



ORIGINAL ARTICLE

Orbital magnetic resonance imaging is useful in age-related distance esotropia



Pilar Gómez de Liaño Sanchez, Gloria Olavarri González*, Pilar Merino Sanz, Jose C. Escribano Villafruela

Ocular Motility and Strabismus Department, General University Hospital Gregorio Marañón, Madrid, Spain

Received 23 November 2016; accepted 19 April 2017
Available online 7 June 2017

KEYWORDS

Age-related distance esotropia;
Aging;
Extraocular rectus muscles;
Orbital magnetic resonance imaging;
Sagging eye syndrome;
Superior rectus–lateral rectus intermuscular band

Abstract

Purpose: To describe findings for orbital magnetic resonance imaging (MRI) in patients with age-related distance esotropia (ARDE).

Methods: We compared 31 orbital MRI from patients with ARDE (77 ± 7 SD years) with 2 control groups: 32 orbits from individuals aged 18–50 years (33 ± 8 SD years) and 16 orbits from individuals aged >60 years (77 ± 7 SD years). MRI scans were acquired using 3D fast field echo in T1 sequence without fat saturation. Exclusion criteria for all groups were neurological or thyroid disease and a relevant ophthalmological history (e.g., high myopia, diplopia from another etiology, complicated cataract surgery, etc.). Muscle displacement and characteristics of the lateral rectus–superior rectus (LR–SR) intermuscular band were analyzed.

Results: The analysis of the muscles and angles revealed a series of statistically significant differences ($p < 0.07$) between the groups. Subjects with ARDE had LR pulley positions 1.32 ± 0.19 mm lower than in younger controls, and the medial rectus (MR) pulley positions were 0.68 ± 0.19 mm lower than in younger. Older controls had LR and MR pulley positions 0.85 ± 0.20 mm and 0.49 ± 0.23 mm lower than in younger. ARDE subjects had LR pulley positions 0.46 ± 0.26 mm lower than in older control group. The LR–SR band was absent in 35.5% of ARDE patients and in 12.5% of older control group ($p = 0.168$).

Conclusions: MRI showed that displacements of LR and LR–SR band degeneration could facilitate the diagnosis of patients with ARDE.

© 2017 Spanish General Council of Optometry. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author at: Instituto Provincial de Oftalmología, Calle General Arrando número 17, 28010 Madrid, Spain.
E-mail address: gloria.olavarri@gmail.com (G. Olavarri González).

PALABRAS CLAVE

Esotropía asociada a la edad;
Envejecimiento;
Músculos rectos extraoculares;
Imagen de resonancia magnética orbitaria;
Síndrome de "sagging eye";
Banda intermuscular recto superior-recto lateral

Utilidad de la resonancia magnética orbitaria en la esotropía asociada a la edad**Resumen**

Objetivo: Describir los hallazgos encontrados en la resonancia magnética orbitaria (RMN) en pacientes con esotropía asociada a la edad (ETAE).

Métodos: Comparamos 31 RMN orbitarias de pacientes con ETAE (77 ± 7 DE años) con 2 grupos control: 32 órbitas de individuos con edades comprendidas entre 18 y 50 años (33 ± 8 DE años) y 16 órbitas de individuos con edades >60 años (77 ± 7 DE años). Las RMN se adquirieron utilizando eco de campo rápido 3D en secuencia T1 sin saturación de grasa. Los criterios de exclusión para todos los grupos fueron enfermedad neurológica o tiroidea y antecedentes oftalmológicos relevantes (ej.: alta miopía, diplopía de otra etiología, cirugía complicada de cataratas ...). Se analizaron el desplazamiento muscular y las características de la banda intermuscular recto lateral-recto superior (RL-RS).

Resultados: El análisis de los músculos y ángulos reveló una serie de diferencias estadísticamente significativas ($p < 0,07$) entre los grupos. Los sujetos con ETAE presentaban la polea del RL $1,32 \pm 0,19$ mm inferior a los controles jóvenes y la polea del recto medial (RM) $0,68 \pm 0,19$ mm inferior a los sujetos jóvenes. Los controles de mayor edad tenían las poleas del RL y del RM posicionadas $0,85 \pm 0,2$ mm y $0,49 \pm 0,23$ mm inferiores a los jóvenes. Los sujetos con ETAE tenían la polea del RL $0,46 \pm 0,26$ mm inferior a la del grupo control de mayor edad. La banda RL-RS estaba ausente en el 35,5% de los pacientes con ETAE y en el 12,5% del grupo control de mayor edad ($p = 0,168$).

