Anterior Segment Characteristics and Risk Factors for Primary Angle Closure Disease With Long Axial Lengths: The Handan Eye Study

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Purpose. To investigate the anterior segment characteristics of primary angle closure disease (PACD) with long axial length (AL) compared with that of those with short and medium AL and explore the risk factors associated with AC with different AL levels.

Methods. This observational cross-sectional study enrolled subjects aged 35 years or older who completed the follow-up examinations of the Handan Eye Study and dichotomized them into normal and PACD groups. Ocular data of the right eye were analyzed. AL was categorized into short (<22.0 mm), medium (22.0–24.0 mm), or long (>24.0 mm) subgroups. Demographic and anterior segment parameters of PACD subjects were compared between the three AL subgroups. Logistic regression analysis was performed to identify the risk factors for PACD in the three subgroups.

Results. Data from 715 PACD and 1446 normal subjects were analyzed. Only 6.6% of the PACD eyes had long AL, with lower spherical equivalent, larger anterior chamber depth ($P < 0.001$), and smaller lens thickness ($P < 0.001$) than those with short and medium AL. No significant differences were found for angle opening distance and iris parameters on comparing the values of eyes with long AL with that of those with short and medium AL. Significant risk factors for the development of PACD with long AL were peripheral iris thickness, anterior chamber width, and lens vault.

Conclusions. PACD with long AL was uncommon. A thicker peripheral iris, larger lens vault, and smaller ACW contributed to angle closure in these patients.

Keywords: angle closure, long axial length, anterior segment biometrics, risk factors

Primary angle closure disease (PACD) is the appositional or synechial closure of the anterior chamber angle, including a continuum of three stages: primary AC suspect (PACS), primary AC (PAC), and PAC glaucoma (PACG).[1,2] Asian populations, especially Chinese, have the highest prevalence of PACD.[2–5] In addition, according to a meta-analysis, 27.0% of PACG patients worldwide are blind.[6] Approximately 5.2 million people in China are blind in at least one eye owing to PACG, resulting in severe ocular morbidity.[5]

Established biometric risk factors for PACD include hyperopia, short axial length (AL), shallow anterior chamber depth (ACD), and increased lens thickness (LT) and anteriorly positioned lens.[7–11] Previous studies have reported that short AL suggests an anatomic predisposition to PACD. Myopic eyes usually have long ALs and are predisposed to deep ACDs and open angles, thereby protecting against PACD because of the divergent ocular biometry of these conditions.[10,12–16] However, although Chinese populations have a higher prevalence of myopia compared with Western populations, many epidemiologic studies also show a high prevalence of AC.[17,18] Moreover, Jin et al.[19] reported that the increasing prevalence of myopia has minimal impact on the prevalence of occludable angles, with myopia prevalence increasing from 10% to 60% and narrow-angle prevalence decreasing from 11.1% to 9.6%. Owing to the incremental

rate of myopia in East Asia, particularly China, PACD with relatively long AL, which was scarce in the past, may increase in number accordingly.[10,17,20–22]

Myopia has been observed in patients with PACD, with a relatively low prevalence of myopia in patients with PACD across the United States, ranging between 0.05% and 1.90%, as opposed to as high as 22.0% in Asia, with 11.7% of them having high myopia.[13–14,20,21] In addition, some studies demonstrated ocular biometrics among different refractive statuses (myopic, hyperopic, or emmetropic subjects) in patients with PACD.[16,20,23,24] However, some studies attributed their refractive statuses to lenticular myopia with relatively short or normal AL rather than axial myopia with long AL.[13,16,20,23,24]

Nevertheless, we should explore whether long AL is a protective factor against PACD and whether the mechanisms or risk factors of atypical PACD with long AL vary from those of typical PACD with relatively short AL. To the best of our knowledge, there have been limited studies on this topic. Therefore, we conducted this study in a rural Chinese population to (1) demonstrate anterior segment biometrics of PACD eyes with long AL and compare them with those with short and medium AL to explore if there are any differences and (2) investigate the risk factors associated with AC in PACD eyes with different AL subgroups.

Methods

Study Population

This observational, cross-sectional study was based on a 5-year follow-up of the Handan Eye Study (HES). The HES was conducted from 2006 to 2007 on 6830 rural Chinese adults aged 30 years or older, including 13 villages in Yongnian County, Handan City, Hebei Province, Northern China.[25] In the follow-up research conducted between 2012 and 2013, 5394 (85.3% of survivors) subjects aged 35 years or older returned for repeat examinations.[26]

The subjects enrolled in our study were subjects of follow-up research who underwent gonioscopic and A-scan ultrasound examinations and anterior segment optical coherence tomography (ASOCT) imaging. We excluded subjects with POAG, primary glaucoma with indeterminate angle status, secondary glaucoma, a history of acute AC attack, pseudophakic or aphakic glaucoma, previous intraocular surgery or laser treatment, penetrating eye injury (ocular trauma), topical or systemic medications that may have affected the angle or the pupillary reflex, and corneal and iris disorders that could influence the anterior chamber assessment. Subjects with ASOCT images of poor quality were also excluded.

Written informed consent was obtained from all subjects, and ethical approval was obtained from the Ethics Committee of Beijing Tongren Hospital. This study was conducted in accordance with the principles of the Declaration of Helsinki.

