Surgical Treatment of Moyamoya Disease in Adults: Combined Direct and Indirect vs. Indirect Bypass Surgery

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Abstract

Combined superficial temporal artery-middle cerebral artery anastomosis and encephalo-duro-arterio-galeo-synangiosis (EDAGS) were retrospectively compared with indirect bypass, EDAGS with or without inversion, in 134 hemispheres of 96 adult patients with non-hemorrhagic moyamoya disease (MMD) in terms of angiographic findings, perioperative complications, and clinical outcome. Angiographic revascularization seemed to be better in the combined bypass group compared with the EDAGS group ($p = 0.045$), but perioperative complication tended to be slightly more common in the combined bypass group. No statistical differences were found in clinical outcome. EDAGS is a very reliable alternative to combined bypass in adult MMD. However, randomized clinical trials are needed to assess the long-term efficacy of any bypass surgery in adult patients with MMD.

Key words: moyamoya disease, adult, combined direct and indirect bypass surgery, indirect bypass surgery

Introduction

Adult patients with moyamoya disease (MMD) seem to have a different response to direct or indirect cerebral revascularization procedures compared to children. In particular, the angiographic findings after indirect bypass surgery have been relatively inconsistent in adults, but are very reliable in pediatric patients.^{14,18,27,31} These differences between adult and pediatric MMD suggest that an age-specific tailored approach is required for the management of patients with MMD.

Direct bypass procedures such as superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis are frequently performed in adult patients with MMD because the donor and recipient vessels have suitable sizes for direct anastomosis in most cases, and this procedure provides immediate augmentation of cerebral blood flow in the ischemic cerebral cortex affected by MMD. However, direct bypass surgery-related various complications such as hyperperfusion, cerebral infarction, intracerebral hemorrhage, or even death

have been reported.^{8,10,12,15,16,20,26,35,36} In contrast, indirect bypass surgery procedures, such as encephalo-duro-arterio-synangiosis (EDAS), encephalo-myo-synangiosis (EMS), and encephalo-duro-arterio-myo-synangiosis (EDAMS), are considered easier and safer even in patients with medical comorbidity, and slow but steady revascularization can be maintained because the STA, deep temporal artery, or middle meningeal artery (MMA) are little affected by MMD.

The present study compared combined STA-MCA anastomosis and encephalo-duro-arterio-galeo-synangiosis (EDAGS) to EDAGS with or without inversion in adult patients with non-hemorrhagic MMD in terms of angiographic findings, perioperative complications, and clinical outcome.

Materials and Methods

The medical records and results of neuroimaging studies were retrospectively reviewed of 134 bypass surgeries (72 combined bypass and 62 EDAGS) performed in 96 adult patients with MMD, 28 males and 68 females aged 18–68 years (mean 38.44 years), who underwent bypass surgery at our institutions between February 1998 and January 2010. The 134 by-

pass surgeries included 74 bilateral (38 combined, 24 EDAGS, 12 mixed) and 60 unilateral procedures (28 combined, 32 EDAGS). Clinical presentations included cerebral infarction in 61 patients (combined in 34, EDAGS in 27), transient ischemic attack (TIA)-reversible ischemic neurological deficit in 49 patients (combined in 25, EDAGS in 24), TIA-infarction in 10 patients (combined in 4, EDAGS in 6), and other symptoms including headache, dizziness, and involuntary movement in 14 patients. Inclusion criteria for bypass surgery were non-hemorrhagic and symptomatic MMD, no recent cerebral infarction within 6 weeks, decreased cerebrovascular reserve on perfusion study using hexamethylpropyleneamine oxime single photon emission computed tomography or perfusion computed tomography, and Karnofsky performance status score ≥ 70 .

The primary surgical modality was combined STA-MCA anastomosis using the M_3 or M_4 cortical branch of the MCA and the larger of the 2 branches of the STA, EDAGS using the other branch of the STA with or without inversion, and dural pedicle inversion (DPI).^{6,19} Inversion of EDAGS¹⁹ was used in 30 procedures (20 combined, 10 EDAGS) in 22 patients aged ≥ 50 years in consideration of poor revascularization of simple EDAS, especially in patients older than 40 years,²⁷ and personal experience (unpublished data). Indirect bypass surgery using EDAGS and DPI was chosen if the size of the donor or recipient artery was unsuitable, contribution of branches of the STA to pre-existing ipsilateral or contralateral transdural collateralization, great difference in size of the branches of the STA, and presence of medical comorbidity.

