (EDAS), the multiple burr hole surgery technique, ribbon encephalo-duro-arterio-myo-synangiosis (EDAMS), encephalo-duro-myo-arterio-pericranio-synangiosis (EDMAPS), and omentum transplantation [6]. It is an easier method to perform but the time to improve the cerebral blood flow is longer than the direct revascularization [16].

Indirect revascularization relies on neovascularization of the cortical surface via angiogenic mechanisms from pedicle-based grafts (ie, pial synangiosis). Although indirect techniques are easier to perform, the cerebral revascularization and hemodynamic protection of the brain may take months to develop and is less predictable in hemodynamic outcome [17]. The one of advantage of indirect revascularization is that it is relatively easier to perform than direct surgery. This makes the operation time shorter, which is important in preventing complications. In addition, post-operative hyperperfusion syndrome rarely develops after indirect revascularization. However, it takes more time to improve cerebral blood flow, because neovascularization from connective tissue is not immediate [18].

A high level of plasticity and angiogenic potential of the brain tissue and vasculature are required for the success of indirect revascularization techniques, which are a hallmark of MMD but not atherosclerosis [19]. Expression of diverse vascular growth factors, such as vascular endothelial growth factor and hepatocyte growth factor, as well as matrix metalloproteinase-9 and interleukin-1β, have been shown to be highly expressed in patients with MMD. Also, the level of circulating endothelial progenitor cells has been shown to be increased in patients with MMD [20].

Shen et al recently presented an enlarged encephalo-duro-myo-synangiosis in children with provided superior results when compared with standard encephalo-duro-myo-synangiosis which enables revascularization of the ACA territory. Thus, the final decision, which technique will be applied to the individual MMD patient, is up to the discretion of the surgeon as the variety of indirect techniques is large, and it remains unknown which of these techniques is superior over the others [21,22].

Besides from abovementioned coverage of the brain surface with adjacent pedicle-based grafts, other strategies exist for indirect revascularization, such as multiple burr holes or omental transplantation to stimulate transcranial angiogenesis [17]. A recent study with 108 hemispheres revealed comparable long-term results to other surgical procedures in children [23]. Zhao et al demonstrated a modified procedure with combination of multiple burr holes with dural inversion and periosteal synangiosis in 62 patients with ischemic MMD, including children and adults [24]. A recent review analyzed 64 patients with MMD treated with omental transposition or transplantation with 98%

improvement in cerebral revascularization, with better results in younger patients [25].

1.3 Combined Revascularization

Combined bypass procedure is a combination of direct and indirect bypass procedures performed simultaneously. Combined bypass procedure may also carry a risk for postoperative hyperperfusion, but has the advantage to immediately improve cerebral hemodynamics followed by further improvement of cerebral hemodynamics through indirect bypass-mediated angiogenesis. A reciprocal and synergistic relationship exists between the direct and indirect bypass in the development of collateral circulation after the combined bypass procedure [26,27].

Combined techniques provide the advantages of both methods, however there is no evidence of one technique having advantages over the other [28]. Most techniques focus on revascularization of the MCA territory. However, revascularization in the frontal territory is receiving gradually more attention: a considerable part of the ischemic presentation of moyamoya patients consists of neurocognitive disorders as well as lower extremity function, caused by frontal hypoperfusion [29]. The strength of this technique is the revascularization of three vascular territories during a single surgical intervention: the MCA unilaterally; and the frontal territories bilaterally. Bifrontal EDPS may also be considered as a supplementary independent procedure for patients who previously underwent revascularization treatment in the MCA territory, but develop symptoms due to frontal hypoperfusion [30].

A recent study demonstrated sufficient development of both direct and indirect bypasses in 54% of children and in 47% of adult hemispheres [31]. A randomized trial from our group comparing hemodynamic outcome of indirect (EMS) versus combined (STA/MCA bypass+EMS) revascularization concluded that only combined revascularization improved cerebrovascular reserve capacity, as measured by Xe-CT and Diamox challenge, significantly compared with preoperative measurements [32]. A recent prospective cohort study by Deng et al40 similarly demonstrated that direct and combined bypass procedures provide significantly longer ischemia-free time in adults and also children compared with indirect bypass [33].

Jeon et al in a meta-analysis indicated in adults that any strategy that includes a direct bypass (direct and combined procedures) is superior in stroke prevention when compared with indirect bypass procedures, whereas the risk profile for perioperative complications is comparable [34]. Another meta-analysis by Qian et al presented similar results: superior efficacy of strategies, including a direct bypass on secondary stroke incidence compared with indirect revascularization techniques, both for the adult and pediatric patient populations [35]. Another analysis, including only comparative studies with adults, concluded that direct and combined revascularization achieved better angiographic revascularization; however, this was the only study that failed to reveal the superiority of the direct revascularization group with respect to stroke prevention [36].

