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Cerebral Circulation in Moyamoya Disease: A Clinical Study Using Transcranial Doppler Sonography

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Transcranial Doppler sonography was performed on eight patients diagnosed as Moyamoya disease. Angiographically, the patients–four adults (mean age 42) and four children (mean age 7.7)–underwent a complete six- or five-vessel angiographic study. The results showed the following: (1) Despite the presence of stenosis, all middle cerebral arteries showed very low-flow velocity compared to their ipsilateral distal internal carotid arteries. In adult cases, the difference was very significant ($p < 0.02$). (2) Relatively high-flow velocity was observed in the posterior cerebral arteries of children, and in the ophthalmic arteries of adult cases. (3) In several occasions, very low-flow velocity values were still detected despite the fact that with angiography, the respective arterial segments were hardly opacified. The relation and discrepancy between these results and the angiographic findings, and the potential application of transcranial doppler in assessing and grading the severity of moyamoya disease are discussed.

KEY WORDS: Cerebral circulation; Cerebrovascular disease; Moyamoya disease; Transcranial Doppler sonography

Moyamoya disease is a form of chronic cerebrovascular occlusive disease, characterized by the angiographic finding of stenosis or occlusion of distal portions of both internal carotid arteries and their major branches, and the appearance of extensive parenchymal, leptomeningeal, and transdural anastomosis [11,16,25]. This particular type of cerebrovascular abnormality was once thought to be confined to the Japanese [12], but similar cases have been reported from all over the world [5,11]. According to the diagnostic criteria of the Japanese Cooperative Research Committee on Moyamoya, only cases with bilateral lesions are diagnosed as "definite," and those with unilateral involvement are classified as "probable" [8]. It was possible for an initially unilateral case to progress bilaterally as reported by Matsushima et al [15]. Its incidence has two peaks, that is, in the first and fourth decade of life [17,26]. Children typically present with recurrent ischemic attacks, such as episodes of sudden hemiplegia [17,26]. On the other hand, adult cases are more commonly present with evidence of intracranial hemorrhages, either intracerebral hemorrhages with intraventricular rupture or subarachnoid hemorrhage [26]. Although there are several supporting diagnostic methods such as computed tomographic (CT) scan and electroencephalographic (EEG) findings [17,26], definite diagnosis and its classification still depend largely on angiography of the main cerebral arteries, which is invasive and not without risk. In children it is usually necessary to give general anesthesia in performing the angiography, and this may make this procedure more risky.

In 1982 Aaslid et al [1] introduced a high-energy, pulsed-doppler system, operating at low frequency, which facilitated a reliable measurement of flow velocity from distinct cerebral arteries, at a defined depth, at the base of the skull. Since then, transcranial doppler (TCD) sonography was suggested and even indicated for examination and follow-up of patients with vasoconstriction of any cause, especially vasospasm after subarachnoid hemorrhage [14,21]. Even, using TCD sonography, the process of relaxation or normalization of the spastic segment of a middle cerebral artery was clearly observed [19]. Using one of the three cranial windows mentioned by many authors [1,2,9,22], it is possible to measure the normal flow velocity of the basal cerebral arteries and their main branches.

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Table 1. *Patients, Their Symptoms and Findings on CT and Angiograms*

Case no.	Patients	Age	Symptoms	CT findings	Angiographic patency		
					ICA	MCA	ACA
1.	M	49	Hemorrhage	Normal	+	+	+
					+	+	+
2.	F	51	Infarction and hemorrhage	Lt. and rt. frontal LDA	+	+	−
					−	−	−
3.	M	44	Infarction	Lt. occipital LDA	+	+	−
					+	+	−
4.	F	28	Hemorrhage	Rt. parietooccipital LDA	+	−	−
					−	−	−
5.	F	13	TIA	Normal	−	−	−
					−	−	−
6.	M	4	TIA	Normal	+	+	−
					+	+	−
7.	F	6	TIA	Normal	+	+	+
					+	+	+
8.	F	8	TIA	Normal	+	+	+
					+	+	+

Abbreviations: F, female; LDA, low density area; Lt, left; M, male; Rt, right; TIA, transient ischemic attack; other abbreviations as per text.

Reported here are the results of TCD examinations in eight Moyamoya cases (four adults and four children). The potential application of TCD for classification of severity and evaluation of collateral circulation in this chronic cerebrovascular occlusive disease is discussed in relation to the clinical and angiographic findings.

