Anaesthetic Management for Extracranial-Intracranial Bypass Surgery in Patients With Moyamoya Disease

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KEY POINTS

- Moyamoya disease (MMD) is a chronic progressive occlusive cerebrovascular disease of unknown aetiology.
- The manifestations of MMD can be very diverse, from being asymptomatic to having transient ischaemic attacks, cerebral infarction, intracranial haemorrhages, or seizures.
- Surgical revascularization for symptomatic patients with MMD is widely accepted to be superior to medical treatment, with better neurological prognosis and further reduction to the risks of ischaemic or haemorrhagic stroke.
- The overriding goal of perioperative anaesthetic management in extracranial-intracranial bypass surgery is to balance the cerebral oxygen supply and demand, ensuring adequate cerebral protection.
- Heightened vigilance and tightly controlled physiologic parameters throughout the whole perioperative period together form a cornerstone to control cerebral oxygen supply and demand deficiencies.
- Continuous intra-arterial blood pressure monitoring is essential in extracranial-intracranial bypass surgery. Processed electroencephalogram and somatosensory evoked potentials are commonly used for additional neurophysiological monitoring.
- Keeping patients in a neuro-intensive care unit for 24 to 48 hours postoperatively is important for ensuring tight blood pressure control and timely management of any complications, including any neurological deterioration and superficial temporal artery patency issues.

INTRODUCTION

Moyamoya disease (MMD) is a rare, chronic, and progressive occlusive cerebral vasculopathy with no known aetiology. Surgical revascularization has been shown to be superior to medical treatment in preventing ischaemic and haemorrhagic strokes in MMD. Perioperative management of these patients is challenging for anaesthesiologists. To reduce perioperative cerebrovascular events, understanding the underlying pathophysiology of the disease and ensuring adequate cerebral perfusion and neuroprotection are crucial. Perioperative management has a direct impact on the outcome of surgery.

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TAKE ONLINE TEST

Criterion 1. Cerebral angiography	(i) Stenosis or occlusion of the distal portion of the ICA or proximal portions of the ACA and/or MCA (ii) Abnormal vascular networks close to the stenotic lesions (iii) Bilateral findings of (i) and (ii)
Criterion 2. MRI/MRA(if MRI/MRA meet all the criteria, cerebral angiography can be omitted)	(i) Stenosis or occlusion of the distal portion of the ICA or proximal portions of the ACA and/or MCA (ii) Abnormal vascular networks in the basal ganglia (iii) Bilateral findings of (i) and (ii)
Criterion 3. Exclusion of the following	(i) Brain tumours (ii) Cerebrovascular lesions after head irradiation (iii) Autoimmune disease (iv) Von Recklinghausen disease (v) Meningitis (vi) Down syndrome (vii) Head injury (viii) Atherosclerosis

Table 1. Diagnostic Criteria for Moyamoya Disease.[5] ICA indicates internal carotid artery; ACA, anterior cerebral artery; MCA, middle cerebral artery; MRI/MRA, magnetic resonance inaging/magnetic resonance angiography. Note: Paediatric patients can be diagnosed with criteria 1 or 2 (only item i + item ii unilaterally) plus visible stenosis around the terminal portion of the contralateral ICA

BACKGROUND AND CHARACTERISTICS OF MMD

MMD is an occlusive cerebral vasculopathy, seen both in children and adults. It is characterized by bilateral or unilateral occlusive or stenotic changes at the distal portion of the internal carotid arteries and the proximal portions of the anterior cerebral arteries and middle cerebral arteries (MCAs), with the posterior cerebral arteries rarely involved. Dilated collateral vessels are abnormally formed, which give the pathognomonic appearance of "a puff of cigarette smoke" on angiogram, which is "moyamoya" in Japanese.[1–3]

In MMD, patient demographics differ significantly across ethnicities. Asian populations have a higher incidence of MMD, especially the Japanese, with an incidence of 0.54 per 100,000 persons, and a female:male ratio of 1.8, compared to a 0.086 per 100,000 persons incidence in the United States.[2] For Asian ethnicity, MMD is mainly a primary disease which has a familial predisposition and bimodal distribution, with 2 peaks observed, at the ages of 10 and 40. Cerebral ischaemia is the most common precipitating event in both adults and children, presenting as strokes, transient ischaemic attacks (TIAs), headaches, or seizures. Another common presentation in adults is intracranial haemorrhage, with the rate of haemorrhage amongst adults being 7 times that of children. In Caucasian populations, MMD mainly presents with ischaemia, which is secondary to other diseases, such as radiation exposure and atherosclerosis, and occurs more commonly in adults.[1,4]

