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Relevance of relationships between eye structure measurements for risk of anterior chamber angle closure

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ABSTRACT

Aim of the study: To analyze the relationships between eyeball length, anterior chamber depth and lens thickness with respect to age and refractive state and in chronic versus acute angle-closure glaucoma.

Material and methods: 240 patients were evaluated: 180 patients with different refractive states and 60 patients with primary angle-closure glaucoma, acute angle closure glaucoma and cataract.

Results: We propose a predictive factor (PF) for anterior chamber angle closure based on ultrasound biometrics. PF = AC / AL / LT × 100. A significant decrease in PF with age was noted in all refractive states. In hypermetropia, PF was significantly lower than in myopia and emmetropia. PF is more sensitive than Lowe's coefficient towards a tendency for angle closure with respect to age and refractive state. A significant difference in PF was observed between acute angle closure and cataract groups, and between chronic angle-closure glaucoma and cataract groups. Its significance was higher than the significance of Lowe's coefficient between the respective groups. PF below 2.5 is a significant risk factor of anterior chamber angle closure.

Conclusions: The risk of anterior chamber angle closure is primarily determined by relationships between measurements of eyeball structures (eyeball length, anterior chamber depth, lens thickness). We propose a PF coefficient calculated from these relationships, which reliably predicts the risk of anterior chamber angle closure.

KEY WORDS: angle-closure glaucoma, anterior chamber depth, age-related anterior chamber peculiarities, ultrasound biometrics, angle closure prediction factor, Lowe's coefficient.

INTRODUCTION

Anatomical factors predisposing to iridocorneal angle closure and ways to predict it are relevant to understanding the mechanism of primary angle-closure glaucoma (PACG). Acute angle closure, which is often the first presentation of PACG, frequently leads to irreversible optic disk damage with a decline in vision. If the iridocorneal angle is narrow, identification of angle closure threat is crucial for timely preventive intervention (laser iridotomy, laser peripheral iridoplasty, phacoemulsification of lens).

Iridocorneal angle closure is known to be anatomically associated with shorter eyeball length, thicker lens and shallow anterior chamber [1-4]. Lowe [5, 6] analyzed the role of changes in the lens in iridocorneal angle closure. He identified three key factors which lead to a decrease of anterior chamber depth. These are constitutional lens thickening, thickening of the lens with age, and lens edema secondary to cataract [7] According to Lowe, anterior displacement of the lens (relative lens position) plays a special role in iridocorneal angle closure [5]. The latter factor was identified by Lowe as an important and reliable factor leading to iridocorneal angle closure. This factor is termed Lowe's coefficient or relative lens position (RLP). RLP = (AC + 1/2 LT) / AL × 10, where AC stands for anterior chamber depth (in mm), 1/2 LT is half thickness of the lens (in mm), and AL is the axial length of the eyeball (in mm).

Like Lowe, Markowitz *et al.* (1985) [8] view changes in the lens, specifically the age-related ratio of lens thickness (LT) to eyeball axial length (AL), as key factors in angle closure. This relationship (lens thickness/axial length) is termed length axial factor (LAF). Studies by Markowitz demonstrated a significant difference in LT:AL ratio between patients with 'normal' eyes and angle-closure glaucoma patients of the same age.

Marchini [9] used ultrasound biometrics to study the mechanism of different types of angle-closure glaucoma and obtained data comparable to those of Lowe and Markowitz. High reliability of Lowe's coefficient in prediction of ante-

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rior chamber angle closure was further confirmed by Saxena *et al.* [10]

However, Razeghinejad *et al.* [11] failed to demonstrate a significant difference in biometrics of eyes with suspected iridocorneal angle closure versus primary angle-closure glaucoma. Huang *et al.* [12] were unable to demonstrate any significant role of lens thickening, lens position, or eyeball length in transition from suspected angle closure to angle-closure glaucoma. Sihota *et al.* noted shallow anterior chamber and lens thickening in relatives of angle-closure glaucoma patients, but shorter eyeball length was considered the only reliable risk factor for iridocorneal angle closure [3]. Similarly, Li *et al*. (2019) demonstrated that shorter eyeball length is the only marker of severe angle-closure glaucoma.

However, constitutional difference in the ratio between anterior chamber depth (AC) and eyeball axial length (AL) is an important factor in development of angle-closure glaucoma. Decrease in this ratio is an obvious risk factor for anterior chamber angle closure [12].

