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Original article

# Superficial temporal artery-middle cerebral artery anastomosis patency correlates with cerebrovascular reserve in adult moyamoya syndrome patients

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ABSTRACT

*Objectives.* – To evaluate the effectiveness of superficial temporal artery-middle cerebral artery (STA-MCA) bypass in improving cerebrovascular reserve (CVR) in Moyamoya syndrome.
*Patients and methods.* – This prospective study included 10 consecutive patients treated for Moyamoya syndrome by STA-MCA bypass in our institution between June 2016 and January 2018. Perfusion MRI, transcranial Doppler and 99 m Tc-HMPAO SPECT with acetazolamide challenge were performed before and after treatment to evaluate perfusion and cerebrovascular reserve. STA-MCA bypass was indicated for patients with history of ischemic or hemorrhagic stroke and when CVR was diminished on both transcranial Doppler and 99 m Tc-HMPAO SPECT with acetazolamide challenge or brain perfusion was deteriorated on MRI.
*Results.* – Bypass anastomosis was patent in all patients at end of surgery. One patient presented partial postoperative sensorimotor deficit related to an ischemic lesion in the frontal cortical area. One patient presented regressive chronic subdural hematoma without neurological deficit. Three months after treatment, CVR was significantly improved in 8 patients and unchanged in 2, probably related to low flow. Further follow-up found CVR deterioration in 1 patient, with anastomosis occlusion at 1 year.
*Conclusion.* – Our data suggest that improvement in cerebral perfusion and CVR depends on flow in the STA-MCA anastomosis in patients with Moyamoya syndrome. Systematic long-term follow-up of anastomosis flow, brain perfusion and CVR improves quantification of the benefit of STA-MCA anastomosis in terms of disease progression.



## 1. Introduction

Cerebrovascular reserve (CVR) is defined as the ability of brain parenchyma to adjust cerebral blood flow in response to altered metabolic demand or vasoactive stimulation. It may be used to identify new or recurrent stroke risk in patients with cerebrovascular disease [1]. Deterioration of CVR plays an important role in the occurrence of stroke in patients with Moyamoya syndrome [2]. As CVR is diminished in these patients, the risk of ischemic or hemorrhagic stroke increases. Some authors [3,4] have reported an annual risk of ischemic stroke close to 13% and an annual risk of hemorrhagic stroke close to 8% in patients with Moyamoya syndrome when CVR is impaired. CVR and cerebral perfusion can be evaluated by transcranial Doppler [5], 99 m Tc-HMPAO SPECT [6] with acetazolamide challenge, MRI [7] and CT scan [8] perfusion. Monitoring CVR is essential for treatment decision-making and treatment evaluation in Moyamoya syndrome [2]. The purpose of the treatment is to improve CVR in order to reduce risk of stroke [9]. Superficial temporal artery-middle cerebral artery (STA-MCA) bypass is the main treatment in adult patients with Moyamoya syndrome [10].

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The goal of this study was to evaluate the effectiveness of STA-MCA bypass in improving CVR in patients with Moyamoya syndrome.

## 2. Materials and methods

This prospective study included 10 consecutive patients treated for Moyamoya syndrome by STA-MCA bypass in our institution between June 2016 and January 2018. Approval was obtained from the local institutional review board (ref. DEC19-002). The series comprised 5 men and five women, with mean age at diagnosis of 44.8 years (range: 19–62 years).

### 2.1. Preoperative evaluation

All patients were clinically evaluated at our institution prior to treatment. Age at diagnosis, medical history, neurological status and American Society of Anesthesiology (ASA) score [11] were recorded. Moyamoya syndrome was diagnosed in all patients using conventional cerebral angiography and cranial magnetic resonance imaging (MRI). The STA main trunk and frontal and parietal branches were studied on conventional external carotid angiogram. Perfusion MRI, transcranial Doppler with acetazolamide challenge and 99 m Tc-HMPAO SPECT with acetazolamide challenge were performed before treatment to evaluate baseline perfusion and CVR.