Subject and Method

The study involved eight patients, diagnosed angiographically as "definite" Moyamoya disease. They were admitted to the Department of Neurosurgery, Hiroshima University Hospital between January 1991 and July 1992. There were four adults, aged between 28 and 51 (mean 42), and four children, aged between 4 and 13 (mean 7.75). The children all presented with symptoms of transient ischemic attack and their CTs showed normal images. Three of the adult cases had intraventricular hemorrhage and the one had cerebral infarction at presentation. Low-density lesions were observed on the CT scans of cases 2, 3, and 4 (Table 1).

All patients underwent six- or five-vessels selective angiographic study using conventional or digital subtraction methods via a transfemoral catheter. As had been reported previously [23], the internal carotid arteriograms were categorized, according to the degree of stenosis, into five stages: stage 1, slight to moderate stenosis of internal carotid artery (ICA) bifurcation (lumen $\geq$ 10%); stage 2, severe stenosis of ICA bifurcation (lumen $<$ 10%); stage 3, occlusion of middle cerebral artery (MCA) or anterior cerebral artery (ACA); stage 4, occlusion of ICA or ACA and MCA with partial retention of trunk of ACA or MCA; stage 5, occlusion of ICA or ACA and MCA with no filling of main trunk of either ACA or MCA (Table 2).

TCD examinations, using a TC2-64 Transcranial Doppler (EME, Uberlingen, Germany), were done through the temporal bone window for the insonation of the supraclinoid portion of the internal carotid, middle cerebral, anterior cerebral, and posterior cerebral arteries, and through the orbital window for insonation of the ophthalmic artery. Doppler intensity was set at 75% and 10% of spatial peak temporal average for temporal bone window and orbital window, respectively [9]. Techniques of TCD examinations were as follows: The temporal window is a region through which the doppler signal can penetrate because of the thin bone in this area. The middle, anterior, and posterior cerebral arteries, as well as distal portion of ICA can usually be insonated by placing the ultrasound probe over this window. Flow of MCA (from 40 to 55 mm) is toward the transducer and can often be followed to the distal ICA. Once the MCA is identified, the orientation and depth of the insonation has to be adjusted until the maximal or the best of the doppler signals are received. At the distal ICA, the observed flow is usually bidirectional, and flow of the ACA which is normally away from the transducer is detected. The posterior cerebral artery (PCA) is detected by using the ICA bifurcation as a reference, increasing the depth by 5 mm, and directing the probe slightly posteriorly. Signals from the PCA can usually be recorded at a depth between 60 and 80 mm. The

Table 2. *MFV and PI of ICA and MCA and its Ratio in Relation to Stage of IC Occlusion*

Case no.	Stage (Satoh et al) rt./lt.	ICA		MCA		Ratio of V_{MCA}/V_{ICA}	
		MFV	PI	MFV	PI	Rt.	Lt.
1.	3/3	42/86	1.03/0.61	34/40	0.67/0.71	0.81	0.47
2.	3/3	50/n.r.	0.87/n.r.	46/n.r.	0.86/n.r.	0.92	n.r.
3.	3/3	50/60	0.67/0.7	32/46	0.73/0.62	0.64	0.77
4.	3/3	42/64	0.56/0.36	30/26	0.28/0.33	0.71	0.41
5.	5/4	42/24	0.65/0.59	n.r./n.r.			
6.	2/2	52/60	0.79/0.81	42/34	0.67/1.0	0.81	0.57
7.	2/1	108/80	0.56/0.91	80/82	0.82/0.91	0.74	1.02
8.	2/3	72/92	0.90/0.88	50/26	0.69/0.28	0.69	0.28

Abbreviations: n.r., not recorded; other abbreviations as per Table 1 and text.

flow is directed toward the probe in the proximal (P1) segment, and away from the probe in the distal (P2) segment as well as the contralateral P1. In contrast to that of MCA, the signal is lost when the depth is below 50–55 mm. Normal values for mean flow velocities (MFVs) of the above-mentioned arteries have been published elsewhere [2,8,22]. The ophthalmic artery (proximal intraorbital segment) is insonated through the orbital window, from the superior palpebrae, over a closed eye, with a depth of 45–55 mm. It is characteristically directed toward the probe, has MFV values of 21–23.6 cm/s [20,22], and its waveform is characteristic of extracranial vessels, that is, a relatively higher pulsatility index than that for the other intracranial vessels [5,20]. All measured MFV are displayed in centimeter per second (cm/s), and Gosling's pulsatility index [PI = (peak systolic velocity − end diastolic velocity)/mean velocity] (2) was also calculated. Student's t test was applied to calculate the statistical significance of all measurement.