Conclusiones: La RMN reflejó que los desplazamientos del RL y la degeneración de la banda RL-RS podrían facilitar el diagnóstico de los pacientes con ETAE.

© 2017 Spanish General Council of Optometry. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Age-related distance esotropia (ARDE) is an acquired benign entity that manifests as comitant esotropia in adults patients with no history of neurological events or strabismus.¹ Degeneration of orbital connective tissue is associated with ARDE and manifests as blepharoptosis, superior sulcus defect, loss of inferior palpebral elasticity,² and esotropia, which in turn manifests as diplopia mainly in distant vision with orthoposition or phoria in near vision.

The role of orbital connective tissue in the etiology and pathogenesis of strabismus was unknown until recently. Imaging techniques have made it possible to analyze the muscle structures of the orbit^{3,4} and determine some of the causes of strabismus.

In 2002, Clark and Demer⁵ described inferior displacement of LR in older people that predisposed them to strabismus. Subsequent studies² reported degeneration of the lateral rectus–superior rectus (LR–SR) band in patients with ARDE.

Orbital magnetic resonance imaging (MRI) is a helpful diagnostic tool that is increasingly used in conditions affecting ocular motility. It could shown muscle position abnormalities, muscle contractures, intermuscular angle changes, and band and pulley alterations.

In some cases, positional abnormalities and connective tissue degeneration require surgical treatment; therefore, a complete presurgery workup is necessary so that treatment can be tailored.

The purpose of the present study was to describe orbital MRI findings in ARDE patients and compare them with those of controls aged 18–50 years and >60 years, in a European population.

Methods

This study was conducted according to the principles of the Declaration of Helsinki and approved by the ethics committee of Hospital General Universitario Gregorio Marañón (HGUGM), Madrid, Spain. All participants gave their written informed consent.

The subjects were recruited in the Ocular Motility and Diplopia department derived from the General Ophthalmology department of our hospital. The examinations performed for the recruitment were: complete medical history, best corrected visual acuity, motor and sensory examination and Lancaster-Hess chart. We asked the patients about the characteristics of the diplopia as well as if its perception was similar in primary position, side gaze and near vision. The measurement of the deviation in side gaze, near and far vision with horizontal and vertical prisms bar were performed. Worth, Lang and TNO tests were used for the sensory examination.

We analyzed 32 orbits from patients with ARDE (G.ARDE: 75% women, mean age 77 ± 7 SD years) and compared them with the control groups: G.1, 32 orbits from adult individuals aged 18–50 years (37.5% women, mean age 33 ± 8 SD years); and G.2, 16 orbits from individuals aged >60 years

