# Changes in Cerebral Hemodynamics Following Encephalo-Duro-Arterio-Synangiosis (EDAS) in Young Patients with Moyamoya Disease

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**To evaluate the effect of encephalo-duro-arterio-synangiosis, (EDAS), we obtained follow-up angiograms and measured regional cerebral blood flow in 21 young patients with Moyamoya disease. Carotid fork stenosis continued to progress after EDAS, although angiography demonstrated a marked increase in the number of middle cerebral artery branches via implanted arteries. Preoperative cortical blood flow was lower than normal. The post-EDAS increases in hemispheric and cortical flow were significant in patients with transient ischemic attacks, but not in patients with infarction. The increase in cortical flow at the site of EDAS was first noted 2 weeks after EDAS.**

KEY WORDS: Moyamoya disease; Cerebral blood flow; Cerebral angiography; Encephalo-duro-arterio-synangiosis; Pediatric neurosurgery

## Introduction

In the past, surgery was thought to be of little value in Moyamoya disease. Recent attempts to create a collateral blood supply from extracranial sources have resulted in the development of several surgical procedures for this disease. They include superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis [6], encephalo-myo-synangiosis [5], omentum transplantation [7], and encephalo-duro-arterio-synangiosis (EDAS) [10,11]. EDAS has frequently been cited as the procedure of choice [1,15].

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EDAS, which was introduced in 1980 by Matsushima and colleagues [10], accelerates extra-cranial to intracranial anastomosis by means of indirect bypass surgery [12,13]. These researchers [12,13] reported the clinical and angiographic results in patients with Moyamoya disease, noting that the procedure appears promising. Most young patients with Moyamoya disease have transient ischemic attacks (TIAs) of hemodynamic origin as well as infarctions [16,22]. In the studies by Matsushima and Inaba [12,13], most patients' TIAs disappeared, at varying intervals, following EDAS. However, it must be remembered that EDAS and other surgical approachs to Moyamoya disease are palliative rather than curative, so that the disease may continue to progress postoperatively.

In this EDAS follow-up study, we obtained cerebral angiograms and measured regional cerebral blood flow (rCBF). We discuss our hemodynamic findings as well as the post-EDAS progression of Moyamoya disease.

## Patients and Methods

Between July 1980 and September 1987, we performed EDAS in 56 patients with Moyamoya disease. The 21 patients who were under 20 years of age, and who were followed with both angiography and xenon-enhanced computed tomography (Xe-CT) were included in this study. Table 1 provides a clinical summary of the patients. Their mean age was 8.5 ± 4.7 years. In each case the initial symptom was transient ischemia, and all patients had occasional paroxysmal ischemic attacks perioperatively. At the time of surgery, the primary clinical manifestation was infarction in 6 patients and TIA in 15. The TIAs disappeared in 17 cases, at intervals ranging from 1 to 27 months postoperatively (mean, 10.5 months).

Selective angiography via the femoral artery was performed preoperatively and postoperatively in most cases; a few patients underwent direct carotid angiogra-



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**Table 1.** *Clinical Summary of the Patients*

| Case | Age/sex | Primary manifestation | Disappearance of TIA (months after EDAS) |
|---|---|---|---|
| 1 | 3/M | Infarction | +15 |
| 2 | 10/F | Infarction | +21 |
| 3 | 11/M | TIA | +4 |
| 4 | 9/F | Infarction | — |
| 5 | 13/M | Infarction | +2 |
| 6 | 8/M | TIA | +1 |
| 7 | 2/F | Infarction | — |
| 8 | 8/M | TIA | +9 |
| 9 | 2/F | Infarction | +27 |
| 10 | 5/F | TIA | +10 |
| 11 | 13/F | Frequent TIA | +11 |
| 12 | 9/M | TIA | +6 |
| 13 | 1/M | Frequent TIA | — |
| 14 | 9/M | TIA | +12 |
| 15 | 6/M | TIA | +12 |
| 16 | 6/M | TIA | +25 |
| 17 | 20/M | Frequent TIA | +1 |
| 18 | 17/F | TIA | +2 |
| 19 | 10/F | TIA | +1 |
| 20 | 10/F | TIA | +8 |
| 21 | 6/M | TIA | — |

TIA, transient ischemic attacks.