CVR was assessed on HMPAO SPECT. After keeping the patient in a dark and quiet area for 30 minutes, SPECT and planar images were acquired with intravenous injection of 732 mBq 99 mTc HMPAO. Scans were repeated within 3 to 7 days with acetazolamide challenge. Acetazolamide was injected intravenously at 20 mg/kg body weight and, 20 minutes later, the patient received 732 mBq 99 mTc HMPAO. SPECT and planar images were acquired 20 minutes after administration of 99 mTc HMPAO. Images were compared with and without acetazolamide challenge, to obtain the differences between gamma-ray counts in 2 cerebral hemispheres to assess CVR, a difference of more than 6% being defined as impaired CVR. Two of the 10 patients (20%) did not have baseline perfusion MRI, and CVR was evaluated by SPECT HMPAO and transcranial Doppler.

The treatment strategy was systematically discussed and decided upon by a multidisciplinary team including neurologists, neurosurgeons, neuroradiologists and intensivists. The STA-MCA bypass procedure was indicated for patients with history of ischemic or hemorrhagic stroke and when CVR was diminished on both transcranial Doppler and 99 m Tc-HMPAO SPECT with acetazolamide challenge and on perfusion MRI. However, 1 patient without history of stroke nevertheless underwent the STA-MCA procedure because of severely deteriorated CVR. In accordance with the COSS study [12], the bypass procedure was never performed within 3 months of an acute episode of stroke [13]. Antiplatelet medication was not discontinued perioperatively.

### 2.2. Surgery

The course of the STA is marked on the skin by palpation and portable continuous-wave Doppler ultrasonography. A frontotemporal incision is carefully made, conserving STA integrity. A frontotemporal craniotomy is performed over the Sylvian fissure and the dura is opened to identify suitable recipient M3–M4 cortical arteries. Once a recipient artery has been identified, the STA is dissected under an operating microscope.

Depending on STA length and diameter, the frontal, parietal or both branches are carefully dissected, distally cut and proximally clipped with a temporary aneurysm clip. The recipient cortical artery or arteries are dissected from the overlying arachnoid and isolated with a rubber-leaf/foil layer. The cortical artery is temporarily clipped with a small aneurysm clip and arteriotomy is performed. Subsequently, end-to-side anastomosis of the STA to the cortical artery is performed using microneurosurgical techniques with 10-0 interrupted nylon sutures. During bypass anastomosis clamping time, blood pressure is raised to normotensive values. STA-MCA anastomosis patency is confirmed by intraoperative indocyanine green video-angiography.

### 2.3. Postoperative evaluation

Early postoperative clinical examination was performed within the first week, with transcranial Doppler, MRI with diffusion and

**Table 1**
Functional outcomes.

| Patient | Age at diagnosis | Disease | Preoperative symptoms | Preoperative mRS score | mRS score 3 months after bypass |
|---|---|---|---|---|---|
| 1 | 50 | Atheromatous Moyamoya | 3 ischemic strokes with motor aphasia | 2 | 2 |
| 2 | 19 | Unilateral Moyamoya | Headache and paresthesia, no stroke | 2 | 2 |
| 3 | 49 | Bilateral Moyamoya | 2 left ischemic strokes with transient motor aphasia | 2 | 2 |
| 4 | 49 | Unilateral Moyamoya | 1 right ischemic stroke without symptoms | 2 | 2 |
| 5 | 43 | Unilateral Moyamoya | 2 left ischemic strokes with hemiparesis | 2 | 2 |
| 6 | 62 | Cavernous sinus meningioma with ICA occlusion | 1 left ischemic stroke with transient motor aphasia | 0 | 0 |
| 7 | 30 | Bilateral Moyamoya | 1 right ischemic stroke and 1 left brain hemorrhage with hemiparesis | 2 | 2 |
| 8 | 55 | Unilateral Moyamoya | 1 left ischemic stroke with motor aphasia | 1 | 2 |
| 9 | 47 | Bilateral Moyamoya | Headache without stroke | 1 | 2 |
| 10 | 45 | Bilateral Moyamoya | Right ischemic stroke with hemiparesis | 3 | 3 |

