Effectiveness of Ipsilateral Stroke Prevention Between Conservative Management and Indirect Revascularization for Moyamoya Disease in a North American Cohort

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BACKGROUND: Few reports have compared surgical intervention with conservative treatment for moyamoya disease (MMD) in non-Asian cohorts. This study describes the effectiveness of follow-up stroke prevention by indirect revascularization relative to conservative management in a Northeast United States study population.

METHOD: We retrospectively reviewed records of patients with MMD at our institution from 1990 to 2014. Baseline characteristics and follow-up results including subsequent ipsilateral strokes were collected, and compared between an indirect revascularization group and a conservatively treated group on a per-hemisphere basis.

RESULTS: A total of 94 patients with 184 hemispheres were included. The average age was 23.9 ± 18.1 years, with 76.6% (n = 141) being female. Racial distribution comprised white (n = 75, 40.8%), African-American (n = 57, 31.0%), Asian (n = 30, 16.3%), and other (n = 22, 12.0%). Eighty-three hemispheres (45.1%) presented with ipsilateral stroke and 54 (29.3%) with ipsilateral TIA. Management strategies included either conservative management (51.1%) or indirect bypass (48.9%). Patients who were male (P < 0.001), on baseline antiplatelets (P = 0.043), or with speech disturbance (P = 0.002) were more likely to receive indirect revascularization. Patients with headache history were more likely to be treated conservatively (P = 0.046). History of ipsilateral stroke was borderline associated with indirect bypass (P = 0.058). During a follow-up period of 6.37 ± 5.81 years, the annual risk of stroke for indirect revascularization group was 0.93% and 2.70% for the conservative group. Multivariate analysis found that increasing age (P = 0.029), posterior cerebral artery involvement (P = 0.040), and conservative treatment (P = 0.048) were associated with follow-up stroke.

CONCLUSION: Our results suggests that indirect revascularization provides symptom relief and lower risk of stroke during follow-up compared with conservative management. Indirect revascularization should be considered for symptomatic MMD patients with a low surgical risk profile in a similar patient population.

INTRODUCTION

Moyamoya disease (MMD) is a cerebrovascular arteriopathy with progressive spontaneous occlusion of the intracranial internal carotid arteries. The Japanese term “moyamoya” is used to describe something hazy, like a “puff of smoke,” which in MMD arises as the result of the formation of an anastomotic capillary network allowing blood flow distal to diseased vessels. Upon progressing, MMD may affect other portions of the circle of Willis, including the proximal middle cerebral artery (MCA), the anterior cerebral artery (ACA), and more rarely the vertebrobasilar system. With progression, MMD leads to recurrent strokes; therefore, the
prevailing standard of treatment for symptomatic disease is revascularization surgery. Existing literature reports suggest that the annual stroke rate for untreated MMD patients is between 3.2% and 13.3%. By contrast, annual stroke rates for treated patients are reported between 0.41% and 4.5%. Surgical treatment of MMD is generally approached by either of 2 revascularization strategies: direct bypass, where a superficial temporal artery (STA) branch is anastomosed to a MCA branch, or indirect bypass, whereby well-vascularized tissue composed of the STA with its vascularized pedicle and the temporalis muscle is placed in direct contact with the affected cortex to promote collateral vessel formation. The decision whether to treat MMD with direct or indirect revascularization is debatable. Direct bypass is reported to be the superior modality by some authors, who advocate its use when possible. Abla et al. described direct and indirect bypass as equally effective for preventing stroke in adults, but that direct bypass patients experienced greater symptom relief. Despite these reported advantages, patient circumstances can often preclude the use of direct revascularization, and alternative strategies should remain available.

The merit of indirect bypass is not completely understood, but mounting evidence suggests that it can provide long-term relief from ischemic and hemorrhagic manifestations of MMD for pediatric and adult populations. Additionally, despite numerous reports describing the natural history of MMD and the benefit of surgical intervention relative to conservative management, non-Asian MMD is not well described in the literature. In this study, we aimed to elucidate the role of indirect revascularization for MMD in non-Asian patients for preventing follow-up ipsilateral strokes—an undertaking that is under-reported in the literature.

