Major Article

Comparison of the anterior chamber angle structure between children and adults

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The prevalence of acute primary angle closure and
primary angle closure (PAC) increases with
age.^{1,2} A shorter axial length (AL) is also
associated with a risk of developing angle closure.³⁻⁵ primary angle closure (PAC) increases with age.^{1,2} A shorter axial length (AL) is also associated with a risk of developing angle closure.³⁻⁵ However, children rarely develop PAC or PAC glaucoma even when their AL is short. Other reported risk factors for angle closure in adults include a shallow anterior chamber, $3-5$ steep corneal curvature, thick lens, $3,5,6$ $3,5,6$ $3,5,6$

Presented in part at the World Ophthalmology Congress of the International Council of Ophthalmology, Tokyo, Japan, April 2-6, 2014.

Submitted March 12, 2016.

Revision accepted October 26, 2016.

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<http://dx.doi.org/10.1016/j.jaapos.2016.10.005>

anterior lens position,^{[5](#page-5-0)} large lens vault,⁵ advanced age,⁵ and cataracts.^{[5](#page-5-0)} The reasons for children with a short AL not developing acute angle closure are thought to lie in the differences in risk factors between children and adults.

The recent development of swept-source anterior segment optical coherence tomography (AS-OCT), with a scan duration of 0.3-2.4 seconds for anterior segment three-dimensional images and a waveband light source measuring 1.3 μ m in wavelength, allows clinicians to obtain a deeper penetration into tissues, making it possible to quantitatively measure the anterior chamber angle configuration in young children in a noncontact and noninvasive manner relatively rapidly. The purpose of the present study was to compare the anterior chamber angle configuration between children and adults with similar ALs using swept-source anterior segment optical coherence tomography and to investigate why children, despite their short AL, rarely develop PAC.

Subjects and Methods

This study conformed to the tenets of the Declaration of Helsinki; written informed consent was obtained from either the subjects or

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Japan Clinical Trials Register: <http://www.umin.ac.jp/ctr/index/htm9> number, UMIN000012527.

FIG 1. The definition of angle-opening-distance 500 (AOD 500) and lens vault on a cross-sectional image of the anterior chamber angle obtained using swept-source anterior segment optical coherence tomography. A, The AOD 500 is indicated by the double-headed white arrow. The arrowhead indicates the scleral spur; the white bar represents 500 μ m in length. B, The lens vault is indicated by the doubleheaded white arrow. SS, scleral spur.

their legal guardians after providing an explanation of the nature and possible consequences of the study. Approval was obtained from the Institutional Review Board of Saneikai Tsukazaki Hospital for this clinic-based, cross-sectional comparative study.

Children and adults with AL of \leq 24 mm were recruited from among the patients treated at Saneikai Tsukazaki Hospital between October 2012 and July 2013. Children with any history of prematurity or ocular surgery were excluded. Adults with glaucoma accompanied by visual field deficits, ocular hypertension with an eye pressure of \geq 21 mm Hg, uveitis, or a history of any ocular surgery or other eye diseases were also excluded. In addition, patients in whom we were unable to obtain clear images due to poor fixation were excluded.

The degree of refraction and corneal radius of curvature (corneal curvature) were measured using an auto keratorefractometer (KR-8900; TOPCON, Tokyo, Japan). The average of 10 measurements was used to determine the spherical equivalent, using the formula spherical power $+$ cylindrical power \div 2, and corneal curvature. AL measurements were obtained using optical biometry (IOL Master; Carl Zeiss Mesitec, Jena, Germany) based on an average of 5 measurements. Only the findings from the right eyes were included in the statistical analysis.

SD, standard deviation.

^aMann-Whitney U test.

bWelch t test.

Following 5 minutes of dark adaptation, cross-sectional images were obtained using the anterior segment mode and angle mode on swept-source anterior segment OCT (AS-OCT; SS-1000 CA-SIA, TOMEY, Nagoya, Japan). The alignment was subsequently corrected using an internal fixation lamp. The clearest images of several scans were selected for the analysis (see [Video 1,](#page-0-0) available at jaapos.org). The central corneal thickness (CCT), anterior chamber depth (ACD), and angle opening distance 500 (AOD 500) were then calculated automatically using the built-in software.

