Universal Bypass for Treatment of Symptomatic Moyamoya Disease or Moyamoya Syndrome. Analysis of a Personal Case Series on Behalf of the Italian Moyamoya Association

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Abstract

Background

Moyamoya (MM) is a very rare cerebrovascular disease, particularly in Caucasians. We describe the results of an Italian case series where the mainstay of treatment was a bypass or a combined approach.

Methods

An analysis of a prospectively collected database was carried out. The main objective was to investigate (1) the risk of perioperative stroke and surgical complications, (2) the risk of new ischemic events, and (3) the risk of new hemorrhages at follow-up (mean follow-up: 2.2 years).

Results

Between January 2011 and January 2015 we carried out 34 bypasses in 23 patients with MM (15 MM disease, 5 unilateral MM, 3 MM syndrome); mean age was 34 (range:1–57). The mortality and definitive morbidity rates were 0 %. Two patients suffered from transient aphasia and one developed partial palsy of the facial nerve. Five of the 12 patients with preoperative fixed deficits improved. No patient with preoperative ischemia experienced new ischemic symptoms. Rebleeding occurred in 1 of the 11 patients with a hemorrhagic presentation (9 %).

Conclusions

The bypass/combined approach to MM appears to have a favorable risk profile and preventive effectiveness, particularly on TIAs and ischemic stroke.

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Introduction

Moyamoya (MM) is a very rare cerebrovascular disease, particularly in Caucasians. MM is characterized by the progressive occlusion of the terminal internal carotid artery (ICA) with the secondary development of compensatory collateral networks [15]. Clinically, patients with MM may present with either ischemic or hemorrhagic events. A small subset of patients may have subtle cognitive deficits, headache, epilepsy, or, very rarely, may be asymptomatic. Children more frequently have symptoms related to cerebral ischemia, while adults may be either ischemic or hemorrhagic [2, 15, 16]. Although the natural history of MM is still debated, the disease is usually progressive, with relapsing ischemic or hemorrhagic events. The treatment of MM is surgical revascularization that may be achieved with various methods including direct bypass, different types of synangiosis (indirect revascularization procedures), or a combination of the two approaches [8].

We describe the mid-term results of an Italian case series of patients affected by MM who were treated with either a direct bypass or a combined approach.

Materials and Methods

Methodology and Definitions

An analysis was carried out of a prospectively collected database of patients with MM who underwent surgical revascularization. MM and its variants were defined according to the criteria proposed by the Research Committee on Spontaneous Occlusion of the Circle of Willis [14]. In brief, MM disease (MMD) was diagnosed when there was a stenosis or occlu-

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sion of the terminal ICA on both sides without an underlying cerebrovascular disease being responsible for the pathology. When only one of the ICAs was affected, we made a diagnosis of unilateral moyamoya (uMM), and when there was an underlying disease we classified the case as moyamoya syndrome (MMs).

Data Collection Diagnosis and Treatment

We collected the baseline demographic (e.g., age at presentation, gender, ethnicity, familial occurrence), and clinical data (e.g., type of presentation categorized as hemorrhage or ischemia; type of MM categorized as MMD, uMM or MMs). The angiographic grade was defined according to the Suzuki scale [15]. In addition to angiography and MR, all patients routinely underwent CT or MR perfusion studies with and without the acetazolamide challenge before surgery. For investigative purposes, a subgroup of patients underwent preoperative near-infrared spectroscopy to study cerebral O_2 saturation. The treatment was dichotomized into bypass or combined approach; the latter consisted of a bypass associated with the pan-synangiosis (encephalo-duro-myo-pericranio synangiosis). The bypass was performed using one or both branches of the superficial temporal artery or the occipital artery as donors and, typically, a distal branch of the middle cerebral artery (MCA) as recipient. When the patient had symptoms or hypoperfusion related to the anterior cerebral artery (ACA), we targeted the ACA territory using the middle internal frontal artery as recipient. In the event of symptoms related to the posterior cerebral artery (PCA), the recipient was the parieto-occipital artery coming off the interhemispheric fissure.

Complications and Results

Surgical complications were categorized as (1) cerebral ischemic lesions, (2) intracranial hemorrhages, (3) infections, (4) postoperative seizures, and (5) skin necrosis or delayed wound closure. The patients were followed up and any new ischemic or hemorrhagic event was recorded. For patients with preoperative deficits, we used the Activities of Daily Living (ADL) scale according to Choi et al [3].

Results

From January 2011 to January 2015, at the neurosurgical department of the Papa Giovanni Hospital of Bergamo, 67 bypasses were performed. All the bypasses were carried out by a single surgeon (LAL). Thirty-four bypasses were performed on 23 patients with MM. The remaining procedures were performed for complex aneurysms (17 bypasses), chronic ischemia related to ICA or MCA occlusion (14 bypasses), and skull base tumors (2 cases).

As regards the 23 patients with MM, 15 were affected by MMD, 5 by uMM and 3 by MMs. Two of the three patients with MMs were affected by Recklinghausen's disease and one had MMs associated with an arteriovenous malformation (proliferative angiopathy). There were no familial cases and all patients were Caucasians. These patients had been referred to our department from all over Italy. The mean age was 34 (range: 1–57), with a female-to-male ratio of 3:1. The presentation was hemorrhage in 11 cases (47.8 %), cerebral infarction in 7 cases (30.4 %), and transient ischemic attacks (TIA) in five patients (21.7 %). All pediatric cases (<18 years) presented with either infarctions or TIAs. The Suzuki grade was 3–4 in 7 patients (30 %), 5 in 12 (52 %), and 6 in 4 (17 %).

