Paretic Side/Normal Side Ratios of Cross-Sectional Areas of the Superior Oblique Muscle Vary Largely in Idiopathic Superior Oblique Palsy

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• PURPOSE: **To search for a new definition of muscle hypoplasia in congenital or idiopathic superior oblique muscle palsy.**
• DESIGN: **Retrospective case-control study.**
• METHODS: **Cross-sectional areas of the superior oblique and 4 rectus muscles near the eye globe–optic nerve junction were measured by an image analysis software on magnetic resonance images of 50 patients with congenital or idiopathic superior oblique muscle palsy and 45 patients with other disease conditions serving as a control. The paretic side/contralateral normal side ratios of the cross-sectional areas and the left side/right side ratios were calculated for the superior oblique muscle palsy patients and the control patients, respectively.**
• RESULTS: **The 95% confidence intervals in paretic side/contralateral side ratios of cross-sectional areas of the superior oblique muscle were 0.55 to 0.80 in the right-side superior oblique muscle palsy, and 0.48 to 0.75 in the left-side palsy, while the 95% confidence interval in the left side/right side ratios was 0.99 to 1.00 in the control. The 95% confidence intervals in the left side/right side ratios of the 4 rectus muscles were 1.00, both in the superior oblique muscle palsy and in the control.**
• CONCLUSIONS: **The muscle hypoplasia could be defined as such when the paretic side/contralateral side ratios of cross-sectional areas of the superior oblique muscle on magnetic resonance images fell outside the 95% confidence interval of the ratios in normal controls.**

CONGENITAL OR IDIOPATHIC SUPERIOR OBLIQUE muscle palsy is a common form of incomitant strabismus. Its etiology remains unknown, but genetic background is suggested based on the familial occurrence[1–6] or the structural abnormalities, such as muscle aplasia and hypoplasia.[7–11] Recently, magnetic resonance imaging has been used clinically to assess the status of the superior oblique muscle before surgery.[12–16] The hypoplasia of the superior oblique muscle is the major finding on imaging, and etiologic classification of the palsy is proposed based on the absence or the presence of muscle hypoplasia.

Some authors have suggested that idiopathic superior oblique muscle palsy with muscle hypoplasia be designated as true muscle palsy while palsy without muscle hypoplasia be designated as simulated muscle palsy.[17] A problem in this classification is the definition of the hypoplasia: for instance, the cross-sectional area of the muscle is less than 50% compared with that on the contralateral side. The extent of the muscle hypoplasia may have a spectrum ranging from aplasia to almost normal. In this study, we measured cross-sectional areas of the superior oblique muscle on both sides of patients with idiopathic superior oblique muscle palsy to obtain basic data for the definition of the hypoplasia.

METHODS

THIS STUDY INVOLVED 50 PATIENTS WHO WERE DIAGNOSED with idiopathic or congenital superior oblique muscle palsy and underwent orbital magnetic resonance imaging at Okayama University Hospital over 10 years, from January 1999 to December 2008. Of these 50 patients, 42 underwent surgery while the remaining 8 patients were followed without surgery. During the same 10-year period, 98 consecutive patients in total were diagnosed at Okayama University Hospital as having congenital or idiopathic superior oblique muscle palsy. Of these 98 patients, 48 patients were excluded from this study because magnetic resonance imaging was not done (16 patients) or the films for magnetic resonance images were not available (32 patients; imaging was done at other hospitals in 25 patients and at this hospital in 7 patients). Informed consent for magnetic resonance imaging was obtained in written form from each patient. Patients with acquired superior oblique muscle palsy, such as traumatic, ischemic, and vascular accident-related palsy, were excluded from the study.