phy. Follow-up angiograms were obtained at 7 to 22 months (mean, 10.7 months) following EDAS. We classified each hemisphere according to the system of Fukuyama and Umezu [2] and Umezu [21], which is a modification of Suzuki and Kodama's [16] angiographic classification of Moyamoya disease. Preoperatively and postoperatively we examined the angiographic demonstrability of the C1 portion of the internal carotid artery (C1), the proximal portion of the middle cerebral (M1), anterior cerebral (A1), and distal basilar (BA) arteries, and the cortical branches of the middle (MCA), anterior (ACA), and posterior (PCA) cerebral arteries. The diameters of the C1, M1, A1, BA, middle meningeal artery (MMA), and superior temporal artery (STA) were also measured. The postoperative decrease in basal Moyamoya vessels was rated as none, poor, good, or excellent [13].

We planned to measure rCBF at 2 weeks and again at over 6 months postoperatively. Using the Xe-CT technique of Suzuki et al [18,19], we obtained rCBF maps for eight patients, all of whom had TIAs at 2 weeks and for 19 patients in the long-term period (mean, 9.8 months following EDAS). Patients under 6 years of age were sedated before examination. After baseline CT scans had been obtained, the patient inhaled a mixture of 40% xenon in oxygen for 3–4 minutes, during which time a series of 9-second scans were obtained at 60-second intervals. A topographic rCBF map was constructed from the CT images. The rCBF values were compared with normal values [18], and the patients' preoperative and postoperative rCBF were compared.

## Results

### *Angiographic Staging and Basal Moyamoya Vessels*

Preoperative angiography indicates various stages, but most of the hemispheres were stage III. The angiographic staging was not predictive of the clinical symptomatology (Figure 1). In 12 cases the angiographic stage advanced postoperatively. The degree of the reduction in basal Moyamoya vessels was none in 2 hemispheres, poor in 18, good in 19, and excellent in 3. Among patients with infarction 6 of 12 hemispheres were rated as poor. On the other hand, 17 of 30 hemispheres were rated as good in patients with TIA.

### *Carotid Fork and Basilar Arteries*

Angiographic demonstrability of the C1, M1, and A1 decreased postoperatively in both the infarction and TIA groups (Tables 2 and 3). Also, the diameter of the visible C1, M1, and A1 were smaller postoperatively in both groups. However, both angiographic demonstrability and the diameter of the BA were unchanged postoperatively.

**Figure 1.** *Number of the hemispheres in each angiographic stage preoperatively and postoperatively. Note that the angiographic stages advanced even after surgery.*

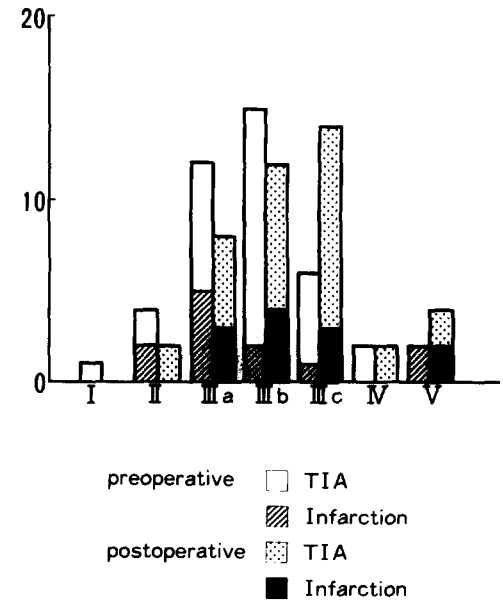

Table 2. *Changes in Arterial Diameters on Angiography in Patients with Transient Ischemic Attacks*

| Artery | Number of occluded side | | Diameter (mean ± SD in mm) | |
|---|---|---|---|---|
| | Pre-EDAS | Post-EDAS | Pre-EDAS | Post-EDAS |
| C1 | 5 | 10 | 1.7 ± 0.7 | 1.5 ± 0.9 |
| M1 | 10 | 21 | 1.3 ± 0.7 | 1.1 ± 0.6 |
| A1 | 11 | 22 | 1.2 ± 0.5 | 1.0 ± 0.3 |
| BA | 0 | 0 | 2.7 ± 0.5 | 2.7 ± 0.6 |
| STA (stem) | | | 1.7 ± 0.5 | 2.3 ± 0.6** |
| Frontal | | | 1.3 ± 0.4 | 1.5 ± 0.4 |
| Parietal | | | 1.1 ± 0.3 | 1.9 ± 0.6** |
| MMA (stem) | | | 1.5 ± 0.5 | 2.0 ± 0.5** |
| Anterior | | | 0.9 ± 0.3 | 1.3 ± 0.4** |
| Posterior | | | 0.9 ± 0.3 | 1.3 ± 0.4** |