Results

Except for the left side of case 2, the temporal bone windows were present in all 15 sides of the eight patients. From these successfully insonated windows, doppler signals of the distal ICAs, the proximal middle cerebral, precommunicating segment of posterior cerebral, and precommunicating segment of anterior cerebral arteries were successfully recorded in 100%, 100%, 100%, and 66.67% of the angiographically patent arterial segments respectively. Orbital insonation for ophthalmic arteries gave a 87.5% success rate. The MFV and PI values for all the successfully identified basal cerebral arteries and the ophthalmic arteries from both sides of each subject and the stage of ICA occlusion on angiograms are summarized in Tables 2 and 3, and briefly analyzed below (displayed in mean ± standard deviation):

Internal Carotid Artery

Doppler signals of the distal ICAs were successfully recorded from all the other 15 sides of the eight patients. In case 5, interestingly, very low-flow velocity values were still detected, while both supraclinoid ICAs were hardly opacified on angiogram (stage 4 of ICA stenosis). The mean flow velocity values were 56.28 ± 15.51 cm/s in adult cases and 66.25 ± 27.37 cm/s in child cases. The values for pulsatility index were 0.69 ± 0.21 in adult and 0.76 ± 0.14 in children.

Middle Cerebral Artery

In adult cases, the mean flow velocity value of MCAs (36.28 ± 7.8 cm/s) was significantly lower ($p < 0.02$) than the value of the respective ipsilateral ICAs (Figure 1). In children, the value (52.33 ± 23.61 cm/s) was also lower than that of the respective ICAs but no statistical difference was observed. Signals of the MCAs were not observed bilaterally in case 5 with total occlusion of the distal ICAs. In case 4, however, very low MFV values were still detected despite the presence of very severe stenosis of bilateral MCAs on angiogram (Figure 2).

Posterior Cerebral Artery

In all insonated temporal bone windows, PCAs were successfully insonated in all sides except the left side of case 5. In this particular case, angiography revealed occlusion of the interpeduncular segment of the left PCA. Children typically showed very high mean flow velocity values (100–250 cm/s). And the mean value (124.57 ± 60.53 cm/s) was significantly higher ($p < 0.05$) compared to that of the adult cases (69.43 ± 19.34 cm/s) (Figure 3). Angiography showed excellent leptomeningeal anastomosis in 15 out of 16 parietal regions and 15 out of 16 temporal regions.

Table 3. *MFV and PI of Posterior Cerebral Artery and Ophthalmic Artery*

Case no.	Posterior cerebral artery		Ophthalmic artery		Comments on angiography
	MFV	PI	MFV	PI	
1.	56/42	0.70/0.79	46/34	0.86/0.58	No stenosis of PCA
2.	86/n.r.	0.69/n.r.	20/30	1.35/0.92	VA stenosis proximal to VB junction
3.	80/50	0.60/0.46	52/34	0.70/0.82	No stenosis of PCA
4.	86/86	0.50/0.63	44/42	0.63/0.56	Rt. PCA hypoplasia lt. distal stenosis
5.	52/n.r.	0.65/n.r.	42/46	1.27/1.04	Rt. distal and lt. proximal PCA occlusion
6.	122/112	0.68/0.59	28/24	1.72/1.71	No stenosis of PCA
7.	126/250	0.58/0.49	n.r.	n.r.	No stenosis of PCA both OA hypoplasia
8.	100/110	0.63/0.76	16/18	1.60/1.89	Distal stenosis of bilateral PCA

Abbreviations: OA, ophthalmic artery; VA, vertebral artery; other abbreviations as per Tables 1, 2, and 3 and text.

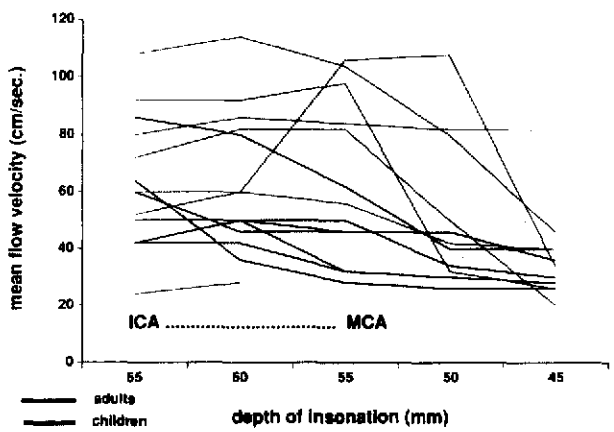
Anterior Cerebral Artery

Angiography revealed the opacification of patent ACAs in six sides of three patients, and TCD successfully recorded their doppler signals in four out of these six sides, two in adult and the other two in children. The mean value of mean flow velocities was 64 ± 19.8 cm/s. Statistical comparison was not done on these results.