ACD was defined as the distance from the corneal endothelium to the anterior lens. AOD 500 is a parameter defined by Pavlin and colleagues^{\prime} as the perpendicular distance between a point 500 μ m anterior to the scleral spur and the opposite iris (Figure 1). In children with relatively small palpebral fissure, capturing the superior and inferior quadrant images in AS-OCT was challenging. Measurements obtained at the nasal quadrant were used for analysis of AOD 500 values. The lens vault was measured using built-in caliper software by identifying the perpendicular distance between the midpoint of the horizontal line connecting the scleral spurs and the anterior pole of the crystalline lens (Figure 1), with the distance at the cornea defined as positive and the distance at the retina defined as negative^{[7](#page-5-0)} (Figure 1). The distance between the scleral spurs (inter–scleral spur distance) and the perpendicular distance of the midpoint of the scleral spurs to the corneal endothelium at the apex (distance from the inter–scleral spur line to the corneal endothelium; perpendicular distance) were measured using a built-in software caliper. Thereafter, for cycloplegic refraction testing in the children, the first set of cyclopentolate hydrochloride 1% eyedrops was administered, followed by an interval of 10 minutes, after which the second set of eyedrops was administered; 50 minutes later the refraction test was conducted at the end of all examinations.

Statistical Analysis

The t test, Welch t test, Mann-Whitney U test, and a stepwise regression analysis were performed using a commercially available software program (JMP, v. 10.0; SAS Institute Inc, Cary, NC). In addition, to reduce the risk of type 1 error, we adjusted the level of the cut-off value for significance using Bonferroni correction. A P value of $<$ 0.0045 (0.05/11) was considered statistically significant.

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Table 2. Comparison of the structural parameters of anterior chamber angle and the refractive parameters between the children and adults

Characteristic	Mean values \pm SD (range)		
	Children	Adults	P value
AL, mm	22.21 ± 0.88 (20.67 to 23.97)	22.34 ± 0.53 (20.50 to 22.96)	0.18^{a}
SE power, D	1.36 ± 2.52 (-3.75 to 8.5)	1.01 ± 1.8 (-3.88 to 5.25)	0.43 ^b
Corneal curvature, mm	7.70 \pm 0.21 (7.24 to 8.19)	7.40 \pm 0.24 (6.77 to 7.81)	${<}0.0045$ ^c
Keratometry, mm			
Anterior	7.73 ± 0.30 (6.82 to 8.48)	7.40 \pm 0.23 (6.75 to 7.81)	$<$ 0.0045 $^{\circ}$
Posterior	6.48 ± 0.19 (6.17 to 6.97)	6.18 ± 0.21 (5.67 to 6.66)	${<}0.0045$ ^c
Inter-scleral spur distance, mm	11.65 \pm 0.33 (10.76 to 12.40)	11.20 \pm 0.39 (10.38 to 11.88)	${<}0.0045$ ^c
Perpendicular distance, mm	3.09 ± 0.21 (2.63 to 3.66)	3.08 ± 0.38 (2.27 to 4.99)	0.09^{a}
CCT, μ m	560.1 \pm 32.97 (503 to 635)	522.6 ± 30.42 (464 to 582)	${<}0.0045$ ^c
ACD, mm	3.05 ± 0.27 (2.33 to 3.74)	2.53 ± 0.43 (1.53 to 4.40)	${<}0.0045$ ^c
AOD 500, mm	0.56 ± 0.15 (0.3 to 1.11)	0.37 ± 0.15 (0.11 to 0.81)	${<}0.0045$ ^a
Lens vault, mm	0.04 ± 0.22 (-0.436 to 0.594)	0.54 ± 0.31 (-0.09 to 1.352)	${<}0.0045$ ^c

ACD, anterior chamber depth; AL, axial length; AOD, angle opening distance 500; CCT, central corneal thickness; SD, standard deviation; SE, spherical equivalent.

^aMann-Whitney U test.

 $\frac{b}{c}$ Welch *t* test.

 c Independent samples *t* test, with level of significance adjusted by Bonferroni correction.

Results

[Table 1](#page-1-0) shows the patient demographics. A total of 50 children and 50 adults were recruited. Mean age, with standard deviation, of the children was 7.1 ± 3.3 years (range, 3-16 years); of the adults, 73.7 ± 7.8 years (range, 50-85 years). We were able to obtain clear images capturing the angle recess in all eyes exhibiting fixation stability on swept-source AS-OCT. In the children group, 3 eyes required manual correction due to incorrect identification of the scleral spur by the integrated analysis software program; in the adult group 10 eyes required correction. The anterior surface of the crystalline lens was clearly identified in all studied eyes.