The subjects were categorized into the normal group (open-angle) and PACD group, which included PACS, PAC, and PACG. In our study, the classification and definition of PACD developed by the International Society for Geographical and Epidemiological Ophthalmology were used to categorize PACD.[5] In addition, suspected PAC was defined as an eye with occludable angles (the pigmented posterior trabecular meshwork was not visible on gonioscopy for at least 180° in the primary position) and IOP of 21 mm Hg or less in the absence of peripheral anterior synechiae or glaucomatous optic neuropathy (GON).[5] PAC was defined as the presence of occludable angles with peripheral anterior synechiae and/or an IOP of more than 21 mm Hg, but without GON.[5] Additionally, PACG was defined as eyes with PAC associated with GON.[5] The following conditions were identified as possible GON: a vertical cup disc ratio (VCDR) of 0.6 or greater (95th percentile of the HES population), VCDR asymmetry of 0.2 or greater, optic disc hemorrhage, and visible retinal nerve fiber layer defect. A final diagnosis of glaucoma in the HES was made by a panel of glaucoma specialists through three steps, as reported in our previous studies.[27]

Study Examinations

All subjects underwent a comprehensive and standardized eye examination, which included the following tests: presenting visual acuity and best-corrected visual acuity (BCVA) measurements using the logMAR 4-m charts, automated refraction, and keratometry using a KR-8800 auto keratorefractometer (Topcon, Tokyo, Japan), slit-lamp examination, IOP measurement using a Kowa applanation tonometer (HA-2, Kowa Company Ltd. Tokyo, Japan), gonioscopic examination, A-scan ultrasound examination, and fundus examination using a 78-diopter (D) or 90-D lens.

One in 10 subjects and all patients with a limbal ACD of 40% or less, an IOP of greater than 21 mm Hg, and those with a history of glaucoma or suspected glaucoma underwent gonioscopy, which was performed in the dark with a one-mirror Goldmann lens (Ocular Instruments, Bellevue, WA) at high magnification (×25). A static examination was performed under dim ambient illumination with a shortened slit that did not fall on the pupil. Indentation gonioscopy was performed with increased illumination after static gonioscopy to determine the presence of peripheral anterior synechiae. Gonioscopy was performed by one of the two observers (Z.P. and Y.S.H.). The two observers attained a κ of 0.76 for the assessment of the occludable angle in 30 eyes (observers attained a study).

Refraction status was derived from the spherical equivalent (SE) of the subject's autorefraction. Average keratometry was performed using an auto-kerato-refractometer. The central corneal thickness (CCT), central ACD, LT, and AL were measured by A-scan ultrasound biometry using OcuScan RxP (Alcon, Inc., Fort Worth, TX, USA). The AL was categorized into short (<22.0 mm), medium (22.0–24.0 mm), or long (>24.0 mm).[28–31]

ASOCT Imaging and Image Processing

ASOCT (Visante, Carl Zeiss Meditec, Dublin, CA, USA) imaging was performed under dark room conditions (approximately 3 lx). All images were obtained in the "anterior segment quadrant" mode at the meridians of 0° to 180°, 45° to 225°, 90° to 270°, and 135° to 315°. For image acquisition of the anterior chamber angle at the 6 and 12 o'clock positions, the upper and lower eyelids were gently retracted as needed to avoid inadvertent pressure on the globe. Imaging was repeated if the scleral spur visibility was poor; the best set of images was selected.

The images were processed using customized software, the Zhongshan Angle Assessment Program (ZAAP, Guangzhou, China), by a single observer (Y.Z.) blinded to clinical data.[32] Angle, anterior chamber, lens, and iris configuration, including angle opening distance at 500 µm

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(AOD500), anterior chamber width (ACW), anterior chamber volume (ACV), iris thickness at 750 µm (IT750), iris cross-sectional area, iris curvature, lens vault (LV), and pupil diameter were analyzed and calculated using ZAAP after the scleral spur was marked on each side of the image.[32]

Statistical Analyses

All statistical analyses were performed using SPSS statistical software (version 25.0; SPSS, Inc., Chicago, IL, USA). Demographic data and ocular characteristics of the right eye were included in the analysis. The ASOCT parameters represent the average of measurements from the four cross-sections of the anterior segment. The one-sample Kolmogorov–Smirnov test was used to assess the normality of continuous data. Normally distributed continuous data are presented as means and standard deviations, whereas medians and interquartile ranges are presented for numerical data that are not normally distributed. The results are presented as frequencies and percentages for categorical data.

The one-way ANOVA or Kruskal–Wallis test was used to compare continuous data among the three subgroups divided by ALs in PACD subjects; the χ^2 test was used to assess differences in categorical data. The Bonferroni post hoc test or Mann–Whitney U test was performed to ascertain which pair of groups had a significant difference. The Pearson correlation was calculated to assess the correlation between central ACD and AL in normal and PACD eyes.

Univariate and multivariate logistic regression analyses were performed to identify the risk factors for PACD diagnosis in the AL subgroups; this included age, sex, BCVA, SE, IOP, keratometry, CCT, ACD, LT, VCDR, IT750, iris cross-sectional area, iris curvature, ACW, LV, and pupil diameter. The multivariate regression analysis included variables with a P value of less than 0.05 in the univariate logistic regression. We assessed the multicollinearity of the independent variables using variance inflation factors. A variance inflation factor of less than < 2 was acceptable in our study. Statistical significance was set at a P value of less than 0.05.