Ophthalmic Artery

Doppler signals of the ophthalmic arteries could be traced in all orbital insonations, except in case 7, whose angiogram revealed bilateral hypoplastic ophthalmic arteries. The mean flow velocities of the ophthalmic artery were significantly higher ($p < 0.05$) in adult cases (37.75 ± 10.22 cm/s) compared to child cases (29.0 ± 12.44 cm/s), whereas the vessel's resistance or pulsatility indices were significantly lower ($p < 0.01$) in adult cases (0.8 ± 0.26) as compared to child cases (1.53 ± 0.32) (Figure 4). This low pulsatility index in adult cases was expressed in the recorded doppler signal as the flow pattern similar to that of intracranial vessels. Normally, as also observed in all the child cases except case 5, signal flow pattern of the ophthalmic artery is similar to that of the extracranial vessels, that is, relatively lower flow velocity and higher pulsatility index (Figure 5).

Figure 1. *Results of transtemporal doppler insonation for distal internal carotid artery (ICA, depth of 60–65 mm) and middle cerebral artery (MCA, depth of 55–45 mm). Except for one MCA of case 6, the mean flow velocity value was much lower in the MCA side even in the presence of stenoses. In adult cases, the difference is statistically very significant ($p < 0.02$).*



Discussion

The flow velocity of the terminal portion of the ICAs were generally lower in adult than in childhood Moyamoya cases, as also observed in normal individuals [10]. In some cases, very low doppler signals could still be detected even when the respective arterial segments (supraclinoid ICAs in case 5 and bilateral MCAs in case 4) were hardly opacified on angiograms (Figure 2). This discrepancy might have been caused by the very prolonged regional circulation time in Moyamoya vessels [28]; the contrast medium did not reach the "stenotic but patent" vessels on time. Or it might have been the result of the relatively large size of the "sample volume" in the presently available TCD instrument (10 × 4 mm^2), so that the nearby patent segment of the same vessel was simultaneously insonated. Angiography is not necessarily accurate, since the opacification of a particular vessel and its direction of flow depend on the pressure of contrast injection [5,20].

When a vessel narrows, regardless of the cause, the velocity of the bloodflow increases to allow the same volume of blood to pass the narrowed lumen. This "law of continuity" is the basis for the compensatory flow velocity increase found in vascular spasm after aneurysmal subarachnoid hemorrhage [5,9]. Velocity also in-

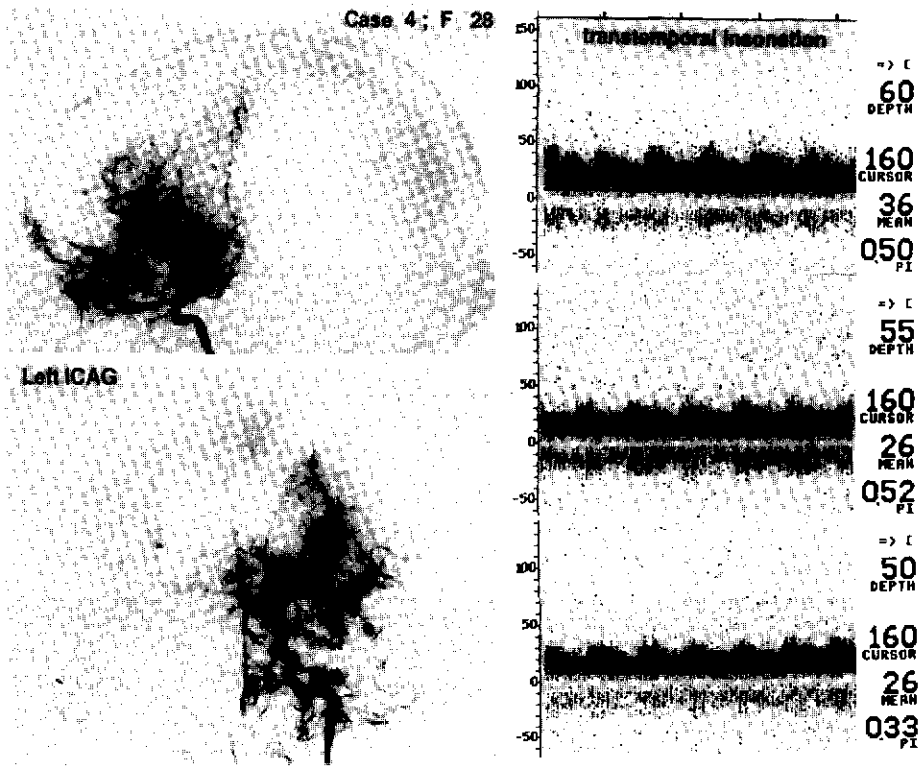
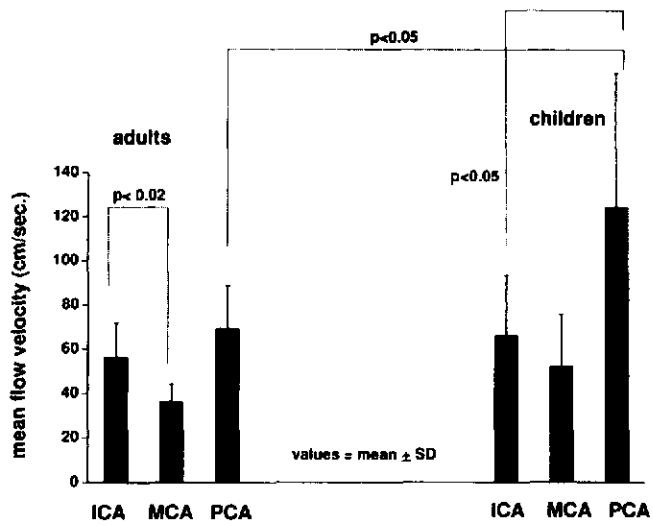