We hypothesized that better reliability in predicting the risk of angle closure may be achieved by combining all these factors in one equation. The coefficient we propose is termed the 'predictive factor' (PF). PF is calculated as follows: anterior chamber depth (AC) is divided by axial eyeball length (AL), then divided by lens thickness (LT), and multiplied by 100. PF = AC / AL / LT × 100.

This formula is more sensitive to the ratio of the depth of the anterior chamber to the length of the eyeball (the smaller the ratio of the depth of the anterior chamber to the length of the eyeball, the higher the risk of anatomically narrow angle of the anterior chamber) and the ratio of eyeball length to lens thickness (the smaller the ratio of the length of the eyeball to the thickness of the lens, the greater the risk of closing the angle of the anterior chamber due to age-related changes in the lens). Thus, the lower the prediction factor, the greater the risk of closing the angle of the anterior chamber.

The aim of the study was to analyze the relationships between eyeball axial length, anterior chamber depth and lens thickness with respect to age and refractive state, and in chronic versus acute angle-closure glaucoma. From these data we aimed to derive a predictive factor for angle closure and to test its significance and reliability in patients with PACG, acute angle closure and age-related cataract.

MATERIAL AND METHODS

We evaluated 240 patients: 180 patients with different refractive states and 60 patients with primary angle-closure glaucoma, acute angle closure and cataract.

Age-related biometric data were collected from 60 patients with emmetropia (28 women and 32 men) aged 20, 40, and 60 years, 60 patients with moderate myopia (31 women and 29 men) aged 20, 40, and 60 years, and 60 patients with moderate hypermetropia aged 20, 40, and 60 years (37 women and 23 men).

To confirm the reliability of different mathematical models predicting iridocorneal angle closure, we collected biometric data from sixty eyes of 60 patients (34 women and 26 men) aged 62 to 75 years, including 20 patients with acute angle closure, 20 patients with primary chronic angle-closure glaucoma, and 20 patients with cataract.

Ultrasound biometry was conducted using a Scanmate Flex scanner, DGH Technology. We measured anterior chamber depth, lens thickness, and eyeball axial length. In all groups we calculated the PF we are proposing, along with Lowe and LAF coefficients.

Statistical analysis was performed in MS Excel. Results of the study are presented as mean and standard deviation (M ±SD). Significance of difference (p) in the dependent group parameters was assessed using Student's t-test for related sets. The difference was deemed significant if $p < 0.05$. Post-hoc analysis, such as Bonferroni's correction, was used to correct Student's t-test between three groups: acute angle-closure glaucoma, chronic angle-closure glaucoma, and cataract.

RESULTS

Table I shows biometric data in relation to age and refractive state, and indices derived from the biometrics. As can be seen from the Table, in all refractive states anterior chamber depth gradually decreased with age. Similarly, lens thickness increased with age. For all groups, $p < 0.001$.

Table I. Biometric data for different age and different refractive states, and derived indices

Refraction, age	AC (mm)	AL (mm)	LT (mm)	RLP	LAF	PF
Emmetropia, 20 years	3.79 ±0.26	23.88 ±0.52	3.66 ±0.09	2.356 ±0.1	1.533 ±0.05	4.526 ±0.35
Emmetropia, 40 years	3.46 ±0.16	23.66 ±0.36	3.87 ±0.086	2.28 ±0.06	1.635 ±0.03	3.782 ±0.23
Emmetropia, 60+ years	3.36 ±0.35	23.13 ±0.47	4.82 ±0.23	2.498 ±0.14	2.085 ±0.1	3.03 ±0.39
Myopia, 20 years	3.77 ±0.21	25.43 ±0.36	3.47 ±0.087	2.163 ±0.09	1.364 ±0.04	4.275 ±0.27
Myopia, 40 years	3.69 ±0.21	26.11 ±0.77	3.73 ±0.09	2.129 ±0.1	1.428 ±0.04	3.797 ±0.28
Myopia, 60+ years	3.35 ±0.11	26.23 ±0.39	4.55 ±0.09	2.144 ±0.06	1.735 ±0.04	2.85 ±0.13
Hypermetropia, 20 years	3.72 ±0.2	22.47 ±0.4	3.45 ±0.08	2.421 ±0.15	1.534 ±0.04	4.785 ±0.33
Hypermetropia, 40 years	2.98 ±0.1	21.82 ±0.31	4.32 ±0.12	2.132 ±0.1	1.983 ±0.11	2.638 ±0.33
Hypermetropia, 60+ years	2.67 ±0.5	21.62 ±0.35	4.88 ±0.33	2.362 ±0.2	2.259 ±0.15	2.549 ±0.59

