Neurosurgical Focus

Neurosurg Focus 5 (5): Article 3, 1998

Comparison of positron emission tomography study results of cerebral hemodynamics in patients with bleeding- and ischemic-type moyamoya disease

Toru Iwama, M.D., Yoshinori Akiyama, M.D., Masafumi Morimoto, M.D., Akio Kojima, M.D., and Kohei Hayashida, M.D.

Departments of Neurosurgery and Radiology, National Cardiovascular Center, Suita, Osaka, Japan

The purpose of this study was to elucidate the difference in cerebral hemodynamics and metabolic status between patients with bleeding- and ischemic-type moyamoya disease. Regional cerebral blood flow (rCBF), regional cerebral metabolic rate of oxygen ($rCMRO_2$), regional oxygen extraction fraction (rOEF), and regional cerebral blood volume (rCBV) in the cortex of the middle cerebral artery (MCA) territories and rCBV in the striatum were measured using positron emission tomography (PET) in 17 patients with moyamoya disease. Patients were divided into three subgroups according to type of disease manifestation and age: adult bleeding type (five cases), adult ischemic type (10 cases), and childhood ischemic type (two cases). When compared with adult controls, statistically significant reductions in rCBF and $rCMRO_2$, elevation in rOEF in the MCA territories, and elevation of rCBV in the striatum were observed in PET studies for all three subgroups. Between the adult bleeding type and ischemic type, rCBF, $rCMRO_2$, and rOEF in the MCA territories were not different, but rCBV in the striatum was higher in patients with ischemic-type moyamoya disease than in those with the bleeding type. In adult patients with bleeding and ischemic types, rOEF and rCBV in the MCA territories and rCBV in the striatum were significantly lower than in patients with childhood ischemic-type moyamoya disease. In adult patients with bleeding-type moyamoya disease, cerebral hemodynamics were impaired and similar to those in adult ischemic type.

Key Words * bleeding type * ischemic type * moyamoya disease * positron emission tomography * adult

Moyamoya disease is a clinical entity characterized by progressive cerebrovascular occlusion and a spontaneously developing collateral vascular network, the so-called moyamoya vessels.[11,13,14,19] The main manifestations are recurrent cerebral ischemia or intracranial bleeding.[11,14,19] In patients with moyamoya disease who present with cerebral ischemia, cerebral hemodynamic status has been well studied, and forms of impairment in cerebrovascular reserve have been documented by many investigators.[2,8,15-17,20] Efficacy of various revascularization surgeries to prevent further ischemia

has been also well recognized.[6,7,10] However, the therapeutic strategy for the treatment of patients with bleeding-type moyamoya disease is still controversial, although intracranial bleeding is the most catastrophic event and the main cause of death.[3,11,13,19] It is also unclear whether the ischemic and bleeding types share the same pathogenesis and pathophysiology. To establish the treatment of bleeding-type moyamoya disease, elucidation of cerebral hemodynamic status is thought to be important. However, hemodynamic disturbances in bleeding-type moyamoya disease have never been fully investigated.[17,20] In the present study, we measured the hemodynamic and metabolic status in patients with bleeding-type moyamoya disease by using positron emission tomography (PET) scanning and compared these results with those obtained in patients with ischemic-type moyamoya disease to clarify the differences in cerebral hemodynamics and metabolic status between these two types.

CLINICAL MATERIAL AND METHODS

In the last 6 years, we performed PET studies in 17 patients with moyamoya disease. Of these patients, 12 presented with cerebral ischemia and five with intracranial bleeding. Two patients were younger than 18 years of age (11 and 14 years), and the other 15 patients were older than 18 years of age (range 19-53 years, mean 40.5 years). All of the five patients who presented with intracranial bleeding were adults.

