Rectus Extraocular Muscle Paths and Staphylomata in High Myopia

YUNPING LI, QI WEI, ALAN LE, BOLA AYOUB GAWARGIOUS, AND JOSEPH L. DEMER

• PURPOSE: To investigate the relationship between displacement of extraocular muscles (EOMs) and staphyloma in high myopia using magnetic resonance imaging (MRI).
• DESIGN: Retrospective case-control study.
• METHODS: SETTING: Institutional study. POPULATION: Twenty-nine highly myopic patients (46 eyes), 11 age-matched healthy control subjects (21 eyes), and 34 patients (66 eyes) with sagging eye syndrome. PROCEDURES: MRI was analyzed for aspect ratio (AR) of the ocular cross section, locations of staphylomata and EOMs, and status of superior rectus to lateral rectus (SR-LR) band ligament. MAIN OUTCOME MEASURES: Association between staphylomata with EOM paths and the LR-SR band.
• RESULTS: Several associations of staphylomata were statistically significant ($P < .05$). Most staphylomata were superotemporal. Myopic patients with staphyloma had larger ARs in quasi-coronal images than in myopic subjects without staphyloma or normal controls. Compared to patients with high myopia without staphyloma and normal controls, when staphyloma was present, there was more inferior LR displacement, larger LR-globe angle, and larger SR-LR displacement angle than in myopic subjects without staphyloma. Staphyloma in the superotemporal quadrant was associated with greater SR-LR angle than in other quadrants. There were significantly more ruptures of SR-LR band ligament in highly myopic patients with staphyloma than in those without staphyloma.
• CONCLUSIONS: Local staphylomata in high myopia reflect ocular asphericity and correlate with EOM paths. Myopic staphylomata are associated with inferior displacement of LR path and defect of the LR-SR band ligament. (Am J Ophthalmol 2019;201:37–45. © 2019 Elsevier Inc. All rights reserved.)

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High myopia is a leading cause of blindness worldwide, especially in Asia,[1–3] where 2.4%-4.2% of people over age 30 years have high myopia.[4] Complications of high myopia may be sight-threatening, including the formation of scleral ectasias called staphylomata. While causes of the current myopia epidemic are obscure, high myopia is associated with axial globe elongation and chorioretinal lesions that can represent vision-threatening maculopathies.[5–7]

Staphylomata in high myopia are increasingly common with advancing age.[8–10] Rotation of a staphyloma against an extraocular muscle (EOM) in eccentric gaze can augment mechanical tension in the EOM or displace its path.[10] Although there is a paucity of studies investigating the relationship between staphylomata and EOM paths, Demer recently reported that irregular equatorial or posterior staphylomata are common in individuals with strabismic axial high myopia, and posited the existence of the "knobby eye syndrome" in which such irregularity in globe contour contributes to strabismus.[10] Yokoyama and associates reported that superotemporal displacement of the highly myopic globe in heavy eye syndrome (HES),[11] a striking form of acquired pulley heterotopy with limited abduction and supraduction, could disturb EOM paths, yet these authors did not comment on the possible impact of staphylomata.[12] No studies to date have quantitatively explored the relationship between presence of myopic staphyloma and EOM paths.

The present study employed 3-dimensional (3D) high-resolution magnetic resonance imaging (MRI)[13] to demonstrate and characterize staphylomatous globe deformation in axial high myopia, and to identify the relationship of staphylomata to EOM paths.

METHODS

• SUBJECTS: After obtaining patient informed consent according to a protocol approved by the Institutional Review Board of the University of California, Los Angeles, and in conformity with the Health Information Portability and Accountability Act and the Declaration of Helsinki, we studied 29 consecutive highly myopic subjects (aged 54 ± 17 years [mean ± standard deviation]; 10 male and 19 female). These subjects participated in a prospective MRI study of strabismus at the University of California, Los Angeles, from 1991 to 2016. Eleven age-matched, healthy,

