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· Clinical Research ·

Magnetic resonance imaging of extraocular rectus muscles abnormalities in acute acquired concomitant esotropia

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Abstract

● **AIM:** To investigate the difference of medial rectus (MR) and lateral rectus (LR) between acute acquired concomitant esotropia (AACE) and the healthy controls (HCs) detected by magnetic resonance imaging (MRI).

● **METHODS:** A case-control study. Eighteen subjects with AACE and eighteen HCs were enrolled. MRI scanning data were conducted in target-controlled central gaze with a 3-Tesla magnetic resonance scanner. Extraocular muscles (EOMs) were scanned in contiguous image planes 2-mm thick spanning the EOM origins to the globe equator. To form posterior partial volumes (PPVs), the LR and MR cross-sections in the image planes 8, 10, 12, and 14 mm posterior to the globe were summed and multiplied by the 2-mm slice thickness. The data were classified according to the right eye, left eye, dominant eye, and non-dominant eye, and the differences in mean cross-sectional area, maximum cross-sectional area, and PPVs of the MR and LR muscle in the AACE group and HCs group were compared under the above classifications respectively.

● **RESULTS:** There were no significant differences between the two groups of demographic characteristics. The mean cross-sectional area of the LR muscle was significantly greater in the AACE group than that in the HCs group in the non-dominant eyes (P=0.028). The maximum cross-sectional area of the LR muscle both in the dominant and non-dominant eye of the AACE group was significantly greater than the HCs group (P=0.009, P=0.016). For the dominant eye, the PPVs of the LR muscle were significantly greater in the AACE than that in the HCs group (P=0.013), but not in the MR muscle (P=0.698).

● **CONCLUSION:** The size and volume of muscles dominant eyes of AACE subjects change significantly to overcome binocular diplopia. The LR muscle become larger to compensate for the enhanced convergence in the AACE.

● **KEYWORDS:** acute acquired concomitant esotropia; magnetic resonance imaging; extraocular muscles
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INTRODUCTION

Acute acquired concomitant esotropia (AACE) is a type of esotropia with sudden binocular diplopia[1-3]. They present with diplopia in the horizontal direction and good eye movements in all directions. Since the visual system of adolescents and adults is mostly well developed, the binocular diplopia symptoms produced at the onset of AACE are more difficult to eliminate naturally. Symptoms such as visual fatigue, dizziness, nausea, and inability to perform fine work can easily occur, seriously affecting the visual quality and daily life of subjects. AACE has divided into three categories by Burian and Miller[4]: Swan (type 1), Franceschetti (type 2) and Bielschowsky (type 3)[5]. The prevalence and incidence of AACE have been rarely reported. Recently, the number of AACE subjects has been increased dramatically, but its pathogenesis remains unclear. According to previous studies, the risk factors of AACE was considered to be accommodative spasm, uncorrected myopia, intracranial diseases, excessive near work, and physical or psychic exhaustion[6-12], all of which eventually caused an imbalance in the strength of the extraocular muscle (EOM) with an acute onset of esotropia.

EOM maintains the eye position by balancing the strength of interacting muscles. The disturbance of the strength could be evaluated through the size and volume of EOM. Several research has examined the connection between EOM size and clinical signs of EOM motility, and several of them have found a specific link between radiographic EOM enlargement and motility restriction. The two-dimensional measurement of mean cross-sectional area would give a more precise indication of the true “size” of the muscles, particularly in thyroid eye illness[12-14]. A systematic study of human horizontal rectus EOM contractility has demonstrated that EOM morphologic changes in single-plane maximum cross-sectional areas and posterior partial volumes (PPVs) provide accurate and quantitative measures of EOM contractility[15], which indicated the morphologic changes of EOM in response to EOM strength. Orbital magnetic resonance imaging (MRI)[16] was a noninvasive technique for characterizing EOM in the size and volume, which described the muscle insertion location, pulley position, cross-section and volume[17-19]. The previous study has demonstrated high correlations to conjugate horizontal duction angle for both maximum cross-sectional area and PPV, a morphometric that integrates area over multiple contiguous cross-sections and thus can be considered a noninvasive indicator of contractility[20].