All patients were questioned about age at onset, a history of previous head trauma, and family history of strabismus. Photographs at earlier ages were obtained to check abnormal head postures in some patients. Clinical

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TABLE 1. Clinical Features in 50 Patients With Congenital or Idiopathic Superior Oblique Muscle Palsy

	Mean (SD) of Deviation (Prism Diopters) in Primary Gaze With Head Straight, Determined by Alternate Prism and Cover Test[a]			
	Horizontal Deviation at 5 m	Vertical Deviation at 5 m	Horizontal Deviation at 0.3 m	Vertical Deviation at 0.3 m
Superior oblique muscle palsy in total (n = 50)	−6.9 (7.0)	19.9 (9.7)	−10.9 (10.3)	18.9 (11.7)
Right-side palsy (n = 29)	−8.4 (7.1)	R/L 20.4 (10.1)	−10.9 (10.3)	R/L 17.8 (9.6)
Left-side palsy (n = 20)	−5.3 (7.2)	L/R 19.0 (8.7)	−11.9 (10.7)	L/R 21.0 (14.2)
Bilateral palsy (n = 1)	−2.0	L/R 8.0	−2.0	L/R 5.0

[a]"Minus" indicates exodeviation; R/L, right hypertropia(phoria); and L/R, left hypertropia(phoria).

TABLE 2. Paretic Side/Contralateral Side Ratios or Left Side/Right Side Ratios of Cross-Sectional Areas of the 5 Extraocular Muscles in Patients With Idiopathic Superior Oblique Muscle Palsy and Patients With Other Conditions (Control Group)

		Paretic Side/Normal Side Ratio or Left Side/Right Side Ratio of Muscle Cross-Sectional Areas[a]				
Group	Muscle	Mean	SD	Median	Range	95% Confidence Interval
Idiopathic superior oblique muscle palsy group (n = 50)	Superior oblique (SO)					
	In total (n = 50)	0.66	0.33	0.67	0–1.03	0.57–0.75
	In total excluding SO aplasia (n = 45)	0.73	0.26	0.72	0.19–1.03	0.66–0.80
	Right-side palsy (n = 29)	0.67	0.35	0.80	0–1.03	0.55–0.80
	Right-side palsy excluding SO aplasia (n = 26)	0.75	0.27	0.86	0.19–1.03	0.65–0.86
	Left-side palsy (n = 20)	0.61	0.31	0.64	0–1.02	0.48–0.75
	Left-side palsy excluding SO aplasia (n = 18)	0.68	0.23	0.66	0.19–1.02	0.57–0.79
	Bilateral palsy (n = 1)	1				
	Superior rectus	1.00	0	1.00	0.99–1.01	1.00–1.00
	Inferior rectus	1.00	0	1.00	0.99–1.01	1.00–1.00
	Medial rectus	1.00	0.01	1.00	0.99–1.02	1.00–1.00
	Lateral rectus	1.00	0	1.00	0.99–1.01	1.00–1.00
Control group (n = 45)	Superior oblique	1.00	0.02	1.00	0.96–1.07	0.99–1.00
	Superior rectus	1.00	0	1.00	0.99–1.01	1.00–1.00
	Inferior rectus	1.00	0	1.00	0.99–1.01	1.00–1.00
	Medial rectus	1.00	0	1.00	0.99–1.01	1.00–1.00
	Lateral rectus	1.00	0	1.00	0.99–1.01	1.00–1.00

In superior oblique (SO) muscle palsy patients, paretic side/contralateral side ratios are shown for the superior oblique muscle in the right-side palsy or the left-side palsy while left side/right side ratio is shown in 1 patient with the bilateral palsy. In control patients, left side/right side ratios are shown for the superior oblique muscle. For the 4 rectus muscles, left side/right side ratios are shown in the superior oblique muscle palsy patients and the control patients.

[a]Paretic side value when contralateral normal side value = 1 or left side value when right side value = 1.

examinations included visual acuity, slit-lamp biomicroscopic and fundus examinations, tonometry, inspection of head posture, deviation measurement at 5 m and 0.3 m by alternate prism and cover test in 9 diagnostic positions of the gaze (Table 1), version, Bielschowsky head-tilt test, vertical fusional amplitude, and TNO stereotest.

Orbital magnetic resonance imaging was performed preoperatively in all patients to evaluate the status of the superior oblique muscle. The patients were instructed to close the eyes during the imaging. Of the 50 patients, 26 were male and 24 female, with age at magnetic resonance imaging ranging from 2 to 80 years (mean and standard deviation, 30.9 and 22.7 years). The palsy was on the right side in 29 patients, on the left side in 20 patients, and on both sides in 1 patient. The superior oblique muscle aplasia was found on the right side in 3 patients (1 male and 2 female) and on the left side in 2 patients (1 male and 1 female).