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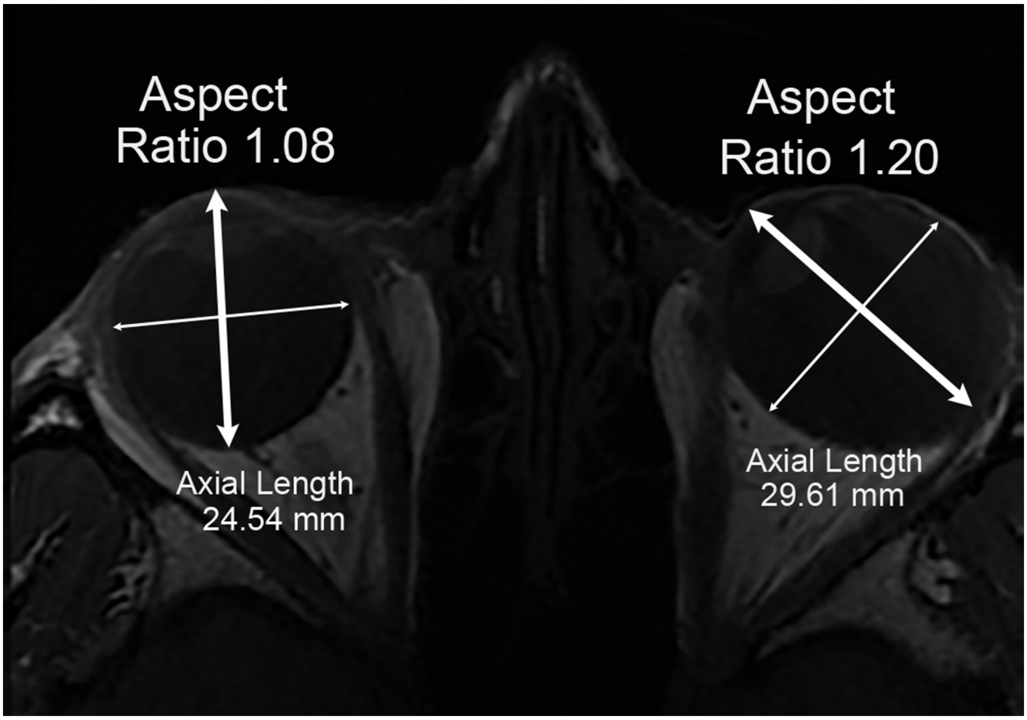

FIGURE 1. Axial magnetic resonance image of esotropic subject with left unilateral axial myopia. Major axes of ellipses fitting each globe cross section are indicated by bold bidirectional arrows and minor axes by thin arrows. Emmetropic right eye cross section is nearly circular, even including the cornea for aspect ratio 1.08, while cross section of diffusely staphylomatous, myopic left eye is oval with aspect ratio 1.20. Axial length of the myopic left eye is about 5 mm greater than emmetropic right eye.

orthotropic subjects without myopia (aged 61 ± 16 years, 4 male and 7 female, spherical equivalent more than -0.50 diopter [D]) from this study served as normal controls. All subjects underwent visual acuity assessment, motility examination, slit-lamp and funduscopic examination, refraction, photography of ocular versions, and surface coil MRI of the orbits. High myopia was defined by a spherical equivalent of -5.00 D or less, or axial length exceeding 26.5 mm measured from MRI if there had been prior cataract or refractive surgery. Axial globe length was determined from high-resolution MRI as the distance from the anterior corneal surface to the retinal surface along a line perpendicular to the iris plane, measured in the axial image plane closest to the globe equator. This is a robust approach employed elsewhere.[14,15] We also studied another control group consisting of 66 orbits of 34 subjects (aged 68 ± 12 years, 15 male and 19 female) clinically diagnosed with sagging eye syndrome (SES).[16] Staphylomata were identified in all groups using MRI.

• **MAGNETIC RESONANCE IMAGING:** High-resolution T1- or T2-weighted MRI was performed using a 1.5 T scanner (Signa, General Electric, Milwaukee, Wisconsin, USA) using published techniques.[10,17] Axial images were obtained in contiguous 2-mm slices over a 10- or 11-cm field of view, yielding 390 μm or 430 μm in-plane resolution. Quasi-coronal images perpendicular to the long axis of each orbit, and quasi-sagittal images parallel to the long axis of each orbit, were obtained at high resolution (312 μm pixels) in planes of 2 mm thickness in target-controlled central gaze for each eye. The scanned eye was monocularly centered on an afocal, fiberoptic target that does not induce convergence.

• **ANALYSIS:** Images were analyzed using the program ImageJ 64.[18] Ocular shapes were quantitatively described from contiguous axial, quasi-coronal, and quasi-sagittal image sets. Left orbits were digitally reflected into the orientation of right orbits and all orbits corrected for variations in head positioning. Roll rotation was performed first to vertically align the inter-hemispheric fissure of the brain in quasi-coronal images.[19] Axial globe length[6] was measured from axial MRI.[14]

Each eye was first categorized as spherical or nonspherical from MRI in all 3 planes. Posterior segment curvature was assessed. Staphyloma was defined as an ectasia of the sclera with a local radius of curvature less than that of the surrounding areas in any of the 3 orthogonal MRI planes.[20] We employed a polar coordinate system in axial and sagittal images to categorize staphyloma location into quadrants: superotemporal, inferotemporal, superonasal, and inferonasal. Counterclockwise angles were taken as positive.