Results

Among the 5394 subjects who participated in the follow-up study, 2911, 48, and 173 did not undergo gonioscopic examination, A-scan ultrasound examination, and ASOCT examination or had low-quality ASOCT images, respectively. The remaining 2262 subjects completed all ocular examinations. Among these, another 101 (101 eyes) were excluded for the following: (1) diagnosed with POAG, 36 subjects (36 eyes); (2) pseudophakia, 29 subjects (29 eyes); (3) aphakia, 1 subject (1 eye); (4) underwent argon laser peripheral iridoplasty, laser peripheral iridotomy, or iridectomy, 27 subjects (27 eyes); (5) with iris synechia, 7 subjects (7 eyes); and (6) iridocoloboma (1 eye). Accordingly, 2161 subjects (2161 eyes) were included in the final analysis. Figure 1 shows the enrolment of the subjects.

In comparison with nonexaminees, the enrolled examinees tended to be older (P < 0.001), more often female (P < 0.001), and have worse presenting visual acuity (P < 0.001), worse BCVA (P < 0.001), steeper keratometry (P = 0.039), higher SE (P < 0.001), lower IOP (P < 0.001), larger VCDR (P < 0.001), thinner CCT (P < 0.001), smaller central ACD (P < 0.001), larger LT (P < 0.001), and smaller AL (P < 0.001) (Supplementary Table S1).

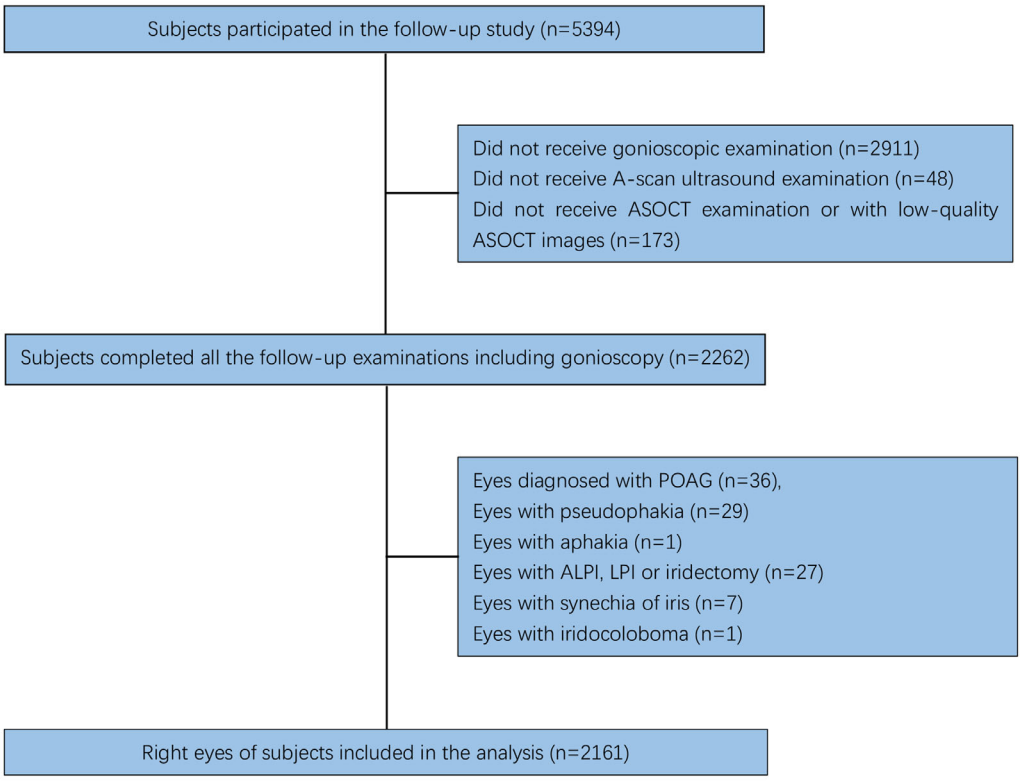

Figure 1. Flow chart showing the enrollment of subjects in this study. ALPI, argon laser peripheral iridoplasty; LPI, laser peripheral iridotomy.

Table 1. Demographic and Biometric Characteristics of the PACD Subjects With Short, Medium, and Long ALs

Parameter	1 = Short AL (n = 190)	2 = Medium AL (n = 478)	3 = Long AL (n = 47)	P Value	P Value 1 and 2	P Value 2 and 3	P Value 1 and 3
Age, years	63.0 (58.0–68.0)	63.0 (58.0–67.0)	62.0 (57.0–67.0)	0.823*			
Gender							
Male	42 (22.1)	161 (33.7)	15 (31.9)				
Female	148 (77.9)	317 (66.3)	32 (68.1)	0.013†	0.003†	0.807†	0.159†
Diagnosis							
PACS	174 (91.6)	444 (92.9)	44 (93.6)				
PAC	15 (7.9)	24 (5.0)	3 (6.4)				
PACG	1 (0.5)	10 (2.1)	0 (0.0)	0.297†			
PVA	0.30 (0.15 to 0.46)	0.24 (0.10 to 0.40)	0.30 (0.10 to 0.50)	0.049*	0.015‡	0.471‡	0.626‡
BCVA	0.08 (0.00 to 0.20)	0.00 (0.00 to 0.18)	0.06 (0.00 to 0.20)	0.328*			
AK, diopter	45.50 (44.50 to 46.25)	44.25 (43.25 to 45.00)	44.00 (42.75 to 45.50)	<0.001*	<0.001‡	0.448‡	<0.001‡
SE, diopter	1.13 (0.63 to 1.92)	0.75 (0.13 to 1.38)	–0.19 (–2.19 to 0.38)	<0.001*	<0.001‡	<0.001‡	<0.001‡
IOP, mm Hg	11.6 (10.0 to 13.8)	11.9 (10.2 to 13.9)	13.1 (10.6 to 15.8)	0.046*	0.259‡	0.042‡	0.016‡
VCDR	0.30 (0.20 to 0.40)	0.30 (0.20 to 0.40)	0.30 (0.40 to 0.50)	0.002*	0.006‡	0.078‡	0.001‡
CCT, µm	527.0 (504.0 to 547.0)	528.0 (514.0 to 547.8)	537.0 (527.0 to 550.0)	0.019*	0.057‡	0.067‡	0.011‡
Central ACD, mm	2.37 (2.25 to 2.57)	2.63 (2.43 to 2.78)	2.86 (2.70 to 3.07)	<0.001*	<0.001‡	<0.001‡	<0.001‡
LT, mm	4.90 (4.66 to 5.10)	4.83 (4.36 to 5.09)	4.28 (4.10 to 4.73)	<0.001*	0.034‡	<0.001‡	<0.001‡
AL, mm	21.62 (21.27 to 21.84)	22.65 (22.24 to 23.02)	24.14 (24.07 to 24.21)	<0.001*	<0.001‡	<0.001‡	<0.001‡