All patients underwent magnetic resonance imaging and PET studies at least 1 month after the last ischemic attack or bleeding episode. The PET scanner we used was a four-ring, seven-plane scanner (Headtome IV; SHIMADZU, Japan) that has a transaxial resolution of 6.5 mm and an axial resolution of 4.5 mm full width at half maximum in clinical use. A transmission scan was obtained for attenuation correction of positron annihilation gamma-rays in the brain. Regional cerebral blood flow (rCBF), regional cerebral metabolic rate of oxygen ($rCMRO_2$), regional oxygen extraction fraction (rOEF), and regional cerebral blood volume (rCBV) were measured after the patients inhaled ^{15}O-labeled carbon dioxide, oxygen, and carbon monoxide, with arterial activity corrected through a radial artery catheter.[9] During the acquisition of PET scans, each patient was firmly immobilized by a plastic collar placed around the neck and by a head restraint. The patient's ears were plugged and eyes were covered. Before each group of PET measurements were obtained, the head position was checked according to its alignment relative to six reference points. Blood gas levels were measured by a blood gas autoanalyzer (280 Blood Gas System; Ciba-Corning Diagnostics Corp., Meadfield, MA). Blood pressure was monitored throughout the examinations.[4] Regions of interest (ROIs) were placed both in the cortex in middle cerebral artery (MCA) territories and in the striatum bilaterally (Fig. 1). Areas of cerebral infarction and periventricular hematoma were excluded from the ROIs based on magnetic resonance imaging findings. Measurements of rCBF, $rCMRO_2$, rOEF, and rCBV in the cortex in MCA territories and rCBV in the striatum were obtained bilaterally in each patient. Control values for PET parameters were obtained from the same ROIs in five healthy adult patients who served as controls (age range 27-51 years, mean 34.8 years). These control values were expressed as the mean ± standard deviation as follows: 47 ± 7 ml/100 g/minute for rCBF; 3.8 ± 0.3 ml/100 g/minute for $rCMRO_2$; 0.41 ± 0.04 for rOEF; 2.4 ± 0.6 ml/100 g for rCBV in the MCA territories; and 2.5 ± 0.4 ml/100 g for rCBV in the striatum.

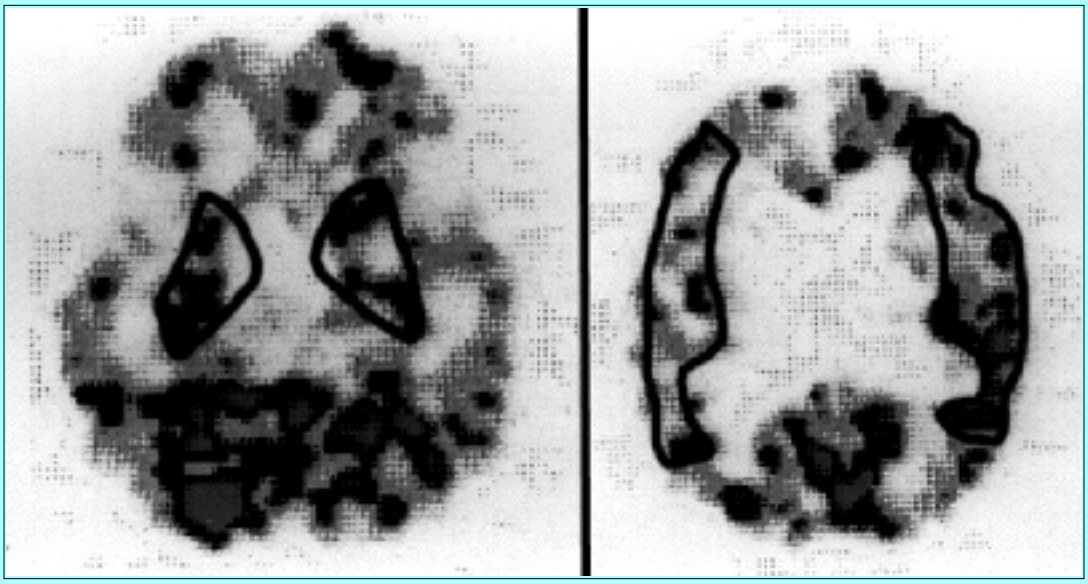

Fig. 1. Representative PET studies demonstrating ROI indicted on the CBF mapping obtained in the striatum (left), and the cortex in the MCA territory (right).