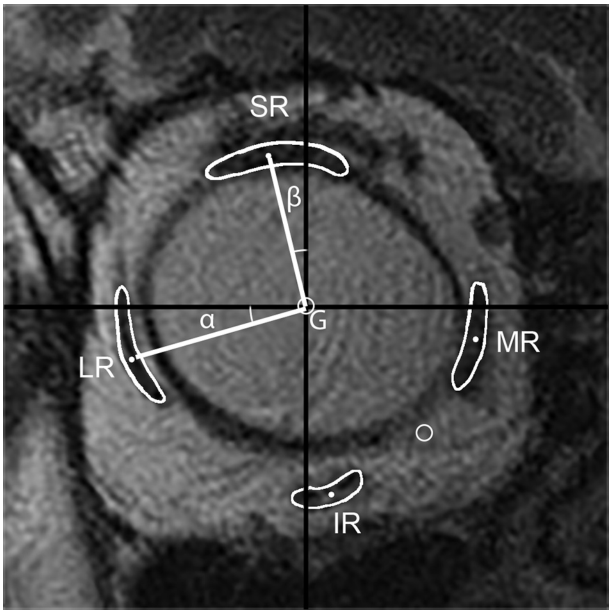

FIGURE 2. Quasi-coronal magnetic resonance image of right orbit of highly myopic subject, 4 mm posterior to the largest globe cross section, illustrating the lateral rectus (LR) angle (α) to the horizontal, and the superior rectus (SR) angle to the vertical (β), formed with white lines connecting the centroids (white dots) of the respective muscles. Globe centroid is designated G. IR = inferior rectus muscle; MR = medial rectus muscle.

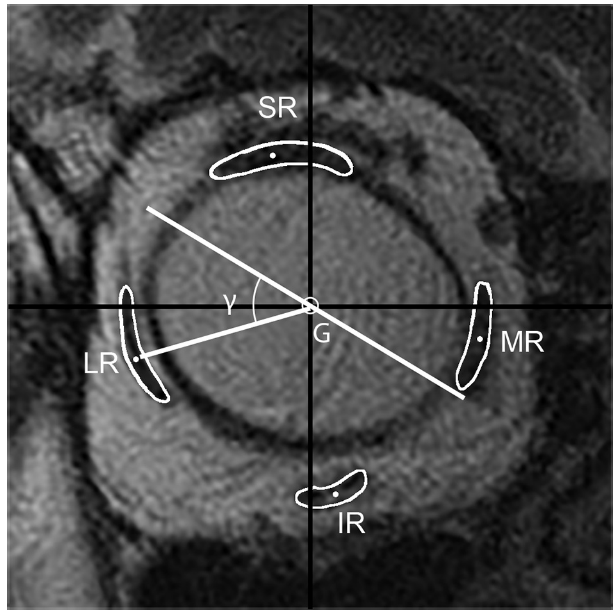

FIGURE 3. Quasi-coronal magnetic resonance image of right orbit of the highly myopic subject illustrated in Figure 2, but marked to illustrate lateral rectus (LR)–globe angle (γ), formed by white line between the centroids (white dots) of muscle and globe (G), and the major axis of the ellipse best fitting the globe. IR = inferior rectus muscle; MR = medial rectus muscle; SR = superior rectus muscle.

Classification was made by consensus of 2 authors (Y.L., J.L.D.), who were masked to refractive errors and other clinical findings. The traced globe contour was automatically fit to an ellipse in ImageJ in the image plane containing the largest globe cross section including the cornea. As an index of asphericity, aspect ratio was computed as the ratio of the major (long) axis to minor (short) axis length of the ellipse fitted to the globe. Such an approach is independent of ellipse orientation (Figure 1).[10]

To examine the association between rectus EOM paths and globe shape, we described geometric relationships among orbital structures by several angle measurements. The EOM displacement angle measures the displacement of horizontal rectus EOMs from the anatomic horizontal line, or of vertical rectus EOMs from the anatomic vertical (midsagittal) line. The angle was calculated between the horizontal or vertical, and a line connecting the respective EOM and globe centroid (Figure 2). These angles quantify the polar position of each EOM's centroid. The rectus EOM–globe angle measures the EOM's polar angle relative to the elliptical axes of the globe as computed by fitting in ImageJ. The angle was then calculated between the major (minor) axis of the globe and the line connecting the horizontal (vertical) rectus EOM and globe centroids (Figure 3). We found that for the control and the high myopia groups without staphyloma, the globe was close to spherical so that the quasi-coronal aspect ratio was less than 1.05. This caused angular indeterminacy of the fitted ellipses because aspect ratios near 1.0 describe circles, for which major and minor axes cannot be mathematically defined. Therefore, we arbitrarily assigned the major axis to be the cranial horizontal axis for these groups with nearly spherical eyes. Rectus-to-rectus angles, including the superior rectus (SR) to lateral rectus (LR) angle, the SR to medial rectus (MR) angle, the inferior rectus (IR) to LR angle, and the IR to MR angle, were also measured, analogous to the approach proposed by Yokoyama and associates for the SR-to-LR angle.[12] These angles measure the polar relationships between the respective adjacent rectus EOMs and are obtained from lines connecting the rectus EOM centroid to the globe centroid in quasi-coronal MRI (Figure 4).

Main outcome measures were quantitative MRI geometry, ocular versions, and binocular alignment. Statistical analyses were performed using GraphPad Prism (GraphPad Software, La Jolla, California, USA). Significant effects of groups were evaluated using analysis of variance, with subsequent pair-wise contrasts by unpaired t tests and χ^2 tests.

