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Opinion paper

Encephaloduroarteriosynangiosis versus conservative treatment for patients with moyamoya disease at late Suzuki stage

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ABSTRACT

The purpose of this study is to investigate the long-term outcomes after conservative and encephaloduroarteriosynangiosis procedures for patients with moyamoya disease at late Suzuki stage. We retrospectively reviewed 64 patients (128 hemispheres) with moyamoya disease at late Suzuki Stage at Beijing Tiantan Hospital. Clinical features, radiologic findings, and outcomes were analyzed. The mean age at diagnosis was 29.0 ± 14.9 years. The distribution of the initial Suzuki stage of MMD was as follows: stage 4, $n = 75$; stage 5, $n = 46$; stage 6, $n = 7$. PCA involvement was observed in 4 (37.5%) hemispheres. The incidence of postoperative stroke was 6.7%. During the average follow-up of 46.9 ± 21.1 months, including postoperative and follow-up strokes, seven of 75 (9.3%) conservatively treated hemispheres and 10 of 87 (10.1%) surgically treated patients experienced a stroke event there was not statistically significant in the Kaplan-Meier curve of stroke incidence between the surgical group and conservative group (log-rank test, $p = .848$). However, the rate of perfusion improvement in indirect bypass surgically treated patients was higher than in those conservatively treated patients 3 months after discharge ($p < .05$). Although indirect bypass surgery was shown to be effective in improving the cerebral perfusion in patients with MMD at late Suzuki stage, it failed to reduce the risk of recurrent stroke compared to conservative treatment. Further study is needed to determine whether direct bypass surgery is effective in MMD patients at late Suzuki stage.

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1. Introduction

Moyamoya disease (MMD) is characterized by progressive stenosis of terminal portion of internal carotid artery and its main branches, leading to ischemic or hemorrhagic symptoms. The aim of MMD treatment is to supplement the intracranial circulation from the external carotid system with direct bypass to an intracranial cortical branch, or by stimulation of collateral formation via indirect methods.

Abbreviations: DSA, digital subtraction angiography; EDAS, encephaloduroarteriosynangiosis; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; MMD, moyamoya disease; mRS, modified Rankin Scale; PCA, posterior cerebral artery; SAH, subarachnoid hemorrhage.

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Recently, one of our study reported the long-term outcomes after conservative and direct surgical treatment for patients with moyamoya disease at late Suzuki stage. Unfortunately, although the direct bypass may improve cerebral perfusion, it does not offer significant advantages in terms of stroke prevention in patients with late Suzuki stages. Is there any other way that may prevent stroke in late stage MMD? Fortunately, indirect bypass using various connective tissues is effective, possibly due to the nature of the disease in promoting spontaneous leptomeningeal collateral formation.

However, although several studies reported the role of indirect bypass played in preventing further stroke for patients with MMD, there is little information the comparison of long term outcomes of indirect revascularization and conservative therapy of MMD at late Suzuki stage, which made us question whether indirect bypass surgery beneficial for the patients with MMD in patients with

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advanced MMD stage. In this retrospective study, we reviewed patients with MMD at late Suzuki stage and focused on whether encephaloduroarteriosynangiosis (EDAS) could prevent further stroke in this patient population.

2. Materials and methods

2.1. Patient selection

We searched our electronic medical records to identify eligible patients who were admitted to Beijing Tiantan Hospital between February 2008 and June 2015. All patients who met the following criteria were included in this study: 1) diagnosis of definite MMD via digital subtraction angiography (DSA); 2) Suzuki Angiographic Stage 4–6 in both hemispheres; 3) having only undergone EDAS or conservative therapy for the treatment of MMD; 4) patients with unilateral MMD or the presence of secondary moyamoya phenomenon caused by meningitis, Down syndrome, systemic vasculitis, neurofibromatosis, leptospiral infection, or previous skull-base radiation therapy were excluded from the analysis. Among these patients, 67 patients with MMD were identified. 1 patients with follow-up periods shorter than 24 months and 2 patients without complete radiologic data were excluded. Therefore, a total of 64 patients (128 hemispheres) were included.

2.2. Clinical and radiologic characteristics

The Ethics Committee of Beijing Tiantan Hospital, Capital Medical University, Beijing, China, approved the study. Clinical information on the sex, age at diagnosis, family history, hypertension, DM, hyperlipidemia, smoking or alcohol use, aneurysm and thyroid disease was obtained by clinical chart review. Radiologic data were reviewed blindly by 2 neurosurgeons, including Suzuki stage, posterior cerebral artery (PCA) involvement, aneurysm. Any disagreement on the radiologic findings was re-evaluated by a third reader.