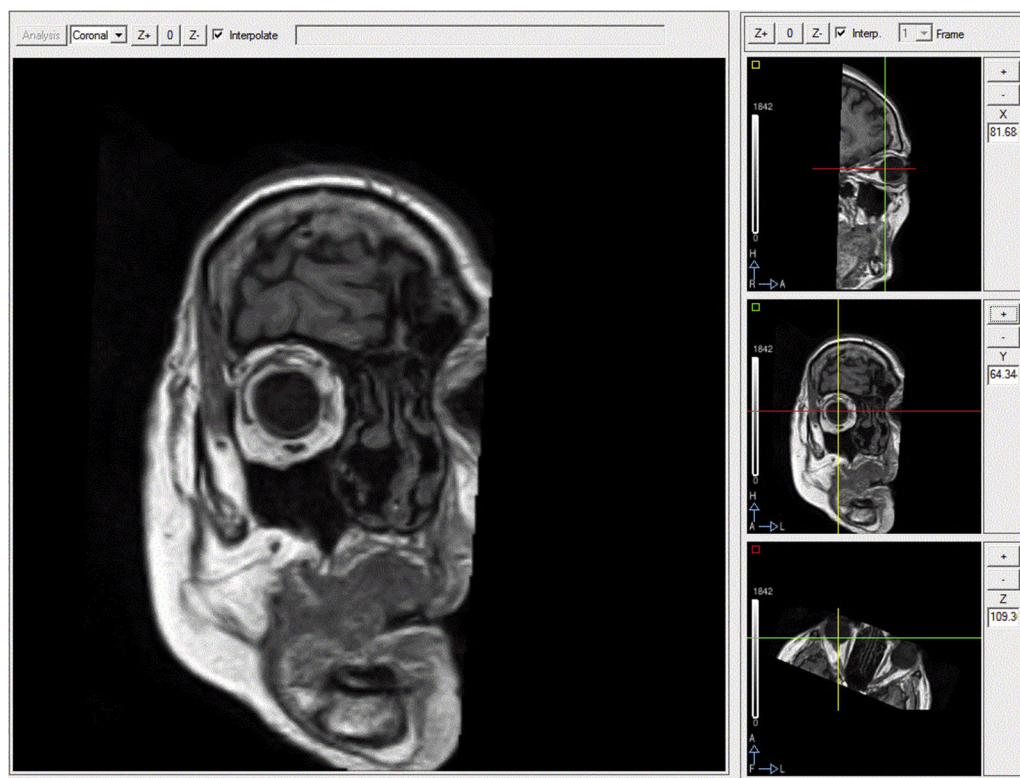


Figure 1 Processing images with MRI. Plane between 4 and 7 mm anterior to the point where the optic nerve enters the eyeball allows the visualization and the study of the LR–SR band.

(50% women, mean age 77 ± 7 SD years). We excluded from the study one orbit from an ARDE patient because of an error in the image processing process, limiting the analysis to 31 orbits.

The inclusion criteria for G.ARDE were age over 60 years, diplopia, lateral comitant esotropia less than 5 PD difference between primary position and side gaze, a greater deviation in far vision than in near vision, and no limitations of ductions and versions.

In the control groups, the inclusion criteria were as follows: in G.1, age 18–50 years and good health; in G.2, age >60 years and good health.

The exclusion criteria in all 3 groups were history of neurological or thyroid disease and relevant ophthalmological complaints such a high myopia, diplopia from another etiology or complicated cataract surgery.

MRI scans were acquired on a Philips Intera 1.5T system (Best, Netherlands) using 3D fast field echo in T1 sequence without fat saturation. Multiple contiguous quasicoronal planes were obtained.

The parameters of the acquisition were: flip angle 30° , repetition time 32 ms, echo time 4.6 ms, 60 slices, 256×256 matrix, 0.8 mm isometric voxel, total acquisition time of each image 4 min and 6 s.

The individual was instructed to fix his/her gaze on a point on the roof of the MRI tunnel. The patient's head was semi-immobilized.

Before performing the biometric study, it was necessary to perform rotations and 3D translations of the orbital image so that the longitudinal, axial and coronal axes of each eye corresponded to the axial, sagittal and coronal planes of the

MR image. For calculating angles of rotation and 3D translation it was necessary to determine reference points in the geometric center of the eyeball and in the apex of the orbital cone.

The images were processed using Multimodality Works Station, which was developed at the Medical Imaging Laboratory of our center (HGUGM) in 2006 with prototypes to apply 3D image reorientation methods to reposition the eyeball.

In reoriented images, it was necessary to obtain coordinates for each rectus from its geometric center on 2 lines perpendicular to each other and passing through the geometric center of the eye ("x" axis is the horizontal one and "y" axis is the vertical one), all in a plane 3 mm anterior to the point where the optic nerve enters the eyeball. This location makes it possible to analyze the position of the muscle pulleys and the intermuscular angle.

The eye of each side was analyzed separately, obtaining a value in "x" axis and a value in "y" axis for each rectus muscle. Values from the center of coordinates toward medial or nasal directions have been taken as positive on the horizontal axis ("x") and values from the center of coordinates to upper been taken as positive on the vertical axis ("y"). This made it possible to compare right and left eyes equally.

The LR–SR band was studied 4–7 mm in front of the point at which the nerve enters the eyeball, using the slice in which the extraocular muscles were best defined (Fig. 1).