RESULTS

A TOTAL OF 52 EYES OF 32 HIGHLY MYOPIC SUBJECTS WERE examined by MRI. Six eyes of 3 subjects were excluded

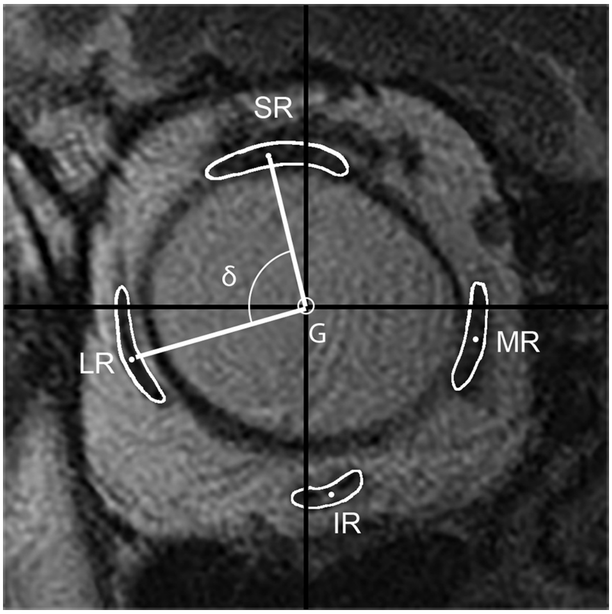

FIGURE 4. Quasi-coronal magnetic resonance image of the right orbit of the highly myopic subject illustrated in Figure 2, but marked to illustrate the superior rectus (SR)–lateral rectus (LR) angle (δ), formed by lines connecting the centroids (white dots) of the SR and globe (G), with the line connecting the centroids of the globe and the LR. IR = inferior rectus muscle; MR = medial rectus muscle.

because of MRI artifacts owing to eye movements. Ultimately, 46 eyes of 29 subjects (mean axial length: 29.1± 2.7 mm) were studied. Among these, staphylomata were identified in 17 subjects (29 eyes, mean age 58 ± 15 years), of whom 8 had strabismus (1 with exotropia, 4 with esotropia, 2 with HES, 1 with SES). Among the 12 subjects without staphyloma (17 eyes, mean age 50 ± 20 years), of whom 4 had strabismus (2 had esotropia, 1 had SES, and 1 had HES). There were 21 eyes of 11 age-matched normal controls (mean age 61 ± 16 years, axial length 24.1 ± 0.6 mm). There were no significant differences in age and sex distribution among myopic subjects with and without staphyloma and normal controls. No significant difference in age distribution was found between staphylomatous highly myopic patients with and without SR-LR band rupture (mean age 59 ± 14 vs 53 ± 16 years, respectively, $P = .45$). Myopic subjects with staphyloma had a longer mean axial length than myopic subjects without staphyloma (mean axial length 29.9 ± 3.0 vs 27.9 ± 1.7 mm, respectively, $P = .02$).

Among the 46 highly myopic eyes, in 17 (12 patients, 37%), MRI showed no evidence of staphyloma; these eyes were axially elongated, but in spherical or uniformly ellipsoidal shape. There were 35 staphylomata in 29 eyes, including nasally distorted, temporally distorted, cylindrical, or barrel shaped. Diffuse posterior staphylomata were present in 26 eyes, with 3 exhibiting 2 distinct staphylomata. Three eyes had both posterior and equatorial staphylomata.

Axial globe aspect ratio was 1.10 ± 0.09 (mean ± standard deviation) in staphylomatous myopic subjects and 1.10 ± 0.05 in nonstaphylomatous myopic subjects, both significantly greater than 1.00 ± 0.02 in normal controls ($P < .0001$). Aspect ratio in quasi-coronal MRI was 1.10 ± 0.04 in staphylomatous myopic subjects, and 1.00 ± 0.01 in both nonstaphylomatous myopic subjects and normal controls. Control subjects had spherical cross-sections in quasi-coronal planes as the mean aspect ratio was near unity, as expected. The quasi-coronal aspect ratio of staphylomatous myopic subjects significantly differed from both other groups ($P < .0001$).

Displacement angles of the rectus EOMs at the approximate pulley positions are summarized in Figure 5. The staphylomatous myopic subjects exhibit LR ($P = .0004$) and IR ($P = .02$) displacements significantly different from normal. The inferior displacement of LR in staphylomatous (18 ± 8 degrees) was significantly larger than in nonstaphylomatous myopic subjects (12 ± 7 degrees, $P = .03$). The IR was also nasally displaced in nonstaphylomatous myopic subjects, indicating association of nasal displacement of IR with high myopia in general. Displacement angles of the SR and MR were similar among groups ($P > .05$).

Rectus-globe angles are summarized in Figure 6. Staphylomatous myopic subjects had significantly larger LR-globe angles (22 ± 9 degrees) than the nonstaphylomatous myopic subjects (12 ± 7 degrees, $P = .008$) and normal controls (9 ± 5 degrees, $P < .0001$). The IR-globe angles of the staphylomatous (15 ± 9 degrees, $P = .002$) and nonstaphylomatous myopic subjects (13 ± 6 degrees, $P = .005$) were both significantly higher than the normal controls (8 ± 5 degrees), indicating that nasal displacement of IR is associated with high myopia in general. No other EOM-globe angles differed among groups.