2.3. Treatment

Hemispheres were divided into 2 groups according to treatment received: group 1: hemispheres with EDAS surgeries: EDAS is the preferred indirect bypass at our institution. Briefly, EDAS involves placement of an external carotid artery branch beneath the dura in ischemic territories. Most commonly, the STA is used. In certain circumstances, depending on the territory at risk, the occipital artery may also be used; and group 2: hemispheres with conservative treatment. In patients with bilateral symptoms, surgery was initially performed on the more symptomatic side. If the patient exhibited equal symptomatology bilaterally, we initiated surgery on the dominant hemisphere. A second surgery was performed 6 months after the first surgery. During this period, patients were maintained under antiplatelet therapy coverage (aspirin 100 mg/d), which was stopped 3 days before the second surgery and restarted 24 h after intracranial hemorrhage had been ruled out by CT scan.

2.4. Clinical follow-up

After discharge, the long-term outcome was ascertained through clinical visits, telephone, or letter interviews. Neurological outcome was assessed using mRS. Postoperative stroke was defined as new neurologic deficits that persisted for more than 24 h and was associated with a new infarct or hemorrhage on magnetic resonance (MR) or computed tomography (CT) imaging after the revascularization. CT perfusion or SPECT was used to assess the changes in cerebral blood flow of patients in the surgical revascularization group at the 3rd postoperative months.

2.5. Statistical analysis

The data were analyzed statistically using SPSS for Windows, version 19.0 (SPSS, Inc.). Continuous and categorical data were compared with the *t*-test and chi-square test, respectively. Stroke-free survival analysis was performed using Kaplan-Meier curves tested for statistical significance with the log-rank test.

A probability value of $< .05$ was considered to indicate statistical significance.

3. Results

3.1. General patient characteristics

We identified 64 patients who met the criteria for study inclusion. The mean age at diagnosis was 29.0 ± 14.9 years. The ratio of female to male patients was 2.2:1.0. Of the 64 patients, 12 (18.8%) had a history of hypertension, 5 (7.8%) had diabetes mellitus, 2 (3.1%) had hyperlipidemia, 3 (4.7%) had a history of tobacco or alcohol use and 1 (1.6%) had thyroid disease (Table 1).

The initial symptom was ischemia or hemorrhage in 45 and 19 patients, respectively. The majority of ischemic patients presented with transient ischemic attack (TIA); infarction was the second most common presentation for these patients. In patients with hemorrhagic MMD, intraventricular hemorrhage and intracranial hemorrhage was the most common type, and intracerebral hemorrhage was the second most common. The distribution of the initial Suzuki stage of MMD was as follows: stage 4, $n = 75$ (58.6%); stage 5, $n = 46$ (35.9%); stage 6, $n = 7$ (5.5%), PCA involvement was observed in 48 (37.5%) hemispheres, and 1 (0.8%) aneurysm was observed in 128 hemispheres (Table 2).

3.2. Treatments and outcomes

Eighty-seven hemispheres (54.3%) in 60 patients underwent EDAS surgeries, and 41 hemispheres underwent conservative treatment for initial management. Of the 60 patients who underwent EDAS surgeries, 27 were bilateral. In 87 operations, a total of 16 complications in 15 hemispheres occurred prior to hospital discharge. Postoperative infarctions of variable size were the most clinically relevant complications and occurred in 4 cases (6.7% per patient; 4.6% per operation) after 87 operations (< 48 h after surgery). Of the 4 hemispheres suffering a new stroke, 3 had made a complete recovery when evaluated at 3 months after surgery. What's more, 3 hemispheres experienced transient ischemic attack prior to discharge, 3 hyperperfusion syndrome, 3 subdural hygroma and 3 subdural hemorrhage and all patients made a full recovery at 3 months after surgery.

3.3. Long-Term clinical outcome

Over a mean follow-up of 46.9 ± 21.1 months, there were a total of 13 new strokes (7 infarcts and 6 hemorrhages) events (Table 3). In the surgical group, the strokes occurred in 6 of 87 hemispheres (6.9%); among the 62 hemispheres with ischemic MMD, there were 3 (4.8%) ischemic strokes and 1 (1.6%) hemorrhagic stroke; and among the 25 hemispheres with hemorrhagic MMD, there were 2 (8.0%) hemorrhagic strokes. However, in the conservative group, the recurrent strokes occurred in 7 of 41 hemispheres (17.1%); among the 28 hemispheres with ischemic MMD, there were 4 ischemic strokes (14.2%) and 1 hemorrhagic stroke; and among 13 hemispheres with hemorrhagic MMD, there were 2 hemorrhagic strokes (15.4%). Regarding the stroke recurrence over a mean follow-up of 46.9 ± 21.1 months in 128 hemispheres, including postoperative and follow-up strokes, seven of 41

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