Table II. Biometric data for eyes with acute angle closure, angle-closure glaucoma and cataract, and derived indices (M ±SD)

Groups	AC (mm)	AL (mm)	LT (mm)	RLP	LAF	PF
Acute angle closure	2.30 ±0.16	22.35 ±1.06	4.67 ±0.34	2.067 ±0.16	2.039 ± 0.2	2.213 ±0.25
Chronic ACG	2.40 ±0.21	21.55 ±0.65	4.81 ±0.42	2.245 ±0.12	2.235 ±0.1	2.386 ±0.22
Cataract	3.32 ±0.33	23.38 ±0.49	4.75 ±0.19	2.439 ±0.14	2.033 ±0.09	2.998 ±0.33

ACG – angle-closure glaucoma.

Table III. Results of least significant difference in Lowe's index, predictive factor and length axial factor by Student's *t*-test and post-hoc Bonferroni correction among study groups

	p-value					
	Student's t-test ($p < 0.05$)			Bonferroni correction ($p < 0.017$)		
	Lowe	PF	LAF	Lowe	PF	LAF
Group 1 vs. group 2	0.0037	0.6021	0.177	0.00057	0.1786	0.007236
Group 1 vs. group 3	0.0000000447	0.00000000033	0.2157	0.0000062	0.00000000037	0.0000000043
Group 2 vs. group 3	0.000068	0.0000000036	0.000000082	0.00000000098	0.000000000011	0.1420

Group 1 – patients with acute angle closure; group 2 – patients with chronic angle closure glaucoma; group 3 – patients with cataract.

Age-related increase in lens thickness directly and significantly affects the increase in LAF ratio (LT:AL) in all groups, $p < 0.001$. Lowe's coefficient (RLP) did not differ significantly with age or refraction state ($p > 0.05$). Conversely, a significant decrease of PF (in all groups, with $p < 0.001$) was observed with age in all refractive states, indicating the role of age-related changes in lens thickness. In hypermetropia, PF was significantly lower than in myopia and emmetropia ($p < 0.001$ in all groups). This suggests that the constitutional relationship between anterior chamber depth and eyeball axial length plays a role in anterior chamber angle narrowing.

Table II shows biometric data for eyes with acute angle closure, angle-closure glaucoma and cataract, and indices derived from the biometrics. As seen from the table, anterior chamber depth in acute angle closure (2.3 ±0.16 mm) was lower than anterior chamber depth in chronic angle-closure glaucoma (2.4 ±0.21 mm) and significantly differed from anterior chamber depth in cataract (3.32 ±0.33 mm), $p < 0.001$ for all groups. However, the difference in lens thickness between acute angle closure, chronic angle-closure glaucoma and cataract was not significant ($p > 0.05$). The difference in LAF coefficient between these groups was not statistically significant either. A significant difference in Lowe's coefficient was observed between acute angle closure and cataract groups, and between chronic angle-closure glaucoma and cataract groups, $p < 0.001$ for all groups. The same was observed for the PF coefficient. However, significance of the difference in PF coefficient between these groups was higher than that of the difference in Lowe's coefficient. Specifically, significance of the difference in PF between acute angle closure and cataract groups was $p = 0.000000000033$, while significance of the difference in Lowe's coefficient (RLP) between the same groups was $p = 0.000000044$. Significance of the difference in PF between chronic angle-closure glaucoma and cataract groups was $p = 0.0000000036$, while significance of the difference in Lowe's coefficient (RLP) between the same groups was $p = 0.000068$.

Bonferroni correction shows similar significant statistical difference (Table III). Significance of the difference in PF between acute angle closure and cataract groups was $p = 0.00000000037$, while significance of the difference in Lowe's coefficient between the same groups was $p = 0.0000062$. Significance of the difference in PF between chronic angle-closure glaucoma and cataract groups was $p = 0.00000000098$, while significance of the difference in Lowe's coefficient between the same groups was $p = 0.000000000011$. There was no statistically significance between groups of acute angle closure and chronic angle closure glaucoma.

