Long-term follow-up study after extracranial-intracranial bypass surgery for anterior circulation ischemia in childhood moyamoya disease

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Between May, 1974, and March, 1991, 104 patients with moyamoya disease, all under 16 years old at the time of first surgery, underwent superficial temporal-to-middle cerebral artery anastomosis and/or encephalomysynangiosis. The mean follow-up period was 9.6 years (range 4.8 to 16.0 years). Hemiplegia was the most frequent symptom before the first operation. Transient ischemic attacks (TIA's) were noted in 57 patients and minor stroke with hemiplegia in 44. The most frequent type of cortical dysfunction was aphasia (21 cases). Postoperatively, the incidence of TIA's and/or completed stroke with motor weakness of the extremities was markedly decreased, but visual disturbance progressed and major or minor stroke with visual disturbance was found in two cases. In patients under the age of 3 years, a major stroke prior to surgery resulted in a poor outcome in 36% of cases. Preoperative major stroke in patients between the ages of 3 and 7 years was less frequent, and poor outcomes were seen in 17% of this group. There were no major preoperative strokes in patients with surgery after the age of 7 years, and no poor outcomes were recorded in this group. A major preoperative stroke prior to surgery had adverse impact on the ultimate patient intelligence quotient (IQ) following surgery. All patients operated on after the age of 7 years had a normal or borderline IQ at follow-up examination.

KEY WORDS • moyamoya disease • revascularization • stroke • children

MOYAMOYA disease is a progressive occlusive cerebrovascular disease with the following characteristic angiographic features: stenosis or occlusion of the distal internal carotid arteries (ICA’s) with poor visualization of the proximal segments of the anterior and/or middle cerebral arteries (MCA’s), as well as the compensatory development and enlargement of a fine vascular network at the base of the brain. These features should be present bilaterally for a diagnosis to be made. The clinical manifestations in these patients are variable and include hemiplegia, paraplegia, speech disturbance, visual disturbance, seizures, headaches, involuntary movements of the extremities, and mental retardation.

The present study was undertaken to determine the long-term result of patients with moyamoya disease who underwent superficial temporal artery (STA)-MCA anastomosis and/or encephalomysynangiosis for the treatment of ischemia related to deficiencies of the anterior cerebral circulation.

Clinical Material and Methods

Patient Population

Between May, 1974, and March, 1991, 400 patients with moyamoya disease underwent surgery at our institution while aged less than 16 years. Of these, 104 were enrolled in this study. All patients had undergone STA-MCA anastomosis and/or encephalomysynangiosis. Patients who had been previously operated on at another hospital or who have been followed for 4 years or less were excluded. The mean follow-up period was 9.6 years (range 4.8 to 16.0 years). Sixty-three patients were girls and 41 were boys. Ninety-two patients were operated on bilaterally and 12 had unilateral surgery. In the bilaterally treated group, 32 first underwent STA-MCA anastomosis on the right side and 60 had a left-sided procedure first. The average interval between the first and subsequent operations was 3.6 months.

The neurological symptoms exhibited before the first operation are shown in Tables 1 and 2. Hemiplegia was the most frequent symptom, and transient ischemic attacks (TIA's) and minor stroke with hemiplegia were noted in 57 and 44 of these patients, respectively. The second most common ischemic symptom was motor weakness of one or both lower extremities, which was found in 25 cases. The most frequent type of cortical dysfunction was aphasia (21 cases); five patients had severe aphasia before their first operation. Visual symp-
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**TABLE 1**

Neurological deficits associated with ischemic disorders in 104 cases of moyamoya disease before and after the first operation*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>TIA Preop</th>
<th>Postop</th>
<th>RIND Preop</th>
<th>Postop</th>
<th>Completed Stroke Preop</th>
<th>Postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>hemiplegia</td>
<td>57</td>
<td>28</td>
<td>1</td>
<td>1</td>
<td>44</td>
<td>5</td>
</tr>
<tr>
<td>paraplegia</td>
<td>22</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>hemihypesthesia</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>quadriplegia</td>
<td>13</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>monoplegia (upper extremity)</td>
<td>14</td>
<td>13</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>dysarthria</td>
<td>13</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>aphasia</td>
<td>10</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>acaulcia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>apraxia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>dysphagia</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>urinary incontinence</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>visual disturbance</td>
<td>7</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

* TIA = transient ischemic attack; RIND = recurrent ischemic neurological deficits.

**TABLE 2**

Other symptoms in 104 cases of moyamoya disease before and after the first operation

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Preop</th>
<th>Postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>loss of consciousness</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>headache</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>epilepsy</td>
<td>29</td>
<td>1</td>
</tr>
<tr>
<td>involuntary movement</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>mental retardation</td>
<td>12</td>
<td>3</td>
</tr>
</tbody>
</table>

...toms were detected in nine patients: two had minor strokes with visual symptoms and seven had TIA's with visual disturbance. Other symptoms included epilepsy in 29 cases, headache in 17, involuntary movements in five, and urinary incontinence in two.