**Table 2**
Cerebrovascular reserve evaluation on different examinations.

| Patient | Preoperative perfusion MRI (mean transit time) | Flow in anastomosis on early transcranial Doppler (mL/minute) | Early postoperative perfusion MRI (mean transit time) | Perfusion MRI 3 months after anastomosis (mean transit time) | 99 m Tc-HMPAO SPECT with acetazolamide challenge 3 months after anastomosis (improvement in cerebrovascular reserve) | Transcranial Doppler with acetazolamide challenge 3 months after anastomosis (improvement in cerebrovascular reserve) |
|---|---|---|---|---|---|---|
| 1 | 5 seconds | 85 | 5 seconds | 5 seconds | + | + |
| 2 | 2 seconds | 82 | 2 seconds | 0 seconds | + | + |
| 3 | 4 seconds | 70 | 2 seconds | 1 second | + | + |
| 4 | 2 seconds | 55 | 2 seconds | - | + | + |
| 5 | – | 45 | – | 3 seconds | + | + |
| 6 | 7 seconds | 35 | 3 seconds | 3 seconds | + | + |
| 7 | – | 120 | – | 0 seconds | + | + |
| 8 | 4 seconds | 45 | 3 seconds | 3 seconds | – | – |
| 9 | 7 seconds | 19 | 5 seconds | 4 seconds | – | – |
| 10 | 4 seconds | 48 | 3 seconds | 2 seconds | + | + |

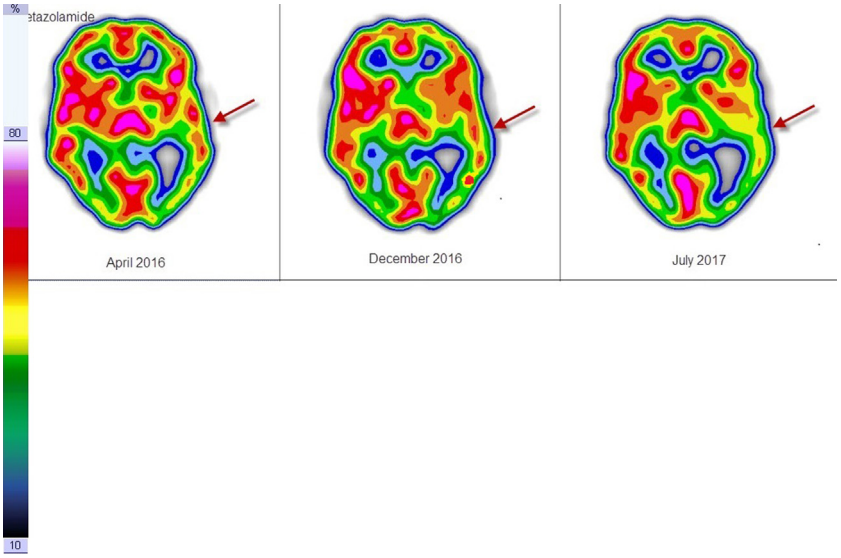


**Fig. 1.** Patient 2, 19 years old, with a deterioration of CVR in left middle cerebral artery territory (red arrow) related to unilateral left-side Moyamoya disease. STA-MCA anastomosis was performed in June 2016. CVR increased after treatment, as demonstrated on 99 m Tc-HMPAO SPECT with acetazolamide challenge in December 2016. STA-MCA anastomosis occlusion occurred one 1 year after treatment and CVR decreased as demonstrated on 99 m Tc-HMPAO SPECT with acetazolamide challenge in July 2017.

perfusion sequences, and CT angiography for each patient 1) to confirm bypass patency, 2) to measure flow in each anastomosis, 3) to detect any ischemic lesions and 4) to assess brain perfusion.