For the control, we selected 45 patients who underwent magnetic resonance imaging at Okayama University Hospital over 4 years, from 2003 to 2006, for other reasons: 11 patients suspected with orbital tumors, 10 patients suspected with optic neuropathy, 4 with thyroid diseases, 8 with other types of strabismus, 4 with anterior segment diseases, and 8 with screening for other conditions such as retinal diseases, uveitis, and glaucoma. The findings in the orbital structure were within normal parameters in these 45 patients. The 45 patients who served as controls in this

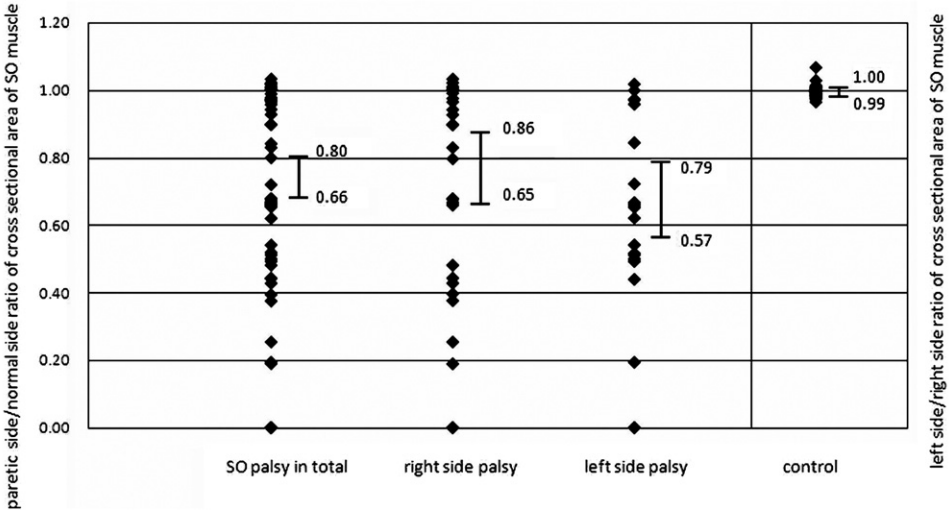

FIGURE. The distribution of paretic side/contralateral normal side ratios of cross-sectional areas of the superior oblique (SO) muscle in 50 patients with idiopathic superior oblique muscle palsy and the distribution of right side/left side ratios of cross-sectional areas of the superior oblique muscle in 45 patients with other conditions serving as a control. The left side/right side ratio is used in 1 patient with bilateral superior oblique muscle palsy. The number of patients with right-side palsy is 29, including 3 patients with muscle aplasia, while the number of patients with left-side palsy is 20, including 2 patients with muscle aplasia. The paretic side/contralateral side ratios are 0 in these 5 patients with muscle aplasia. The 95% confidence intervals for the superior oblique muscle palsy in total, right side palsy, and left side palsy do not include these 5 patients with muscle aplasia. Note a wide range of the 95% confidence interval in the patients with superior oblique muscle palsy in total, compared with the control. The 95% confidence intervals in the right-side superior oblique muscle palsy and in the left-side palsy do not overlap with the 95% confidence interval in controls.

study were 20 male and 25 female subjects, with age at magnetic resonance imaging ranging from 2 to 88 years (mean and standard deviation, 51.0 and 19.7 years). Between the 50 patients with the superior oblique muscle palsy and the 45 control patients, the male-female ratio was not statistically different ($P > .05$, χ^2 test), while the age of the 50 patients with the muscle palsy was significantly younger than that of the 45 control patients ($P = .0001$, Mann-Whitney U test).