Abbreviations: C1, internal carotid artery; M1, middle cerebral artery; A1, anterior cerebral artery; BA, basilar artery; STA, superficial temporal artery; MMA, middle meningeal artery.
* $p < 0.05$; ** $p < 0.01$ relative to pre-EDAS measurement.

### *External Carotid Artery*

Angiographic demonstrability of the STA and MMA increased, mainly due to the widening of their diameters, including the diameters of their stems and branches (Tables 2 and 3). In patients with TIA, the stem and parietal branch of the STA and the stem and the anterior and posterior branches of the MMA were markedly widened ($p < 0.01$). However, in those with infarction, only the parietal branch of the STA and the posterior branch of the MMA which were used in the EDAS procedure increased in diameter ($p < 0.05$).

### *Cortical Arteries*

The number of angiographically visible cortical branches of the MCA increased postoperatively. Preoperatively they were fed mainly by a parent artery or by basal Moyamoya vessels, and postoperatively by implanted STA branches. On the contrary, visible cortical branches of the ACA, particularly the callosomarginal, posterior internal frontal, and paracentral arteries were fewer in number postoperatively. The number of visible cortical branches of the PCA was unchanged. These results are summarized in Figure 2.

### *Preoperative rCBF Values*

The preoperative rCBF values in various brain regions are listed in Table 4. In patients with TIA, rCBF values in the cerebral hemispheres and the cortices of the frontal and temporal lobes were significantly lower than normal. In the same regions, in patients with infarction, they were dramatically lower than normal and also lower than in patients with TIA (Table 4). A representative rCBF map of a patient with TIA is shown in Figure 3.

Table 3. *Changes in Arterial Diameters on Angiography in Patients with Infarction*

| Artery | Number of occluded side | | Diameter (mean ± SD in mm) | |
|---|---|---|---|---|
| | Pre-EDAS | Post-EDAS | Pre-EDAS | Post-EDAS |
| C1 | 4 | 5 | 1.8 ± 0.5 | 0.9 ± 0.3* |
| M1 | 4 | 7 | 1.0 ± 0.3 | 0.6 ± 0.2 |
| A1 | 5 | 8 | 0.7 ± 0.2 | 0.8 ± 0.4 |
| BA | 0 | 0 | 2.5 ± 0.9 | 2.5 ± 0.3 |
| STA (stem) | | | 1.6 ± 0.4 | 1.7 ± 0.6 |
| Frontal | | | 1.1 ± 0.4 | 1.3 ± 0.4 |
| Parietal | | | 1.0 ± 0.4 | 1.4 ± 0.3* |
| MMA (stem) | | | 1.3 ± 0.5 | 1.7 ± 0.4 |
| Anterior | | | 0.9 ± 0.3 | 1.1 ± 0.5 |
| Posterior | | | 0.9 ± 0.5 | 1.4 ± 0.4 |

Abbreviations are the same as those in Table 2.

