Ocular Biometry in the Subtypes of Primary Angle Closure Glaucoma in University Malaya Medical Centre

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Summary

Thirty-seven consecutive patients (41 eyes) diagnosed with primary angle closure glaucoma (PACG) attending the Glaucoma Clinic in University Malaya Medical Centre, over a period of 6 months were categorized into acute, subacute and chronic PACG from their clinical presentation. Each case was subjected to automated refraction, A-scan biometry for anterior chamber depth, axial length and lens thickness, keratometry and corneal diameter measurement. Calculations for the relative lens position and the lens thickness: axial length index were performed. The data collected was analysed by the nonparametric test (Kruskal-Wallis), one way analysis of variance (ANOVA), chi-square test, Spearman's nonparametric correlations and regression analysis. For controls 15 eyes from 15 normal subjects matched for age, sex, refractive error and race were chosen and subjected to the same examinations. Chronic PACG was the predominant subtype (53.6% of patients and 58.5% of eyes). The ocular biometric measurements of acute PACG eyes deviated most from normals in having the shallowest anterior chamber depth, shortest axial length, smallest corneal diameter, steepest corneal radius, thickest and most anteriorly situated lens, and the greatest lens thickness: axial length index. The subacute subtype was closest to normal and chronic PACG subtype fell in between in most of the biometric characteristics. These findings were not statistically significant. All PACG eyes as a group however showed statistically significant shallower anterior chamber depth (p<0.05), and a more anterior relative lens position (p<0.05) compared to normals.

Key Words: Primary open angle glaucoma, Subtypes, Ocular biometric measurements

Introduction

Primary angle closure glaucoma (PACG) is the predominant form of glaucoma in Asian countries[1]. In whites PACG typically presents as an acute attack. In Asians and Blacks however the tendency is to develop a gradual asymptomatic chronic angle closure[2]. Known risk factors for primary angle closure glaucoma include a shallow

anterior chamber, thick lens, anterior lens disposition, small corneal diameter, shorter axial length of globe, and small radius of corneal curvature. However, other than the studies by Sihota et al [3,4] and Marchini et al [5], little is known regarding differences in ocular dimensions that may be responsible for the clinical differences among the acute, subacute and chronic subtypes of PACG. This cross sectional study aims to study the differences in the biometric measurements

amongst the different subtypes of PACG, which might explain the variations in the types of presentation of primary angle closure glaucoma. All biometric measurements were performed by one person.

Materials and Methods

The study comprised of 37 consecutive patients (41 eyes) diagnosed with primary angle closure glaucoma (PACG) attending the eye clinic over a period of 6 months. Fifteen controls free from ocular disease were taken from patients and medical staff and matched for age, refraction, race and sex. Exclusion criteria included patients who had undergone any form of surgery like drainage surgery, surgical iridectomy or laser iridotomy and those with other intraocular diseases. Patients on pilocarpine had the drops stopped at least 2 weeks before the biometry was performed. Also excluded were patients with angle closure glaucoma due to secondary causes such as lens abnormalities and rubeosis iridis. Each patient's particulars and detailed history including family history of glaucoma were recorded. PACG patients/eyes diagnosed from narrow angles on gonioscopy (non-indentation) were further staged from their presenting features into acute, subacute and chronic PACG as follows:

Acute PACG:

a. Presence of periocular pain, congestion with severe elevation of intraocular pressure (IOP) and accompanying corneal oedema at presentation
b. Angle of Grade 0 by Shaffer's classification

Subacute PACG:

a. At least one eye with an occludable angle with or without an increase in pigmentation or presence of peripheral anterior synechiae.
b. Patient may or may not have a history of intermittent attacks including those precipitated by physiological mydriasis with IOP greater than 21 mmHg

c. A rise in IOP greater than or equal to 8 mmHg on dark-prone provocative testing (30 minutes face-down in the dark) if the IOP is less than or equal to 21 mmHg
d. A normal optic disc

Chronic PACG:

a. IOP greater than 21mmHg with a variable amount of synechial angle closure
b. Presence of an increased cup disc ratio of 0.4 and above and field abnormalities

Each case underwent a thorough ophthalmic examination which included measurement of the best corrected visual acuity, automated refraction, slit-lamp examination, funduscopy with grading of the vertical cup:disc ratio, applanation tonometry, gonioscopy, keratometry, corneal diameter measurement, A-scan ultrasound biometry and a dark room provocative test where applicable. The vertical and horizontal 'white to white' corneal diameters were measured using Castroviejo callipers and averaged. The keratometry readings were taken in two meridians using the Takata Cooper Vision EB-020 Javal-Schiotz Keratometer and averaged.