1.4 Perioperative Complications

Various studies have reported complications after revascularization surgery for MMD. Fragile MMD vessels and unstable hemodynamics result in a very high surgical risk, and direct bypass is associated with a high incidence of surgical complications, especially in patients with unstable MMD [37]. The main causes of MMD complications are hemodynamic fluctuations caused by bypass surgery, as well as other types of surgery and anesthesia. Complications mainly include hyperperfusion syndrome, postoperative cerebral hemorrhage, postoperative cerebral infarction, vascular bypass occlusion, bypass anastomotic aneurysm, and scalp necrosis, among others [38]. A patient with an advanced Suzuki stage with a lower CBF is prone to intraoperative stroke development. During surgery, maintaining euvolemic status and the appropriate blood pressure are important, along with appropriate anesthetic care. In addition, both hypotension and hypercapnia can aggravate hypoperfusion during surgery. Maintaining the level of hemoglobin is also essential in for oxygen delivery capacity. Thus, it is very important to communicate with the anesthesiologist while planning revascularization surgery.

The exact incidence of MMD complications occurring after direct bypass is still unknown. Postoperative stroke with permanent neurologic deficits developed in 1.6%-16.0% of patients and was more frequent in adults than in pediatric patients. In addition, permanent neurologic deficits developed in 0.9%-8.0% of those with

peri-operative ischemic stroke. However, the radiologic incidence of ischemic stroke was higher than symptomatic stroke [39].

Guzman et al. evaluated the effects of 450 revascularization procedures performed on MMD patients on their clinical outcomes; they found that the surgical morbidity rate was 3.5% and that the mortality rate was 0.7% per treated hemisphere [40]. Kim et al. found that MMD surgery performed within 6 weeks after the last ischemic infarction resulted in a higher incidence of postoperative ischemic complications [41].

Hyperperfusion syndrome-induced local neurological impairment has gradually been recognized in recent years, and it is the most common complication of direct bypass in MMD. Fujimura et al. reported that among 80 hemisphere surgeries of 50 MMD patients, the incidence of HS was 27.5% (22/80) [42]. This group updated their research in 2011 and found that among 121 hemisphere surgeries of 80 MMD patients, the incidence of HS was 21.5% (26/121) [43]. They updated their data again in 2012, reporting that among 150 hemisphere surgeries of 106 consecutive MMD patients, the incidence of HS was 18% (27/150) [44].

In addition to headaches and local neurofunctional deficits, the most serious consequence of HS is intracranial hemorrhage [45]. The occurrence of HS-induced intracerebral hemorrhage is not rare after direct revascularization of MMD. In 2014, Kazumata et al. found that the frequency of postoperative stroke was 1.3% in MMD patients following combined revascularization and the appearance of hemorrhagic complications [46].

Postoperative infarction and non-HS-induced hemorrhage have similar mechanisms and prognoses. These postoperative complications are closely related to the hemodynamic instability characteristic of MMD. Unilateral direct bypass in symptomatic hemispheres of MMD patients could cause impairment of cerebrovascular regulation in primary asymptomatic hemispheres shortly after surgery, which may result in the occurrence of infarction and hemorrhage in the whole brain. Even anesthesia can induce intraoperative, acute brain swelling [47].

The cortex arteries should be blocked temporarily during STA-MCA bypass, which results in local hypoperfusion of the cerebral cortex. Clinical symptoms often occur after surgery due to the poor compensatory ability of MMD vessels. In 2015, Mukerji et al. studied postoperative cerebral perfusion in 31 MMD patients who underwent direct ECA-ICA bypass in 2015 and suggested that hyper-perfusion was the cause of transient neurological events [48].

MMD direct bypass requires separation of the STA from the scalp, which destroys the blood supply to the scalp; therefore, the scalp is prone to poor healing and infection. In particular, revascularization surgery seems to be associated with a higher risk of wound-related complications [49]. Houkin et al. studied direct and indirect revascularization in the context of MMD surgical techniques and perioperative complications and found that among 112 surgically treated hemispheres, skin necrosis along the skin incision occurred in 2 [50]. Abla et al. studied 153 revascularization surgeries in 140 affected hemispheres and found that 1 patient required reoperation due to scalp infection [51].

Epilepsy can also occur in HS. In 2007, Narisawa et al. performed STA-MCA anastomosis on 64 sides of 44 consecutive patients, of whom 3 suffered from seizures at between 1 and 10 days after surgery. STA-MCA anastomosis can cause hyperperfusion in patientsSTA-MCA anastomosis can be caused by hyperperfusion in patients [52].

2. CONCLUSION

At present, surgical re-vascularization is the mainstay MMD treatment. It is an effective treatment modality for preventing both ischemic and hemorrhagic stroke. Early diagnosis of moyamoya disease coupled with timely surgical intervention is of utmost importance as medical therapies act only as secondary prevention and do not halt disease progression. However, surgical treatments pose various complications due to the sudden increase in cerebral blood flow or hemodynamic changes caused by perioperative risk factors and anesthesia, such as HS, cerebral hemorrhage and cerebral infarction, bypass occlusion caused by distal vascular resistance, bypass occlusion caused by compression of the temporalis, and anastomotic aneurysm.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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