All 3 planes (coronal, sagittal, and axial) were always visible; therefore, the slice could be modified manually and the location of the muscle pulleys established.

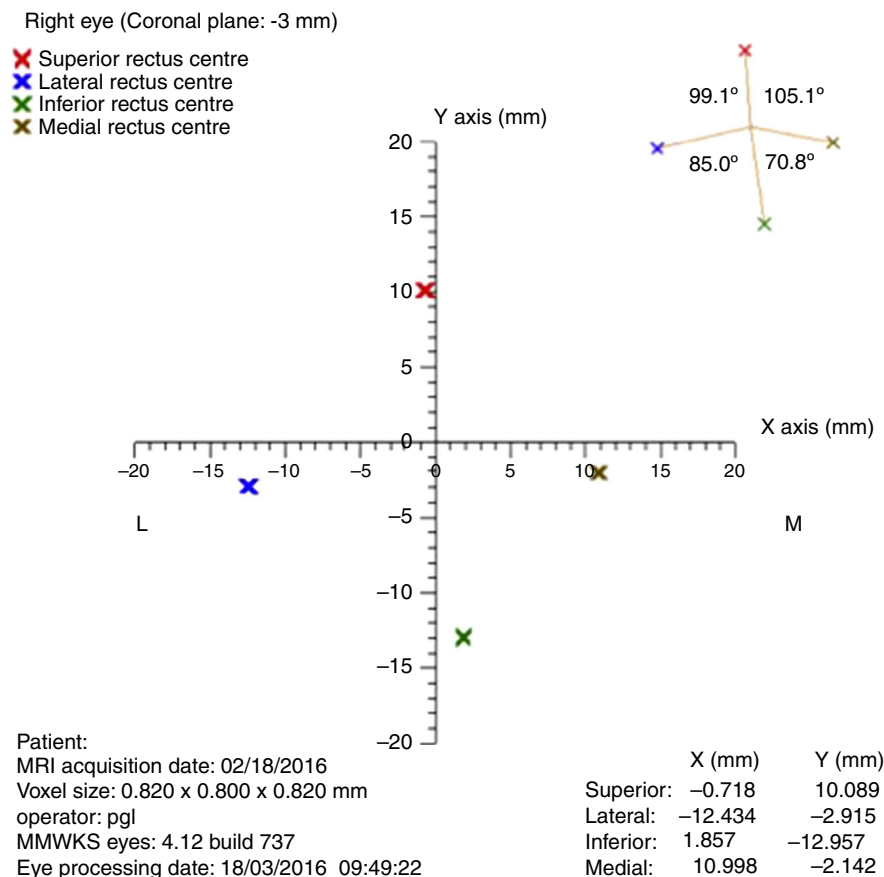


Figure 2 Final graphic obtained after the use of the computer tool in a subject. From the central axis (0,0) the location of the geometric center of the 4 rectus muscles (marked in crosses of different colors – legend in the upper left corner) is obtained, with the corresponding values in millimeters in the lower right corner. In the upper right corner the angles between the 4 muscles appear, and finally, in the lower left corner data of the characteristics of the image along with the date and time of the intervention and the initials of the one that made the measurement. Positive values in the horizontal axis or “x” axis correspond to the medial rectus and the negatives to the lateral rectus. On the vertical axis or “y” axis the positive values correspond to the superior rectus and the negative ones to the inferior rectus.

The software tool allowed the location of the centers of the rectus muscles (superior, medial, inferior and lateral) in the selected coronal plane. The computer program automatically generated the morphometric study, obtaining as final result a graph representing the position of the muscles with respect to the center of the ocular globe, providing the displacement (in millimeters) with respect to the horizontal (“x”) axis and vertical (“y”) axis, and the angles (in degrees) between the four muscles (Fig. 2). Thanks to this tool, we were able to obtain the position of the extraocular rectus muscles (in millimeters) and the size of the angles for each of the 3 study groups.

We also analyzed the qualitative values of the LR–SR band between G.ARDE and G.2, continuity or discontinuity of the band, and the thickness of the band (thinned or normal). The obliquity of the band was not studied.