Rectus-rectus displacement angles are presented in Figure 7. The SR-LR displacement angle in staphylomatous myopic subjects was 109 ± 11 degrees, which was significantly greater than in both the normal controls at 97 ± 7 degrees ($P < .0001$) and nonstaphylomatous myopic subjects at 101 ± 8 degrees ($P = .02$), with the latter 2 groups not differing significantly from one another ($P = .07$). The IR-LR displacement angle in staphylomatous myopic subjects was 83 ± 6 degrees, which was significantly less than in both normal controls at 89 ± 6 degrees ($P = .002$) and in nonstaphylomatous myopic subjects at 91 ± 9 degrees ($P = .0009$). In general, in staphylomatous myopic subjects there was greater IR and counterclockwise LR displacement, although nonstaphylomatous myopic subjects did not differ significantly from normal ($P = .32$). The IR-MR displacement angles in staphylomatous and nonstaphylomatous myopic subjects were identical at 74 ± 8 degrees and 74 ± 5 degrees, respectively, significantly less than in normal controls at 78 ± 6 degrees ($P = .04$ for both). The SR-MR displacement angles did not differ significantly among groups.

The Table shows that staphylomata were most abundant in the superotemporal quadrant ($P = .002$, χ^2 test). The

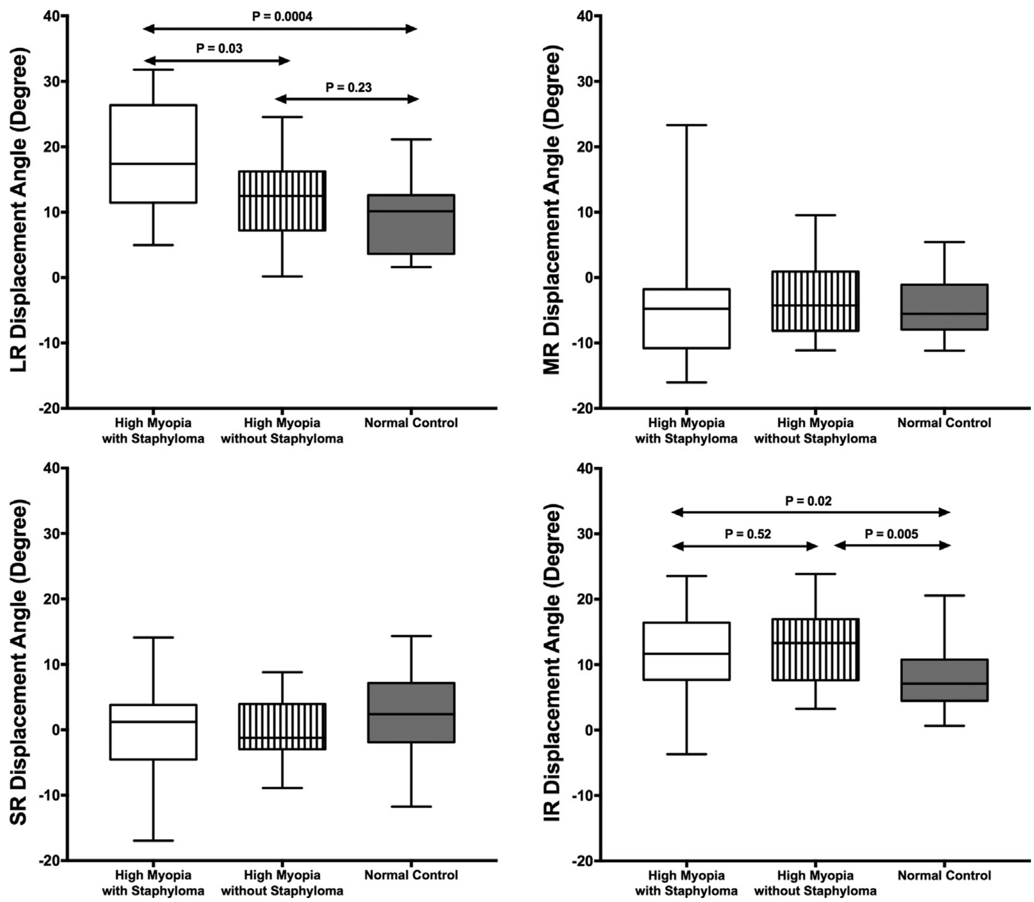

FIGURE 5. Displacement of horizontal rectus extraocular muscles from the anatomic horizontal line, or of vertical rectus extraocular muscles from the anatomic vertical (midsagittal) line, counterclockwise positive. Horizontal bars indicate the median, rectangles the interquartile range, and error bars the minimum and maximum values. IR = inferior rectus; LR = lateral rectus; MR = medial rectus; SR = superior rectus.

SR-LR displacement angle varied significantly for staphylomata located in different quadrants in highly myopic subjects ($P = .009$, 1-way analysis of variance), being greatest when staphyloma was superotemporal ($P = .004$, *t* test).