To analyze these hemodynamic and metabolic values, patients were divided into three subgroups: adult bleeding type (five patients), adult ischemic type (10 patients), and childhood ischemic type (two patients). Statistical significance was analyzed using the modified Bonferroni t test. A value of $p < 0.05$ indicated a significant difference.

RESULTS

Hemodynamic and metabolic data in patients with moyamoya disease are summarized in Table 1.

TABLE 1
SUMMARY OF HEMODYNAMIC AND METABOLIC DATA OBTAINED IN SUBGROUPS OF PATIENTS WITH MOYAMOYA DISEASE*

			Cortex in MCA territory				Striatum
Type	No. of Cases	No. of Hemis-pheres	CBF (ml/100 g/minute)	$CMRO_2$ (ml/100 g/minute)	OEF	CBV (ml/100 g)	CBV (ml/100 g)
adult bleeding	5	10	32.8 ± 7.3†	3.0 ± 0.7‡	0.53 ± 0.06†	3.5 ± 1.5	3.8 ± 0.8†
ischemic	10	20	37.1 ± 6.3‡	3.0 ± 0.5†	0.54 ± 0.06†	5.1 ± 1.0†	5.1 ± 1.0†
childhood ischemic	2	4	32.7 ± 4.1‡	3.4 ± 0.2§	0.65 ± 0.03†	8.8 ± 1.8‡	11.1 ± 0.5†
adult control	5	10	47.0 ± 7.0	3.8 ± 0.3	0.41 ± 0.04	2.4 ± 0.6	2.5 ± 0.4

* Values are expressed as the mean ± standard deviation.
† Significance compared to adult controls $p < 0.001$.
‡ Significance compared to adult controls $p < 0.01$.
§ Significance compared to adult controls $p < 0.05$.

Mean rCBF in the MCA Territories

Mean rCBF in the MCA territories was significantly reduced in all subgroups compared with that of adult controls. The mean rCBF in adult patients with bleeding-type moyamoya disease was lower than that of adult ischemic-type moyamoya disease, but the difference was not significant. Among the three

subgroups, there were no differences in the mean rCBF between any pairs of the subgroups.

Mean $rCMRO_2$ in the MCA Territories

Mean $rCMRO_2$ in the MCA territories was also significantly decreased in all the three subgroups compared with that of adult controls. Among the subgroups, there were no differences in the mean $rCMRO_2$.

Mean rOEF in the MCA Territories

Mean rOEF in the MCA territories was significantly elevated in all the three subgroups compared with that of adult controls. Among the subgroups, the mean rOEF values in both subgroups of adult patients were significantly lower than in the pediatric subgroup ischemic-type moyamoya disease ($p < 0.01$ and $p < 0.01$, respectively). There were no differences in rOEF between the adult bleeding and ischemic types.

Mean rCBV in the MCA Territories

Mean rCBV in the MCA territories was significantly increased in adult and childhood ischemic types compared with that of adult controls. The mean rCBV value in the MCA territories in the adult bleeding type was higher than that of adult controls, but the difference was not significant. Among the subgroups, the mean rCBV value in the juvenile ischemic type was significantly higher than values in the two adult types ($p < 0.001$), but there were no differences between the adult bleeding and ischemic types.

Mean rCBV in the Striatum

Mean rCBV in the striatum was significantly elevated in all the three subgroups compared to adult controls. Among the subgroups, the mean rCBV in the striatum was higher in the order of childhood ischemic, adult ischemic, and adult bleeding types. The differences in rCBV between each pair of the subgroups were statistically significant ($p < 0.001$ each).