To minimize error due to residual corneal indentation, keratometry was performed prior to A-scan biometry and at least half an hour after gonioscopy and applanation tonometry. The Nidek Echoscan US-800 was used to measure the anterior chamber depth, lens thickness, and axial lengths of the eyeball. Five axial length measurements with the most acceptable A mode waveforms were recorded and the 3 most consistent measurements obtained and averaged. Lowe's formula[6] which is the sum of the anterior chamber depth + half lens thickness divided by the axial length was used to determine the relative lens position. The lens thickness: axial length index[7] was calculated as the ratio of the lens thickness to the axial length multiplied by 10.

Analysis

To assure statistical independence between eyes, both eyes of each patient were analysed to see if the PACG was unilateral or bilateral. Bilaterally affected patients had their right eyes analysed unless each eye presented as different subtypes when the eyes were analysed separately. The data was analysed using the Microsoft SPSS 7.5 software. As the number of eyes in the acute and subacute groups were small, p-values were obtained using both the non-parametric test (Kruskal-Wallis) and the oneway analysis of variance (ANOVA). Correlations were done using the Spearman's nonparametric test. Multivariate analysis using linear regression was also performed, with each parameter being made the dependant variable.

Results

Age, sex, and racial distribution of PACG

Thirty-seven patients were recruited. There were 6 patients in the in the acute subtype (14.6%), 9 (21.9%) with subacute and 22 (53.3%) with the chronic subtype of PACG. Four patients had bilateral involvement with the fellow eye belonging to a different subtype of glaucoma. Thus 41 eyes were studied; 6 eyes presented with an acute PACG, 11 with subacute and 24 with the chronic subtype of PACG.

The 4 bilateral cases were put under acute subgroup for age, sex and racial distribution as all presented with acute PACG in one eye and either subacute or chronic in the other. There were 21 males and 16 females with the male to female ratio of 1.3:1. In the acute PACG subtype, 5 of 6 patients were females (83.3%) while in the subacute and chronic subtypes 6 of 9 patients and 14 of 22 patients respectively were males. For all 3 subtypes of PACG, the most commonly affected age group was between 60 - 69 years (20 patients) with an overall age range of 41 - 81 years, and a mean of (63.8±9.4). There was a significant age difference (p<0.05) between all 3 subtypes of PACG. Subacute PACG patients tended to be

younger (mean age 56.8±10.0 years), whereas patients with chronic PACG were in the older age range (mean age 66.5±9.0 years). The mean age for female patients was 63.4±9.2 and male patients 64.0±9.8 years. Of the 37 patients, 4 (10.8) were Malays, 18 (48.6%) Indians and 15 (40.5%) Chinese. In the acute subtype there were 1 Malay, 4 (66.6%) Chinese and 1 Indian; in the subacute- 1 Malay, 2 Chinese and 6 (66.6%) Indians while in the chronic subtype, 2 Malays, 8 Chinese and 11 (50%) Indians.

Biometric values

The mean and standard deviation of each biometric parameter studied in the four groups are detailed in Table I.

Anterior chamber depth

The anterior chamber depth was not significantly different among the 3 subtypes of PACG.

The mean anterior chamber depths of all subtypes of PACG (2.74±0.48mm) was however significantly shallower than in normal (3.17±0.43mm) with (p<0.05). This is especially in the acute PACG (p=0.019) and chronic PACG subtype (p=0.027). There is a considerable overlap in values in the normal and PACG groups. The shallowest anterior chamber was seen in the acute PACG subtype (mean depth of (2.49±0.27) which also had the smallest range of values of 2.14 - 2.83 mm. Chronic PACG had a shallower mean anterior chamber depth than the subacute subtype.

Axial length, keratometry readings, corneal diameter and lens thickness

There was a considerable overlap in axial length measurements between all four groups; and no statistically significant differences were found between them. The mean axial length was shortest in the acute PACG subtype (22.30±0.78mm) and longest in eyes with chronic

Table I
Comparison of Ocular Biometric Measurements and Refractive Status
for the Acute, Subacute and Chronic Subtypes of PACG and Normal Eyes