The statistical study was performed using IBM SPSS Statistics 21.0 for Windows (IBM Corp., Armonk, New York, USA). Statistical significance was set at $p < 0.07$. For quantitative variables, a bivariate analysis of the 3 groups was performed using the Kruskal–Wallis test for independent samples. Qualitative variables were analyzed using the chi-square test (or

the Fisher exact test if fewer than 5 values appeared in the contingency table).

Results

Analysis of the location and displacement of the extraocular muscles

The location of the extraocular muscles on both axes is reported in Table 1.

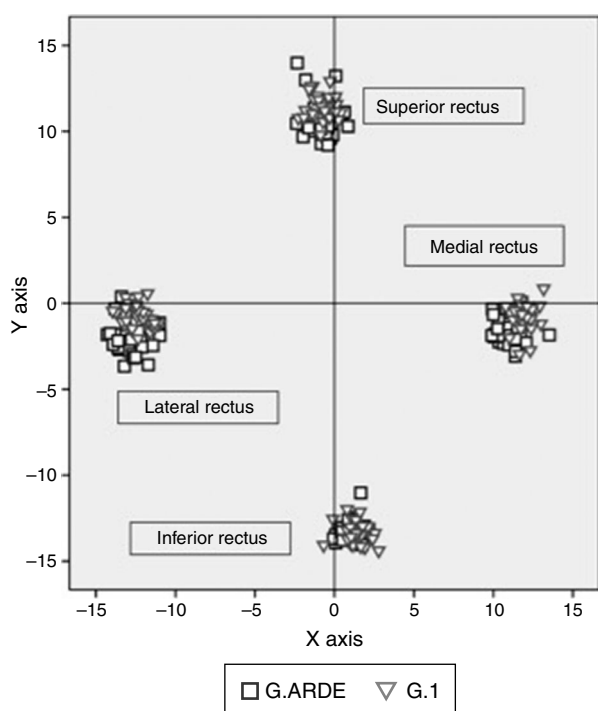
Comparison between G.ARDE and G.1 revealed a lower displacement of the LR muscle in G.ARDE with a difference between the means of 1.32 mm (SD, 0.19) ($p < 0.01$). The medial rectus (MR) muscle was displaced downward 0.68 mm (SD, 0.19) ($p = 0.001$) in G.ARDE (Fig. 3).

Comparison between G.ARDE and G.2 revealed a lower displacement of LR (0.46 mm; SD, 0.26) in G.ARDE ($p = 0.066$) (Fig. 4).

Comparison between G.1 and G.2 also revealed a lower displacement of the LR muscle by 0.85 mm (SD, 0.20)

Table 1 Coordinates “x” and “y” with respect to the geometric center of the ocular globe (0,0) of the pulleys of the rectus muscles (measurements in millimeters) for the 3 study groups.

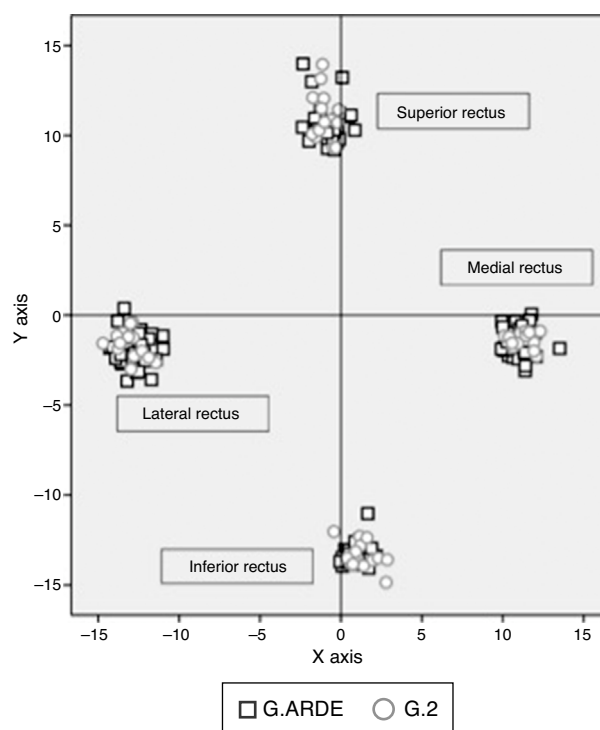
	Location of rectus muscles on MRI, average (SD) in mm							
	Medial rectus		Lateral rectus		Superior rectus		Inferior rectus	
	x axis	y axis	x axis	y axis	x axis	y axis	x axis	y axis
G. ARDE	11.08 (.88) ^a	-1.49 (.81) ^a	-12.79 (.89) ^a	-2.0 (.9) ^{a,c}	-.72 (.82)	10.59 (1.08) ^a	1.14 (.58)	-13.24 (.58)
G.2	11.24 (.68) ^b	-1.30 (.43) ^b	-12.96 (.85) ^b	-1.5 (.76) ^{b,c}	-.87 (.59)	11.01 (1.3)	1.34 (.88)	-13.41 (.78)
G.1	11.95 (.54) ^{a,b}	-0.80 (.77) ^{a,b}	-12.38 (.71) ^{a,b}	-.68 (.62) ^{a,b}	-.77 (.68)	11.48 (.69) ^a	1.41 (.72)	-13.33 (.60)