DISCUSSION

Hemodynamic Status in Adult Bleeding-Type Moyamoya Disease

Hemodynamic status in moyamoya disease has been studied using dynamic computerized tomography, single photon emission computerized tomography, or PET scanning.[2,8,15-17,20] However, hemodynamic studies on bleeding-type moyamoya disease have been rare,[8,17] and PET scanning is thought to be the gold standard for quantitative hemodynamic study. Therefore, using PET scanning, we measured the hemodynamic and oxygen metabolic levels in patients with moyamoya disease who had sustained intracranial bleeding. Analysis of the results revealed that the hemodynamic and oxygen metabolic status in adult patients with bleeding-type moyamoya disease is impaired and nearly similar in status in adult patients who present with ischemia. Although rCBV values in the cerebral cortex and the striatum and rCBF in the cortex were lower in bleeding type than those of ischemic type, rOEF values in the cerebral cortex were significantly elevated even in those adult patients with bleeding-type moyamoya disease.

Taki, et al.,[17] have reported elevated rCBV and reduced rCBF/rCBV ratios in adult patients with bleeding-type moyamoya disease. In their six adult patients who presented with bleeding, rOEF values were within normal range, but rCBF was decreased compared with those of controls. The authors

suggested that the reduction in of rCBF was caused by diaschisis and brain atrophy posthemorrhage. In the present study, adult patients with bleeding-type moyamoya disease showed an increase in rOEF as well as a reduction in rCBF. The reason for this difference in rOEF status between our study and theirs is not clear. There may be variability in hemodynamic status in adult bleeding-type patients. The number of the patients in both series is not large because this disease is relatively rare. Although accumulation of data from a large series would be required to clarify this question, the present findings are compatible with two facts: 1) the incidence of perioperative ischemic complication are almost equal between bleeding and ischemic types of adult moyamoya disease,[5] and 2) the cases of patients who present with hemorrhage are often further complicated by infarction near the ictus.[1] Hemodynamic compensation by dilation of vessels is thought to be less active in adult bleeding-type moyamoya disease based on the known slight elevation of rCBV in the cortex, but hemodynamic insufficiency exists and is compensated by increasing oxygen extraction.

Treatment Strategy in Adult Bleeding-Type Moyamoya Disease

Hemodynamic improvements have been reported in patients with moyamoya disease who presented with ischemia and underwent cerebral revascularization surgery.[2,20] Intracranial bleeding is thought to result from increased hemodynamic stress caused by the tiny moyamoya vessels that act as collateral channels around the basal ganglia.[3,12,18] Although it is thought that revascularization has the potential to reduce the hemodynamic stress on moyamoya vessels,[3,19] this point remains controversial. Based on analysis of hemodynamic data in bleeding-type moyamoya disease, it is not clear whether or not cerebral revascularization surgery is effective in preventing further bleeding in patients with moyamoya disease. However, our analysis does indicate that adult patients who present with bleeding should undergo treatment that assumes that their hemodynamic status is impaired. Overdehydration or hypotension must be avoided to prevent ischemic complications.

Hemodynamic Status in Adult Ischemic-Type Moyamoya Disease

The present series included only two pediatric cases of moyamoya disease, because PET scans are difficult to obtain in children as the process requires that patients remain still for an appropriate length of time. However, comparison between the hemodynamic status in adult ischemic-type moyamoya patients and that in childhood moyamoya disease patients provides interesting findings. In adult patients who present with ischemia, hemodynamic insufficiency is obvious (significantly decreased rCBF and increased rOEF and rCBV) compared with adult controls; however, hemodynamic status is thought to be more stable in pediatric patients. When compared with hemodynamic status in childhood ischemic-type, rCBF in the cortex was higher and rCBV in the striatum was significantly lower in adult patients with ischemic-type moyamoya disease. These differences may indicate that leptomeningeal collateral pathways have been developed in adults instead of collateral flow through the basal moyamoya vessels, which exist in and around the striatum in children. Angiographic studies reveal that the basal moyamoya vessels fade with aging.[13,14]

References

1. Hashimoto N, Iwama T, Tsukahara T, et al: Potential hazard of intracranial bleeding and cerebral ischemia in patients with moyamoya disease, Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) (eds) **Annual Report 1995.** Tokyo: Ministry of Health and Welfare, 1996, pp 55-60