Postoperative angiographic revascularization was evaluated on the lateral view of selective external carotid angiography and was classified into 3 groups: good, fair, and poor.²⁴ The clinical outcomes were divided into 4 categories: excellent, good, fair, and poor.²¹ Follow-up duration was 2 to 16 months (mean 6.8 months) for the evaluation of postoperative angiographic findings, 1 day to 6 weeks (mean 4.2 weeks) for early perioperative complications, and 1 day to 108 months (40.2 months) for clinical outcome. Statistical analysis used the unpaired t-test, chi-square test, and Fisher's exact test, and adopted a significance level of 0.05.

Results

The postoperative angiographic revascularization findings, perioperative complications, and clinical outcomes are summarized in Table 1. Good revascularization was found in 57 of 71 sides (80.3%)

treated by combined bypass and 46 of 61 sides (75.4%) treated by indirect bypass. Fair revascularization was obtained in 10 of 71 sides after combined bypass and in 9 of 61 sides after indirect bypass. However, only poor revascularization was achieved in 4 sides with combined bypass and 6 with indirect bypass. The 2 bypass groups showed significant statistical difference in the extent of angiographic collateralization ($p = 0.045$). Perioperative overall neurological complications occurred in 17 of 71 procedures (23.9%) in the combined bypass group, which included 5 major complications (modified Rankin scale [mRS] 3–5) and 12 minor complications (mRS 1–2), and in 12 of 61 procedures (19.7%) in the indirect bypass group, which included 3 major and 9 minor complications. Seven of 8 major neurological complications in both bypass groups were related to ipsilateral ($n = 4$) and contralateral ($n = 3$) cerebral infarction and one intracerebral hemorrhage occurred with combined bypass surgery. Perioperative neurological complications tended to be slightly more common in the combined bypass group, but no significant difference was found between the two bypass groups. Perioperative non-neurological complications such as delayed wound healing or wound infection occurred in 3 sides of the combined bypass group and 2 sides of the indirect bypass group. Clinical outcome was favorable (excellent and good) in 59 of 71 procedures (83.1%) in the combined bypass group and in 50 of 61 procedures (82.0%) in the indirect bypass group, and unfavorable (fair and poor) in 12 of 71 procedures (16.9%) in the combined bypass group and in 11 of 61 procedures (18.0%) in the indirect bypass group. Two deaths, one in each group, were related to acute myocardial infarction after bypass surgery, but before postoperative angiographic evaluation. Clinical outcome showed no statistical difference between the two bypass groups.

Discussion

Extracranial to intracranial bypass surgery has proven a reliable method for the treatment of patients with non-hemorrhagic MMD in terms of clinical outcomes as well as angiographic revascularization. Direct or combined direct and indirect or indirect bypass procedures have been utilized in patients with MMD, especially with ischemic presentation, but the safety and efficacy of these surgical techniques remain largely unproven. Furthermore, the optimal surgical treatment in adult patients with MMD is unknown.³³ Direct bypass such as STA-MCA anastomosis^{15,17,22,24,25} or combination of direct and indirect bypass surgery^{11,13,27,29} have been recommended in adult patients with

Table 1 Summary of clinical data of 96 adult patients with moyamoya disease who underwent 134 bypass surgeries

	Indirect bypass (n = 45, procedure = 62)	Combined bypass (n = 51, procedure = 72)	p Value
Sex			NS*
male	13 (17 procedures)	15 (17 procedures)	
female	32 (45 procedures)	36 (55 procedures)	
Age (years)			0.027**
range	20–61	18–68	
mean $\pm$ SD	36.17 $\pm$ 9.94	41.08 $\pm$ 14.57	
Presentation			NS***
infarction	27	34	
TIA-RIND	24	25	
TIA-infarction	6	4	
others	5	9	
Angiographic findings			0.045***
good	46 (75.4%)	57 (80.3%)	
fair	9	10	
poor	6	4	
Perioperative complications			NS*
non-neurologic	2	3	
neurologic	12 (19.7%)	17 (23.9%)	
mRS 1–2	9	12	
mRS 3–5	3	5	
Clinical outcome			NS***
favorable	50 (82.0%)	59 (83.1%)	
excellent	37	42	
good	13	17	
unfavorable	11 (18%)	12 (16.9%)	
fair	7	7	
poor	4	5	
dead [#]	1	1	
Follow-up period (months)			
angiographic findings	8 (3–16)	6 (2–12)	
clinical outcome	46 (1–108)	38 (1–89)	

*Chi-square test, **unpaired t-test, ***Fisher's exact test. [#]Two patients died before postoperative angiographic evaluation. mRS: modified Rankin scale, NS: not significant, RIND: reversible ischemic neurologic deficit, SD: standard deviation, TIA: transient ischemic attack.