The research committee on MMD of the Ministry of Health, Labour and Welfare of Japan developed diagnostic criteria in 2012, which are presented in Table 1.[5]

MMD has been linked with a variety of associated diseases, as shown in Table 2.[1] These patients present with a characteristic vasculopathy and are categorized as having moyamoya syndrome.[1]

MMD commonly leads to significant debilitation within 2 years after initial presentation in about 20% of adults and 75% of children.[6] No methods have been found to stop disease progression. Surgical revascularization is the recommended treatment for MMD patients who present with either ischaemic or haemorrhagic symptoms, as it reduces the risk of subsequent ischaemic or haemorrhagic strokes, improves long-term activities of daily living performance and better preserves higher brain

Diseases and conditions		Prevalence (%)
Common	Down syndrome	10-20
	Cranial therapeutic irradiation	
	Neurofibromatosis type 1	
	Sickle cell disease	
Rare	Renal-artery stenosis	< 10
	Giant cervicofacial hemangiomas	
	Hyperthyroidism	
	Congenital cardiac anomaly	

Table 2. Moyamoya Syndrome–Associated Diseases and Conditions[1]

functions.[5,7] If surgical treatment is deemed too high risk, oral antiplatelet agents can be considered for ischaemic-type MMD. Other commonly used drugs for symptom control include vasodilators such as calcium channel blockers, and anticonvulsants.[1,5] However, management for asymptomatic MMD is less well established, with the current consensus focusing on lifestyle modification, risk factor control, and regular magnetic resonance inaging/magnetic resonance angiography examinations. Antiplatelet drugs are not recommended for asymptomatic patients due to the risk of haemorrhagic strokes. Surgical revascularization may be considered in asymptomatic patients with impaired cerebral haemodynamics, if assessed as having a low surgical morbidity. The Asymptomatic Moyamoya Registry study is currently underway, which aims to generate an evidence base for guidelines and management recommendations.[8]

SURGICAL TREATMENT FOR MMD

Cerebral revascularization surgeries can be for either flow augmentation or flow replacement.[3] In MMD, surgical revascularization is for flow augmentation to the ischaemic brain, either by a direct bypass procedure, an indirect bypass procedure, or a combination of both. All these options have been reported to be effective in different situations.[5] A direct bypass refers to anastomosing a branch of the external carotid artery, commonly the superficial temporal artery (STA), to a branch of the internal carotid artery. The MCA is the most utilised target, particularly its M4 branch, which is a terminal cortical segment. A direct bypass achieves an increase in blood flow to the ischaemic brain immediately. This procedure is commonly done in adults but is technically more challenging in children as the vessel calibre is much smaller.[2]

An indirect bypass aims to improve collateral blood flow via angiogenesis, by creating direct contact between an extracranial source of vascularized tissue and the meninges.[3] This is done commonly by encephalo-duro-arterio-synangiosis, in which the STA is mobilized and seamed to the open edges of the dura, or encephalo-myo-synangiosis, in which the temporalis muscle is placed on the surface of brain.[2] The type of revascularization chosen is dependent on the patient's age group, symptoms, and comorbidities, and the surgeon's preference. As typically both sides of cerebral vasculature are involved, surgery is usually staged, with the more symptomatic side often revascularized first.[2] These different procedures are discussed in Table 3.[2,9] In adults, direct bypasses have shown better efficacy for stroke prevention than indirect bypass,[10] whilst better angiogenesis in children and the technical difficulty of a direct bypass make indirect bypass often the preferred choice in the younger age group.