A coronal section slice at the nearest location posterior to the eye globe and optic nerve junction was chosen from T1-intensified orbital magnetic resonance images. These magnetic resonance images were taken by different machines with different slice thickness and were printed on films with varying magnifications. Of the 50 patients with the superior oblique muscle palsy, the coronal images were at 3-mm intervals in 41 patients and at 4-mm intervals in 9 patients, while the images were at 3-mm intervals in 2, at 4-mm intervals in 39, and at 5-mm intervals in 4 of the 45 control patients. The selected slices of the magnetic resonance imaging films placed on a show case were captured by a digital camera at the highest magnification possible with good focus, and captured images were transferred to a computer. Using Scion Image for Windows software (Scion Corporation, Frederick, Maryland, USA), cross sections of the superior oblique muscle and 4 rectus muscles were encircled manually with a mouse and the number of square pixels in the encircled area was measured to obtain the area of the cross section. The measurements were repeated 5 times and a mean was calculated to get a representative value for the cross-sectional area of the muscle.

For the superior oblique muscle of patients with either right-side or left-side superior oblique muscle palsy, the value on the paretic side was divided by the value on the contralateral normal side to obtain the paretic side/contralateral normal side ratios. For the superior oblique muscle of control patients and 1 patient with bilateral superior oblique muscle palsy, the value on the left side was divided by the value on the right side to obtain the left-to-right ratio for statistical analysis. The left side/right side ratios of the cross-sectional areas were calculated for the 4 rectus muscles both in the superior oblique muscle palsy patients and in the control patients.

RESULTS

THE PARETIC SIDE/CONTRALATERAL NORMAL SIDE RATIOS of cross-sectional areas of the superior oblique muscle varied widely in 50 patients with idiopathic superior oblique muscle palsy. In contrast, the left side/right side ratios for the superior oblique muscle in a control group of 45 patients with other conditions showed no variation at all (Table 2, Figure).

The 50 patients with idiopathic superior oblique muscle palsy were classified into 3 groups: 29 patients with right-side palsy, 20 patients with left-side palsy, and 1 patient with bilateral palsy. The paretic side/contralateral

side ratios of cross-sectional areas of the superior oblique muscle in the right-side palsy distributed from 0 to 1.03 (mean and standard deviation, 0.67 and 0.35) while the ratios distributed from 0 to 1.02 in the left-side palsy (mean and standard deviation, 0.61 and 0.31). In contrast, the left side/right side ratios of cross-sectional areas of the superior oblique muscle in 45 control patients distributed from 0.96 to 1.07 (mean and standard deviation, 1.00 and 0.02). The paretic side/contralateral side ratios in 9 of the 29 right-side palsy patients and in 5 of the 20 left-side palsy patients fell within this range of 0.96 to 1.07 for the left side/right side ratios in the control patients. The paretic side/contralateral side ratios in all the palsy patients, in the right-side palsy patients, and in the left-side palsy patients were significantly different from the left side/right side ratios of cross-sectional areas of the superior oblique muscle in the control patients ($P < .05$, Tukey-Kramer test; $P < .001$, 1-factor ANOVA).

After the 5 patients with superior oblique muscle aplasia (3 with right-side aplasia and 2 with left-side aplasia) were excluded, the 95% confidence intervals of the paretic side/contralateral side ratios for the superior oblique muscle were in the range of 0.65 to 0.86 in the right-side palsy and 0.57 to 0.79 in the left-side palsy patients, respectively (Table 2, Figure). The 95% confidence interval of the left side/right side ratios for the superior oblique muscle in control patients was in a small range of 0.99 to 1.00 and did not overlap with the 95% confidence intervals of the paretic side/contralateral side ratios in the right-side superior oblique muscle palsy or in the left-side palsy (Figure).

The left side/right side ratios of cross-sectional areas of the other extraocular muscles were also calculated in the 50 patients with idiopathic superior oblique muscle palsy and in the 45 control patients. The left side/right side ratios in the 4 rectus muscles showed extremely small ranges around 1 and the 95% confidence intervals were at 1 both in the superior oblique muscle palsy patients and in the control patients (Table 2).

DISCUSSION

THE GOAL OF THIS STUDY IS TO ESTABLISH THE DEFINITION of superior oblique muscle hypoplasia in patients with congenital or idiopathic superior oblique muscle palsy. Magnetic resonance imaging has shown that aplasia or hypoplasia is a hallmark of congenital or idiopathic superior oblique muscle palsy. The aplasia is rather rare but is understood easily, while the definition of muscle hypoplasia is arbitrary. Most studies have defined hypoplasia as when the cross-sectional area of the muscle on the affected side is less than 50% of the muscle on the contralateral side. However, it is speculated that the hypoplasia of the muscle might have a spectrum ranging from aplasia to the nearly normal muscle.