AK, average keratometry, PVA, presenting visual acuity.
Values are number (%) or median (interquartile range).
* Kruskal–Wallis test.
† χ^2 test.
‡ Mann–Whitney U test (<0.05/3 = 0.017 = significant difference).

Table 2. Anterior Chamber, Angle, Lens, and Iris Parameters Measured by ASOCT in PACD Subjects with Short, Medium, and Long ALs

Parameter	1 = Short AL (n = 190)	2 = Medium AL (n = 478)	3 = Long AL (n = 47)	P Value*	P Value 1 and 2	P Value 2 and 3	P Value 1 and 3
AOD500, mm	0.096 (0.057–0.145)	0.115 (0.074–0.167)	0.114 (0.077–0.159)	0.004*	0.001†	0.638†	0.161†
ACW, mm	11.07 ± 0.39	11.36 ± 0.37	11.33 ± 0.41	<0.001‡	<0.001‡§	0.575§	<0.001§
ACV, mm^3	57.00 (49.05–64.26)	64.14 (55.72–71.77)	63.60 (54.08–71.69)	<0.001*	<0.001†	0.700†	0.003†
IT750, mm	0.49 ± 0.07	0.49 ± 0.06	0.50 ± 0.05	0.426‡			
IA, mm^2	2.85 ± 0.35	2.92 ± 0.39	2.96 ± 0.42	0.141‡			
IC, mm	0.32 (0.27–0.36)	0.31 (0.27–0.36)	0.30 (0.26–0.33)	0.146§			
LV, µm	687.0 (541.5–799.8)	637.7 (515.5–761.4)	598.1 (453.3–717.3)	0.003§	0.009†	0.069†	0.003†
PD, mm	4.53 ± 0.68	4.68 ± 0.72	4.65 ± 0.71	0.040‡	0.034§	0.767§	0.867§

IA, iris cross-sectional area; IC, iris curvature; PD, pupil diameter.
Values are mean ± standard deviation or median (interquartile range).
*Kruskal–Wallis test.
† Mann–Whitney U test (<0.05/3 = 0.017 = significant difference).
‡One-way ANOVA.
§ Bonferroni test.

Among the 2161 subjects included in our study, 715 presented with PACD, including 662 with PACS, 42 with PAC, and 11 with PACG. In addition, 1446 subjects presented with a normal open angle. In the PACD group, short, medium, and long AL was observed in 190 (26.6%), 478 (66.9%), and 47 (6.6%) subjects, respectively. In the normal group, short, medium, and long AL was noted in 193 (13.3%), 1121 (77.5%), and 132 (9.1%) subjects, respectively. A significant difference (P < 0.001) existed in AL between PACD (median, 22.40 mm; interquartile range, 21.97–22.99 mm) and normal (median, 22.80 mm; interquartile range, 22.19–23.33 mm) groups. In the short AL subgroup, the proportion of PACD subjects among the total number of subjects in that subgroup was 49.6%; the proportions were 29.9% and 26.3% in the medium and long AL subgroups, respectively.

Table 1 shows the demographic and ocular biometric data of PACD subjects with three different AL levels. Across the three PACD subgroups, significant differences were observed in sex (P = 0.013), presenting visual acuity (P = 0.049), keratometry (P < 0.001), SE (P < 0.001), IOP (P = 0.046), VCDR (P = 0.002), CCT (P = 0.019), central ACD (P < 0.001), LT (P < 0.001), and AL (P < 0.001). No differences were noted in age, the proportion of PACD diagnosis, or BCVA among the three subgroups. In addition, PACD eyes with long AL had flatter keratometry (P < 0.001), lower SE (P < 0.001), higher IOP (P = 0.016), larger VCDR (P = 0.001), thicker CCT (P = 0.011), larger central ACD (P < 0.001), and smaller LT (P < 0.001) than those with short AL, as well as lower SE (P < 0.001), larger central ACD (P < 0.001), and smaller LT (P < 0.001) than the medium AL subgroup.