METHODS

Study Population
This study was approved by the institutional review board from our institution, and patient consent was waived for retrospective review of medical records. We performed a retrospective review of MMD patients at our institution from 1990 to 2014 using an actively maintained institutional database. After excluding patients without definitive documentation of MMD or nonidiopathic internal carotid artery occlusion, we identified 114 patients with 212 hemispheres confirmed to have MMD. Of these 212 hemispheres, we excluded patients with single-hemisphere involvement (n = 15) and those having undergone direct revascularization (n = 13). The patients who underwent direct STA-to-MCA bypasses occurred earlier and likely represented a practice paradigm shift. The final cohort for our study included 184 hemispheres from 94 patients with confirmed bilateral MMD who were treated either conservatively or with indirect revascularization. Patient information was collected and analyzed on a per-hemisphere basis. Exclusion criteria included patients with incomplete clinical and angiographic data, and patients lost to follow-up.

Definition of Variables
Baseline demographic and clinically related variables such as vessel patency and ischemic events were obtained from our institution’s database of medical records. We investigated patient age, sex, associated medical conditions, clinical manifestations of cerebral vasculopathy, and surgical records. Age was defined as age at diagnosis, and race was categorized as white, African-American, Asian, or others. The diagnosis of MMD was confirmed through digital subtraction angiography. Treatment groups included patients receiving indirect revascularization or conservative management. Our primary adverse outcome was whether ipsilateral stroke occurred during the follow-up interval defined as the time between date of diagnosis (for conservatively managed patients) or first surgical treatment and last follow-up visit. Secondary functional outcomes were determined by modified Rankin Scale (mRS) at last follow-up visit. Annual risk of stroke was calculated as number of adverse events per hemisphere divided by follow-up years.

Management Strategy and Surgical Techniques
For patients presenting with prior stroke or symptoms affecting their daily activities such as weakness or speech disturbances, surgical revascularization is generally recommended. At our institution, patients are generally offered indirect revascularization. Conservative management maximizing medical therapy was usually undertaken in patients who were asymptomatic, those with only mild symptoms such as headaches, those who were naïve to antiplatelet therapy, or patients declining surgery. Indirect revascularization techniques included encephaloduroarteriosynangiosis (EDAS) or encephaloduroarteriomyosynangiosis (EDAMS) with pial synangiosis. Preoperative evaluation included angiography to include external carotid artery injections. For all cases, the STA was first identified intraoperatively using Doppler and carefully mapped. After an incision was made directly over the course of the STA, both anterior and posterior branches of the STA were exposed using blunt dissection, and a pedicle of the STA branch was isolated. At least 2 burr holes were made for the temporal craniotomy, 1 at the entry point and the other at the exit point of the implant artery. Microscopic arachnoid dissection of the exposed sulci was performed before suturing of the STA pedicle to the pia. The dural leaflets were loosely reaproximated for EDAS. Additional transposition of a portion of the temporalis muscle to the epidural compartment constituted the EDAMS. Patients received maintenance intravenous fluids and given aspirin 325 mg on the night of surgery.

Statistical Analysis
Comparative statistics were used in this study to describe patient demographics, baseline clinical parameters, treatment modality, and follow-up outcomes between indirect vascualrization and conservative treatment. The Wilcoxon rank sum test was used for continuous variables, and the χ² test was used for categoric variables. Patient baseline characteristics were compared on a per-hemisphere basis to determine variables significantly associated with propensity for inclusion into a specific treatment group. Univariate Cox proportional hazard regression was performed to determine significant factors associated with follow-up ipsilateral strokes; descriptive analysis using Kaplan-Meier curves was also performed to visualize relationships between follow-up ipsilateral stroke and associated variables. Variables that were significant in baseline comparison or in univariate Cox regression, or that were clinically significant, were selected into a multivariate Cox
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