Status of the SR-LR band is presented in Figure 8. The SR-LR band was ruptured in 18 of 29 orbits (13 of 17 subjects; 7 of 13 subjects with band ruptured had strabismus including 1 with SES) in staphylomatous myopic subjects, significantly more than in nonstaphylomatous myopic subjects ($P = .01$), in whom the band was ruptured in only 4 of 17 orbits (3 of 12 subjects; 1 of 3 subjects with band rupture had SES and the other 2 had no strabismus). This may be compared with the SES group, in whom the SR-LR band was defective (ruptured or elongated and attenuated) in all 66 orbits, consistent with prior report.[16] Nine out of 66 orbits with SES exhibited staphylomata, and there was SR-LR band rupture in 7 of these 9. In the 57 orbits with SES but without staphyloma, the SR-LR band was ruptured in 9. Thus, SR-LR band rupture was significantly more likely in the presence of staphyloma ($P < .0001$). Most subjects with SES without staphyloma did not have SR-LR band rupture, but most highly myopic subjects with staphylomata did.

DISCUSSION

THIS STUDY DEMONSTRATES THAT LOCAL STAPHYLOMATA in highly myopic people influence ocular asphericity and are related to EOM positions. The LR is likely to be displaced more inferiorly in staphylomatous than in nonstaphylomatous subjects with high myopia. Staphylomata were particularly common in the superotemporal quadrant, where the SR and LR were more widely separated owing to a defect of the SR-LR band ligament in this same quadrant. This suggests that the degeneration of orbital connective tissues, especially the LR-SR band, is associated with development of highly myopic staphylomata. Of course, that clear association may or may not be causal, leaving open 3 possible interpretations: LR-SR band ligament degeneration might cause staphyloma, or staphyloma

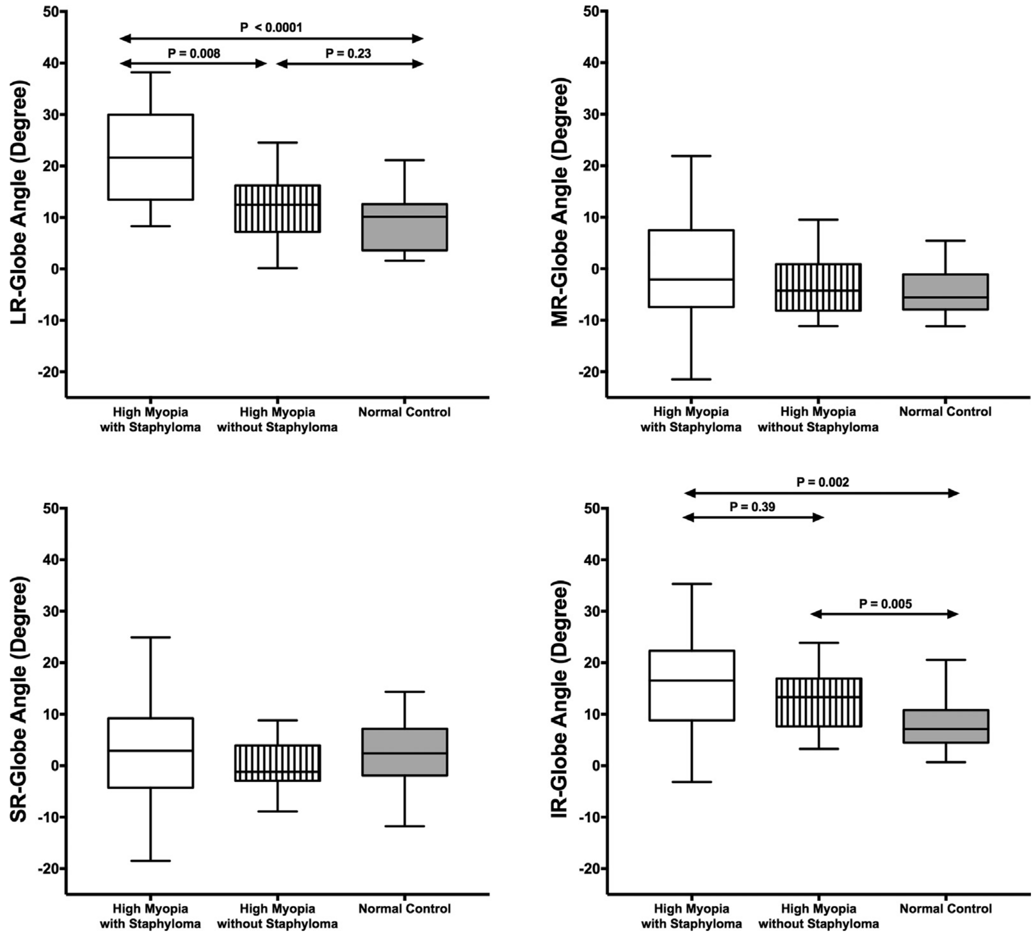

FIGURE 6. Angle between the major (minor) axis of the globe and the polar angle to from the horizontal (vertical) rectus extraocular muscle centroid to the globe centroid. Conventions and abbreviations as in Figure 5.

may cause or accelerate ligament degeneration, or the 2 phenomena might progress independently under the influence of some common factor. However, additional evidence argues for the possibility that LR-SR band ligament degeneration may promote or accelerate staphyloma formation, as discussed below.