MMD because these procedures are effective at preventing future ischemic events and improve the quality of life.¹⁰⁾ Recent studies have documented real augmentation of collateral blood flow using color or laser Doppler flowmetry, indocyanine green angiography, or perivascular ultrasonic flowprobe investigations.^{2,3,9,23,37)} On the other hand, some complications are related to direct bypass surgery such as symptomatic hyperperfusion and cheiro-oral syndrome, which are mostly not permanent, cerebral infarction, intracerebral hemorrhage, or even death.^{8,10,12,15,16,20,26,32,35,36)} The long-term durability of direct bypass surgery for cerebral perfusion in MMD has yet to be elucidated because the long-term patency of the recipient artery such as the MCA branches in MMD remains unknown.^{1,28)}

In contrast, indirect bypass surgery is generally

considered easier and safer, with shorter surgery time, less invasive compared with direct anastomosis, and more feasible in patients with inadequate recipient or donor arteries.^{5,35)} However, indirect bypass requires several weeks to form collateral vessels,^{15,35)} and angiographic revascularization is relatively inconsistent in adult patients compared with pediatric patients.^{14,18,27,31)} Our study showed that combined direct and indirect bypass is slightly superior to EDAGS in the extent of postoperative angiographic revascularization ($p = 0.045$). A recent quantitative angiographic comparison between the direct and indirect revascularization modalities in adult patients with MMD concluded that the extent of revascularization was highest after STA-MCA anastomosis with EDAMS and lowest after only EDAS.⁴⁾ This study supports our angiographic find-

ings, although the detailed surgical technique is not the same as our procedure.

Considering the poor revascularization achieved by simple EDAS, especially in patients older than 40 years,²⁷⁾ we have adopted inverted EDAGS and DPI for obtaining abundant and widespread revascularization through the STA and the attached wide galeal tissue by direct contact with the ischemic cerebral cortex in adult patients with MMD 50 years or older. The combined bypass group tended to have slightly higher rates of surgery-related neurological complications compared to the indirect bypass group, especially for major complications. The hemodynamic changes in the STA after direct bypass surgery mainly occurred in the early period after the operation and seems to be related to low resistance or lower perfusion pressure of the intracranial vascular bed, or the large pressure gradient between the donor and recipient vessels.^{3,23,37)} Only EDAS promoted adequate pial collateral development and increased perfusion in the majority of North American adult patients with MMD with low rates of postoperative TIAs, infarction, and hemorrhage.³⁴⁾ However, the present study found no significant difference in overall clinical outcome between the groups. Therefore, indirect bypass such as EDAGS seems to be a reasonable approach considering the surgery-related early postoperative complications and overall clinical outcome in our study.

Indirect revascularization by EDAS and burr holes for MMD resulted in long-term resolution of ischemic and hemorrhagic manifestations in 95% of adults (n = 33) and children (n = 9) with emphasis on the significant contribution of the MMA in angiographic revascularization.⁷⁾ Our personal experience regarding the main contributor to postoperative revascularization in MMD indicates that the contribution of the dural arteries including the MMA was not inferior to the STA in both the EDAGS group and the combined bypass group (unpublished data). Dominance of EMS compared with the STA was found in the combined group as well as the indirect (EMS) group in eventual patterns of revascularization based on dominance of donor arteries in MMD.³⁰⁾ These factors including dominance of the dural arteries in revascularization and slightly fewer major perioperative complications in the indirect bypass group may have contributed to the absence of significant difference in long-term clinical outcome compared with the combined bypass group.

This study has some limitations. First, this is a non-randomized, controlled study with different indications for combined bypass surgery and indirect bypass surgery, and application of EDAGS and in-

verted EDAGS according to the patient's age. The second limitation is inherent to a retrospective study from medical records, which carries the risk of selection bias in the data collection.

The present study suggests that EDAGS with or without inversion and DPI is a very reliable alternative to combined STA-MCA anastomosis and indirect bypass surgery because the clinical outcome and surgery-related complication rates are not significantly different, although combined bypass surgery is slightly superior to indirect bypass surgery in terms of postoperative angiographic revascularization. However, randomized clinical trials are needed to assess the safety and long-term efficacy of bypass surgery in adult patients with MMD.

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