Figure 2. *Proximal middle cerebral artery was hardly opacified during left internal carotid arteriography (ICAG) in case 4 (left), but a very low-flow velocity was still detected on transcranial doppler recording (right). Note also the very low pulsatility index (PI) values.*

creases when there is augmentation due to collateral contribution to other vessels' territories [2,5,9]. This latter reason applies for the abnormally high flow velocity of the PCAs in children, and of the ophthalmic arteries in adult Moyamoya cases, since no stenotic lesion was observed in those insonated arterial segments. Even, dilatation and hypertrophy of the ophthalmic arteries were observed in cases 1 to 5 (Figure 5). Whitnal [33], and Bock and Schwarz-Karsten [3] wrote that, anatomically, the ophthalmic artery branches off at right angles from, and at once turns to lie almost parallel with, the ICA. The main stream of the ICA would tend to suck blood out of the ophthalmic artery rather than force blood into the artery. Narrowing of the arterial segment distal to the origin of the ophthalmic artery as in Moyamoya disease, would then tend to dam up the main bloodstream and force the blood back into the ophthalmic artery. This factor might have some influence on the enlargement of the ophthalmic arteries in adult Moyamoya cases and the change of their waveforms from the extracranial type to the intracranial type (Figure 5). If the assumption is true, then it will explain the chronicity of the disease process.

Figure 3. *Comparison of mean flow velocity values of the internal carotid (ICA), middle cerebral (MCA), and posterior cerebral (PCA) arteries in adult cases (left) and in child cases (right). In adults, MCA is significantly ($p < 0.02$) lower than ICA, and in children, PCA is significantly higher ($p < 0.05$) than ICA. And compared to adult cases, children showed significantly higher flow velocity of PCA ($p < 0.05$).*



Normally, the MCA has the highest flow velocity among the basal cerebral arteries [2,9,22]. This is related to the fact that it carries about 80% of flow to the hemisphere [30], has a smaller diameter compared to that of ICA [6,7,33], and has the smallest degree of insonation angle in TCD sonography [1]. Mild to moderate stenosis increases flow velocity, and this increase is inversely correlated to the residual lumen's diameter [9,13,22]. De-