Ocular Features	Acute PACG (n=6)	Subacute PACG (n=11)	Chronic PACG (n=24)	Normal Eyes (n=15)	P Value Between			
					All groups (inc. normals)		PACG Subtypes only	
					ANOVA	KW	ANOVA	KW
Anterior Chamber Depth (mm)	2.49±0.27@ (2.14-2.83)	2.91±0.75 (2.13-4.82)	2.73±0.33 (2.13-3.42)	3.17±0.43 (2.13-4.82)	0.010*	0.006*	0.228	0.302
Axial Length (mm)	22.30±0.78 (21.55-23.52)	23.05±1.76 (20.69-27.14)	23.11±0.83 (21.71-25.30)	23.05±0.80 (21.61-24.24)	0.408	0.240	0.299	0.154
Corneal Radius (D)	45.00±1.34 (42.50-46.50)	44.59±1.76 (42.00-47.50)	43.73±1.64 (41.00-48.00)	44.33±1.18 (42.00-45.50)	0.202	0.138	0.148	0.127
C Diam (mm)	11.12±0.18 (10.50-11.75)	11.48±0.14 (10.75-12.50)	11.53±0.08 (10.75-12.50)	11.60±0.39 (11.00-12.50)	0.140	0.213	0.140	0.183
LT (mm)	4.61±0.57 (3.92-5.26)	4.19±0.69 (2.87-5.41)	4.30±0.79 (2.23-5.72)	4.21±0.57 (3.05-5.33)	0.646	0.561	0.538	0.458
RLP	0.21±0.01 (0.20-0.22)	0.22±0.03 (0.19-0.28)	0.21±0.03 (0.15-0.31)	0.23±0.02 (0.19-0.25)	0.384	0.074	0.969	0.920
SPH. EQ. (D)	0.14±2.19 (-3.58-+2.50)	-0.68±2.68 (-7.37-+2.04)	0.47±1.77 (-5.87-+2.75)	-0.05±0.82 (-1.60-+1.25)	0.398	0.303	0.333	0.486
LT:AXL Index	2.07±0.31 (1.73-2.42)	1.82±0.33 (1.29-2.53)	1.86±0.35 (0.96-2.37)	1.83±0.26 (1.41-2.39)	0.410	0.473	0.569	0.562

Indicators: LT: lens thickness
AXL: Axial Length
RLP: Relative lens position
SPH. EQ (D): Spherical equivalent (Dioptres)
Range values are bracketed
p-value obtained using one way ANOVA and nonparametric test
KW:Kruskal-Wallis
@ : mean ± standard deviation
* : significant (p<0.05)

PACG (23.11±0.83). The keratometric readings in the various subgroups did not vary significantly. There was however a trend of an increasing corneal steepness with acute ACG eyes having the steepest cornea (45±1.34 Dioptres), followed by subacute (44.59±1.70 Dioptres) and chronic eyes (43.73±1.64 Dioptres). The controls eyes had steeper corneas compared to PACG eyes. The smallest mean corneal diameter was seen in the acute PACG subtype (11.12±0.18mm) and the largest in the control eyes (11.60±0.39 mm). No statistically significant differences were found between the 4 groups.

Although the lens was thickest in the acute PACG subtype (4.61±0.57) and thinnest in the eyes with subacute PACG (4.19±0.69), the statistical differences were also not significant.

Relative lens position/lens thickness, axial length ratio

The relative lens position was calculated using Lowe's formula[6]. The lens in the PACG group were situated more anteriorly (mean 0.21±0.03) compared to control eyes (mean 0.23±0.02) This was statistically significant when the nonparametric test was used (p<0.05). The lens was situated most anteriorly in eyes with acute PACG (0.21±0.01). The range of relative lens position was largest in the chronic PACG subtype (0.15 - 0.31). The lens thickness to axial length ratio multiplied by ten provides an index with values of one or more, which is also referred to as the lens thickness/axial length factor[7]. Acute PACG eyes had the greatest value (2.07±0.31) followed in decreasing order by chronic PACG (1.86+-0.35), controls (1.83+-0.26) and subacute PACG eyes (1.82+-0.33). There was no statistical significance in these values between the groups.

Refraction in spherical equivalence revealed that only 5/37 (13.5%) of patients with PACG had hyperopia of >2 Dioptres.

Correlations

The strongest correlation was seen when lens thickness:axial length index was made the dependant variable, and the rest of the parameters as independent variables. Statistically significant correlations were noted with the corneal radius measurements (Table II). Anterior chamber depth also correlated significantly with axial length, lens thickness and relative lens position (R^2 = 0.76).

Discussion

PACG occurs in anatomically predisposed eyes and aqueous outflow is obstructed solely as a result of closure of the angle by the peripheral iris. PACG is subdivided into the acute, subacute and chronic subtypes and each presents differently. In the acute form, there is sudden and severe elevation of the IOP due to a total closure of the angle. In the subacute subtype, the angle is narrow in only one part. A rapid partial closure and reopening of the angle occurs and the level of elevation of IOP is proportional to the extent of angle closure. The chronic subtype has similar clinical features as the primary open angle glaucoma except that the angle shows a variable amount of closure on gonioscopy.