2. Ikezaki K, Matsushima T, Kuwabara Y, et al: Cerebral circulation and oxygen metabolism in childhood moyamoya disease: a perioperative positron emission tomography study. **J Neurosurg 81:** 843-850, 1994

3. Iwama T, Hashimoto N, Nozomu Murai B, et al: Intracranial rebleeding in moyamoya disease. **J Clin Neurosci 4:** 169-172, 1997

4. Iwama T, Hashimoto N, Takagi Y, et al: Hemodynamic and metabolic disturbances in patients with intracranial dural arteriovenous fistulas: positron emission tomography evaluation before and after treatment. **J Neurosurg 86:** 806-811, 1997

5. Iwama T, Hashimoto N, Tsukahara T, et al: Peri-operative complications in adult moyamoya disease. **Acta Neurochir 132:** 26-31, 1995

6. Karasawa J, Kikuchi H, Furuse S, et al: Treatment of moyamoya disease with STA-MCA anastomosis. **J Neurosurg 49:** 679-688, 1978

7. Karasawa J, Touho H, Ohnishi H, et al: Long-term follow-up study after extracranial-intracranial bypass surgery for anterior circulation ischemia in childhood moyamoya disease. **J Neurosurg 77:** 84-89, 1992

8. Kuwabara Y, Ichiya Y, Otsuka M, et al: Cerebral hemodynamic change in the child and the adult with moyamoya disease. **Stroke 21:** 272-277, 1990

9. Lammertsma AA, Jones T: Correction for the presence of intravascular oxygen-15 in the steady-state technique for measuring regional oxygen extraction ratio in the brain: 1. Description of the method. **J Cereb Blood Flow Metab 3:** 416-424, 1983.

10. Matsushima Y, Fukai N, Tanaka K, et al: A new surgical treatment of moyamoya disease in children: a preliminary report. **Surg Neurol 15:** 313-320, 1981

11. Nishimoto A, Takeuchi S: Abnormal cerebrovascular network related to the internal carotid arteries. **J Neurosurg 29:** 255-260, 1968.

12. Oka K, Yamashita M, Sadoshima S, et al: Cerebral haemorrhage in moyamoya disease at autopsy. **Virchows Arch A Pathol Anat Histol 392:** 247-261, 1981

13. Suzuki J, Kodama N: Moyamoya disease--a review. **Stroke 14:** 104-109, 1983

14. Suzuki J, Takaku A: Cerebrovascular "moyamoya" disease. Disease showing abnormal net-like vessels in base of brain. **Arch Neurol 20:** 288-299, 1969

15. Tagawa T, Naritomi H, Mimaki T, et al: Regional cerebral blood flow, clinical manifestations, and age in children with moyamoya disease. **Stroke 18:** 906-910, 1987

16. Takeuchi S, Tanaka R, Ishii R, et al: Cerebral hemodynamics in patients with moyamoya disease. A study of regional cerebral blood flow by the ^{133}Xe inhalation method. **Surg Neurol 23:** 468-474, 1985

17. Taki W, Yonekawa Y, Kobayashi A, et al: Cerebral circulation and metabolism in adults' moyamoya disease--PET study. **Acta Neurochir 100:** 150-154, 1989

18. Yamashita M, Oka K, Tanaka K: Histopathology of the brain vascular network in moyamoya disease. **Stroke 14:** 50-58, 1983

19. Yonekawa Y, Okuno T, Handa H: "Moyamoya" disease: clinical review and surgical treatment, in Fein JM, Flamm ES (eds): **Cerebrovascular Surgery**. New York: Springer-Verlag, Vol. 2, 1985, pp 557-580

20. Watanabe H, Ohta S, Oka Y, et al: Changes in cortical CBF and vascular response after vascular reconstruction in patients with adult onset moyamoya disease. **Acta Neurochir 138:** 1211-1217, 1996

Manuscript received September 21, 1998.

Accepted in final form October 7, 1998.

Address reprint requests to: Toru Iwama, M.D., Department of Neurosurgery, Gifu University School of Medicine, 40 Tsukasa-machi, Gifu 500-8705, Japan.