In addition to ordinary forms of strabismus, highly myopic patients can develop 3 special forms of syndromic strabismus: "heavy eye syndrome,"[11] "sagging eye syndrome," and "knobby eye syndrome."[10,16,21] HES is due to inferonasal shift of the LR and nasal shift of the SR paths, both closely opposed to the superotemporally displaced globe[22]; SES is a less severe, age-related inferolateral shift of the LR path with generalized elongation of rectus EOM lengths.[21] Previous studies of HES and SES in high myopia did not address the existence of staphyloma. In the present study, there were 2 subjects with HES and 1 with SES who had staphylomatous high myopia; 1 highly myopic subject with SES lacked staphyloma.

Staphylomatous subjects with high myopia in the current study exhibited more inferior LR displacement than nonstaphylomatous subjects with high myopia or normal controls. The mean SR-LR angle in staphylomatous subjects with high myopia was larger than in both other groups. The mean SR-LR angle in HES has been reported to be 121 ± 7 degrees and in SES 104 ± 11 degrees.[21] The mean SR-LR angle (109 ± 11 degrees) in staphylomatous subjects with high myopia here is intermediate between HES and SES. While most staphylomata were located in the superotemporal and inferotemporal quadrants, the SR-LR angle was significantly larger with supratemporal vs inferotemporal staphylomata ($P = .04$).

Aging is associated with degeneration of the orbital connective tissue bands that couple the pulleys to one another.[23,24] The SR-LR band originates from the lateral border of the SR pulley and terminates in the superior border of the LR pulley.[24] The SR-LR band typically degenerates in elderly people, allowing inferior displacement of the LR pulley and EOM.[16,25–27] Subject groups in the current study were all similarly elderly. There was significantly more frequent LR-SR rupture in staphylomatous than in nonstaphylomatous subjects with high myopia.

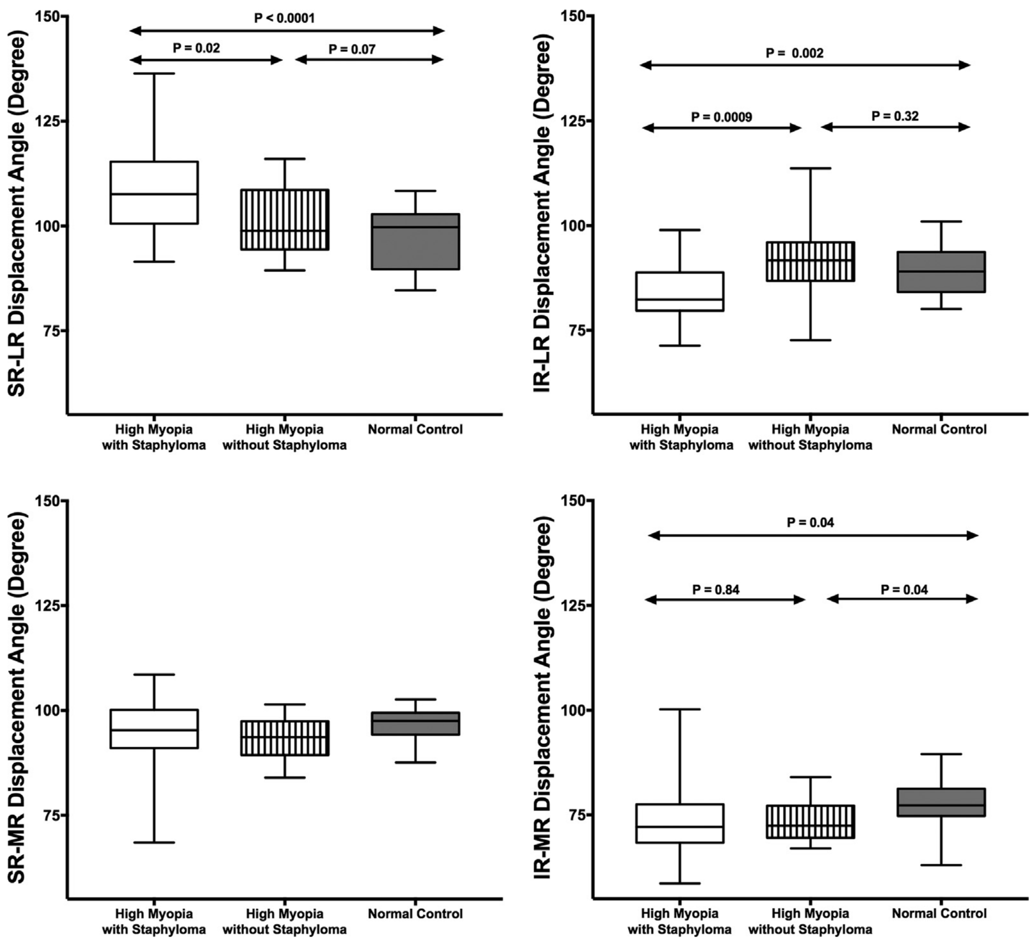

FIGURE 7. Polar relationships between the respective adjacent rectus muscles, from lines connecting muscle centroids to globe centroid in quasi-coronal magnetic resonance image. Conventions and abbreviations as in Figure 5.