Operative Technique

The surgical procedures used in treating those patients were fundamentally identical to those reported by Donaghy and Yaşargil. The side of operation was selected on the basis of clinical symptoms. When symptoms appeared bilaterally and equally on the left and right sides, the left side was surgically treated first.

Patients were placed in the supine position, the head was rotated about 80° to 90° toward the contralateral side, and the sagittal sinus was placed parallel to the horizontal plane. A horseshoe-shaped scalp incision was made surrounding the parietal branch of the STA, and the galea was separated from the pericranium and temporals fascia. The scalp flap was reflected toward the auricle and the temporalis fascia was dissected all along the horseshoe incision for encephalomyosynangiosis, after which a craniotomy was performed. Before the dura mater was opened, the branches of the STA were dissected free from the surrounding connective tissue. The central branch of the MCA was also dissected out and isolated after the opening of the dura mater (Fig. 1 left). Following these procedures, the cut end of the STA was joined to the central branch of the MCA by an end-to-side anastomosis with 11-0 monofilament nylon. An encephalomyosynangiosis was then performed (Fig. 1 right). In this procedure, the dura was removed along the meningeal artery which was left intact. The temporal muscles were detached from the bone flap and placed over the brain surface. The outer edge of the muscles was then sutured to the remaining dura, and a cranioplasty was performed with skin closure. Figure 2 illustrates the effect of these procedures with pre- and postoperative angiograms.

Evaluation of Results

We analyzed the neurological symptoms before the first and second operations and investigated the relationship between symptom onset and the clinical outcome. The relationship between symptom onset and the patients' intelligence quotient (IQ) as classified by Taf, et al., was also investigated. This classification is as follows: 1) normal (IQ > 83); 2) borderline (IQ 68 to 83), in the lower levels of normal school classes; 3) mild retardation (IQ 52 to 67), able to function independently as adults; 4) moderate retardation (IQ 36 to 51), semi-independent; 5) severe retardation (IQ 20 to...
Fig. 2. Angiograms in a patient with superficial temporal (STA)-to-middle cerebral artery (MCA) anastomosis and encephalomyosynangiosis.  
Left: Preoperative external carotid angiogram showing transdural anastomoses via the middle meningeal branch.
Center: External carotid angiogram 3 months postoperatively. A major part of the MCA is filled via the STA and deep temporal artery. Right: Selective angiogram showing that a large part of the MCA is filled via the two arteries.

35), minimum self-care; and 6) profound retardation (IQ < 20), total supervision necessary. We further evaluated the relationship between the clinical outcome and the severity of IQ disturbance.

The results immediately after the last operation were rated as follows: 1) complete recovery = disappearance of TIA's plus a complete recovery from neurological deficits, except for homonymous hemianopsia and disturbance of intelligence; 2) marked improvement = a few minor TIA's without neurological deficits, the disappearance of minor neurological deficits and several minor TIA's, or the improvement of neurological deficits with or without TIA's; 3) slight improvement = small improvement in major neurological deficits; 4) unchanged; and 5) worsened.

Results

Follow-Up Angiographic Examination

Angiograms were performed in all patients (total 196 sides) and filling was considered to be excellent in 124 sides and good in 72 sides. The angiograms illustrated in Fig. 2 center and right are interpreted as showing excellent filling.

Neurological Recovery

The neurological symptoms appearing between the first and second operations on the contralateral side are shown in Tables 1 and 2. The incidence of TIA's and/or completed stroke with motor weakness of the extremities (including paraplegia) was markedly decreased, and major stroke with hemiplegia was found in only one patient. Cortical dysfunction was also decreased after the first operation, and the incidence of epilepsy or involuntary movements was markedly reduced. However, visual disturbance progressed regardless of the operation, and major or minor stroke with visual disturbance was found postoperatively in two cases (Table 1).