^a Statistically significant differences between G.ARDE and G.1.^b Statistically significant differences between G.1 and G.2.^c Statistically significant between G. ARDE and G.2.**Figure 3** Comparative chart of the location of the geometric center for each rectus muscles between G. ARDE (quadrates) ($n=31$) and in G.1 (inverted triangle) ($n=32$). “x” axis=horizontal axis, “y” axis=vertical axis. Positive values in the horizontal axis correspond to the medial rectus and the negatives to the lateral rectus. On the vertical axis the positive values correspond to the superior rectus and the negative ones to the inferior rectus.

($p=0.001$). Likewise, the MR muscle was displaced downward 0.49 mm (SD, 0.20) ($p=0.002$) (Fig. 5).

Analysis of the SL-LR intermuscular band

The study of the LR-SR band revealed that the band was absent in 11 cases of G.ARDE (35.5%) and 2 cases of G.2 (12.5%) ($p=0.168$). In G.ARDE, 11 bands had a normal thickness and 9 were thin. Out of a total of 20 cases (64.5%) in which the bands were present, 12 were continuous and 8 discontinuous. In G.2, 9 bands had a normal thickness

**Figure 4** Comparative chart of the location of the geometric center for each rectus muscles between G. ARDE (quadrates) ($n=31$) and (circumference) G.2 ($n=16$). Positive values in the horizontal axis correspond to the medial rectus and the negatives to the lateral rectus. On the vertical axis the positive values correspond to the superior rectus and the negative ones to the inferior rectus.

and 5 were thin; out of a total of 14 cases, 10 bands were continuous and 4 discontinuous.

Therefore, the bands were discontinuous in 40% of cases of G.ARDE and 28.58% of cases of G.2 ($p=0.121$). Respectively, 45% and 35.72% of cases were thinned ($p=0.172$).

Analysis of the intermuscular angles

Table 2 shows the average angles formed between the extraocular muscles.

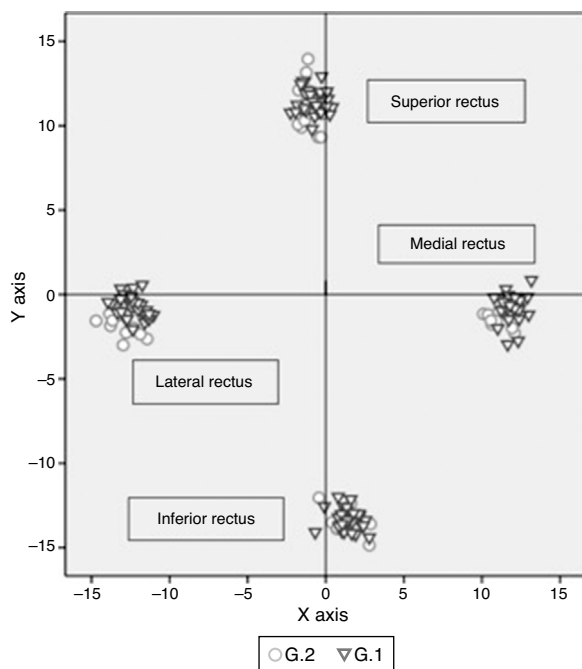


Figure 5 Comparative chart of the location of the geometric center for each rectus muscles between G.1 (inverted triangle) ($n=32$) and G.2 (circumference) ($n=16$). Positive values in the horizontal axis correspond to the medial rectus and the negatives to the lateral rectus. On the vertical axis the positive values correspond to the superior rectus and the negative ones to the inferior rectus.