Table 2 summarizes the quantitative anterior chamber parameters measured using ASOCT, along with the differences among the three AL subgroups. Significant differences in AOD500 (P = 0.004), ACW (P < 0.001), ACV (P < 0.001), LV (P = 0.003), and pupil diameter (P = 0.040) were observed among the three subgroups. Bonferroni-corrected

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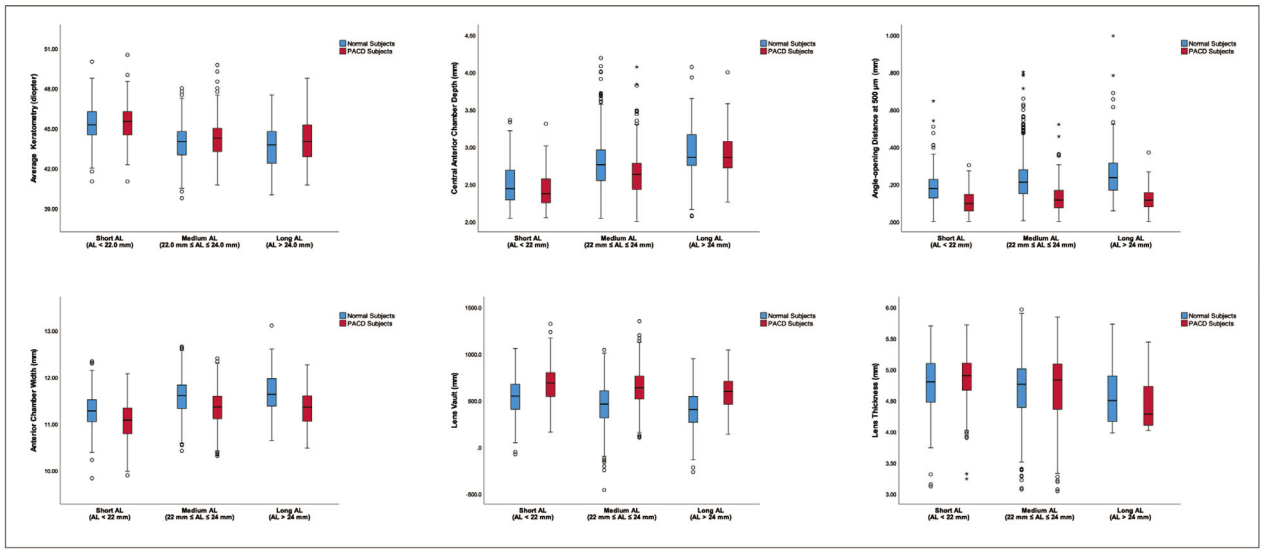

Figure 2. Box plots showing **keratometry**, central ACD, AOD500, ACW, LT, and LV in normal and PACD subjects with short, medium, and long ALs.

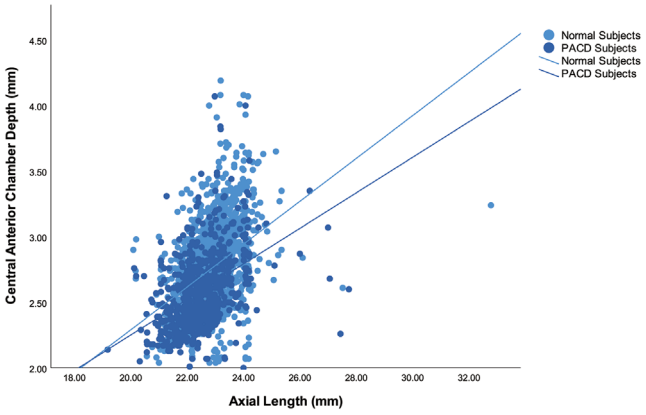

Figure 3. Scattergram showing correlations between AL and central ACD in normal and PACD subjects. The Pearson correlation coefficients for central ACD and AL were 0.426 ($P < 0.001$) for eyes with PACD and 0.420 ($P < 0.001$) for normal eyes.

comparisons showed that PACD eyes with a long AL had larger ACW ($P < 0.001$), larger ACV ($P = 0.003$), and smaller LV ($P = 0.003$) than those with a short AL. No significant differences were found in IT750, iris cross-sectional area, or iris curvature among the three subgroups.

Figure 2 shows the parameters keratometry, central ACD, AOD500, ACW, LT, and LV among the three AL subgroups in PACD and normal subjects. Supplementary Tables S2, S3, and S4 show the results of comparisons of demographic and biometric characteristics between PACD and normal subjects with short, medium, and long ALs, respectively. The central ACD increased with increasing AL in the PACD and normal groups (Fig. 3). The Pearson correlation coefficients for central ACD and AL were 0.426 ($P < 0.001$) for PACD eyes and 0.420 ($P < 0.001$) for normal eyes. There was no difference in the ACD change per AL increase between the PACD and normal subjects ($P = 0.401$).

Tables 3, 4, and 5 show the results of the univariate and multivariate logistic regression analyses for the diagnosis of PACD in the short, medium, and long AL subgroups, respectively. In the short AL subgroup, the significant risk factors for the diagnosis of PACD were IT750 ($\beta = 0.007$; $P = 0.001$), ACW ($\beta = -1.339$; $P < 0.001$), and LV ($\beta = 0.004$; $P < 0.001$). In the medium AL subgroup, the significant risk factors for the diagnosis of PACD were central ACD ($\beta = -0.732$; $P = 0.005$), IT750 ($\beta = 0.008$; $P < 0.001$), ACW ($\beta = -1.690$; $P < 0.001$), and LV ($\beta = 0.005$; $P < 0.001$). In the long AL subgroup, significant risk factors for PACD diagnosis were IT750 ($\beta = 0.018$; $P < 0.001$), ACW ($\beta = -1.637$; $P = 0.003$), and LV ($\beta = 0.007$; $P < 0.001$).