To search for a better definition of hypoplasia, we measured cross-sectional areas of the 5 extraocular muscles, including the superior oblique muscle and the 4 rectus muscles, in patients with idiopathic superior oblique muscle palsy and in control patients with other conditions. The measurement of cross-sectional areas of the muscle was adopted for simplicity, in contrast with muscle volume measurements reported in past studies.[18,19] In this study, we demonstrated that the paretic side/contralateral side ratios of the cross-sectional areas of the superior oblique muscle showed a large range of variation only in the patients with idiopathic superior oblique muscle palsy.

It should be noted that the ranges of left side/right side ratios of the cross-sectional areas of the 4 rectus muscles were in an extremely small range at 1 in the patients with idiopathic superior oblique muscle palsy, including 5 patients with muscle aplasia and 1 patient with bilateral muscle palsy. Furthermore, the left side/right side ratios of the cross-sectional areas of the superior oblique muscle were in an extremely small range at 1 in the control patients. These facts indicate that the cross-sectional areas of the extraocular muscles in normal conditions were the same between the right side and the left side. In contrast, the cross-sectional areas of the superior oblique muscle varied between the right side and the left side of the patients with idiopathic superior oblique muscle palsy, indicating the hypoplasia of the muscle in varying degrees.

This study also showed that the 95% confidence intervals of the paretic side/contralateral side ratios of cross-sectional areas of the superior oblique muscle in 2 separate groups of the right-side superior oblique muscle palsy and the left-side palsy were located clearly outside the small range of the 95% confidence interval of the left side/right side ratios in the control patients. In this context, muscle hypoplasia could be defined as such when the paretic side/contralateral side ratios of the cross-sectional areas of the superior oblique muscle fall outside the 95% confidence interval of the ratios in the normal conditions. Another way of defining the muscle hypoplasia is to use the paretic side/contralateral side ratios that are located outside the range of the left side/right side ratios of cross-sectional areas of the superior oblique muscle in normal controls.

The drawbacks in this study involve 2 points: 1 is the definition of the normal conditions and the other is the use of magnetic resonance images taken in varying conditions at different clinical settings. Firstly, magnetic resonance images in 45 patients with other disease conditions were used as a control in this study. Ideally, images from normal subjects should be used as a control. Secondly, magnetic resonance images of the patients with idiopathic superior oblique muscle palsy and the patients with other disease conditions were taken under markedly different conditions with different appliances. Coronal sections of magnetic resonance images varied from patient to patient at the interval of 3 or 4 or 5 mm and 1 section nearest posterior to the eye globe–optic disc junction was chosen to measure the cross-sectional areas

of the muscles. The exact location of the coronal sections, relative to the eye globe–optic disc junction, thus varied from patient to patient up to 5 mm. Furthermore, coronal sections of magnetic resonance images were not perpendicular to the orbital axis along the optic nerve, and therefore cross sections of the muscles were cut obliquely.[20] The patients closed the eyes in the usual condition of magnetic resonance imaging. In contrast, patients are instructed to open 1 eye with the fellow eye occluded to gaze at a certain target in the standardized condition to obtain quasi-coronal images perpendicular to the long axis of the orbit.[20] To overcome these weak points, we used the paretic side/contralateral side or the left side/right side ratios of the cross-sectional areas of the muscles and also measured the 4 rectus muscles as references.

In conclusion, this study showed a wide range of paretic side/contralateral side ratios of the cross-sectional areas of the superior oblique muscle only in the patients with congenital or idiopathic superior oblique muscle palsy. Magnetic resonance images at the usual clinical setting can be used as such to obtain a rough estimation of the muscle hypoplasia. The hypoplasia of the superior oblique muscle would be defined when the paretic side/contralateral side ratios of the cross-sectional areas of the muscle fall outside the narrow range of the ratios in normal conditions. Better definition of the muscle hypoplasia would lead to the establishment of the diagnostic entity of congenital or idiopathic superior oblique muscle palsy, and hence would provide a better basis for genetic analyses of the disease.[6,21,22]

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