In recent years, variations in MRI of the horizontal rectus muscles have been recorded from diverse types of strabismus. A and V syndromes were considered to be associated with vertical displacement of media rectus (MR) and lateral rectus (LR), as well as horizontal displacement of superior rectus (SR) and inferior rectus (IR)[21]. In the subjects with paralytic strabismus, the cross-sectional area of the paralytic muscle was smaller than that of the normal side in different fixation directions, and the variation range of the cross-sectional area was smaller when the paralytic muscle contracted and relaxed[22]. The rectus muscle cross-sectional area was increased in subjects with thyroid-related eye disease while that was decreased in contraction and relaxation[23]. In subjects with Duane regression syndrome, MRI also confirmed the significantly increased cross-sectional area of the affected MR muscle and the simultaneous contraction of the MR and LR muscles. All the above studies proved that it was feasible to use MRI for detecting the morphology of EOM to evaluate muscle strength. Until now, no study documented the changes of size and volume in EOM for AACE subjects, which could highlight the pathogenesis of AACE in the changing of EOM strength.

In the present study, the hypothesis was that the morphology of horizontal rectus EOM was changed in AACE, which reflects the misbalancing of EOM strength. The purpose was to investigate the difference in the size and volume of LR and MR muscles between AACE and the healthy controls (HCs) detected by MRI. The clinical application of MRI to investigate extraocular rectus muscles abnormalities in AACE would be a useful tool to detect the pathogenesis of AACE, which could improve the understanding of the disease in a radiography way.

SUBJECTS AND METHODS

Ethical Approval The study was approved by the medical research ethics committee and institutional review board of Capital Medical University, Beijing Tongren Hospital (No. TRECKY2021-228), and written informed consent was obtained from all participants or their guardians. The study protocols were in accordance with the Declaration of Helsinki.

Subjects We used a case-control study to explore changes in the morphology of the EOMs in subjects with AACE. Eighteen subjects with AACE were enrolled in the study (8 men and 10 women), with a mean age of 23.00±10.80y (range 10–47y) from Beijing Tongren Hospital between 1 March 2021 and 1 September 2021 while 18 HCs were also recruited for matching sex and age (mean age 22.61±10.38y, range 10–41y, 7 men and 11 women) from the local community. All participants underwent detailed ophthalmological examinations that included measurement of best-corrected visual acuity (BCVA), dominant eye, refraction (cyclopentolate hydrochloride for participants under 14 years old; compound tropicamide mydriatic for the 14–40 years old; manifest refraction for participants over 40 years old), synoptically, alternate cover test, eye movement and strabismus deviation measured at distance and near using alternate and prism cover tests.

MRI Data Acquisition MRI scanning data were performed with a 3-T magnetic resonance scanner (Prisma, Siemens, Germany). A matched 64-channel phase-array head coil was utilized, with earplugs and foam padding to reduce scanner noise and head motion. During scanning, all subjects were asked to lie on the examination bed and remain as still as possible. The subject could view the projected visual stimuli on a translucent screen through an angled mirror that was placed above the subjects’ eyes. The visual angle was 45°, and there was a space of about 1 m between the translucent screen and the subjects’ eyes. Subjects wore MRI spectacles to correct ametropia[24]. The target was focal and visible to only one eye, the other eye was covered, so accommodation and binocular convergence on it was impossible, as verified by axial MRI. Targets were placed in the central position for the scanned eye. The 192 high-resolution images for each eye were acquired parallel to the anterior commissure-posterior commissure line, which took 4min and 6s. The sagittal three-dimensional T1-weighted sequence comprised the following parameters:

Table 1 Demographics and clinical measurements of AACE subjects and HCs

Parameters	AACE	*n*	HCs	*n*	t/χ^2(95%CI)	*P*
Sex (male/female)	10/8	18	7/11	18	N/A	0.317
Age (y)	23.00±10.80	18	22.61±10.38	18	-6.7861, 7.5639	0.913
Symptom duration (mo)	33.34±22.84	18	N/A	18	N/A	N/A
Dominant eye (R/L)	8/10	18	12/6	18	N/A	0.180
BCVA (R)	0.98±0.04	18	1.00±0.00	18	-0.0357, 0.0024	0.083
BCVA (L)	0.97±0.08	18	1.00±0.00	18	-0.0689, 0.0133	0.172
SER (D)-R	-4.28±2.30	18	-3.81±2.81	18	-2.2053, 1.2748	0.590
SER (D)-L	-3.82±2.51	18	-3.89±2.67	18	-1.6864, 1.8252	0.936
Preop. esodeviation (Δ)-near	32.50 (27.50)	18	N/A	18	N/A	N/A
Preop. esodeviation (Δ)-far	35.00 (27.50)	18	N/A	18	N/A	N/A
Simultaneous vision (°)	22.72±10.62	18	-0.31±1.30	16	17.7246, 28.3448	<0.001[b]
Collective fusion (°)	33.43±10.60	14	14.50±6.47	16	12.4560, 25.4012	<0.001[b]
Diffuse fusion (°)	13.21±13.01	14	-13.00±7.94	16	18.2678, 34.1608	<0.001[b]
Fusion range (°)	20.21±8.10	14	27.5±7.53	16	1.3993, 13.1722	0.017[a]
Stereopsis (+/-)	7/11	18	18/0	18	N/A	<0.001[b]