The AC mechanisms in three PAC subjects with an AL longer than 24.0 mm were manifold, including pupillary block (PB) and non-PB mechanisms (Fig. 4). Patient A had plateau iris configuration (PIC) and thick peripheral iris roll (TPIR) as AC mechanisms, with PIC being the major one, using the guidelines determined by ASOCT images.[33] Patient B had components of PB, PIC, and TPIR as AC mechanisms with PB being the major one. Patient C had PB and PIC as AC mechanisms, with PIC being the major one. Additionally, we also illustrated the AC mechanisms of seven PACS subjects with an AL longer than 25.0 mm on ASOCT images, which were also manifold (Fig. 5). Patients A, B, and C presented with PIC and TPIR, with PIC being the major AC mechanism. Patients D and E had PB as the major AC mechanism, whereas TPIR existed as a minor AC mechanism in patient D. In patients F and G, PIC affected the left anterior chamber angle and PB affected the right anterior chamber angle; an exaggerated LV existed as a minor AC mechanism in patient G.

We further investigated the distribution of the major AC mechanisms of PACD subjects with different ALs. In the short AL subgroup, 114 had PB (59.7%), 19 had PIC (9.9%), 57 had TPIR (29.8%), and 1 had an exaggerated LV (0.5%); in the medium AL subgroup, 243 had PB (50.9%), 85 had PIC (17.8%), 148 had TPIR (31.0%), and 1 had an exaggerated L (0.2%); in the long AL subgroup, 21 had PB (44.7%), 12 had PIC (25.5%) and 14 had

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Table 3. Risk Factors for PACD With Short AL

	Univariate Logistic Regression		Multivariate Logistic Regression		
Variable	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**VIF**
Age (years)	1.044 (1.021–1.068)	<0.001	—	—	1.208
Female	1.199 (0.748–1.922)	0.451			
BCVA	1.699 (0.485–5.945)	0.407			
SE (diopter)	1.311 (1.091–1.576)	0.004	—	—	1.199
IOP (mm Hg)	1.018 (0.945–1.097)	0.633			
AK (diopter)	1.060 (0.919–1.222)	0.422			
CCT (µm)	0.999 (0.992–1.005)	0.648			
Central ACD (mm)	0.207 (0.085–0.504)	0.001	—	—	1.170
LT (mm)	1.501 (0.937–2.405)	0.091			
VCDR	0.295 (0.059–1.479)	0.138			
IT750 (0.1 mm)	1.875 (1.354–2.597)	<0.001	1.935 (1.309–2.862)	0.001	1.097
IA (mm^2)	1.186 (0.671–2.098)	0.558			
IC (0.1 mm)	1.482 (1.122–1.956)	0.006	—	—	1.509
ACW (mm)	0.260 (0.151–0.448)	<0.001	0.262 (0.135–0.511)	<0.001	1.173
LV (µm)	1.004 (1.002–1.005)	<0.001	1.004 (1.003–1.006)	<0.001	1.475
PD (mm)	0.975 (0.745–1.274)	0.851			

AK, average keratometry; BCVA, best-corrected visual acuity; CI, confidence interval; IA, iris cross-sectional area; IC, iris curvature; OR, odds ratio; PD, pupil diameter; VIF, variance inflation factor.

Table 4. Risk Factors for PACD With Medium AL

	Univariate Logistic Regression		Multivariate Logistic Regression		
Variable	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**VIF**
Age (years)	1.046 (1.034–1.059)	<0.001	—	—-	1.604
Female	1.485 (1.188–1.857)	0.001	—	—	1.155
BCVA	3.031 (1.624–5.658)	<0.001	—	—	1.366
SE (diopter)	1.266 (1.151–1.393)	<0.001	1.101 (0.998–1.215)	0.054	1.122
IOP (mm Hg)	1.018 (0.979–1.058)	0.367			
AK (diopter)	1.137 (1.050–1.231)	0.001	0.902 (0.802–1.015)	0.087	1.454
CCT (µm)	1.000 (0.996–1.004)	0.974			
Central ACD (mm)	0.182 (0.123–0.271)	<0.001	0.481 (0.288–0.804)	0.005	1.192
LT (mm)	1.242 (0.974–1.585)	0.081			
VCDR	0.582 (0.274–1.239)	0.160			
IT750 (0.1 mm)	2.132 (1.773–2.563)	<0.001	2.122 (1.677–2.686)	<0.001	1.2217
IA (mm^2)	1.210 (0.911–1.608)	0.189			
IC (0.1 mm)	1.786 (1.539–2.074)	<0.001	—	—	1.727
ACW (0.1 mm)	0.847 (0.820–0.874)	<0.001	0.845 (0.806–0.885)	<0.001	1.740
LV (µm)	1.005 (1.004–1.005)	<0.001	1.005 (1.004–1.006)	<0.001	1.5993
PD (mm)	0.830 (0.719–0.958)	0.011	—	—	1.535

AK, average keratometry; CI, confidence interval; IA, iris cross-sectional area; IC, iris curvature; OR, odds ratio; PD, pupil diameter; VIF, variance inflation factor.

TPIR (29.8%). No difference was found in the distribution of the major AC mechanisms among the subgroups ($P = 0.082$).