Chronic PACG is the commonest form[3] as found in this study (58.5% of eyes) followed by subacute (26.8%) and acute (14.6%) groups. With age there is increasing percentage of occludable angles and increase incidence of PACG[8]. The mean age in this study was 64 years and that no one was below 41 years agrees with the fact that PACG is rare below 40 years[9]. The subacute patients tended to be younger (mean age 56.8±10.0) while the chronic PACG (p>0.05) were in the older age group (66.5±9.0). Sihorta and Agarwal[10] also found a statistically significant difference in the age distribution of subtypes; the acute predominated between the 3rd and 4th decade while the subacute between 4th to 5th.

Table II
Statistical Correlations between Ocular Biometric Measurements
Taken from all PACG Eyes and Controls

Dependant Variable	P Value	Predictors								
		ACD	AXL	C.RAD	C.DIAM	LT	RLP	S.EQ	LT:AXL	R²
ACD	0.000		0.000	0.753	0.617	0.000	0.000	0.756	0.888	0.76
AXL	0.000	0.000		0.003	0.125	0.002	0.002	0.000	0.000	0.56
C.RAD	0.001	0.753	0.003		0.578	0.609	0.439	0.003	0.000	0.27
C.DIAM	0.187	0.825	0.102	0.585		0.879	1.000	0.267	0.491	0.06
LT	0.000	0.000	0.002	0.608	0.962		0.000	0.805	0.000	0.59
RLP	0.000	0.000	0.02	0.439	0.924	0.000		0.734	0.212	0.74
S.E	0.001	0.756	0.000	0.003	0.287	0.805	0.734		0.027	0.27
LT:AXL	0.000	0.888	0.000	0.000	0.491	0.000	0.212	0.027		0.99

Correlations are calculated from multivariate using linear regression

Indicators:

ACD	:	Anterior chamber depth	LT	:	Lens thickness
AXL	:	Corneal radius	RLP	:	Relative lens position
C.RAD	:	Corneal radius	S.E	:	Spherical equivalent
C.DIAM:		Corneal diameter	R²	:	Adjusted R square

PACG is one and half to three times as great in females as it is in males[11,12]. The female Chinese is the major risk factor for PACG in Singapore[9]. Females have narrower angle width[12] and are 4 to 5 times more likely to have occludable angles[8]. This study however showed that there were more males (56.1%) than females (34.1%) with PACG. There were more females only in the acute subtype where 5 of 6 patients (83.3%) were females. Quigley[13] presumed that males and females were equally affected, as the stratification by sex produced groups too small for analysis. The average age of males (64.0±9.8 years) and that of females (63.4±9.2 years) in this study were almost similar. Leighton et al[14] found that their males were younger, with an average age of 58.8 years compared to that of females, 67.6 years.

The Chinese majority in PACG[9,15] is true in this study in the acute subtype only. The Indians, the third majority ethnic group in Malaysia,

unexpectedly made up the largest number of patients with PACG (43.9%). They were mainly in the subacute and chronic subgroups. The normal Chinese population was found not to differ from other ethnic groups in many of the biometric risk factors known to be of importance for PACG[16]. Oh et al[17] noted that the higher incidence of PACG in Asians could be due to a more anterior insertion of the thick, rigid irides to the cilliary body which was thought to predispose these patients to gradual angle closure.

In this study significant differences between all PACG groups and normals were seen only in two ocular biometric values namely, the anterior chamber depth and in the relative lens position. The differences were not significant in other values. Among the subtypes there was no statistically significant difference noted in any of the ocular biometric measurements.

The average anterior chamber depth of 2.74±0.48mm for all PACG eyes in this study was slightly deeper than in other studies[6,12,18] which ranged from 1.76mm to 2.48mm. The shallowest was seen in the acute subtype. Shallower anterior chamber in PACG could be due to an increased thickness of a normally positioned lens, a forward displacement of the whole lens or a combination of both factors. PACG rarely occurs with an anterior chamber depth greater than 2.5mm and the risk of angle closure increases with depths less than 2.5mm[19]. The larger number of eyes (35 out of 41) in the subacute and chronic groups could explain the deeper anterior chamber depth found in this study. These subtypes have nearer to normal anterior chamber depths and less anteriorly placed lens compared to the acute subtype.

