



Role of Crystalline Lens on Angle Closure in the North Indian Population

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Abstract

Purpose: To evaluate the role of crystalline lens on angle closure in the North Indian Population

Methodology: It was a prospective, comparative study. A total of 313 eyes of 162 participants underwent Anterior Segment Optical Coherence Tomography (AS-OCT) and biometry using IOL Master-700. Measurements included axial length (AL), anterior chamber depth (ACD) and lens thickness (LT). Lens vault (LV) was measured as the perpendicular distance from the anterior pole of the lens to a line connecting the scleral spur on AS-OCT. Lens position (LP) was calculated as $ACD + 1/2 LT$, and relative lens position (RLP) was calculated as LP / AL . The receiver operating curve (ROC) was plotted, and the Area under the curve (AUC), sensitivity, and specificity were calculated for all parameters to quantify their discriminating ability.

Results: Lens vault was significantly higher in the eyes with Primary Angle Closure Suspect (PACS: $503.85 \pm 181.03 \mu\text{m}$), Primary angle closure (PAC: $641.69 \pm 197.04 \mu\text{m}$) and Primary angle closure disease (PACD: $591.31 \pm 211.06 \mu\text{m}$) compared to normal ($141.39 \pm 191.33 \mu\text{m}$) ($p > 0.01$) Lens vault along with ACD demonstrated the highest area under curve (AUC= 0.95) with sensitivity of 89.7%, followed by lens position (AUC=0.92) with sensitivity 82.4 % and specificity 89%.

Conclusion: The eyes with angle closure have thicker lenses with a greater LV, shallower ACD, and shorter AL. Lens vault, ACD and lens position were associated strongly and independently with angle closure and distinguished eyes with angle closure from those with open angles better than traditional biometric parameters.

Keywords: Lens vault, Lens position, relative lens position, AS-OCT

Introduction

Primary angle-closure glaucoma is a leading cause of blindness, for the most part in Asian countries. A survey in an urban population in southern India has reported a high prevalence of 4.3% for primary angle closure glaucoma (PACG) in the 30- to 60-year age group. (1) The Hooghly River Glaucoma Study showed that 1.54% have angle closure. (2) The Andhra Pradesh eye study showed that 41.7% of those with manifest PACG had blindness in one or both eyes resulting from PACG. (3) Previous studies have demonstrated that ocular risk factors for angle-closure glaucoma are shallow anterior chamber depth (ACD), short axial length (AL), and increased lens thickness (LT). (4–7) Among these parameters, the lens is considered to play a critical role in the pathogenesis of angle closure disease either because of an increase in its thickness or a more anterior position, causing a decrease in ACD. The result is angle crowding and a greater predisposition to pupillary block resulting from iridolenticular apposition in eyes with small anterior segments. However, the involvement of different lens parameters such as the lens position (LP; defined as $ACD / 2 \cdot LT$), relative lens position (RLP; defined as $LP / axial\ length$), and LT-to-AL (LT / AL) ratio have not been recognized categorically, and there have been inconsistent reports on the importance of LP and RLP with angle closure. (8–13)

Now it is possible to capture in a single image the whole anterior chamber using anterior-segment optical coherence tomography (AS OCT). This allows enhanced imaging of the lens compared to other structures. We hypothesize that the degree of lens that is located anterior to the plane of the angles plays a role in the pathogenesis of angle closure. One way to determine the grade of this parameter is to calculate the lens vault (LV), defined as the perpendicular distance between the anterior pole of the crystalline lens and a horizontal straight line joining the two scleral spurs. The present study aimed to evaluate the relative importance of lens parameters (LV, LP, and RLP) with respect to angle closure by comparing eyes with angle closure with eyes of patients with open angles. Lens thickness increases with age and has a linear relationship. (30) Lens growth continues throughout life, and there is no difference between sexes. Although in Chinese (24) and Japanese(25)population studies, lens thickness was different between in control group and the study group, but there was a significant difference in age between the two groups.

Materials and Methods

This was a prospective, comparative study of North Indian subjects with angle closure attending a glaucoma clinic and of normal control subjects recruited from the Comprehensive Eye clinic.

Definition of Angle-closure Glaucoma: The definitions of occludable angle and manifest PACG were based on definitions used in a recent report on glaucoma in Mongolia. (14) Occludable angle was defined as pigmented posterior trabecular meshwork not visible by gonioscopy in three-quarters or more of the angle circumference, raised intraocular pressure, or both, but without glaucomatous optic neuropathy. Manifest PACG was defined as an IOP of 22 mmHg or more or glaucomatous optic disc damage with visual field loss in the presence of an occludable angle and the presence of at least 3 of the following signs: conjunctival injection, corneal epithelial oedema, mid dilated unreactive pupil, and shallow anterior chamber. (15)

Patients diagnosed with secondary angle closure (such as neovascular or uveitic glaucoma), patients who had corneal abnormalities that would affect imaging, and patients who had a previous laser iridoplasty or intraocular surgery history were excluded. All subjects with angle closure previously had undergone laser peripheral iridotomy.