Comparison between G.ARDE and G.1 revealed differences between the means of the superolateral (SL), inferolateral (IL), and superomedial (SM) angles: the G.ARDE SL and SM angles were 5.67° (SD 1.28°) ($p=0$) and 3.99° (SD, 1.38°) ($p=0.003$) more obtuse, respectively. The IL angle was 6.77° (SD, 1.08°) ($p=0$) more acute in G.ARDE.

Comparison between G.ARDE and G.2 revealed differences in the SL and IL angles: the SL angle was 2.68° (SD, 1.55°) ($p=0.044$) more obtuse in G.ARDE, and the IL angle was 2.73° (SD, 1.46) ($p=0.047$) narrower in G.ARDE.

Comparison between G.1 and G.2 revealed differences between the means of the SL, SM, and IL angles: the SL and SM angles were 2.99° (SD: 1.48) ($p=0.037$) and 3.57° (SD, 1.42°) ($p=0.005$) more obtuse in G.2, respectively. The IL angle was 4.04° (SD, 1.35°) ($p=0.008$) narrower in G.2.

Discussion

The horizontal rectus pulleys in age-related distance esotropia were statistically significantly more inferior than in control individuals older than 60 years of age. In all cases, the inferior displacement was greater for the LR than for the MR. Consequently, ARDE patients present esotropia because of a biodynamic alteration of the ocular movements leading to a disparity between the forces of contraction and relaxation.

The pulleys act as a separate entity inside the connective tissues. These structures are located immediately posterior to the equator of the globe and surround the muscles.^{6,7} The orbital pulleys stabilize the orbital position of the muscle through contraction or relaxation.

The connective pulleys are connected by intermuscular bands, the most important of which is the LR–SR band because of its involvement in sagging eye syndrome (SES) and heavy eye syndrome (HES), which is associated with high myopia.⁸

In 2013, Chaudhuri and Demer² described SES as a manifestation of connective tissue degeneration due to aging in a series of patients. They reported significant elongation and rupture of LR–SR band that led to displacement of the extraocular muscles. Such displacements are asymptomatic. Nevertheless, a more inferior, bilateral, and symmetrical displacement of the LR would produce comitant esotropia at distance (i.e., ARDE). Bilateral asymmetrical displacements in the LR pulley can also produce cyclovertical strabismus.

Degeneration of the LR–SR band and displacements of the recti are clearly visible in scans of ARDE patients. However, as in previous studies,^{5,9} inferior sagging of the horizontal recti has been observed in subjects aged >60 years in comparison with younger controls. Modifications of this type are produced by physiological aging.

MRI is used to assess displacement of the LR, increased muscle section, absence of oculomotor nuclei, and intermuscular band degeneration or discontinuity, all of which are observed in conditions such as in high myopia, alphabet patterns, fibrosis, muscle palsy, and congenital esotropia.^{3,4}

The diagnosis of ARDE is based on clinical findings, although orbital MRI can provide additional information in problematic cases. Nowadays, MRI enables us to better understand some types of strabismus and it is increasingly used in our clinical practice. However, because of its cost, long waiting lists, and the situation of public hospitals, we do not consider this kind of supplementary test obligatory.

Table 2 Angles between the rectus muscles (in degrees) for the 3 study groups.

Angles between rectus muscles on MRI, average (SD) in degrees				
	Superolateral	Inferolateral	Inferomedial	Superomedial
ARDE	95.05 (5.18) ^{a,b}	86.01 (4.55) ^{a,b}	77.42 (4.74)	101.50 (5.81) ^b
G.2	92.36 (4.75) ^{a,c}	88.75 (5.09) ^{a,c}	77.78 (3.92)	101.08 (3.37) ^c
G.1	89.37 (4.99) ^{b,c}	92.79 (4.06) ^{b,c}	80.10 (3.62)	97.50 (5.15) ^{b,c}

^a Statistically significant between G. ARDE and G.2.