The axial lengths were found to be shorter than normal in some studies while in others no significant difference was found. In the latter case the authors suggested that the structural abnormality in PACG is in the anterior part of the eye. In our study the average axial length of all PACG eyes was 23±1.5mm and this was shorter by 0.5mm compared to normal.

This study showed that the thickest lenses were seen in the acute PACG eyes (4.61+0.57mm) .The lens was thinner in chronic PACG eyes compared to the acute PACG ones (mean difference of 0.3mm). A thinner lens may explain the lower incidence of acute PACG attacks in the black population[20] as well as why they seldom present as pupillary block glaucoma. In this study although there is a considerable overlap between lens thickness of each PACG subtype and normals, there was a mean difference of 0.1mm between all ACG eyes and normals and an even greater mean difference of 0.4mm between acute PACG eyes and normals.

Lowe[6] found a significant difference in the **relative lens position** (RLP) in normal eyes and eyes with angle closure glaucoma. It was less for eyes with angle closure, meaning that the lens is situated further forward. Similarly in this study, PACG eyes the relative lens position of (0.21±0.03) was significantly anterior (p<0.05) when compared to normals (0.23±0.02). Among the subtypes, the RLP was most anterior in the acute PACG eyes, followed closely by chronic and subacute eyes. This difference was however not significant. Sihota et al [4] found that acute PACG eyes had significantly anterior lenses as compared to subacute PACG and control eyes (p<0.0001) and chronic PACG eyes (p<0.05).

The role of **lens thickness/axial length factor** as a predictor of clinical outcome in PACG has been highlighted by Saxena et al [7], as this factor was found to be significantly greater (p<0.001) for the PACG cases when compared to controls. No such difference was found in this study, although acute PACG eyes had the greatest value, followed in decreasing order by the chronic, normal and subacute subtypes. Markowitz et al [21] found that the lens thickness/axial length factor was age dependent and was greater than normal for most age groups with angle closure glaucoma. They found that the factor standardizes the assessment of eyes with PACG and is highly reliable and reproducible and could easily chart the clinical course of the eye examined.

This study showed no significant differences in **keratometry readings** of PACG eyes and normals and between subtypes. The cornea was steepest in the acute subtype, followed by the subacute, and chronic subtype. The difference however, was not statistically significant. The cornea was found steeper in the normal eyes (44.33±1.17 Dioptre) compared to PACG eyes (44.14±1.67 Dioptres). Congdon et al[5] also found that their normal subjects had a steeper cornea than their Chinese patients with PACG, although this was not statistically significant. On the other hand Tomlinson and Leighton[18] did not find any such difference in corneal keratometric readings between PACG eyes and controls. They attributed this to the careful matching of refraction in their study.

The **corneal diameter** was smaller in PACG eyes compared to normal eyes. There was a trend towards an increasing size of the cornea starting with acute PACG, followed by subacute, chronic, and the normal eyes. All this was however, not statistically significant. Other studies[4,18] reported significantly smaller corneal diameters in PACG eyes than in controls.

There was no significant difference in refractive error found among all subtypes of PACG, and no groups had a mean value of >2 Dioptres of hyperopia. Oh et al[17] reported that refractive error significantly affects both levels of iris insertion (p <0.003) and angle width (p<0.0001). The iris tends to join the ciliary body more anteriorly in hyperopic eyes. An anterior iris insertion may predispose to progressive formation of peripheral anterior synechiae even in the presence of a deep anterior chamber in myopic eyes. This might explain the predominance of PACG despite the high incidence of myopia reported in Asians.

Using regression analysis, the anterior chamber depth correlated well ($R^2=0.76$) with axial length, lens thickness and the relative lens position. Sihota et al [4] found that additonal to this, the corneal diameter, refractive error and central corneal thickness also statistically correlated with the anterior chamber depth ($R^2=0.99$).

Conclusion

Ocular biometric differences occur among the subtypes of PACG and can explain the different clinical presentations of the subtypes. The acute PACG had the greatest deviation from normal in all aspects and had the following characteristics: the shallowest anterior chamber depth, shortest axial length, steepest corneal radius, thickest and the most anteriorly situated lens, and the highest lens thickness to axial length index. The *subacute* PACG subtype were the closest to normal in all biometric characteristics except for a steeper corneal radius and a smaller corneal diameter than chronic PACG eyes. The chronic PACG subtype fell in between acute and subacute PACG in most aspects. Biometric differences alone is not able to explain the spectrum of clinical presentations of PACG. Physiological factors perhaps play a part. Further research with a greater number of cases is needed to investigate the cause of the observed clinical variations between the different subtypes of PACG.

Acknowledgements

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