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ANTERIOR CHAMBER DEPTH, LENS THICKNESS, AND RELATED MEASURES IN AFRICAN-AMERICAN FEMALES WITH LONG ANTERIOR ZONULES: A MATCHED STUDY WITH CONTROL FOR REFRACTIVE ERROR

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Abstract

Purpose—To investigate anterior chamber depth (ACD), lens thickness (LT), vitreous body length (VBL), and axial length (AL) in African-American females with long anterior zonules (LAZ) while controlling for refractive error.

Methods—The eyes of 50 African-American females with LAZ were compared to 50 controls matched on age, race, sex, and refractive error. Central ACD, LT, VBL, and AL measurements were obtained in a masked fashion using a-scan ultrasonography.

Results—LAZ cases had a mean age $\pm$ SD (range) = 67.1 ± 7.6 years (52–85 years) and a mean refractive error = $+1.85 \pm 1.41$ D (–1.75 to +4.75D). Parameters were similar for controls. Mean ACD for cases was 2.45 ± 0.34 mm and 2.57 ± 0.38 mm for controls. Mean LT for cases was 4.94 ± 0.43 mm and 4.83 ± 0.45 mm for controls. Mean VBL for cases was 15.00 ± 0.72 mm and 15.17 ± 0.76 mm for controls. Mean AL for cases was 22.39 ± 0.82 mm and 22.57 ± 0.76 mm for controls. Using multiple logistic regression to control for any residual differences in age and refractive error, no significant differences were present between LAZ eyes and control eyes relative to the a-scan variables ($P > 0.1$).

Conclusions—When refractive error was controlled for, this group of African-American females with LAZ did not exhibit clinically significant differences in ACD, LT, VBL, and AL as compared to controls.

Keywords

anterior chamber depth; crystalline lens; glaucoma; pigment dispersion; zonules

Introduction

Long anterior zonules (LAZ) present as lens zonules central to the normal insertion zone on the anterior capsule (Fig. 1).^(1–12) They often become pigmented due to iris rubbing, and are seen as radial, fine brown lines after pupil dilation. Pigment dispersion signs are common, including Krukenberg spindles and trabecular pigmentation. Iris transillumination defects can occur, which may tend to be peripupillary rather than midperipheral.^(4;13)

There are at least two different groups in which LAZ are found. For one, LAZ may occur in families with late-onset retinal degeneration (L-ORD) in conjunction with a serine 163 arginine (S163R) mutation in the C1q tumor necrosis factor-related protein 5 gene (C1QTNF5/CTRP5).⁽¹⁾ More commonly, LAZ also occur in people without a history of L-ORD, with most being female, hyperopic, and >age 50 years.^(7–9;14) So far there is no evidence that LAZ has any racial/ethnic predilection,^(1–6;8;10) and in the single clinic population we have studied, LAZ prevalence has been nearly 2.0% in multiple racial groups.⁽⁸⁾ Aside from works cited so far, LAZ have also received attention due to concerns for post-operative capsular tearing following cataract surgery, but no connections to L-ORD or other group characteristics have been made in the context of this literature.^(15–20)

Due to pigment dispersal and other potential, unknown mechanisms, it's been suggested that aqueous outflow might be impaired in some people with LAZ,^(1;10) but definitive association with open-angle glaucoma has yet to be made. There has also been speculation that narrow-angle mechanisms, including plateau iris configuration,⁽²¹⁾ may contribute to glaucoma in some people with LAZ. A relationship to angle-closure may seem particularly logical given the LAZ association with older age, female gender, and hyperopia.

Due to the potential angle-closure risk, we began investigating the ocular dimensions of LAZ subjects and recently found that our LAZ subjects had shorter axial lengths on average compared to controls.⁽²²⁾ Herein, we further studied LAZ-related ocular dimensions, with a goal to determine whether subjects matched with the same refractive error as our LAZ subjects tended to have similar ocular dimensions. Understanding this is felt to be important because it would be remarkable if LAZ subjects with a given refractive error had for example even shallower anterior chambers than non-LAZ subjects with similar refractive error.