All patients were re-evaluated 3 months after bypass surgery. Clinical examination findings and modified Rankin Scale score (mRS) were recorded. MRI screened for ischemic lesions and assessed brain perfusion. Transcranial Doppler assessed flow in the anastomoses. At 3, 6 and 12 months after treatment, transcranial Doppler with acetazolamide challenge, 99 m Tc-HMPAO SPECT with acetazolamide challenge and MRI with perfusion sequence were performed to evaluate CVR and brain perfusion. In case of discordance between test results, conventional CT angiography was performed to assess the internal and external carotid arteries.

## 3. Results

Mean age at diagnosis was 44.8 years (range, 19–62 years) and mean follow-up was 24 months (range, 6–30 months). ASA score was 1 in 2 patients, 2 in 7 and 3 in 1. Functional outcomes are presented in Table 1.

### 3.1. Intraoperative findings

STA-MCA bypass anastomosis was systematically feasible. In 2 patients, double STA-MCA anastomosis was performed because both frontal and parietal branches of STA were suitable. Mean occlusion time per anastomosis was 55 minutes (range, 33–85 minutes).

Intraoperative indocyanine green video-angiography demonstrated anastomosis patency in all patients at end of procedure. Mean microsurgical procedure time was 5.4 hours (range, 3.1–8.7 hours).

### 3.2. Microsurgical morbidity

One of the 10 patients (Patient 4) showed postoperative partial sensorimotor deficit related to an ischemic lesion in a frontal cortical area. Another patient (Patient 8) presented chronic subdural hematoma without neurological deficit.

### 3.3. Long-term clinical outcome

One patient (Patient 1) showed a frontoparietal cortical ischemic lesion with hemiparesis and aphasia 1 year after left-sided STA-MCA anastomosis. This stroke occurred during femoral vascular