^b Statistically significant differences between G. ARDE and G.1.

^c Statistically significant differences between G.1 and G.2.

Therefore, the need for orbital MRI should be examined on an individual basis.

We excluded high myopia because patients with this condition may experience extraocular displacements as a result of the size of the ocular globe. However, MRI can be useful in the differential diagnosis between ARDE plus high myopia and strabismus fixus or HES.^{10,11} A major difference between both conditions is the finding of wider SL angles in HES (up to 150°). In our series, the largest SL angle in the ARDE group was 106° (mean [SD], 95.05° [5.18°]).

Consistent with other authors,¹² we found that female sex was more frequent in the ARDE group, although the difference was not statistically significant because of the small sample size. However, the different size and structure of orbital anatomy between the genders may account for the greater incidence of ARDE in women.

Surgical suture of SR and LR is recommended in HES, although conventional surgery is the approach of choice in SES.^{10,11} Surgery is not recommended in every case, and tolerance of diplopia in patients with ARDE is somewhat variable.¹³

In conclusion, inferior displacement of the LR with a consecutive increase in the SL angle and more frequent degeneration of the LR–SR intermuscular band is found in patients with ARDE. In the physiological aging process, the horizontal recti are also displaced inferiorly, although an imbalance between LR and MR may cause esotropia. MRI is a complementary test that offers additional information in uncertain cases of ARDE and facilitates the differential diagnosis and future surgical treatment.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

We are grateful to Image Laboratory and to Radiology Service of Gregorio Marañón General Hospital.

References

1. Mittelman D. Age-related distance esotropia. *J AAPOS*. 2006;10:212–213.
2. Chaudhuri Z, Demer JL. Sagging eye syndrome: connective tissue involution as a cause of horizontal and vertical strabismus in older patients. *JAMA Ophthalmol*. 2013;131:619–625.
3. Schoeff K, Chaudari Z, Demer JL. Functional magnetic resonance imaging of horizontal rectus muscles in esotropia. *J AAPOS*. 2013;17:16–21.
4. Patel SH, Cunnane ME, Juliano AF, Vangel MG, Kazlas MA, Moonis G. Imaging appearance of the lateral rectus–superior rectus band in 100 consecutive patients without strabismus. *AJNR Am J Neuroradiol*. 2014;35:1830–1835.
5. Clark RA, Demer JL. Effect of aging on human rectus extraocular muscle paths demonstrated by magnetic resonance imaging. *Am J Ophthalmol*. 2002;134:872–878.
6. Clark RA. The role of extraocular muscle pulleys in incomitant non-paralytic strabismus. *Middle East Afr J Ophthalmol*. 2015;22:279–285.
7. Kono R, Poukens V, Demer JL. Quantitative analysis of the structure of the human extraocular muscle pulley system. *Investig Ophthalmol Vis Sci*. 2002;43:2923–2932.
8. Rutar T, Demer J. “Heavy Eye” Syndrome in the absence of high myopia: a connective tissue degeneration in elderly strabismic patients. *J AAPOS*. 2009;13:36–44.
9. Demer JL. The Apt Lecture. Connective tissues reflect different mechanisms of strabismus over the life span. *J AAPOS*. 2014;18:309–315.
10. Tan RJ, Demer JL. Heavy eye syndrome versus sagging eye syndrome in high myopia. *J AAPOS*. 2015;19:500–506.
11. Shin MH, Jung JS, Kim DH. Sagging eye syndrome presenting as a form of strabismus fixus. *J AAPOS*. 2015;19:188–191.
12. Ridley-Lane M, Lane E, Yeager LB, Brooks SE. Adult-onset chronic divergence insufficiency esotropia: clinical features and response to surgery. *J AAPOS*. 2016;20:117–120.
13. Gómez de Liaño Sánchez P, Olavarri González G, Merino Sanz P, Escribano Villafuella JC. Age-related distance esotropia: clinical features and therapeutic outcomes. *Arch Soc Esp Ophthalmol*. 2016;91:561–566.