Methods

LAZ subjects were recruited, via mailed invitation, from a database developed over several years during the provision of primary eye care by several practitioners within an urban, academic facility in Chicago, Illinois, USA.⁽⁹⁾ The criterion for LAZ was the presence of zonular fibers 1.0 mm central to the normal zonule insertion zone on the anterior capsule (Fig 1), with exclusion of subjects with <5 zonular fibers to ensure definitive cases. For this analysis, only African-American females were included because of low subject numbers outside this category in the database. Controls were recruited when they presented for regular care within the same setting, and their invitation was based on a one-to-one matching paradigm using age (± 5 years), race, gender, and refractive error spherical equivalent

($\pm 1.00D$). As LAZ subjects entered the study, consecutive potential controls were reviewed until successful matches were enrolled. Potential case and control eyes were excluded if there was a history of significant trauma, uveitis, or surgery.

To establish their characteristics and ensure appropriateness for study, all participants had ocular and medical history, extraocular muscle testing, color vision testing, confrontation visual fields, pupil testing, subjective refraction, Goldmann tonometry, four-mirror gonioscopy, and dilated fundus examination. A-scan measures (CompuScan[®] LT Biometric Ultrasound System; Storz Instrument Co., St. Louis, MO) were obtained by one of three experienced practitioners who were trained according to the protocol and masked to subject type. After topical anesthesia with proparacaine HCL 0.5%, at least five acceptable scans were obtained for each eye and averaged for final analysis, i.e., anterior chamber depth (ACD), lens thickness (LT), vitreous body length (VBL), and axial length (AL). Right eye measures were analyzed unless it was necessary to exclude that eye. Analyses were conducted using the SAS[®] System, Release 9.2 for Microsoft Windows[®] (SAS Institute, Inc., Cary, NC, USA). The paired t-test was used for initial group comparisons, and conditional multiple logistic regression was used for further simultaneous control of age and refractive error. Due to multiple comparisons, Bonferroni correction was used to calculate a planned significance level ($P < 0.01$) for evidence of group differences. Institutional Review Board approval was obtained for this investigation, and subjects provided informed consent prior to participation.

Results

Over the course of the study we identified 92 African-American females with LAZ who appeared to meet our inclusion criteria, and 53 presented for examination. Among those participants, three were excluded from analysis. Two of these were very elderly, i.e., a 92-year-old and a 94-year old, and appropriate matched controls could not be recruited. The other was a 54-year-old who had a traumatic angle recession in her only eye with LAZ. The mean age $\pm$ SD (range) of the 50 subjects included in the analysis was 67.1 ± 7.6 years (52–85 years), and it was similar for the 42 people who didn't present for examination or were excluded after examination (70.1 ± 11.4 years, 44–93 years, $P > 0.1$).

The LAZ eyes analyzed included five with open-angle glaucoma based on characteristic optic nerve cupping and visual field loss. Four of these had history of elevated intraocular pressure, one of which had very narrow iridocorneal angles along with suspicion of a mixed mechanism component to the pressure elevation. The fifth was being treated for presumed normotensive glaucoma. LAZ eyes also included eight with ocular hypertension only. One LAZ subject did not have glaucoma or elevated intraocular pressure, but was at high risk for angle-closure and had prophylactic laser peripheral iridotomy procedures soon after study participation. Thus, at the time of study, 14 of the 50 (28%) eyes studied had open-angle glaucoma, mixed mechanism glaucoma, narrow angles with high risk of angle closure, or ocular hypertension.

As shown in Table 1, the LAZ and control groups were very similar relative to age and refractive error ($P > 0.1$), suggesting a successful subject matching process, and exploration

of all variables indicated each approximated a Gaussian distribution with subjects grouped together or split into case/control groups. Having these comparable groups, the mean ACD, LT, VBL, and AL measures were very similar between the cases and controls, and regression analyses to control for any residual differences in age and refractive error gave the same results. To check possible Type II error, i.e., non-detection of true differences, post hoc analysis indicated >95% power ($\beta > 0.95$) at the $\alpha = 0.01$ level to detect a 15% difference between the group means.

To explore the data further, we examined linear relationships (Figures 2 and 3) and found ACD's strongest correlations to be with LT and AL in both cases and controls, which were in the negative direction with LT (LAZ: $r = -0.46$, $P = 0.009$; Controls: $r = -0.52$, $P < 0.0001$) and in the positive direction with AL (LAZ: $r = +0.31$, $P = 0.02$; Controls: $r = +0.37$, $P = 0.008$). Using multiple linear regression, we then also found similar LAZ and control group models containing LT, VBL, and AL as significant explanatory variables ($P < 0.001$) for the ACD dimension (Table 2). Parameter estimates for the LT, VBL, and AL variables also remained stable with or without simultaneous control for age and refractive error.