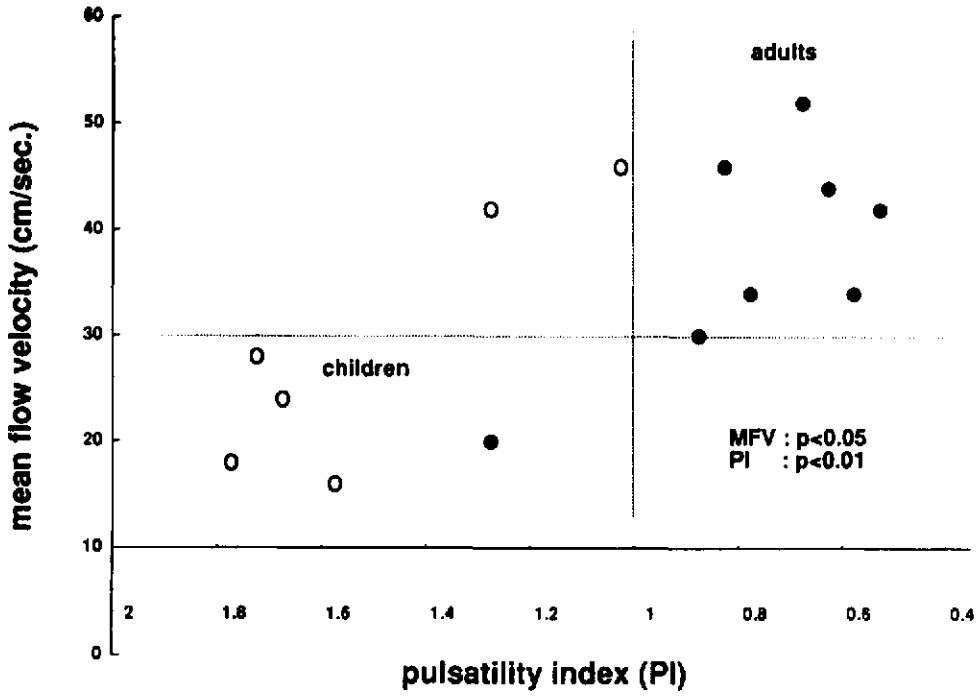


Figure 4. *Results of transorbital doppler insonation for ophthalmic arteries. In adult cases (solid circles), mean flow velocity (MFV) values were significantly higher ($p < 0.05$), and pulsatility index (PI) values were significantly lower ($p < 0.01$) compared to those of children. Most of the adult cases showed absolute values of >30 cm/s for MFV and <1 for PI.*

creased flow velocity occurs distal to the stenotic segment when the stenosis exceeds 60%–80% [10,13,14].

In our cases, the mean flow velocities of the MCAs were generally lower than those of the ipsilateral ICAs and in adult cases they were statistically significant. It is interesting that despite the presence of mild, moderate, or severe stenotic lesions, none of these vessels showed increased flow velocities. The presence of stenotic lesion proximal to the insonated vessels, that is, arterial segment proximal to the supraclinoid ICA, might explain the low flow velocity of the distal ICAs and the MCAs, only if the stenosis was very severe, as had been observed by De Witt and Wechsler [5] in cases of extracranial internal carotid occlusion, and Schneider et al [25] in temporary ICA cross-clamping during carotid endarterectomy.

It is known that arterial occlusion in Moyamoya disease is not only confined to the large arteries of the circle of Willis, but histologic abnormalities such as intimal thickening with elastofibrosis and tortuous internal elastic laminae in the arterial wall are generally observed even in the level of arterioles, medullary arteries of the cerebral white matter, and the small collateral vessels in the subarachnoid spaces over the parieto-occipital region [18,24,36]. These are the reasons behind the prolonged circulation time [28], the decreased volume of blood passing through this particular vessel, and the low hemispheric cerebral blood flow (CBF), as were observed in reported CBF studies [29,31]. The low flow velocity of the middle cerebral compared to that of the internal carotid arteries had to be related to the smaller volume of blood supplied to its vascular territory. And, the smaller the ratio of the MFV value of MCA (V_{MCA}) to the MFV value of ICA (V_{MCA}) (V_{MCA}/V_{ICA}), the smaller the volume of blood carried to the hemisphere through the respective vessel. In our cases, a positive correlation was observed when comparing this ratio with the degree of stenosis of internal carotid artery bifurcation mentioned by Satoh et al [21], but further study with a larger number of subjects will be needed to evaluate the potential application of this ratio for grading the severity of the Moyamoya disease.

Significantly higher flow velocity of the PCAs in children compared to that of adult cases, showed the more important role performed by the PCAs as collateral circulation to the ischemic brain in children than in adult cases. This is in agreement with the results of regional CBF study using the ^{133}Xe inhalation method [30], and the ^{133}Xe clearance method [32] which showed a relatively high regional CBF in the posterotemporal and occipital regions of childhood Moyamoya cases. The higher incidence of aneurysm in the vertebrobasilar system, especially at basilar bifurcation in Moyamoya pa-