Data are presented as mean±SD or median (IQR). HCs: Healthy controls; AACE: Acute acquired concomitant esotropia; BCVA: Best-corrected visual acuity; R: Right eye; L: Left eye; SER: Spherical equivalent refraction; CI: Confidence interval; N/A: Not applicable. [a]$P<0.05$; [b]$P<0.001$.

repetition time =2000ms, echo time =2.25ms, thickness =1.0 mm, no gap, acquisition matrix =256×256, the field of view =256 mm ×256 mm, flip angle =8°.

Image Processing The images were reconstructed by Syngo magnetic resonance E11 workstation of Siemens. The quasi-coronal image plane (perpendicular to the orbital axis) closest to the junction of the globe and optic nerve was defined to be the image plane 0, with more anterior image planes designated positive and posterior planes designated negative. High-resolution (312-μm), axial and quasi-coronal images of 2-mm thickness and matrix of 256×256 perpendiculars to the long axis of the orbit were obtained in target-controlled central gaze for each eye. The MR and LR muscles were outlined in each plane, and their cross-sectional areas were measured using Image J (Figure 1). Mean cross-sectional areas of the horizontal EOMs were computed in contiguous image planes 2-mm thick spanning the EOM origins to the globe equator. Image planes -4, -5, -6, and -7 (8–14 mm posterior to the globe optic nerve junction) were summed and multiplied by 2 mm to form PPVs[19].

Statistical Analysis In this study, frequency and percentage were used to describe gender and stereopsis, and the Chi-square test was used for the comparison between groups. Quantitative data such as age, symptom duration, equivalent spherical refraction, prism diopter, maximum cross-sectional area, mean cross-sectional area, PPVs, were described by mean±standard deviation, and the comparison between the two groups was tested by independent *t*-test. Median and quartile spacing were used if data were not in a normal distribution, and nonparametric tests were used for the comparisons. SPSS 26.0 (IBM Corp, Armonk, NY, USA) was used for data processing, and differences were regarded as statistically significant at $P<0.05$.

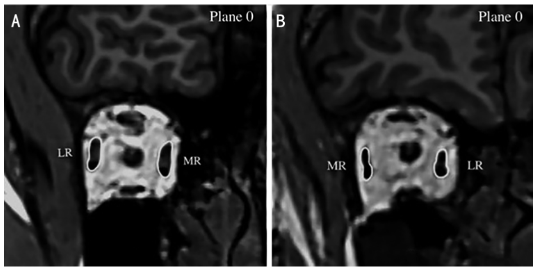

Figure 1 Quasicoronal MRI of the right orbit of the central gaze of AACE group (B) and HCs group (A), of the globe-optic nerve junction at plane 0 LR: Lateral rectus muscle; MR: Medial rectus muscle.

RESULTS

Demographic Characteristics The basic characteristics of the 18 AACE subjects and 18 HCs are given in Table 1. There were no significant differences between the two groups of sex (P=0.317), age (P=0.913), dominant eye (P=0.180), BCVA (right: P=0.083; left: P=0.172) and spherical equivalent refraction (SER; right: P=0.590; left: P=0.936). However, simultaneous vision (P<0.001), collective fusion (P<0.001), diffuse fusion (P<0.001), fusion range (P=0.017) and stereopsis (P<0.001) were significantly reduced in the AACE group than that in the controls.

Subjects in the AACE group all had complaints of binocular diplopia, which started out only when looking at a distance. In some patients, the symptoms worsened over time, *i.e.*, they were also present when looking at near. The course of their disease varied from a minimum of 6d to a maximum of 68mo. All the AACE subjects had not undergone surgery before the MRI scanning.