Discussion

This study helps provide further insight into what appears to be a unique clinical phenotype typically characterized by LAZ, older age, female gender, hyperopia, and anterior segment pigment dispersion. Due to its contribution to the spectrum of pigment dispersion disorders, suspected prevalence, and possible association with glaucoma, further understanding of the LAZ phenotype is important to clinical care. Detection of a Krukenberg spindle should prompt search for LAZ, especially in older, hyperopic females, because recognition of this may lead to enhanced LAZ detection and help avoid potential confusion with the "classic" type of pigment dispersion syndrome and other subtypes.

Since LAZ are associated with hyperopia in our subject population, since refractive error is readily known, and since there is question whether the trait is a risk factor for angle-closure, it is logical to ask whether people with LAZ are likely to have differences in their ocular dimensions when compared to people without LAZ who have similar refractive error. In this analysis, we did not find significant differences between groups relative to ACD, LT, VBL, and AL, and any potential undetected differences would seem to be exceptionally small.

Despite the fact that we did not find differences in the dimensions studied, this does not imply absence of any elevated risk of angle-closure among LAZ eyes because it's still apparent that LAZ eyes are more likely to have higher grades of hyperopia along with shorter axial lengths.^(7–9;22) Perhaps angle-closure risk is in fact elevated among those with LAZ but no more than similar people with similar refractive errors. On the other hand, question remains whether LAZ eyes are also more likely to exhibit plateau iris and/or other differences that may increase the risk of angle-closure.⁽²¹⁾ Thus, further investigation is warranted.

Conclusions

This group of African-American females with LAZ did not exhibit clinically significant differences in ACD, LT, VBL, and AL compared to age, race, gender and refractive error matched controls.

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Figure 1. Normal zonule insertion on anterior capsule (arrows, left) vs. long anterior zonules (arrows, right).

Figure 2.

Scatterplots with least squares regression lines showing the relationship between age and central ACD and refractive error and ACD relative to the LAZ and control groups. In this analysis, the slopes of the regression lines did not differ significantly ($P>0.1$) for either plot, suggesting minimal if any differences between the LAZ and control groups relative to these variable relationships.

Figure 3.

Scatterplots with least squares regression lines showing the relationship between central ACD and LT, VBL, and AL relative to the LAZ and control groups. In this analysis, the slopes of the regression lines did not differ significantly ($P > 0.1$) for any of the plots, suggesting minimal if any differences between the LAZ and control groups relative to these variable relationships.

TABLE 1

Data summary
‡ LAZ and control subjects matched on age and refractive error

	§ Age (Years)	‡ Refractive Error (D)	Anterior Chamber Depth (mm)	Lens Thickness (mm)	Vitreous Body Length (mm)	Axial Length (mm)
LAZ (N=50)	67.1 ± 7.6 (52 to 85)	1.85 ± 1.41 (-1.75 to 4.75)	2.45 ± 0.34 (1.81 to 3.06)	4.94 ± 0.43 (4.07 to 5.91)	15.00 ± 0.72 (13.50 to 16.94)	22.39 ± 0.82 (20.47 to 24.63)
Controls (N=50)	66.6 ± 8.5 (48 to 85)	1.85 ± 1.31 (-0.75 to 4.75)	2.57 ± 0.38 (1.83 to 3.44)	4.83 ± 0.45 (3.5 to 5.87)	15.17 ± 0.76 (13.62 to 16.78)	22.57 ± 0.76 (20.79 to 24.00)

‡ Abbreviations: LAZ, long anterior zonules; mm, millimeters
§ None of the variables statistically different between the LAZ and Control subjects (P>0.1)
‡ Spherical Equivalent Power

TABLE 2Multiple linear regression models response variable = [†]ACD

LAZ SUBJECTS (N=50)			
Variable	Coefficient (β)	Standard Error	P Value
Intercept	0.130	0.170	
X ₁ , LT	-0.954	0.019	<0.001
X ₂ , VBL	-0.952	0.022	<0.001
X ₃ , AL	0.952	0.020	<0.001
CONTROL SUBJECTS (N=50)			
Variable	Coefficient (β)	Standard Error	P Value
Intercept	-0.174	0.060	
X ₁ , LT	-1.000	0.005	<0.001
X ₂ , VBL	-1.002	0.006	<0.001
X ₃ , AL	1.001	0.006	<0.001

[†] Abbreviations: ACD, anterior chamber depth; AL, axial length; LT, lens thickness; VBL, vitreous body length.

[‡] The explanatory variables age and refractive error were not significant and were removed from the models. Parameter estimates remained stable with and without Age and Refractive Error in the models.