The control group of normal subjects (defined as intraocular pressure ≤ 21 mmHg with open angles, healthy optic nerves and normal visual fields, no previous ocular surgery, and no family history of glaucoma) were recruited from the Comprehensive Eye clinic, aged 25 years and older. For this report, complete data were available for 109 eyes of 58 consecutive normal North Indian subjects, and they were included as the control group. All subjects underwent a detailed routine eye examination that included visual acuity measurement using a Snellen's chart, slit-lamp examination, stereoscopic optic disc evaluation with a 90-diopter lens (Volk Optical, Inc., Mentor, Ohio), intraocular pressure measurement by Goldmann applanation tonometer and gonioscopy, performed in a dark room. Indentation gonioscopy with the Sussman 4-mirror lens was used to determine the presence or absence of peripheral anterior synechiae. A-scan biometry (IOL master 700; Zeiss) (16, 17) was used to measure AL, ACD, and LT, and these results were used to calculate LP (defined as $ACD + 1/2LT$) and RLP (defined as LP/AL).

Anterior segment OCT (ASOCT)

All subjects underwent imaging with ASOCT (Cirrus 5000, Carl Zeiss Meditec, Dublin, CA, USA)(18,19,20) performed in dark-room conditions (0 lux) by optometrists who were masked to the results of the clinical ophthalmic examination. Scans were centered on the pupil and taken along the horizontal axis (nasal-temporal angles at 0° – 180°) using the standard anterior segment single-scan protocol. To obtain the best quality image, the examiner adjusted the saturation and noise and optimized the polarization for each scan during the examination. As several scans are acquired by the ASOCT device, the optometrist finalized the best images, without motion artefacts or eyelid image artefacts . One cross-sectional horizontal ASOCT scan

of the nasal and temporal angle was evaluated for each subject. These images were processed using the in-built software, by Carl Zeiss Meditec, 2015, masked to clinical data. For each image, the only observer input was to determine the location of the two scleral spurs, defined as the point where there was a change in curvature of the inner plane of the angle wall, often appearing as an inward protrusion of the sclera. The algorithm then automatically calculated the LV, defined as the perpendicular distance between the anterior pole of the crystalline lens and the horizontal line joining the two scleral spurs. Positive values indicate that the anterior pole of the lens is located anterior to the sclera spur line, whereas negative values occur when the anterior pole of the lens is posterior to the sclera spur line.

Statistical analysis

Statistical analysis was conducted using SPSS software, version 17 (SPSS, Inc., Chicago, IL, USA). Parametric variables were assessed with ANOVA, followed by post hoc Tukey tests. Nonparametric variables were analyzed using the Kruskal–Wallis test. The ROC curve was plotted to assess the diagnostic performance of the parameters in distinguishing between cases and controls. The Area under the Curve (AUC), sensitivity and specificity were calculated for all parameters to quantify their discriminative ability. The Youden Index was used to determine the optimal cutoff point by identifying the threshold that maximized sensitivity and specificity.

Result

We have calculated 313 eyes from 163 patients, out of which 109 eyes were included in the control group and 68 PACS, 107 PAC, and 29 PACG eyes were included in the study group. The mean age group of Angle closure eyes was 52.4 ± 11.06 years, and the mean age group of Normal eyes was 45.6 ± 11.8 years. The mean lens vault of Angle closure was found to be (590.01 ± 203.26) micron, and the control group (141.39 ± 191.33) micron. Significant difference between the angle closure and the control group was found for the lens vault ($P=0.000$). Significant difference between the angle closure and the control group was found for the LP (Lens position) (4.89 ± 0.25 vs 5.34 ± 0.23) mm ($P < 0.001$) and RLP (Relative lens position) (0.21 ± 0.01 vs 0.23 ± 0.01) $P < 0.001$.