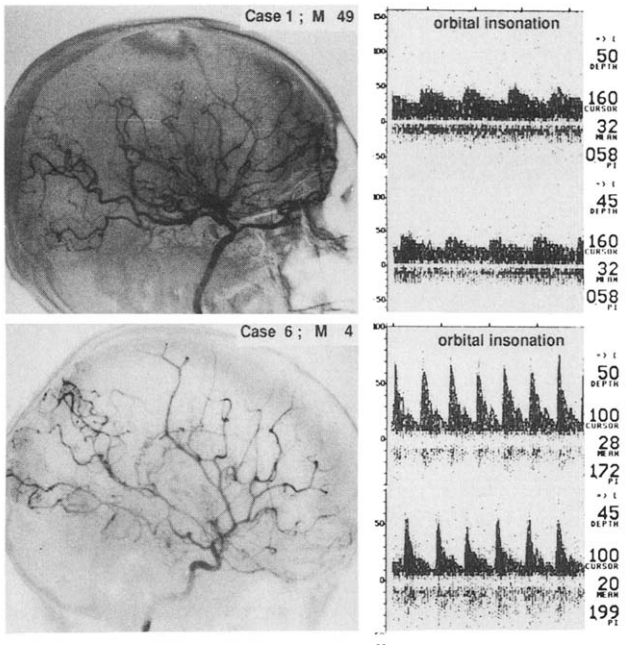


Figure 5. Upper pictures *represented angiographic opacification and doppler signals of ophthalmic artery in adult Moyamoya cases.* **Lower pictures** *were those of children. The doppler flow pattern of the ophthalmic artery in the adult was similar to that of the intracranial vessels (relatively high diastolic flow velocity), whereas children showed patterns similar to that of the extracranial vessels (very low diastolic flow velocity).*

tients [32,35] may be explained by the presence of hemodynamic stress caused by the very high flow velocity at the bilateral PCAs.

It is not the aim of this investigation to compare childhood and adult Moyamoya cases statistically, but the fact that its incidence has two peaks–the first and the fourth decade of life–may lead to the emergence of some differences in many aspects, such as the adaptive capability of the cerebral circulation against the disease process. It is not impossible that there might be some differences in its pathogenesis in children and in adults. The use of TCD has proved to be very beneficial in the assessment of the circulatory state of the main cerebral vessels, especially those directly involved in the disease process, in Moyamoya patients. And as the characteristic doppler flow patterns of the ophthalmic arteries such as that found in adult cases were observed whenever the vessel supplies intracranial circulation (Figure 5), evaluation of the collateral vessels following revascularization measures should be a part of the future benefit of the use of TCD in Moyamoya patients.

References

1. Aaslid R, Markwalder T-M, Nornes H. Noninvasive transcranial doppler ultrasound recording of flow velocity in basal cerebral arteries. J Neurosurg 1982;57:769–74.
2. Aaslid R, Lindegaard KF, Cerebral Hemodynamics. In: Aaslid R, ed. Transcranial doppler sonography. Wien-New York: Springer-Verlag, 1986:60–85.
3. Bock J, Schwarz-Karsten H. Further investigations on the anatomy of the origin of the ophthalmic artery. Am J Ophthalmol 1955;39:160–4.
4. Chen ST, Liu YH, Hsu CY, Hogan EL, Ryu SJ. Moyamoya Disease in Taiwan. Stroke 1988;19:53–59.
5. De Witt LD, Wechsler LR. Transcranial Doppler. Stroke 1988;19:915–21.
6. Gibo H, Carver CC, Rhoton Jr AL, Lenkey C, Mitchell RJ. Microsurgical anatomy of the middle cerebral artery. J Neurosurg 1981;54:151–69.
7. Gibo H, Lenkey C, Rhoton AL Jr. Microsurgical anatomy of the supraclinoid portion of the internal carotid artery. J Neurosurg 1981;55:560–74.
8. Gotoh F. Guideline to the diagnosis of occlusion of the circle of Willis. In: Gotoh F, ed. Annual report of 1978 on the Cooperative Study of Occlusion of the Circle of Willis to the Ministry of Health and Welfare. 1979:132.
9. Harders A. Neurosurgical applications of transcranial doppler sonograsonography. Wien-New York: Springer-Verlag, 1986.
10. Hennerici M, Rautenberg W, Sitzer G, Schwartz A. Transcranial doppler ultrasound for the assessment of intracranial arterial flow velocity, Part 2: Evaluation of intracranial arterial disease. Surg Neurol 1987;27:523–32.
11. Krayenbuhl HA. The moyamoya syndrome and the neurosurgeon. Surg Neurol 1975;4:353–60.
12. Kudo T. Spontaneous occlusion of the circle of Willis. A disease apparently confined to Japanese. Neurology (Minneap) 1968; 18:485–96.
13. Lindegaard K-F, Bakke SJ, Grolimund P, Aaslid R, Huber P, Nornes H. Assessment of intracranial hemodynamics in carotid artery disease by transcranial doppler ultrasound. J Neurosurg 1985;63:890–8.
14. Lundar T, Lindegaard KF, Nornes H. Continuous recording of middle cerebral artery blood velocity in clinical neurosurgery. Acta Neurochir (Wien) 1990;102:85–90.
15. Matsushima T, Take S, Fujii K, Fukui M, Hasuo K, Kuwabara Y, Kitamura K. A case of moyamoya disease with progressive involvement from unilateral to bilateral. Surg Neurol 1988;30: 471–5.
16. Matsushima Y, Fukai N, Tanaka K, Tsuruoka S, Inaba Y, Aoyagi M, Ohno K. A new surgical treatment of moyamoya disease in children: a preliminary report. Surg Neurol 1981;15: 313–20.
17. Matsushima Y, Inaba Y. Moyamoya disease in children and its surgical treatment: introduction of a new surgical procedure and its follow-up angiograms. Child's Brain 1984;11: 155–70.
18. Mauro A, Johnson ES, Chikos PM, Alvord EC. Lipohyalinosis and miliary microaneurysms causing cerebral hemorrhage in a patient with moyamoya: a clinicopathological study. Stroke 1980;11:405–12.
19. Muttaqin Z, Arita K, Uozumi T, Kuwabara S, Oki S, Kurisu K, Nakahara T, Kohno H, Ohba S. Vasospasm after Traumatic Subarachnoid Hemorrhage: Transcranial Doppler Evaluation. Case Report. Neurosurg Rev. 1991;14:321–325
20. Muttaqin Z, Arita K, Uozumi T, Kuwabara S, Oki S, Ohba S, Kurisu K, Nakahara T, Kohno H, Satoh H. Transcranial doppler sonography in carotid–cavernous fistulas: analysis of five cases. Surg Neurol 1992;38:179–85.
21. Petty GW, Wiebers DO, Meissner I. Transcranial doppler ultrasonography: clinical applications in cerebrovascular disease. Mayo Clin Proc 1990;65:1350–64.