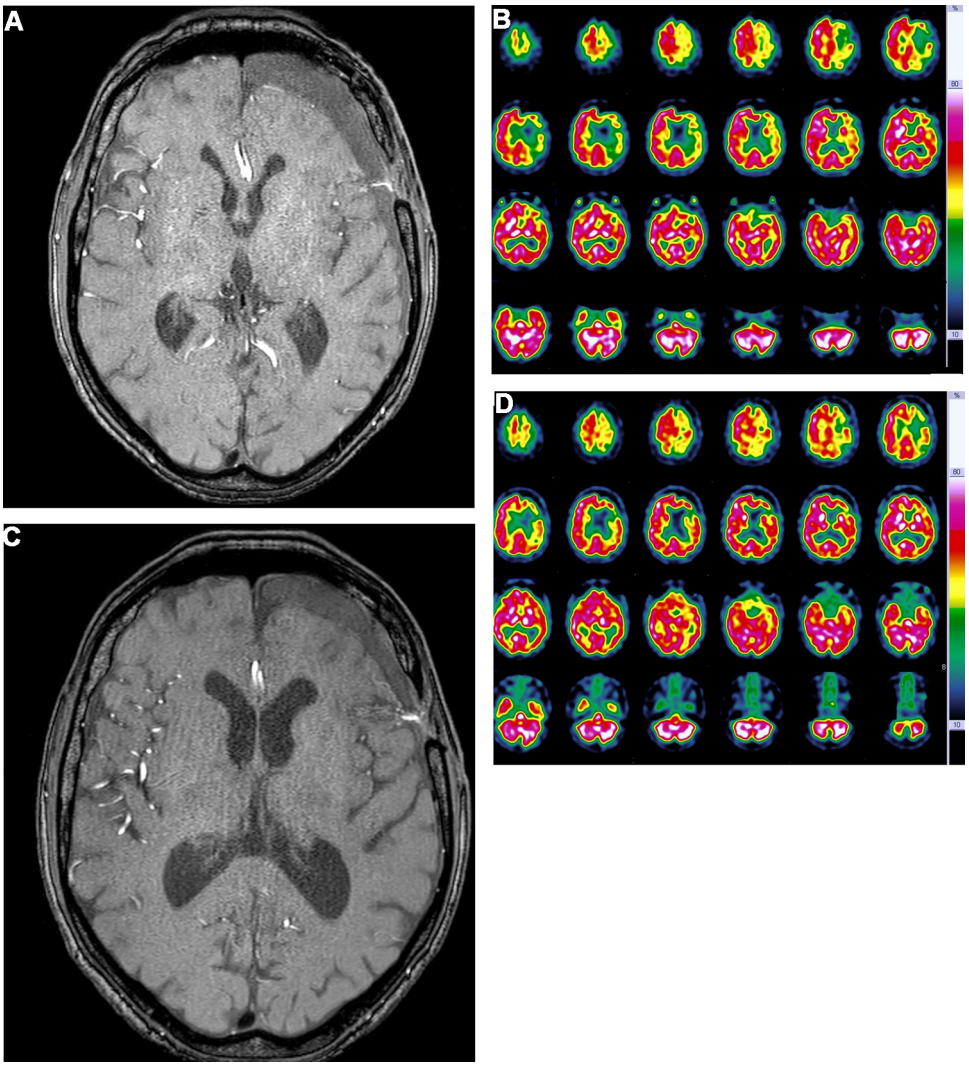


**Fig. 2.** Patient 8, 55 years old, with deterioration of CVR in left middle cerebral artery territory related to unilateral left-side Moyamoya disease. STA-MCA anastomosis was performed but persistent CVR deterioration was noted on 99 m Tc-HMPAO SPECT with acetazolamide challenge 3 months after treatment (Fig. 2A). MRI demonstrated a chronic subdural hematoma, with the STA stretched and thinned (Fig. 2B) and no flow was detected in the STA-MCA anastomosis by cranial Doppler. After administration of corticosteroids, MRI demonstrated regression of the chronic subdural hematoma (Fig. 2C) and transcranial Doppler revealed recanalization of the STA-MCA anastomosis. Improvement in cerebrovascular reserve was noted on 99 m Tc-HMPAO SPECT with acetazolamide challenge (Fig. 2D).

bypass surgery and was related to low intraoperative blood pressure (70 mmHg). There was no change in mRS score in the other patients at 1 year (Table 1).

### 3.4. Radiological outcome

Three months after treatment, brain perfusion and CVR improved significantly in 8 patients and remained unchanged in 2 (Table 2). STA-MCA anastomosis occlusion occurred in 1 patient (Patient 2) at 1 year, without neurological deterioration; CVR had improved after the bypass procedure and decreased after anastomosis occlusion (Fig. 1). On perfusion MRI, transit time was 0 seconds when the STA-MCA anastomosis was patent, but 4 seconds when occluded.

In 1 patient (Patient 8), chronic subdural hematoma occurred after treatment, stretching the STA-MCA bypass; however, the bypass was not definitely occluded, as patency and improved CVR were recorded after regression of the hematoma (Fig. 2).

One patient (Patient 9) showed no significant improvement in CVR after treatment; transcranial Doppler revealed only weak flow (19 mL/min) in the anastomosis.

## 4. Discussion

STA-MCA anastomosis patency correlated strongly with CVR improvement. Therefore, systematic long-term monitoring of flow and CVR on transcranial Doppler, SPECT HMPAO and perfusion MRI seems mandatory in patients with Moyamoya syndrome.

### 4.1. STA-MCA anastomosis morbidity

STA-MCA bypass is a valuable microsurgical procedure that demonstrated efficacy in many intracranial vascular diseases such as Moyamoya disease (MMD), aneurysm and skull base tumor [14]. STA-MCA bypass is usually described as a “low-flow” bypass, but conversion to a “high-flow” state in the late postoperative period

has been reported by many authors [2,15]. In our study, flow was > 50 mL/min in 6 patients by 6 months postoperatively.