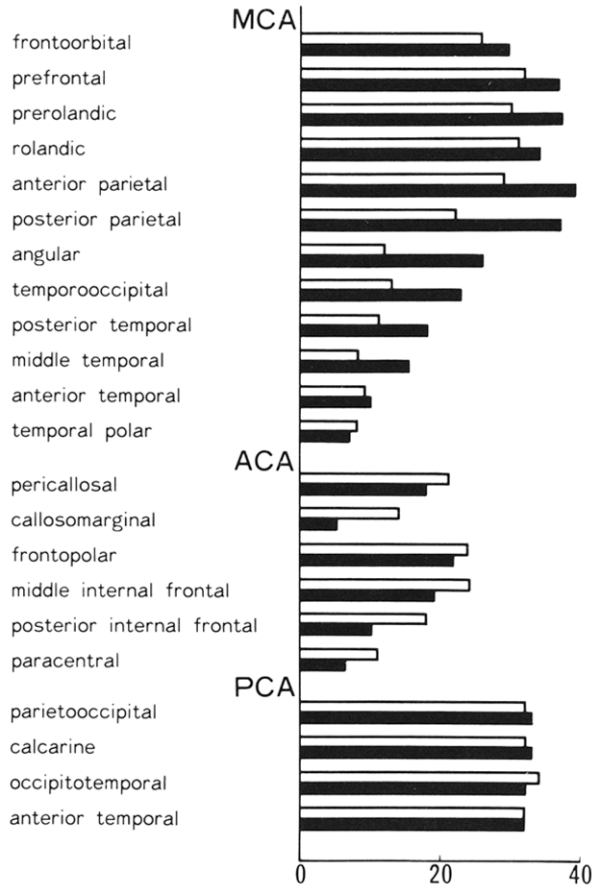


**Figure 2.** *Number of angiographically demonstrated cortical arteries preoperatively and postoperatively. The number of visible branches of the MCA increased after EDAS, while those of the ACA were decreased somewhat.*

### *Changes in rCBF Following EDAS*

Hemispheric blood flow in patients with infarction was unchanged following EDAS, while cortical flow in the frontal, temporal, and occiptal lobes was increased, although not significantly (Figure 4). Thalamic and putaminal blood flow was decreased somewhat. On the other hand, in patients with TIA, in the parietal cortex, where the STA had been implanted, was increased significantly already at 2 weeks after EDAS (Figure 4). Moreover, in these patients rCBF in the hemisphere and the middle frontal, precentral parietal, and superior temporal cortices was significantly increased in the late follow-up period (Figures 4 and 5).

**Table 4.** *Preoperative rCBF Values in Patients with Moyamoya Disease*

| Primary manifestation<br>Number of patients<br>Age in years | Infarction type<br>6<br>6.5 ± 4.8 | TIA type<br>15<br>9.1 ± 4.8 |
|---|---|---|
| Hemisphere | 26.9 ± 6.3** | 35.7 ± 9.3 |
| Superior frontal gyrus | 28.0 ± 14.1 | 38.8 ± 15.2 |
| Middle frontal gyrus | 20.4 ± 13.0* | 32.1 ± 15.0 |
| Frontal white matter | 10.1 ± 6.6 | 14.0 ± 6.1 |
| Precentral gyrus | 21.9 ± 15.9** | 37.6 ± 18.1 |
| Superior temporal gyrus | 20.3 ± 11.4** | 34.6 ± 16.1 |
| Inferior temporal gyrus | 21.1 ± 10.0** | 34.0 ± 13.9 |
| Occipital lobe | 20.1 ± 8.9* | 34.1 ± 18.0 |
| Lingual gyrus | 37.1 ± 10.2 | 45.5 ± 16.6 |
| Putamen | 54.4 ± 17.3 | 45.7 ± 19.6 |
| Thalamus | 47.8 ± 10.0 | 65.2 ± 29.3 |

rCBF values are means ± SD in mL/100 g brain/min.
*$p < 0.05$; **$p < 0.01$ relative to values in patients with TIA.

## Discussion

Moyamoya disease is a rare, chronic cerebrovascular occlusive disorder with an unknown etiology [22]. It is frequently seen in children, and the earliest symptom is commonly paroxysmal ischemic attacks. The prognosis is uncertain [2], although more than half of patients develop permanent, sometimes severe, neurological deficits, including mental retardation, and fatal infarction or intracranial hemorrhage may also occur [3,9,15]. The disease was once considered untreatable, but sev-