Procedure	Technique	Advantages	Disadvantages
Direct bypass	Commonly STA-MCA bypass (end-to-side anastomosis of the branches of the STA to the branches of MCA, typically M4)	Immediate improvement of cerebrovascular haemodynamics Most well-established type of revascularization surgery	Requires experience and comprehensive training in microanastomosis Requires appropriate donor and recipient vessels Is technically difficult in paediatric patients Early postoperative risks include ischaemia from graft occlusion There is a risk of early postoperative hyperperfusion
Indirect bypass	EDAS EMS EDAMS Pial synangiosis Multiple burr holes Etc.	Technically less difficult than direct bypass Shorter operative time Fewer operative complications	Cerebral neovascularization takes 3-4 months Is less predictable; incomplete collateralization may cause variances in the outcome of revascularization
Combined bypass	Combination of direct and indirect bypass procedures	Immediate improvement of cerebrovascular haemodynamics plus additional benefits from diffuse neovascularization	A relatively larger area of surgical exposure is required to perform the dissection

Table 3. Surgical Procedures for Moyamoya Disease.[2,9] STA indicates superficial temporal artery; MCA, middle cerebral artery; EDAS, encephalo-duro-arterio-synangiosis; EMS, encephalo-myo-synangiosis; EDAMS, combination of EDAS and EMS

ANAESTHETIC MANAGEMENT FOR EXTRACRANIAL-INTRACRANIAL BYPASS SURGERY

Preoperative Evaluation

A thorough preoperative assessment is vital. A variety of comorbidities may be associated with MMD, and their anaesthetic implications perioperatively should be considered. Assessment of preexisting symptoms is important, as a history of frequent preoperative TIAs points to a precarious cerebral blood supply that demands meticulous perioperative management and is an important risk factor for complications.[2] Compensatory hypertension may occur with cerebral vascular stenosis and occlusion, and preoperative baseline blood pressures are important for guiding intraoperative hemodynamic goals. In some centres, MMD patients are admitted for aggressive hydration before the day of surgery with the goal of achieving more haemodynamic stability intraoperatively, especially during induction. As comorbidities in MMD patients are common, this population is likely to be prescribed multiple chronic medications. Appropriate medication reconciliation and preoperative adjustment is therefore important to consider. It is commonly recommended that anticonvulsants and calcium channel blockers are continued. For antiplatelet drugs, discussing with neurosurgeons is important, as some centres continue aspirin until the day of surgery, whilst others withhold it for 7 to 10 days prior, with or without bridging therapy such as low-molecular-weight heparin. Aspirin is often restarted on the first postoperative day if haemostasis is satisfactory.[2,3,11]

Intraoperative Considerations and Anaesthetic Goals

The main goal in the anaesthetic management of patients with MMD is balancing the cerebral oxygen supply and demand. Patients presenting for extracranial-intracranial bypass procedures often have exhausted their cerebral oxygen reserve, with the microcirculation maximally dilated and the oxygen extraction ratio raised[2]; therefore, there are multiple perioperative considerations for these patients.

Premedication and Induction

In children, crying and/or hyperventilation can cause *hypo*capnoea, provoking cerebral vasoconstriction and thus ischaemia; sedative premedications should be considered for paediatric and anxious patients. On the other hand, oversedation can cause hypoventilation and in turn *hyper*capnoea, leading to intracerebral steal, as moyamoya collaterals are poorly vasoactive whilst other normal vessels can vasodilate and paradoxically drain blood away.[3] Oral or intravenous midazolam is commonly used in paediatric patients, with the alternative being intranasal dexmedetomidine. Oxygen saturation monitoring and supplemental oxygen should always be considered. Nonpharmacological anxiolytics can also be helpful, such as parental presence at induction, videos, and music.

A smooth and stable induction is beneficial for maintenance of cerebral perfusion. For paediatric patients, calm and cooperative patients, or mildly to moderately sedated patients, inhalational induction with sevoflurane would be ideal to avoid hyperventilation and hypotension. Alternately, if a venous line can be secured, intravenous induction with propofol, thiopentone, or etomidate can be used. Judicious administration of intravenous opioids, such as fentanyl (2-3 μg/kg) or remifentanil (0.5-1 μg/kg), and/or lignocaine (1 mg/kg) should be considered to appropriately blunt the haemodynamic response to laryngoscopy. If induction-induced hypotension occurs, vasoconstrictors such as phenylephrine should be immediately available, and it is reasonable to prophylactically infuse these to allow rapid titration and reduce hypotensive episodes. Non-depolarizing muscle relaxants with minimal histamine release are suitable for induction.