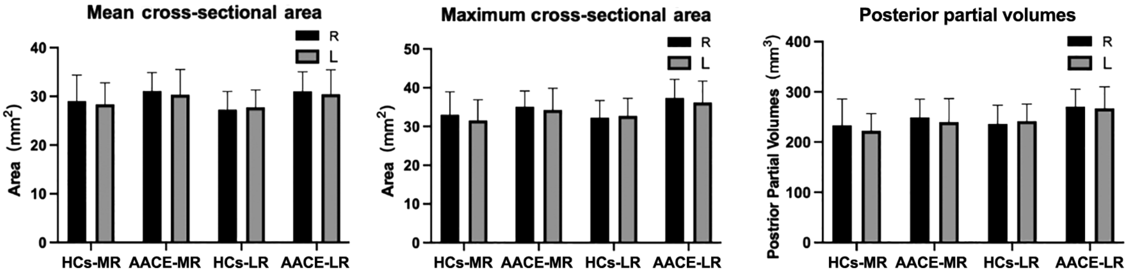

Figure 2 Comparison of the MR or LR muscles within individuals between right and left eyes in both groups Data are presented as mean±SD. R: Right eye; L: Left eye; HCs: Healthy controls; AACE: Acute acquired concomitant esotropia; HCs-MR: Medial rectus muscle of HCs group; HCs-LR: Lateral rectus muscle of HCs group; AACE-MR: Medial rectus muscle of AACE group; AACE-LR: Lateral rectus muscle of AACE group.

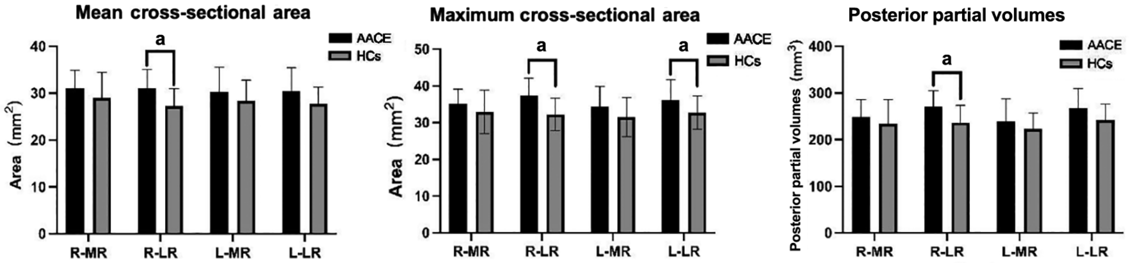

Figure 3 Comparison of the MR or LR muscles in the left and right eyes in different groups Data are presented as mean±SD. R-MR: Medial rectus muscle of the right eye; R-LR: Lateral rectus muscle of the right eye; L-MR: Medial rectus muscle of the left eye; L-LR: Lateral rectus muscle of the left eye. [a]*P*<0.05.

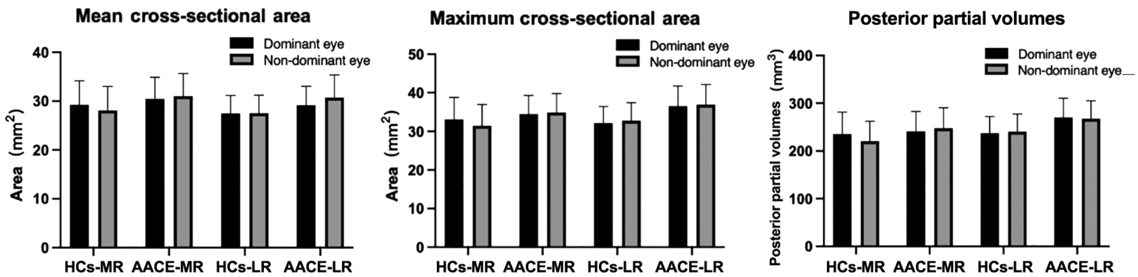

Figure 4 Comparison of the MR or LR muscles within individuals between dominant and non-dominant eyes in both groups Data are presented as mean±SD. HCs: Healthy controls; AACE: Acute acquired concomitant esotropia; HCs-MR: Medial rectus muscle of HCs group; HCs-LR: Lateral rectus muscle of HCs group; AACE-MR: Medial rectus muscle of AACE group; AACE-LR: Lateral rectus muscle of AACE group.

Changes in Mean Cross-sectional Area of Horizontal Rectus EOM The mean cross-sectional area of the LR or MR muscles was measured in the plane of the 0–14 mm image under central gaze in the AACE group and HCs group, respectively.

Changes between the right and left eyes: in the AACE group, the mean cross-sectional area of the MR or LR muscles was not statistically different between the right and left eyes respectively, and the same results were obtained in the HCs group (P>0.05; Figure 2). However, for comparisons between AACE and the controls, the mean cross-sectional area of the LR muscle was significantly greater in the AACE group than that of the HCs group in the right eyes (P=0.006; Figure 3), but no statistical difference existed in the left eyes (P>0.05; Figure 3).