Table 1 Mean value of Lens vault, Axial length, ACD, Lens thickness, Lens position and RLP

	Normal(n=109)	PACS(n=68)	PACD(n=107)	PACG(n=29)	P value
Lens vault(μm)	141.39 \pm 191.33	503.85 \pm 181.03	641.69 \pm 197.04	591.31 \pm 211.06	0.000
Axial length (mm)	23.62 \pm 1.14	22.78 \pm 1.21	22.75 \pm 1.51	23.16 \pm 0.80	>0.01
Anterior chamber Depth (mm)	3.28 \pm 0.27	2.71 \pm 0.27	2.58 \pm 0.26	2.69 \pm 0.35	>0.01
Lens thickness (mm)	4.11 \pm 0.35	4.44 \pm 0.38	4.54 \pm 0.41	4.62 \pm 0.37	>0.01
Lens position(mm)	5.34 \pm 0.23	4.93 \pm 0.24	4.85 \pm 0.26	4.99 \pm 0.24	>0.01
Relative lens position	0.23 \pm 0.01	0.22 \pm 0.01	0.21 \pm 0.02	0.22 \pm 0.01	>0.01

The area under the curve (AUC) for lens vault was 0.95, with a best cutoff point at 361 μm , sensitivity of 89.7%, and specificity of 89%. For axial length, the AUC was 0.73, with a sensitivity of 64.2 %, specificity of 77.1 % and best cut-off point at 22.95 mm. For ACD, the best cut-off point was 2.98, with the AUC of 0.995, sensitivity of 89.7 % and specificity of 89.9 %. For Lens thickness, the AUC was 0.78 with a sensitivity of 76% and a specificity of 67%. For lens position, the AUC was 0.92 with sensitivity of 82.4 % and specificity of 89%. For the Relative Lens position, the AUC was 0.72 with 64.7% sensitivity and 68.8% specificity.

Table 2: Diagnostic performance of biometric parameters based on ROC analysis, including AUC, sensitivity, specificity, and best cutoff values.

	Best Cut off point	Area under curve (AUC)	Sensitivity (%)	Specificity (%)
Lens vault (μm)	361	0.95	89.7	89.0

Axial length (mm)	22.95	0.73	64.2	77.1
Anterior chamber depth(mm)	2.98	0.95	89.7	89.9
Lens thickness(mm)	4.31	0.78	76.0	67.0
Lens position(mm)	5.10	0.92	82.4	89.0
Relative lens position	0.22	0.72	64.7	68.8

For lens vault, the highest AUC was observed in the normal vs PAC group (AUC = 0.97), with the greatest sensitivity (94.4%). The highest specificity for lens vault was noted in the normal vs PACG group (91.7%). The highest AUC for axial length was seen in the normal vs PAC group (AUC = 0.77). The highest sensitivity was in the normal vs PACG group (72.4%), and the highest specificity in the normal vs PACS group (78.0%). For anterior chamber depth, the highest AUC was found in the normal vs PAC group (AUC = 0.97). The highest sensitivity (95.3%) was also observed in this group, while the highest specificity (89.9%) was seen in both the normal vs PAC and normal vs PACG groups.

Table 3: Diagnostic Performance of Anterior Segment Parameters for Differentiating Normal Eyes from PACS, PAC, and PACG

Group comparison		Best cut off point	Area Under Curve (AUC)	Sensitivity (%)	Specificity (%)
Lens vault (µm)	Normal vs PACS	341	0.93	88.2	85.3
	Normal vs PAC	366	0.97	94.4	89
	Normal vs PACG	378	0.94	86.2	91.7

Axial length (mm)	Normal vs PACS	22.94	0.74	66.2	78.0
	Normal vs PAC	22.95	0.77	70.1	77.1
	Normal vs PACG	23.52	0.60	72.4	45.0
Anterior chamber depth (mm)	Normal vs PACS	3.01	0.95	88.2	86.2
	Normal vs PAC	2.98	0.97	95.3	89.9
	Normal vs PACG	2.94	0.93	82.8	89.9

The area under the curve (AUC) for lens thickness was highest in the normal vs PACG group (AUC = 0.84), with the greatest sensitivity (86.2%). The highest specificity was observed in the normal vs PAC group (76.1%). For lens position, highest area of curve was in normal vs PAC group (AUC= 0.93), with the greatest sensitivity (88.8%) and greatest specificity (89%). The relative lens position was highest for both normal vs PAC group and normal vs PACG group.