Glasgow Outcome Scale Score

The relationship between symptom onset and the clinical outcome as assessed by the Glasgow Outcome Scale (GOS) was investigated. Seventy-nine patients were classified as having a good recovery, 13 as having moderate disability, nine as having severe disability, and two as being in a persistent vegetative state. One 6-year-old patient died due to primary pulmonary hyper-

Fig. 3. Graph showing the relationship between patient age at symptom onset and the clinical outcome as assessed by Glasgow Outcome Scale. Major stroke is found in 36.4% of patients under the age of 3 years, but no patients over 7 years of age had major stroke. Open circles denote transient ischemic attacks; closed circles denote reversible ischemic neurological deficits or minor stroke; triangles denote major stroke. Glasgow Outcome Scale grades: GR = good recovery; MD = moderate disability; SD = severe disability; PV = persistent vegetative state; and D = death (asterisk indicates one patient who died of primary pulmonary hypertension).
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![Graph showing the relationship between patient age at symptom onset and the postoperative intelligence quotient (IQ)](image)

**Fig. 4.** Graph showing the relationship between patient age at symptom onset and the postoperative intelligence quotient (IQ) as classified by Taft, et al.: N = normal; B = borderline; Mi = mild retardation; Mo = moderate retardation; S = severe retardation; and P = profound retardation. Open circles denote transient ischemic attacks; closed circles denote reversible ischemic neurological deficits or minor stroke; triangles denote major stroke. Asterisk = one patient who died of pulmonary hypertension. Eight patients (36.4%) with symptom onset earlier than 3 years of age had an IQ of less than borderline. All patients with onset of symptoms at over 7 years old had an IQ of either normal or borderline.

Intelligence Quotient

The relationship between the time of symptom onset and IQ was also investigated. There were 66 patients (63.5%) with a normal IQ, 19 with a borderline IQ, nine with a mildly decreased IQ, four with a moderately decreased IQ, three with a severely decreased IQ, and three with a profoundly decreased IQ. Of the group with symptom onset occurring under 3 years of age, eight patients (36.4%) had a measured IQ lower than borderline; all of these had suffered a major stroke. Of the group with symptom onset occurring between 3 and 7 years old, 11 (18.3%) had an IQ lower than borderline. All patients with symptom onset occurring at more than 7 years old had an IQ of either normal or borderline (Fig. 4).

**Glasgow Outcome Scale Score vs. Intelligence Quotient**

We also evaluated the relationship between the GOS score and the severity of IQ disturbance. A statistically significant correlation was found between the two measures by the chi-squared test for independent variables (4 x 6 contingency table, \(x^2 = 160.807, p < 0.001\)). Patients with only TIA's or minor stroke had both a relatively good GOS score and a relatively high IQ, while most patients with major stroke had a relatively poor outcome and a lower IQ (Fig. 5).

**Immediate Results vs. Glasgow Outcome Scale Score**

Figure 6 shows the relationship between the results immediately after the last operation and the GOS score. There was a significant correlation between the two parameters (\(x^2 = 88.078, \) Cramer's contingency coefficient 0.214, \( p < 0.001\)). The 47 patients with an immediate postoperative result rated as a complete recovery showed a good long-term outcome, except for one who died of primary pulmonary hypertension. Most of the 40 patients with marked improvement immediately after the operation had a good outcome and only nine (22.5%) showed GOS scores of either moderate or severe disability. Fifteen (88.2%) of 17 patients with scores of either slight improvement, unchanged, or worsened had a poor outcome, and only two such patients had a satisfactory result. Two patients classified as worsened had transient deterioration in dysphasia and in motor function, respectively, and both improved markedly by 1 week after their operations.
J. Karasawa, et al.

**Sympathectomy** and indirect anastomosis including encephaloduroarteriosynangiosis have been reported to improve the clinical symptoms, but the most reasonable approach to the treatment of this slowly progressive cerebrovascular disease appears to be the direct construction of anastomotic channels to increase blood supply to the brain.

**STA-MCA Anastomosis and Encephalomyosynangiosis**

Karasawa, et al., reported that both cerebral blood flow (CBF) and cerebral oxygen metabolism were decreased in moyamoya disease, and that patients with TIA's showed less decrease in these parameters than those with minor or major stroke. Immediately after STA-MCA anastomosis and/or encephalomyosynangiosis, CBF increases then decreases within 1 month of the procedure, and thereafter gradually increases again. By 6 months after the operation, CBF is significantly increased compared with the preoperative level.

Encephalomyosynangiosis is usually combined with the anastomatic procedure to augment the direct arterial anastomosis by increasing the formation of indirect and spontaneous anastomoses through the blood supply to the temporalis muscle. Moyamoya disease is characterized by progressive and multiple stenocclusive lesions, and selection of the correct cortical branch of the MCA is very important. Whenever possible, the STA must be anastomosed to a branch overlying the motor cortex. In this study, all patients underwent STA-MCA anastomosis and/or encephalomyosynangiosis.