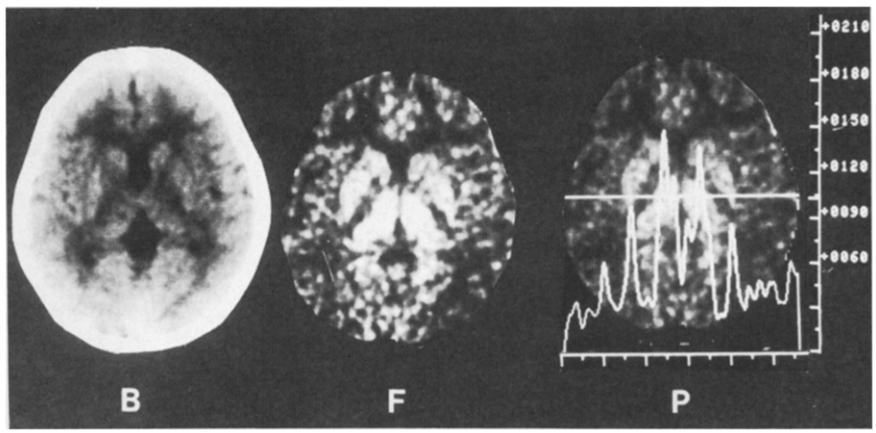


**Figure 3.** *The preoperative CT image (B) and blood flow map (F) in case 10 demonstrates the typical flow pattern in Moyamoya disease. In the cortices rCBF is low, while in the thalamus and putamen it is normal. This pattern is also evident in the rCBF profile (P).*

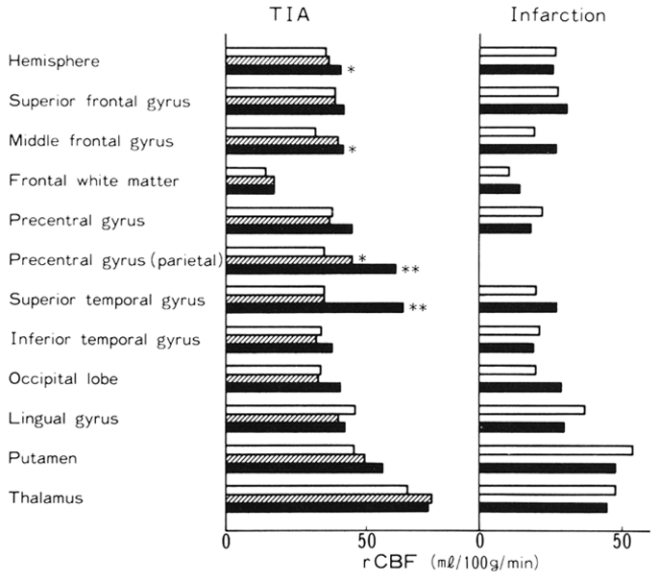


**Figure 4.** *Changes in rCBF after EDAS. Hemispheric and cortical flow increased significantly in patients with TIA. Increases were particularly evident in areas where the STA was implanted. In patients with infarction, hemispheric flow was unchanged and the increases in cortical flow were not significant.* $^{*}p < 0.05$; $^{**}p < 0.01$, *relative to preoperative values.*

eral recently developed surgical procedures designed to revascularize the brain via an extracranial blood source have been effective in inducing remission [5–8,10,11]. Among these procedures, EDAS has certain advantages over the others [12,13] and has been advocated as the surgery of choice for Moyamoya disease [1,15]. Long-term post-EDAS follow-up showed revascularization via the STA to be sufficient [14,15]. Also, the basal Moyamoya vessels diminished and the STA and MMA widened [14], which we also observed in our study. However, to date there have been no reports concerning changes in the carotid fork after the surgical procedures, and only gross changes in CBF have been reported in patients treated by any of the new surgical procedures [4,8,22]. Proper evaluation of surgical treatment of Moyamoya disease will require considerably more data concerning disease progression and changes in rCBF in the postoperative period.

Fukuyama and Umezu [2] and Umezu [21] modified the angiographic classification, which was introduced by Suzuki et al [16,17]. They subdivided stage III into three substages, since most cases are classified as stage III. The natural progression of the stage has been confirmed angiographically [2,17,21], although the time intervals have not yet been determined. Fukuyama and Umezu [2] and Umezu [21] reported that 40% of their patients with TIA showed the progression of angiographic stage with medical treatment over 35 months of follow-up. On the other hand, in our study 60% of patients with TIA who underwent EDAS showed the progression of angiographic stage over 10 months of follow-up. Demonstrability of the C1, A1, and M1, which comprise the carotid fork, markedly declined in