The 50 children had refractive error (39), strabismus (8), or amblyopia (3). All children had been followed or treated with optical correction and/or patching without surgery, and their visual acuity ultimately improved to 20/20. The 50 adults had refractive error (22) or cataract (28). There were no marked differences in sex between groups $(P = 0.22)$. The mean AL was 22.21 \pm 0.88 mm (range, 20.67–23.97 mm) in children and 22.34 ± 0.53 mm (range, 20.50–22.96 mm) in adults. There were no significant differences between the groups in the AL or spherical equivalent ($P = 0.18$, $P = 0.43$, resp.), nor were there any significant differences in the perpendicular distance $(P = 0.49)$. In contrast, the corneal curvature, inter–scleral spur distance, CCT, ACD, and AOD 500 values were significantly larger in the children than in the adults (for all measurements, $P < 0.045$ by Bonferroni correction), whereas the lens vault values were significantly smaller in children than in adults ($P < 0.0045$; Table 2). The statistically significant and important structure parameters are presented in [Figure 2.](#page-3-0)

Compared to the structure of the adult eyes, the corneas in the children were thicker and flatter, with a deeper ACD, longer inter–scleral spur distance, larger AOD 500, and

smaller lens vault. The semicircle structure of the anterior segment was larger in children than in adults [\(Figure 3](#page-3-0)).

We used a stepwise regression analysis to investigate the factors that significantly affected the lens vault, an indepen-dent predictor of angle closure.^{[7](#page-5-0)} The representative factors were age (group), AL, ACD, inter–scleral spur distance, AOD 500, corneal curvature, spherical equivalent, and CCT. The subjects were divided into two age groups, the younger group (mean age, 7.1 ± 3.3 years) and the older group (mean age, 73.7 ± 7.8 years), because the age distribution showed peaks at these ages. Factors with a P value of $<$ 0.2 were included in a stepwise regression analysis.

The significant predictive factors for the lens vault included the ACD (coefficient, –0.407), inter–scleral spur distance (0.307), AOD (–0.650), group (children, –0.108), and corneal curvature (–0.214). See [Table 3](#page-4-0). Contrary to the positive correlation observed between the lens vault value and the inter–scleral spur distance according to a stepwise regression analysis, the lens vault values were smaller and the inter–scleral spur distances were larger in children than in adults.

Additionally, we used a stepwise regression analysis to investigate the factors that significantly affected the AOD 500. The representative factors were age (group), AL, ACD, inter–scleral spur distance, lens vault, corneal curvature, spherical equivalent, and CCT.

The significant predictive factors for the AOD 500 were lens vault (coefficient, –0.310), inter–scleral spur distance (0.140) , and corneal curvature (-0.143) ; [Table 3](#page-4-0)). Contrary to the negative correlation observed between the AOD 500 and the corneal curvature according to a stepwise regression analysis, both the AOD 500 and the corneal curvature were larger in children than in adults. This is explained by the fact that the stepwise regression analysis removed the strong interference resulting from age.

FIG 2. Comparison of important structural parameters in children and adults. ACD, anterior chamber depth; AOD 500, angle opening distance 500; CCT, central corneal thickness.

FIG 3. A diagrammatic representation of the anterior chamber angle structure in children and adults. The inter–scleral spur distance of the children (horizontal solid arrow) is longer than that of the adults (horizontal dashed arrow) despite the similar perpendicular distance (vertical solid and dashed arrow); which is likened to the longer chord of the larger circular arch in children (solid arch) in comparison to adults (dashed arch).

Discussion

The current study showed the difference in the anterior chamber configuration between children and adults with similar ALs. It also demonstrated a larger semicircle structure of the anterior segment in children than in adults despite similar ALs in both groups. In addition, the results of a stepwise regression analysis supported the notion that children rarely develop PAC due to the difference in the anterior chamber configuration between children and adults.

The mean AL in 7-year-olds is reported to be approximately 22.5 mm; thereafter it grows to 23.6 mm (the same length as in adults) at $10-15$ years of age.⁷ The average AL in Japanese adults is reported to be 23.8 ± 1.6 23.8 ± 1.6 23.8 ± 1.6 mm⁸; in the current study, the average AL both in children (22.21 \pm 0.88 mm) and in adults $(22.34 \pm 0.53 \text{ mm})$ was roughly 1 mm shorter. PAC glaucoma and PAC are more common in East Asian countries than in Western countries. The odds ratio of an occludable

ACD, anterior chamber depth; AOD 500, angle opening distance 500.

angle increased with shorter AL (0.7[2](#page-5-0) per 1 mm in length).² In terms of AL, the eyes in the current study may have been at risk of developing an occludable angle.