**Neurological Outcome**

Postoperatively, 87 (83.7%) of 104 patients showed complete or marked improvement in their neurological condition, indicating that direct anastomosis played a role in this improvement by increasing CBF immediately after the operation. This increase was thought to be localized, emphasizing that direct anastomosis should be performed between a branch of the STA and the MCA branch closest to the motor cortex. Seventy-six percent of the patients were classified as having a good recovery, 12.5% as having moderate disability, and 10.5% as having severe disability or a persistent vegetative state. Postoperatively, the incidence of TIA's and/or complete stroke with motor weakness in the lower extremities was extremely low, but visual disturbance with deterioration of visual acuity and/or visual field loss occasionally appeared and in some cases progressed in association with major stroke.

Hemiparesis on the surgically treated side is thought to occur when the local perfusion pressure abruptly increases just after direct anastomosis and produces vasogenic edema in chronically ischemic brain tissue. The reason for hemiparesis on the contralateral side is unknown, but it may be that the underlying pathological condition of moyamoya disease progresses and causes ischemic symptoms on the contralateral side. An increase in oxygen consumption on the contralateral

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**Discussion**

**Moyamoya Disease and Its Treatment**

Since the pathogenesis of moyamoya disease is still unknown, no effective medical treatment has been found for it. The disease provokes chronically progressive stenosis or occlusion starting at the periphery of both ICA's. Childhood moyamoya disease usually manifests with repeated ischemic episodes leading to varying degrees of permanent neurological deficits.

The clinical course of the disease ultimately depends on the rapidity and extent of the vascular occlusion and on the patient's ability to develop effective collateral circulation. The balance between these factors determines the patient's clinical state. Some patients show rapid deterioration from the time of symptom onset, and there is no doubt that early and aggressive treatment is indicated on the basis of these findings. Conservative treatment with corticosteroids, vasodilators, and low-molecular-weight dextran only provides palliation and the results are disappointing. Superior cervical ganglionectomy and cervical perivascular

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Forty-seven patients showed complete recovery, 40 exhibited marked improvement, 12 showed slight improvement, three had no change, and two deteriorated. The patients who deteriorated all had impending stroke, and accordingly surgery was necessitated. One of these patients has mental retardation and attends a school for handicapped children.

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**Fig. 6.** Graph showing the relationship between the operative results and Glasgow Outcome Scale (GOS) score. There is a significant correlation between the two ($\chi^2 = 88.078, p < 0.001$). Open circles denote transient ischemic attacks; closed circles denote reversible ischemic neurological deficits or minor stroke; triangles denote major stroke. Asterisk = one patient who died of pulmonary hypertension. Operative result classifications: CR = complete recovery; MI = marked improvement; SI = slight improvement; U = unchanged; W = worsened. Grades of GOS: GR = good recovery; MD = moderate disability; SD = severe disability; PV = persistent vegetative state; D = death.
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side due to transcallosal metabolic diachisis may also be involved.\(^{10}\) Postoperative TIA's with motor weakness in the lower extremities and visual disturbances were due to a decrease in blood flow in the territory of the anterior and posterior cerebral arteries, respectively. Superficial temporal-to-middle cerebral artery anastomosis with encephalomyosynangiosis is able to increase CBF in the MCA territory, so patients with symptoms related to other regions must be treated with an omental graft to the frontal or occipital lobe.

In patients under the age of 3 years, preoperative major stroke played a large role in both the poor clinical outcome and the lower than normal IQ. Preoperatively, patients older than 7 years had either TIA's or minor stroke and all of these patients had an IQ that was either normal or borderline. The results are thus dependent on the patient's preoperative neurological state and whether irreversible damage to the brain caused by chronic ischemia has already occurred. Thus, early diagnosis and early surgical intervention are essential in treating patients with moyamoya disease.

Patients with a borderline IQ or mild mental retardation have an almost normal life when they attend kindergarten or the lower grades of elementary school. However, their level of performance may drop in the upper years of elementary school or in junior high school, and they then usually attend a school for handicapped children.

The presence of palsy of the extremities, speech disturbance, or visual disturbance early in life affects the clinical outcome of these patients, while the severity of mental retardation defines the patient's social life later. In this series, only three patients attended a university and three women had had children. When neurological symptoms occurred before 6 years of age, the clinical outcome was poor, because these patients showed multiple infarcts on computerized tomography (CT) scans and usually had mental retardation before treatment. In contrast, patients with almost normal CT scans usually have a good outcome. As neurological recovery and final outcome is thought to be correlated with the degree and extent of preoperatively existing neurological deficits, it is suggested that patients with moyamoya disease, especially those under 6 years of age, should be operated on with direct vascular reconstruction and encephalomyosynangiosis as soon as possible.

**Surgical Complications**

There were no major complications during or after STA-MCA anastomosis and/or encephalomyosynangiosis. Two patients classified as worsened postopera-

tively had only transient neurological deterioration and showed marked improvement 1 week later. A subcutaneous collection of fluid sometimes occurred after the procedure but this minor complication subsided by 2 weeks after the operation.

**References**


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