In 14 patients, we performed a combined approach (e.g., bypass and pan-synangiosis), and in 9 we carried out only a direct bypass. The MCA was the recipient in all but six cases, in whom we targeted the bypass to the ACA (five cases) or the PCA (one case). The procedure-related mortality or definitive morbidity rates were 0 %. Two patients suffered from transient motor aphasia lasting less than 72 h and one developed a partial palsy of the supraorbital branch of the facial nerve. One patient deteriorated because of hydrocephalus and underwent a spino-peritoneal shunt procedure. In three patients there was delayed skin closure without the need for reoperation. There were no post-operative seizures or infections. Five of the 12 patients with preoperative fixed deficits improved within 1 month after surgery (mean preoperative ADL of 3.1 and mean postoperative ADL of 1.9). Postoperative angiographies were performed after 3 months of surgery in 17 patients and demonstrated the function of the bypass in all cases. Six patients are still pending postoperative angiography. During a mean follow-up of 2.2 years, no patient with preoperative ischemia experienced any new ischemic symptoms. Rebleeding occurred in 1 of the 11 patients with a hemorrhagic presentation (9 %).

Discussion

This case series represents one of the largest and and most up-to-date single-center Italian experiences of patients with MM where a direct surgical approach (with single or multiple bypass) was the mainstay of treatment. All patients uniformly underwent at least a bypass that, more recently, was combined with pan-synangiosis. The bypasses were usually targeted to the most hypoperfused brain areas and could be directed to the MCA, ACA, or PCA, according to the symptoms and the perfusion maps. The rationale of a universal bypass approach in MM was that such patients might be refractory to simple synangiosis [10, 11], the peri- and postoperative ischemic risk of pure synangiosis might be higher

as it usually takes several weeks or months to develop effective collaterals and, according to a recent literature review, a direct/combined bypass was more often associated with excellent revascularization than indirect approaches [7]. Furthermore, regarding patients with hemorrhage, the recent randomized trial found a possible long-term benefit of treatment, provided that patients were treated with a bypass [13].

The main finding of this study is that the universal bypass approach may be performed with a low risk of major complications. Indeed, no patient died or remained disabled because of the procedure, and we observed no post-operative strokes. Only two patients had transient deficits. These results are in accordance with the literature. Kazumata and colleagues [7] studied a population of 236 patients and 358 revascularization procedures and found a risk of perioperative stroke of less than 5 %. Similar results have been reported by Guzman and colleagues [4] who reported a surgical morbidity rate of 3.5 % and a mortality rate of 0.7 % in a series of 450 revascularization procedures performed in North America. Bao et al., in a cohort of 288 pediatric MM patients, reported a risk of perioperative complications of 4.2 % [1].

Although most of the published reports on the history of the disease describe Asian populations in whom the pathology may be different from that of Caucasians, the effectiveness of the bypass/combined approach in preventing new strokes seems to compare favorably with the natural history. In our series, regarding the risk of new ischemic strokes or relapsing TIAs, to date no patient has suffered from any new ischemic events after treatment. Although this result may be partially biased by a relatively short follow-up period (2 years), the literature appears to be in line with our data. A recent report that included both adults and children who were followed for more than 10 years, found that 97 % of patients were TIA-free after bypass, with nearly 90 % of patients being able to lead an independent life [12].

The preventive effectiveness of the bypass on rebleeding seems to be lower than that on cerebral ischemia and is still being debated. We found a rebleeding rate of 10 % during a 2-year follow-up, a result that largely corresponds to the recent Japanase and Korean studies. The JAM trial disclosed a risk of recurrence of 11.9 % at 5 years and another observational study found a risk of rebleeding of 7 % with a mean follow-up of 7 years [13]. The recurrence risk without treatment was around 30–37 % and was significantly higher than that of the treated patients. It is noteworthy that all the patients included in the JAM trial underwent a bypass or a combined approach. Furthermore, the Korean study found that the risk of rebleeding was lower in patients treated with a bypass than in those treated with synangioses [9].

Revascularization in patients with misery perfusion may be restorative. Five patients with fixed deficits improved, and the mean ADL shifted from 3.2 to 1.8 within 1 month of surgery. We found similar results in patients with chronic ischemia related to ICA or MCA occlusion. Other authors have supported this observation [5, 6]. In our opinion, these data suggest that treatment may be indicated also in selected patients with fixed and dense deficits related to a condition of misery perfusion, particularly in the event of a discrepancy between the severity of the neurological deficits and the lesions shown on the MRI.

The limitations of this study are its limited statistical power and relatively short follow-up. However, the intention of the study was to investigate only the short- and mid-term results and to compare them with the literature. Although we used the combined approach also for children (three cases, five bypasses), and in each case we performed a direct bypass followed by an uneventful postoperative course, the statistical power of the study is too limited to analyze them as a subgroup. The strength of this study is that it describes a relatively homogeneous population of Italian patients with MM treated with a single technique by a single surgeon.

Conclusions

The bypass/combined approach to MM appears to have a favorable risk profile with preventive effectiveness, particularly on TIAs and ischemic stroke. Treatment in selected patients with misery perfusion may be restorative. The bypass/combined approach may be performed also in children.

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Conflict of Interest Statement All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaux, membership, employment, consultancies, stock ownership, or other equity interest, and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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