The average spherical equivalent in Japanese adults is reported to be –0.81 \pm 2.38 D in males and –0.32 \pm 1.85 D^{[9](#page-5-0)} in females. In our study, the average spherical equivalent both in adults $(1.01 \pm 1.8 \text{ D})$ and in children $(1.03 \pm 2.52 \text{ D})$ was more hyperopic by >1 D than that found in 2 Japanese population studies.^{[2,9](#page-5-0)} A shorter AL has been associated with a risk of developing angle closure. $3-5$ Hyperopia is also associated with a substantially increased prevalence of angle closure glaucoma across all racial and ethnic groups.^{[10](#page-5-0)} When the AL and spherical equivalent were considered, both of our study groups were at a relatively high risk of developing angle closure glaucoma.

Our data revealed some differences in anterior segment configuration between groups, with children having a larger radius of corneal curvature than adults (7.70 vs 7.40 $[P < 0.0045]$). Casson and colleagues' reported that patients with an occludable angle have steeper corneal curves than healthy individuals. The average CCT in Japanese adults has been reported to be 521 μ m^{[7,9](#page-5-0)} and 510.7 \pm 30.6 μ m,^{[8](#page-5-0)} which is similar to that observed in our adult subjects. The CCT was significantly thicker in our child subjects, a finding that supports the results of a study showing that the corneal thickness in adults with a normal intraocular pressure becomes thinner with age.^{[9,11,12](#page-5-0)} However, our data did not reveal any correlations between age and corneal thickness in either group; this finding may be due to the small number and/ or limited age of the patients included in this study.

Contrary to our expectations, children had longer inter– scleral spur distances than adults, despite the lack of significant differences in the perpendicular distance between the groups. An eyeball model^{[13](#page-5-0)} joining two hemispheres that forms part of the cornea and the sclera suggests a potential reason for the differences in the anterior structure between children and adults ([Figure 3\)](#page-3-0). Children have greater corneal curvature, namely, the radius of the anterior hemisphere binding to the sclera. Accordingly, children have a longer inter–scleral spur distance than adults; this distance is likened to the chord of a larger circular arch. There is lit-tle change in corneal curvature after 3 years of age.^{[14](#page-5-0)} The increase in AL after 18 months of age depends mainly on the extent of elongation of the vitreous cavity.^{[15,16](#page-5-0)} Thus,

the anterior segment of children in the present study is not expected to change with growth, although their AL may lengthen (to the average level) via the elongation of the posterior segment as they age. In contrast, the adults in the present study may have had a shorter inter–scleral spur distance since childhood. Whether or not an infant with a shorter inter–scleral spur distance will have a shorter AL may be able to be predicted; however, further observations will be required to prove this hypothesis.

The crystalline lens thickens^{[17,18](#page-5-0)} and the lens vault $increases¹⁹$ $increases¹⁹$ $increases¹⁹$ with age in adults; the anterior capsule moves forward and the anterior chamber becomes shallower.^{[17](#page-5-0)} Although no significant differences were found between the adults and children with regard to AL or perpendicular distance in our study, children had deeper anterior chamber and larger AOD 500 than in adults and a smaller lens vault than in adults. Lens thickening, which occurs with aging, results in an increase in the lens vault, the forward displacement of the iris, a decrease in the ACD, and a decrease in the AOD 500. These changes can lead to angle closure in adults. $3-6,20$

The lens vault is a parameter strongly associated with the development of angle closure glaucoma.^{[20](#page-5-0)} Our study found that children have a deeper ACD, larger inter–scleral spur and AODs, and steeper corneal curvature than adults, supporting the results of the stepwise regression analysis and suggesting that children have a lower risk of developing angle closure glaucoma than adults. In addition, the results of the stepwise regression analysis to determine factors associated with the AOD 500 showed that the children have a smaller lens vault, a larger inter–scleral spur distance, and a steeper corneal curvature than adults.

It has been reported that 98% of cases of ocular refraction in adults can be explained by the characteristics of the AL as well as the lens and corneal power.^{[21](#page-5-0)} Based on this background, it is likely that the effects of the difference in the corneal radius of curvature on the spherical equivalent are offset by variation in the shape and power of the lens due to age. In addition, variations in the lens shape result in differences in the anterior chamber angle configuration.

This study has several limitations. First, as a clinic-based study, the subjects were patients and not always healthy volunteers. Second, the prevalence of primary angle closure glaucoma in adults is highest in Asia (1.09%) and varies by ethnicity.^{[22](#page-5-0)} The results of the present study therefore cannot be applied directly to other populations. Third, our investigation assessed the differences in the anterior chamber angle configuration between children and older adults; therefore, the age group in which these configuration changes begin to appear is unclear. Fourth, the present study involved a comparison of children with an average AL and adults with a short (not average) length for their age. The differences in the configuration of the anterior chamber angle are likely to be the most affected by changes in the lens; however, the anterior segment optical coherence tomography that was used in the current study could not be applied to scan the posterior segment of the lens.

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