STA-MCA bypass shows low morbidity [16] and patency is approximately 95% at end of procedure [17–19]. In his systematic review, Schaller [20] reported that long-term bypass patency was excellent, with 1% failure per year following the first year after surgery. In his series of 264 MMD patients, including 450 revascularization procedures, Guzman [16] reported 3.5% surgical morbidity and 0.7% mortality per treated hemisphere. Complications were mainly related to MMD pathophysiology, implicating fragile vessels and hemodynamic instability [21]. Thus, risk of bypass thrombosis is slightly higher in case of MMD. Moreover, MMD can involve extracranial arteries, including the STA [22], which perhaps explains late STA-MCA anastomosis occlusion in our series.

### 4.2. Prognostic value of cerebrovascular reserve evaluation

Perfusion and CVR can be evaluated by various techniques, including perfusion MRI, transcranial Doppler with acetazolamide challenge and 99 m Tc-HMPAO SPECT with acetazolamide challenge. In our study, the results of these techniques correlated [23,24]: when transcranial Doppler showed anastomosis occlusion in Patients 2 and 8, SPECT HMPAO and perfusion MRI showed immediate deterioration of CVR.

In his review, Garrett [2] demonstrated that patients with severe hemodynamic failure were at higher risk of cerebral infarction than those with mild disease, and that patients with severe failure responded better to surgery. In a series of 23 patients who underwent STA-MCA bypass, O [25] reported that (99 m)Tc HMPAO SPECT images of the territory supplied by the bypass graft showed increase in both cerebrovascular flow and reserve at baseline, and that the increase was significantly higher following administration of acetazolamide. Low [10] reported that transcranial Doppler and (99 m)Tc HMPAO SPECT acetazolamide-challenge images repeated at $4 \pm 1$ months showed significant improvement in CVR in the 46 patients who underwent STA-MCA bypass. Moreover, during a mean follow-up of 34 months (range, 18–39 months), only 6 of the 46 patients (13%) developed cerebral ischemic events. In our series, CVR improved significantly in 8 patients 3 months after STA-MCA bypass. However, Patient 9 showed no significant improvement in CVR, probably due to weak bypass-flow as measured on transcranial Doppler. In Patient 8, CVR remained diminished because of postoperative chronic SDH, probably stretching the STA and reducing vessel lumen, with no flow seen on Doppler. A sudden deterioration of CVR was recorded in 1 patient 9 months after surgery, due to late bypass occlusion, without clinical signs of stroke; this late occlusion could be related to MMD involvement of the external carotid artery network, which includes the STA [22]. A cerebral ischemic event was noted in 1 patient with patent STA-MCA bypass 1 year after treatment, during femoral vascular bypass surgery with low intraoperative blood pressure: i.e., iatrogenic; CVR had been satisfactory after STA-MCA bypass, but presumably insufficient to protect the patient against an acute episode during a sudden drop in blood pressure (SBP 70 mmHg).

## 5. Conclusion

STA-MCA bypass is a valid method to improve the brain perfusion and CVR in Moyamoya syndrome. Improvement in CVR depends on the flow and the patency of the STA-MCA anastomosis. Likewise, the success of the anastomosis may be related to the need for bypass to supplement the low blood flow demonstrated on CVR. Our data suggest that improvement in cerebral perfusion and CVR depends on the flow in the STA-MCA anastomosis in patients with Moyamoya syndrome. Systematic long-term follow-up evaluation of anastomosis flow, brain perfusion and CVR should better quantify the benefit of STA-MCA anastomosis in terms of disease progression.

## Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Lille University Hospital/Ethics committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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## Disclosure of interest

The authors declare that they have no competing interest.

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