Discussion

In the present study, PACD eyes with long AL were uncommon (6.6%), indicating that this atypical PACD does occur, but is relatively rare. Furthermore, the 47 PACD subjects with long AL had flatter cornea, lower SE, larger central ACD, ACW, and ACV, thinner lens, and smaller LV than those with short AL, and had lower SE, deeper central anterior chamber, and thinner lens compared with the medium AL subgroup. However, there were no differences in iris parameters among the different AL subgroups. Moreover, although significant statistical differences were found in the AOD500 among the three AL subgroups, no differences were observed when comparing the values of the long AL subgroup with those of the short and medium AL subgroups.

Studies on patients with PACD with different AL levels are limited. A retrospective study conducted by Li et al.[34] found that patients with PACD with a long AL (≥23.5 mm) have a deeper ACD and flatter cornea than those with the medium (22.5 ≤ ALs < 23.5 mm). In another study conducted by Li et al.,[35] the authors reported that PAC patients with a longer AL (≥23.5 mm) had a larger ACW and anterior vault, flatter cornea, and less anteriorly rotated ciliary body compared with those with relatively shorter AL (<22.5 mm), based on low-coherence interferometry and ultrasound biomicroscopy images. The findings of our study are mostly consistent with those of the two studies by Li et al.[34,35]

The flatter cornea in PACD subjects with long AL could be attributed to horizontal expansion of the eyeball and

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Table 5. Risk Factors for PACD With Long AL

	Univariate Logistic Regression		Multivariate Logistic Regression		
Variable	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**VIF**
Age (years)	1.062 (1.024–1.101)	0.001	—	—	1.286
Female	2.483 (1.230–5.012)	0.011	—	—	1.297
BCVA	4.780 (0.741–30.846)	0.100			
SE (diopter)	0.909 (0.780–1.059)	0.222			
IOP (mm Hg)	1.016 (0.909–1.135)	0.781			
AK (diopter)	1.213 (0.986–1.493)	0.068			
CCT (μm)	0.998 (0.985–1.011)	0.747			
Central ACD (mm)	0.720 (0.276–1.878)	0.502			
LT (mm)	0.545 (0.233–1.275)	0.161			
VCDR	1.724 (0.167–17.780)	0.648			
IT750 (0.1 mm)	3.319 (1.774–6.207)	<0.001	6.089 (2.553–14.522)	<0.001	1.181
IA (mm^2)	1.351 (0.617–2.956)	0.451			
IC (0.1 mm)	1.740 (1.135–2.668)	0.011	—	—	1.737
ACW (0.1 mm)	0.130 (0.051–0.328)	<0.001	0.849 (0.762–0.946)	0.003	1.323
LV (μm)	1.005 (1.003–1.007)	<0.001	1.007 (1.004–1.009)	<0.001	1.810
PD (mm)	0.753 (0.469–1.209)	0.241			

AK, average keratometry; CI, confidence interval; IA, iris cross-sectional area; IC, iris curvature; OR, odds ratio; PD, pupil diameter; VIF, variance inflation factor.

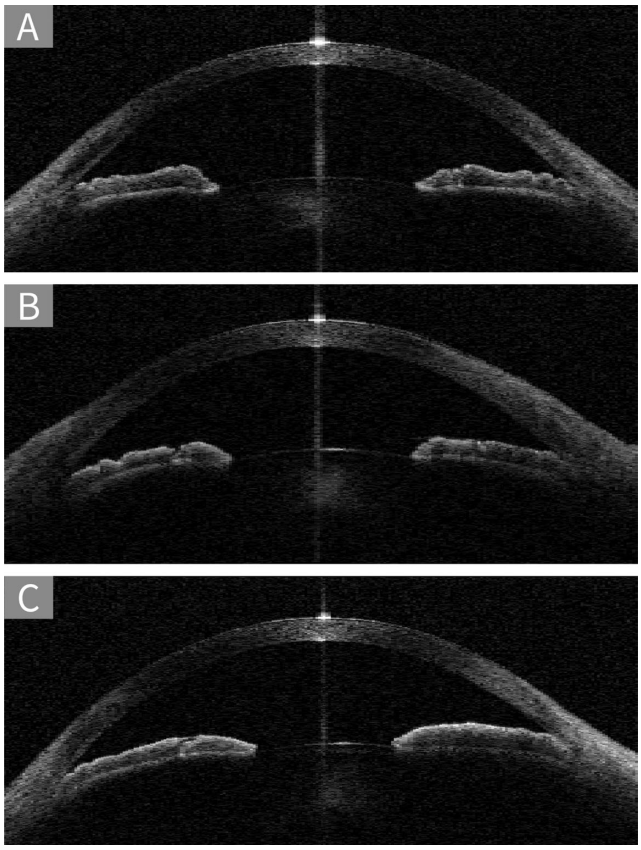

Figure 4. ASOCT images of three PAC subjects with axial length of greater than 24.0 mm.

compensation by decreasing the corneal power in axial myopia.[35,36] The lower SE in these atypical PACD subjects is attributed to a relatively long AL. A larger ACD and ACW in PACD subjects with a long AL indicated larger vertical and horizontal dimensions of the eyeball's anterior segment.[16,35] Furthermore, in disagreement with the findings of the study by Li et al., our findings demonstrated that PACD subjects with long AL had thinner lenses and smaller LV (representing the anterior portion of the lens), compared with those with short AL.[35,37] In a large Chinese cataractous population, LT increased gradually with the increase in AL, apart from eyes with AL of greater than 35 mm.[38] Moreover, it has been hypothesized that with axial elongation, the zonule may be stretched and apply traction to the lens; therefore, the lens might migrate posteriorly.[39]

We further investigated and reported the independent risk factors for AC with different AL levels; to the best of our knowledge, this study is the first to do so. These findings demonstrated that, in atypical PACD with a long AL and relatively large anterior segment dimensions, a thick peripheral iris, small ACW, and larger LV were the most essential risk factors for AC.