Monitoring

Intraoperative monitoring includes all American Society of Anesthesiologists standard monitors (electrocardiogram, non-invasive blood pressure, oxygen saturation, end-tidal carbon dioxide, and temperature), plus an intra-arterial catheter for continuous blood pressure monitoring and blood gas sampling. Expectations for vasopressors such as noradrenaline would validate placement of a central venous catheter after induction (unless complicating factors dictated prior placement). Neuromonitoring devices including electroencephalogram, somatosensory- and motor-evoked potentials, transcranial Doppler, jugular bulb oxygen saturation, and near infrared spectroscopy may be used, according to the institutional experience, although the benefit of these techniques in a flow-augmenting low-flow bypass is not fully established.[3]

In our institution, preoperative discussions with the neurosurgeons regarding their surgical plan are standard practice, covering the planned donor and recipient blood vessels, likely duration of vessel clipping, any need for burst suppression, and any other anticipated surgical difficulties or concerns. In operations involving an STA-M4 bypass, we use only bispectral index for monitoring of anaesthetic depth and in anticipation of the small chance of needing burst suppression. If the anastomosis is to a more proximal MCA segment, electroencephalogram and somatosensory- and motor-evoked potentials are also used to monitor for cerebral ischaemia, as temporary clipping may compromise blood flow to the other vital parts of the brain.

Anaesthetic Drugs

For maintenance of anaesthesia, both total intravenous anaesthesia and inhalational anaesthesia have been used as a standard of practice for this surgery at different institutions, with the ideal technique being debated for many years. A few studies have found that regional cortical blood flow levels are higher, intracranial pressure are lower, and there is a greater reduction in intracerebral steal with propofol than with volatile anaesthetics.[2] However, no significant difference in incidence of postoperative complications has been demonstrated in retrospective studies comparing intravenous anaesthesia to inhalational anaesthesia.[12,13] The use of remifentanil has also been shown to provide more stable haemodynamics during induction, maintenance, and emergence of anaesthesia.[14] Overall, there is not enough evidence to show superiority of one anaesthetic technique over the other.

Haemodynamic Control and Fluid Management

Maintenance of ‘‘normotension’’, based on the preoperative baseline blood pressure, is critical throughout the perioperative period and vital for postoperative neurological outcomes. The intraoperative haemodynamic goal is usually within 10% to 20% of the baseline blood pressure. Careful blood pressure management is essential to maintain adequate cerebral blood flow and reduce the risks of ischaemic or haemorrhagic strokes. It is especially important in children, as they have a higher cerebral metabolic demand, a higher oxygen extraction ratio, and a lower autoregulatory response when compared to adults.[3] Hypotension can lead to cerebral ischaemia perioperatively, graft thrombosis postoperatively, and should be treated with vasoconstrictors such as ephedrine or phenylephrine. Hypertension can exacerbate bleeding, especially at the site of anastomosis, and rupture the fragile collateral vessels causing intracerebral haemorrhage. Hypertension should be aggressively monitored and actively corrected, by ensuring depth of anaesthesia, and using additional medications, such as labetalol, esmolol, or opioids, depending on the cause.

The goal for fluid management is normovolaemia, mainly with crystalloids if there is no significant blood loss, though some would advocate for hypervolaemia to mitigate hypotension. If there is extensive blood loss, haemoglobin and haematocrit should be checked and anaemia corrected as necessary. A haematocrit target of 30% to 42% has been suggested to maintain the balance between blood oxygen-carrying capacity and blood viscosity, as extremes at either end can risk cerebral ischaemia in MMD patients.[2,11]

Ventilation

The goal for intraoperative ventilation is maintenance of normocapnoea and normo-oxygenation. Normo-oxygenation is a basic requirement for adequate cerebral oxygen supply. Carbon dioxide is a powerful modulator of cerebrovascular tone. For MMD patients, the areas of brain supplied by the diseased blood vessels are at higher risk of cerebral ischaemia, with both hypercapnoea and hypocapnoea having negative impacts on cerebral perfusion, by either inducing steal phenomenon or cerebral vasoconstriction, respectively.[3]

Temperature

Maintaining a normal body temperature perioperatively is generally agreed upon by most. Avoiding hyperthermia is widely recommended, as an increased cerebral metabolic rate increases oxygen consumption and can thus precipitate ischaemia. Whilst mild hypothermia (~33°C) during vessel clamping theoretically may offer some degree of neuroprotection by reducing the cerebral metabolic rate, there remains concern regarding its potential influence on vasospasm, and there has also been a lack of evidence regarding outcome improvements.[2,3,11]