Table 4: Diagnostic Performance of Anterior Segment Parameters for Differentiating Normal Eyes from PACS, PAC, and PACG

	Group comparison	Best cut off point	Area Under Curve (AUC)	Sensitivity (%)	Specificity (%)
Lens thickness (um)	Normal vs PACS	4.29	0.72	69.1	66.1
	Normal vs PAC	4.39	0.80	72.9	76.1
	Normal vs PACG	4.35	0.84	86.2	71.6

Lens position (mm)	Normal	vs	5.14	0.91	82.4	85.3
	PACS					
	Normal	vs	5.10	0.93	88.8	89.0
	PAC					
	Normal	vs	5.16	0.86	75.9	78.9
	PACG					
Relative lens position	Normal	vs	0.22	0.69	60.3	65.1
	PACS					
	Normal	vs	0.22	0.74	69.2	68.8
	PAC					
	Normal	vs	0.22	0.74	69.0	68.8
	PACG					

Discussion

The biometric characteristics of eyes with shallow angle have been studied widely, mainly in Asian populations. These eyes typically have shorter axial length, shallower anterior chamber, smaller corneal diameter, and a thicker and more anteriorly located lens than that in open angle eyes.(5,11,21,22,23)

LV is a recently described ASOCT parameter which measures the amount of lens that is situated anterior to the level surface of the scleral spurs. A greater LV has been found to be strongly associated with an increased risk of angle closure in persons of Chinese ethnicity (24) and Japanese ethnicity (25), suggesting its potential role in screening for the condition. In this study, we wished to confirm the role of this parameter in another ethnic group, the North Indian. Compared to the thickness and position of the lens, only the LV was found to be significantly associated with angle closure in the Japanese, comparable to the consequence in the Chinese. Although the lens was thicker and more anteriorly located in eyes with angle closure, after multivariate adjustments the other lens parameters were not significantly associated with angle closure.

Exaggerated LV has been defined quantitatively as LV more than one-third the distance between the corneal endothelium and a line joining the nasal and temporal scleral spurs.(26) LV is a quantitative parameter which measures the portion of the lens in relation to the plane of the scleral spurs, with the scleral spurs being a surrogate marker of the posterior limit of the anterior chamber angle. It is an easily obtained parameter once an ASOCT image is at hand. Lowes and Mapstone proposed a vector model of pupil block mechanism: the

co-contraction of both iris sphincter and dilator muscle, as well as the iris elasticity, will generate a resultant force upright to the lens surface, causing relative or absolute obstruction of aqueous flow in the pupil region (27–29). In eyes with forward movement of the lens–iris diaphragm, the contact between iris and anterior lens surface is anterior positioned; thus, it decreases the angle between the respective vectors, and thus increases the resultant force on the lens surface and resistance to aqueous flow from posterior to anterior chambers. Our results further suggest that the position (relative to scleral spurs) of the anterior lens surface appears to be more important than lens thickness and position itself in angle closure. We hypothesize that a larger LV would occupy more space in the anterior chamber, causing crowding of the anterior segment and aggravation of the pupil block component, resulting in narrowing of the angle. With good ability to predict eyes with angle closure confirmed in two different ethnic groups, as well as its ability to quantify the relationship of the lens with respect to the anterior chamber angle or its structures, LV and LP have the potential to be utilized as a screening and diagnostic parameter for angle closure.

This study guides us to differentiate between normal and angle closure eye with few biometric lens parameters. Where lens vault more than 361 μm or lens thickness more than 4.31mm or lens position more than 5.10 mm firmly alarming for angle closure eye. These lens parameters each plays an important role to indicate the angle closure eye.

Interestingly, although the 3 subtypes of angle closure (PACG, PAC, and PACS) had similar biometric parameter measurements (e.g., ACD and AL), LV was different and was significant ($P>0.01$) among PACS, PAC and PACG in angle closure subgroups. (table) But LP and RLP were not playing in major role in subgroups where in case of normal population LP and RLP were significant factors.

In future studies, it would be important to prospectively evaluate the association of changes in LV with angle-closure progression. One of the limitations to this study was that the groups were not age or gender matched. The angle closure group was slightly older and had more females. Second, this was a cross-sectional study; hence, it is difficult to establish chronological or contributory relationships. Third, the association of lens parameters with cataract type was not investigated (but we excluded significant nuclear cataract). It is possible that the type of cataract may influence LT and LV. Factors such as accommodation, lighting, which may induce changes in the various lens parameters, were not evaluated. The study population was north Indian, and it is not known if the results would be the same in other racial groups. Finally, the relatively small sample size may have affected the ability to detect subtle differences in biometric and lens characteristics.

Conclusion

In summary, this study found that eyes with angle closure have thicker lenses with a greater LV, shallower ACD, and shorter AL. Lens vault was associated strongly and independently with angle closure and distinguished eyes with angle closure from those with open angles better than traditional biometric parameters. Similarly, Position of the lens plays an important role in angle closure ocular structure. But any significant differences were not noted in RLP between eyes with and without angle closure. Lens vault as well as lens position therefore are potential novel markers associated with angle closure.

Conflict of Interest

The authors declare no conflicts of interest.

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