The importance and key role of the iris in the pathogenesis of PAC have been reported in previous studies; greater iris curvature, area, and thickness were independent factors associated with narrow angles.[40,41] A thicker peripheral iris would contribute to angle crowding and subsequent AC as the peripheral iris would be in closer proximity to the trabecular meshwork.[42] A smaller ACW and larger LV are independently associated with AC in previous studies, which was also found to be the case in atypical patients with PACD with long AL in our study.[39,43]

Analyzing three PAC subjects with an AL of greater than 24.0 mm and seven PACS subjects with AL of greater than 25.0 mm revealed that the AC mechanisms of PACD subjects with long AL were complex and diversified, with non-PB mechanism, especially PIC, being the major mechanism in most cases. Hence, in PACD subjects with a long AL, the AC mechanisms should be evaluated to make a preferable treatment decision. It should be considered that the AC mechanisms in our study are factors that contribute to the inability to visualize the trabecular meshwork on gonioscopy, rather than iridotrabecular contact on ASOCT images.

A strength of this study is the large sample size, which included subjects from a population-based survey with international standardized protocols and strict quality control. In addition, we divided the PACD subjects according to their

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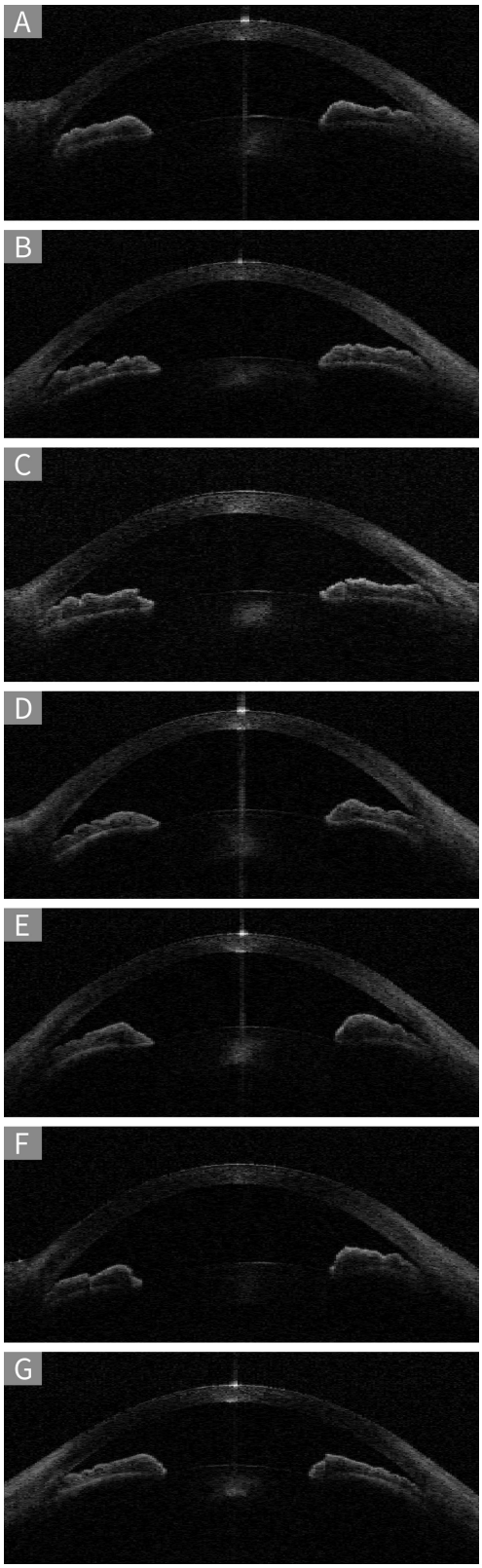

Figure 5. ASOCT images of seven PACS subjects with a AL of more than 25.0 mm.

AL levels rather than their refractive status, which could evaluate the anterior segment biometrics of atypical PACD subjects with long AL and axial myopia.

Our study has several limitations. First, we performed gonioscopy on those with limbal ACD of 40% or less of corneal thickness or suspected glaucoma, as well as one in ten of the examined subjects each day. This strategy might have led to missing some PACD cases, especially those with long AL with a relatively deep anterior chamber. The proportions of eyes with different AL levels in the normal and PACD eyes calculated in our study could not reflect the true proportions and should not be compared with each other. Second, in this study, the differences between the included subjects and those excluded may cause bias. Third, we did not perform ultrasound biomicroscopy, and ciliary body parameters could not be analyzed. Fourth, this observational, cross-sectional study was part of a population-based study, in which the number of PAC/PACG cases was limited. Moreover, we did not include subjects with acute PAC in this study. Hence, in future studies, we will include more patients with PAC/PACG and acute PAC and investigate the anterior segment biometrics in these patients with long AL. Last, because our subjects were all Chinese, the results may not be applicable to other ethnic groups.

In conclusion, the present study found that subjects with a long AL remain a minority in the PACD population. These atypical PACD subjects had flatter cornea, lower SE, larger anterior chamber dimension, thinner lens, and less anteriorly positioned lens, but similar iris parameters compared with those with relatively shorter AL. The AC mechanisms of these atypical PACD subjects were manifold and mainly non-PB. This study indicated that gonioscopy is essential and should be performed on all suspected glaucoma patients with an increased IOP, regardless of the AL level and refractive status.

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