Neuroprotective Methods During Artery Anastomosis

During direct bypass, temporary clipping of the recipient vessel is necessary when the end-to-side anastomosis is sewn. In low-flow augmentation procedures for MMD, the recipient vessel is typically the cortical segment M4, which supplies a relatively superficial area of brain that also has reasonable collateral circulation. For these procedures the temporary arterial clip time is relatively brief, often shorter than 30 minutes. Augmentation of blood pressure to 20% above baseline is encouraged during this period, to maintain and improve collateral flow. Less commonly, if the anastomosis is to a more proximal segment of the MCA, inducing burst suppression by increasing the propofol target concentration, guided by bispectral index or raw electroencephalogram (EEG), is recommended as a means of reducing cerebral demand.

Emergence and Postoperative Care

A haemodynamically stable and smooth emergence is desirable to prevent haemorrhagic or ischaemic complications. Adequate muscular blockade reversal and pain control helps to ensure normocapnoea, reduce stress and prevent agitation, reduce nausea and vomiting, and maintain graft patency. Clinical neurological assessment is performed as soon as possible.

Patients are typically monitored at least overnight in a neuro-intensive care unit for close observation of any signs or symptoms of complications during the first 24 to 48 hours. Avoidance of direct pressure on the side of head where the STA has been used should be emphasized. A bedside transcutaneous micro-Doppler device is commonly used to monitor the STA patency on a daily basis.[6] Targets for postoperative blood pressure should be noted by the neurosurgical team, bearing in mind whether one or both sides of the brain have now been revascularized.

Complications and Outcomes

The surgical morbidity and mortality per treated hemisphere have been reported as 3.5% and 0.7%, respectively, for revascularization procedures in patients with MMD.[2] The most common postoperative complications are new ischaemia and cerebral hyperperfusion syndrome.[15]

A retrospective study concluded that the incidence of postoperative ischaemia is more commonly related to the surgical approach and severity of the disease rather than other factors, such as anaesthetic management. Risk factors for postoperative ischaemia included previous history of frequent TIAs, patients with precipitating factors for TIAs, and indirect revascularization operations.[13] Smaller studies have implicated the role of other risk factors, such as perioperative hypovolaemia, hypercapnoea, hypocapnoea, hypotension, and low haematocrit,[2,15] but these may not independently cause complications if their duration was controlled.

A significant increase in cerebral blood flow above the metabolic demand of the brain can also cause postoperative cerebral hyperperfusion. This condition often presents after a direct bypass surgery, in the acute postoperative period, as temporary neurological deterioration characterised by dysarthria, hand-motor dysfunction, motor/sensory dysphasia, or seizures. Risk factors for symptomatic hyperperfusion include an elevated oxygen extraction fraction in preoperative positron emission tomography studies, which indicates significantly decreased cerebral blood flow. Cerebral hyperperfusion is often temporary, with the cerebral blood flow typically returning to normal levels 3 to 4 months postoperatively.[16] However, as cerebral hyperperfusion syndrome is an important risk factor for intracranial haemorrhage, strict blood pressure control is very important when this is suspected, with the target blood pressure being less than 120/80 mmHg.

It should be noted that postoperative neurological deterioration can be from cerebral hypoperfusion, graft vasospasm, or cerebral hyperperfusion, and it may be difficult to differentiate these aetiologies clinically. Adjuncts such as transcranial Doppler, near infrared spectroscopy, and dynamic imaging techniques (perfusion scans and angiograms) are useful in distinguishing the cause.

SUMMARY

MMD is a rare cerebrovascular disease often with no known aetiology, and there is currently no agreed-upon effective treatment to reverse the disease process. Surgical revascularization is advocated over medical management as an intervention to prevent further ischaemic or haemorrhagic events in symptomatic patients. In patients with MMD, a flow-augmenting low-flow bypass is the most common surgery performed, and the main goal of perioperative anaesthetic management in extracranial-intracranial bypass surgery is balancing the cerebral oxygen supply and demand. A detailed understanding of the underlying pathology of MMD and techniques for providing safe and effective anaesthetic care are important in improving postoperative outcomes and preventing complications.

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