Changes between the dominant and non-dominant eyes: in the AACE group, there were no statistical differences in the mean cross-sectional area of the MR or LR muscles between the dominant and non-dominant eyes, while the same results were obtained for the HCs group (P>0.05; Figure 4). However, the mean cross-sectional area of the LR muscle was significantly greater in the AACE group than in the HCs group in the non-dominant eyes (non-dominant eye, P=0.028; Figure 5).

Changes in Maximum Cross-sectional Area of Horizontal Rectus EOM The cross-sectional areas of the LR or MR muscles in the right and left eyes were measured in the 0–14 mm image plane under the central gaze, respectively. The largest single-plane cross-sectional area of the subjects in the AACE group and the HCs group were selected for statistics.

Changes between the right and left eyes: there was no significant difference between the eyes of the same person in each group (P>0.05; Figure 2). The results showed that the single-plane maximum cross-sectional area of the LR muscle was significantly greater in the AACE group than in the normal

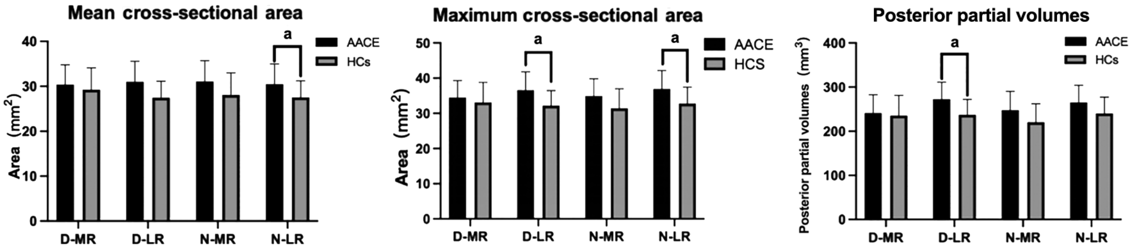

Figure 5 Comparison of the MR or LR muscles in the dominant and non-dominant eyes in different groups Data are presented as mean±SD. D-MR: Medial rectus muscle of the dominant eye; D-LR: Lateral rectus muscle of the dominant eye; N-MR: Medial rectus muscle of the non-dominant eye; N-LR: Lateral rectus muscle of the non-dominant eye. $^{a}P<0.05$.

group in both the right and left eyes (right eye, P=0.002; left eye, P=0.048; Figure 3), while there was no significant difference in the MR muscles (P>0.05; Figure 3).

Changes between the dominant and non-dominant eyes: there was no significant difference between the eyes of the same person in each group (P>0.05; Figure 4). We found that the maximum cross-sectional area of the LR muscle was larger in the AACE group than in the HCs group in both the dominant eye and the non-dominant eye (dominant eye, P=0.009; non-dominant eye, P=0.016; Figure 5).

Changes in PPVs of Horizontal Rectus EOM The PPVs of the LR or MR muscles needed to be measured in the plane of the 8–14 mm image under central gaze in the AACE group and HCs group, respectively.

Changes between the right and left eyes: in the AACE group, the PPVs of MR or LR muscles were not statistically different between the right and left eyes respectively, and the same results were achieved in the HCs group (P>0.05; Figure 2). However, in the right eyes, the PPVs of the LR muscle were significantly greater in the AACE group than in the HCs group (P=0.007; Figure 3), but there was no statistical difference in the left eyes (P>0.05; Figure 3).

Changes between the dominant and non-dominant eyes: there was no statistical difference in the PPVs of the MR or LR muscles between the dominant and non-dominant eyes in the AACE group, and the same results were obtained in the HCs group (P>0.05; Figure 4). For the dominant eye, the PPVs of the LR muscle were significantly greater in the AACE than that in the HCs group (P=0.0013; Figure 5), but not in the MR muscle (P>0.05; Figure 5). Furthermore, in the non-dominant eyes, the MR or LR muscles were not significantly different between the two groups (P>0.05; Figure 5).