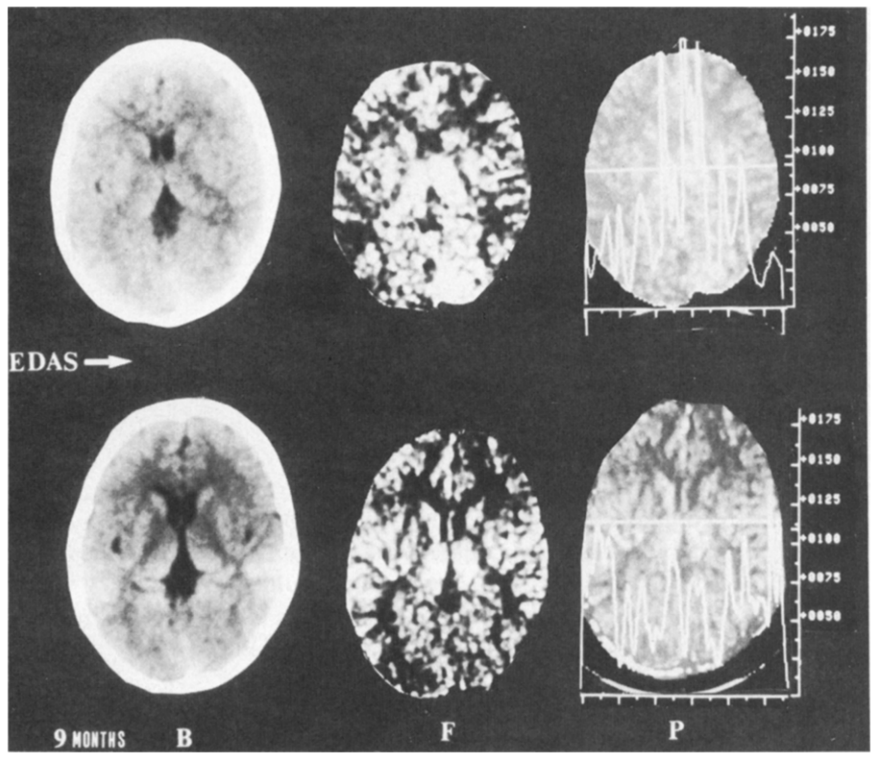


**Figure 5.** *Blood flow maps before and 9 months after EDAS in case 12. Blood flow increased in the bilateral temporal lobes. The increases are also reflected in the profile (P).*

follow-up angiograms, and the portions still visible decreased in diameter. This suggests that carotid fork stenosis may progress faster in patients who underwent EDAS than in patients treated conservatively, even though the clinical improvements occur following EDAS. Also, the variable extent of disappearance of Moyamoya vessels following EDAS may reflect advancement of the angiographic stage. On the contrary, the STA and MMA had markedly increased diameters after EDAS, and statistically significant enlargement was more common in patients with TIA than in those with infarction. Thus, EDAS may be more effective in patients with TIA. The benefit of EDAS was also confirmed by angiographic demonstrability of the cortical arteries. Postoperatively the number of visible MCA branches increased in all areas supplied by the MCA via the implanted STA, which means that collateral formation through the implanted STA exceeded the progression of internal carotid artery stenosis. However, we must note that several cortical branches of the ACA decreased in visibility postoperatively. Clinical and hemodynamic follow-up evaluation of the interhemispheric areas is needed; at this point there is no treatment for vascular occlusion in these regions.

Data on rCBF in Moyamoya disease have been reported by several authors [4,8,20,22], but definite conclusions about the effect of surgery on rCBF cannot yet be made. Reports of increased flow after surgery do not include information on regional flow. Our data demonstrated that rCBF in patients with Moyamoya disease accompanied by TIA was low in the cortices, and that in patients with infarction, perfusion was extremely low in the brain. It must be stressed that children with Moyamoya disease suffer from chronic cortical ischemia, regardless of whether or not they have symptomatic TIA or infarction. Our results lead us to believe that, in cortical ischemia, the demand for blood facilitates the production of a collateral blood supply after EDAS [13].

Assessment of rCBF revealed that patients with infarction had low potential for restoration of rCBF following EDAS, whereas patients with TIA showed improvement in blood flow postoperatively. The benefit of EDAS was first noted 2 weeks after surgery and was corroborated by the observation of clinical improvement in some patients within 1 month of EDAS. In our study, EDAS compared well with direct anastomosis in terms of the establishment of a collateral blood supply. Although the procedure was not curative, the resultant collateral blood supply adequately compensated for the effects of progressive internal carotid artery stenosis. We conclude that EDAS is an effective treatment for young patients with Moyamoya disease.

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