DISCUSSION

Our data on lens thickening with age are in complete agreement with the data published by Marcowitz *et al.* [8]. These authors reported mean lens thickness of 4.87 mm at the age of 60 years. Our measurements are 4.82 mm in emmetropia, 4.55 mm in myopia, and 4.88 in hypermetropia. Lens thickness in chronic angle-closure glaucoma was not significantly different from the normal for age, both according to Marcowitz *et al.* [8] (4.99 mm) and according to our measurements (4.81 mm). The LAF coefficient in chronic angle-closure glaucoma was 2.27 according to Marcowitz *et al.* [8], and 2.24 according to our data. This suggests that age-related cataract (other than swelling cataract) is not a reliable risk factor of angle closure.

Lowe confirmed the relevance of eyeball axial length to development of angle-closure glaucoma (mean eyeball length of 23.10 mm in emmetropia vs. 22.01 mm in angle-closure glaucoma). This is in agreement with our data (23.77 in emmetropia, 21.55 in chronic angle-closure glaucoma, and 22.35 in acute angle closure). However, according to Lowe's data, lens thickness was 4.5 mm in normal eyes and 5.09 mm in eyes with angle-closure glaucoma. According to our data, lens thickness in cataract was 4.75 mm, while lens thickness in angle-closure glaucoma was 4.81 mm. According to Lowe, RLP was 0.22 in normal eyes and 0.2 in eyes with angle-closure glaucoma. According to our data, Lowe's coefficient (RLP) was 2.26 in hypermetropic eyes after the age of 60 years and 2.07 in eyes with acute angle closure (0.226 and 0.207, if divided by 10).

Lowe's coefficient (RLP) shows the relationship between anterior chamber depth and half-thickness of the lens versus eyeball length. Relative lens position is the sum of anterior chamber depth (the higher the value, the lower the risk), and half-thickness of the lens (the higher the value, the higher risk). Actually, this value shows the decrease of anterior chamber depth secondary to lens thickening, and lens-related decrease in anterior chamber depth is seen as the primary factor in anterior chamber angle closure risk.

Eyeball axial length is another important factor in Lowe's equation. The RLP coefficient is defined as relative lens position divided by eyeball axial length. Angle closure is much more prevalent in hypermetropia, in short eyes, but not in all cases.

We believe that the relationship between anterior chamber depth and eyeball axial length is more appropriate to assess constitutional relationships between internal eye structures. A decrease in this parameter may indicate a change in the relationships in terms of angle narrowing and closure.

Lens thickening is the second important factor in angle narrowing. Although lens thickening per se can be related to age or cataract, it cannot be viewed as the cause of iridocorneal angle closure. According to Suwan *et al.* [4], anterior position of the lens is more relevant than lens thickness. A decrease in anterior chamber depth associated with specific constitutional relationships between internal eye structures is of importance. We hypothesized that the ratio between anterior chamber depth and eyeball axial length divided by lens thickness may be more sensitive in detecting the risk of iridocorneal angle closure.

Lowe's studies demonstrate a change in anatomical relationships in eyes with angle-closure glaucoma but fail to indicate the probability of anterior chamber angle closure. We propose a PF, which clearly indicates the risk of angle closure in relation to age and refractive status: the older patient, and the shorter eyeball (the higher the hypermetropic refraction), the higher the probability of iridocorneal angle closure.

Higher reliability of the PF coefficient as opposed to Lowe's coefficient for eyes with angle-closure glaucoma demonstrates the relevance of constitutional relationships between internal eye structures, namely anterior chamber depth and eyeball axial length, in terms of the risk of iridocorneal angle closure.

Our data suggest that PF below 2.5 may be a significant risk factor of anterior chamber angle closure and may justify lens extraction surgery.

CONCLUSIONS

The risk of iridocorneal angle closure is primarily determined by relationships between eyeball structure measurements (eyeball axial length, anterior chamber depth, lens thickness). These relationships depend on the refractive state and age of the patient.

We propose a PF coefficient calculated from these relationships, which reliably predicts the risk of iridocorneal angle closure. PF below 2.5 is a significant risk factor of anterior chamber angle closure.

DISCLOSURE

The authors declare no conflict of interest.

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