TABLE. Quadrant Comparison of Staphylomata and Superior Rectus Muscle–Lateral Rectus Muscle Angle

Quadrant	Superotemporal	Inferotemporal	Superonasal	Inferonasal	*P* Value
Number of staphylomata	16	10	6	3	.002[a]
SR-LR angle (degrees)	114 ± 11	105 ± 8	100 ± 12	105 ± 8	.009[b]

LR = lateral rectus muscle; SR = superior rectus muscle.
[a] χ^2 test.
[b] One-way analysis of variance.

Although attenuation and elongation of the LR-SR band were common in subjects with SES, the more extreme form of SR-LR band rupture was significantly more likely when staphyloma was also present. This indicates that LR-SR degeneration is more likely to be severe when associated with staphylomata.

We suppose 3 main possibilities for the association of LR-SR band degeneration with staphyloma in high myopia. One possibility is that LR-SR band degeneration may allow superotemporal staphylomata to form and progress owing to absence of inward mechanical pressure of the band against the sclera. In the absence of such ligamentous pressure against the superotemporal sclera, it might bulge under the unopposed influence of intraocular pressure. Thus, pulley ligament disease might be a permissive cause of staphyloma formation. Alternatively, the superotemporal staphyloma may bulge against the LR-SR band and mechanically accelerate its degeneration. A third possibility is that development of staphyloma in high myopia is related generalized connective tissue weakness, which may accelerate both scleral and LR-SR band

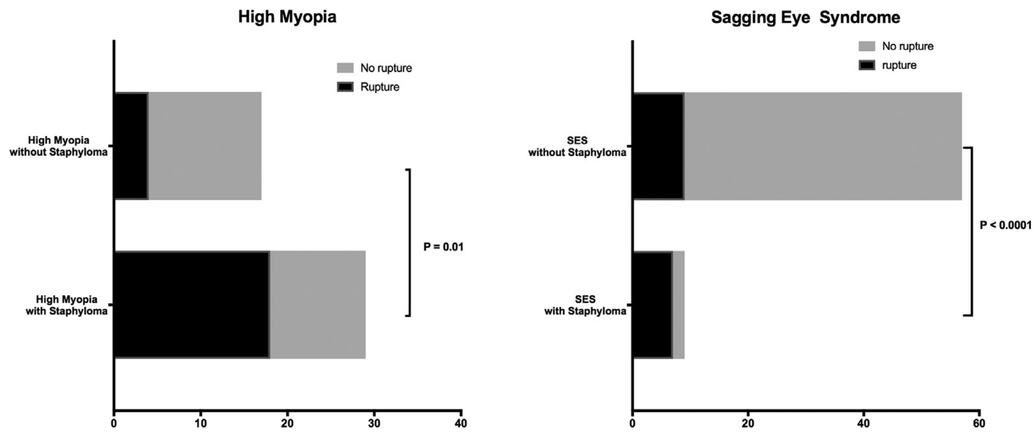

FIGURE 8. Distribution of superior rectus–lateral rectus band rupture in high myopia and sagging eye syndrome (SES) with and without staphyloma, with axis indicating number of cases.

stretching and attenuation. The third possibility of general tendency for connective tissue weakness would, however, not explain why the superotemporal quadrant is especially susceptible, arguing instead for a role of local anatomic and mechanical factors related to the extraocular muscles. If the first possibility that the LR-SR ligament restrains staphyloma formation proves correct, then surgical or photochemical cross-linking repair of the LR-SR ligament might represent options for treatment or prophylaxis of staphylomata. Regardless of the foregoing etiologic considerations, ophthalmic surgeons who treat highly myopic patients with HES or SES should be aware that superotemporal staphylomata are likely to be present, and plan accordingly.

There are limitations to this study. First, it included highly myopic patients who attended a tertiary referral center, so results may not represent the general population. Second, there were small numbers of subjects with axial high myopia and subjects with staphyloma. We employed strict inclusion criteria to assess the exclusive influence of axial high myopia, constituting a study strength but decreasing the sample size. There currently exists no adequate biomechanical model to compute the effects of irregular staphylomata generally; all existing models of binocular alignment, the most complete being Orbit 1.8, assume a spherical globe.[28] Consequently, we cannot provide a quantitative analysis of the potential mechanical interactions among the EOMs, orbital connective tissues, and the globe.

In conclusion, the present results clearly demonstrate a novel relationship between staphylomata, EOM displacement, and LR-SR band ligament degeneration in subjects with axial high myopia. The association between SR-LR band degeneration and equatorial or posterior staphyloma in high myopia may suggest future strategies for prevention and management of staphylomata, which are major contributors to sight-threatening complications of myopia.

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