DISCUSSION

The results of the present study demonstrated that the maximum cross-sectional area and the PPVs of the LR muscle in the dominant eye were significantly greater in the AACE subjects than that in the HCs group, while in the non-dominant eye, only the maximum and the mean cross-sectional area of the LR muscle of AACE was significantly larger than that in the controls. These findings indicated that AACE subjects undergo morphological changes in the LR muscle to overcome binocular diplopia. This is a type of compensatory mechanism. The LR and MR muscles are the interacting muscles to balance the horizontal strength. In this study, the maximum and mean cross-sectional area and PPVs of LR muscle were significantly higher in the AACE group than that in the HCs group either in the dominant eyes or in the non-dominant eyes, but not the MR muscles. Similar results also existed in the PPVs of the LR muscle in the dominant eyes. The PPVs of the LR muscle were significantly greater in the AACE group than that in the HCs group, but not in the MR muscle. The LR muscles always appeared larger in the AACE subjects may be attributed to the compensatory mechanism. The esotropia of AACE may happen with the sudden imbalance of interacting muscles to maintain the converging and diverging forces, in which the converging forces could be stronger[5]. To overcome the enhanced converging force, the LR muscle could become to make up the convergence and increase the diverging forces.

Similar to the results of other related studies[24], our research also found that all subjects were medium myopia, with the SER of -4.28±2.30 (right) and -3.82±2.51 D (left). The accommodative lag and the adjustment demands of near vision may be the reason for the occurrence of AACE. It has also been asserted that ocular dominance plays a major role in the development of myopia[25]. The sighting of dominance has been regarded to be the most closely related to the fixation preference[26]. The dominance or fixation preference is important in the visual function. Sighting dominance[27-29] refers to the preferential use of one eye over the fellow eye in fixating a target. It seems to be an acquired and habitual skill developed mostly at the age of 5 years old[30]. Assessing ocular dominance or fixation preference plays an important role in managing a variety of ocular conditions, especially when choosing the eyes to be operated on or patched for therapy. Some studies also point out the existence of an excellent correlation between sighting dominance and muscle stability. In a previous study[31], 227 out of 229 (99.12%) subjects tested, the sighting dominant eye was matched with the eye with stronger muscle, indicating the dominant eye has a stronger compensatory power. Our results showed that the cross-sectional area of LR muscle was significantly larger in the dominant or non-dominant eyes of AACE than that in the HCs group, which highlighted the importance of dominant or non-dominant eyes in the role of the pathogenesis of AACE. Moreover, only PPVs of LR muscles were observed significantly larger in the dominant eyes of AACE than those in the HCs, but not significant in the non-dominant eyes. Because PPVs are more significant in response to EOM strength[11], this study showed dominant eyes changed more for trying to recover the binocular vision.

In patients with AACE, the eye position is incorrect, causing the images sent to the brain from the two eyes to be too different for the cerebral cortex to fuse the two images, which leads to the development of binocular diplopia[32]. In our study, most of the AACE subjects retained their fusion function, yet their fusion range was much smaller than that of the HCs group, which might be related to the presence of esotropia. Patients with AACE are usually older children and adults who had good binocular vision before the onset of the disease. We hypothesized that the sudden onset of esotropia caused abnormalities in their fusion function and subsequent binocular diplopia. To overcome binocular diplopia, the LR muscles of both eyes receive more nerve impulses and are thickened compensatorily.

There are many treatment options for AACE[10,33-36]. Previous research has suggested that strabismus surgery for AACE can successfully improve diplopia and restore good binocular function in patients who do not have underlying intracranial problems[37-40]. In AACE, surgical approaches include unilateral medial rectus recession and lateral rectus (R&R) resection, bilateral medial rectus recession, or bilateral LR resection. Depending on the surgeon's preferences, different surgical methods may be used. Because it has been demonstrated to be as effective as or even more effective than bilateral medial rectus recession for AACE treatment, particularly for larger-angle deviations[33,41-43], and because it preserves a new eye for potential future surgeries, unilateral R&R is preferred. Our research may offer a theoretical foundation for treatment selection, and R&R may be preferable, particularly in the dominant eye.

There are some limitations in the present study. First, the sample size of AACE subjects should be enlarged and the average age was young, which needs deep investigation to correlated the pathology of MRI and AACE. Second, MRI scanning data were performed only in the central gaze, lacking the scanning data in abduction and adduction, which applies more towards hypertrophy. Further studies are needed to describe the changing of EOM in the muscles status of contraction and stretch.

In conclusion, the maximum cross-sectional area and the PPVs of the LR muscle in the dominant eye were significantly larger in the AACE subjects than that in the controls. To overcome binocular diplopia and esotropia of AACE, the size and volume of dominant eyes changed significantly, and the LR muscle became larger to compensate for the enhanced convergence in the esotropia of AACE.

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