22. Ringelstein EB. A practical guide to transcranial doppler sonography. In: Noninvasive imaging of cerebrovascular disease. New York: Alan R. Liss, 1989:75–121.
23. Satoh S, Shibuya H, Matsushima Y, Suzuki S. Analysis of the angiographic findings in cases of childhood moyamoya disease. Neuroradiology 1988;30:111–9.
24. Sayama I, Fukasawa H, Yasui N, Suzuki A. Child with moyamoya disease after bypass surgery. Report of an autopsy case. Neurol Med Chir (Tokyo) 1985;25:975–80.
25. Schneider PA, Rossman ME, Bernstein EF, Torem S, Ringelstein EB, Otis SM. Effect of internal carotid artery occlusion on intracranial hemodynamics: transcranial doppler evaluation and clinical correlation. Stroke 1988;19:589–93.
26. Suzuki J, Kodama N. Moyamoya disease–a review. Stroke 1983;14:104–9.
27. Suzuki S, Tsuruoka S, Hiratsuka H, Matsushima Y, Fukumoto, T, Inaba Y, Ohno K. Cerebral Circulation in Pediatric Patients with Moyamoya Disease. Tomographic Cerebral Blood Flow Map obtained by Xenon-enhanced Computerized Tomography. Neurol Med Chir (Tokyo) 1985;25:969–974.
28. Takeuchi S, Ishii R, Tsuchida T, Tanaka R, Kobayashi K, Ito J. Cerebral hemodynamics in patients with moyamoya disease. A study of the epicerebral microcirculation by fluorescein angiography. Surg Neurol 1984;21:333–40.
29. Takeuchi S, Tanaka R, Ishii R, Tsuchida T, Kobayashi K, Arai H. Cerebral hemodynamics in patients with moyamoya disease. A study of regional cerebral blood flow by the ^{133}Xe inhalation method. Surg Neurol 1985;23:468–74.
30. Toole JF. Cerebrovascular disorders, 3d ed. New York: Raven Press, 1984.
31. Uemura K, Yamaguchi K, Kojima S, Sakurai Y, Ito Z, Kawakami H, Kutsuzawa T. Regional cerebral blood flow on cerebrovascular moyamoya disease. Study by ^{133}Xe clearance method and cerebral angiography. No To Shinkei 1975;27:385–93.
32. Waga S, Tochio H. Intracranial aneurysm associated with moyamoya disease in childhood. Surg Neurol 1985;23:237–43.
33. Whitnal SE. The anatomy of the human orbit, 2d ed. London: Oxford University Press, 1932.
34. Wollschlaeger G, Wollschlaeger PB. The Circle of Willis. In: Newton TH, Potts DG eds. Radiology of the Skull and Brain Vol 2, book 2. St Louis: C.V. Mosby Company, 1974: 1171–1201.
35. Yaburnoto M, Funahashi K, Fujii T, Hayashi S, Komai N. Moyamoya disease associated with intracranial aneurysm. Surg Neurol 1983;20:20–4.
36. Yamashita M, Oka K, Tanaka K. Histopathology of the brain vascular network in moyamoya disease. Stroke 1983;14:50–8.