Ocular Biometric Determinants of Anterior Chamber Angle Width in Chinese Americans: The Chinese American Eye Study

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• PURPOSE: We sought to investigate anatomic mechanisms of angle narrowing by assessing ocular biometric determinants of anterior chamber angle width.

• DESIGN: Population-based cross-sectional study.

• METHODS: Subjects ≥50 years of age from the Chinese American Eye Study underwent a comprehensive ocular examination, including anterior segment optical coherence tomography imaging and ultrasound A-scan. Independent variables, including anterior chamber depth (ACD), lens vault (LV), iris curvature (IC), anterior chamber width, lens thickness, vitreous cavity depth, and axial length, and dependent variables, including angle opening distance, were measured in 1 randomly selected eye per subject. Univariable and multivariable regression models with standardized regression coefficients (SRCs) and semipartial correlation coefficients squares ($SPCC^2$) were used to assess relative and unique contributions by independent variables to angle width.

• RESULTS: Two thousand two hundred twenty-five subjects (1433 women and 834 men) were included in the analysis. All biometric parameters except lens thickness differed between men and women (age-adjusted $P < .001$). In model 1A ($R^2 = 0.66$), which included ACD, lens thickness, and vitreous cavity depth, ACD (SRC = 0.64, $SPCC^2 = 0.19$) and IC (SRC = −0.26, $SPCC^2 = 0.041$) were the strongest determinants of angle opening distance. In model 1B ($R^2 = 0.58$), which included LV and axial length, LV (SRC = −0.46, $SPCC^2 = 0.1$) and IC (SRC = −0.3, $SPCC^2 = 0.047$) were the strongest determinants of angle opening distance. Determinants of angle width were similar in separate multivariable models for men and women.

• CONCLUSIONS: ACD, LV, and IC are the strongest determinants of angle width in Chinese Americans. Sex-related differences in angle width are explained by differences among biometric measurements. These results provide insights into anatomic mechanisms of angle narrowing and have important implications for quantitative assessments of angle closure eyes. (Am J Ophthalmol 2020;220:19–26. © 2020 Elsevier Inc. All rights reserved.)

THE WIDTH OF THE ANTERIOR CHAMBER ANGLE (ACA) plays a central role in the pathogenesis of primary angle closure glaucoma (PACG), a leading cause of permanent vision loss and blindness worldwide.[1] The position and configuration of anatomic structures of the anterior segment, such as the iris and lens, are risk factors for developing progressive angle narrowing and closure.[2–4] This process leads to impaired aqueous humor outflow through the trabecular meshwork (TM) and elevations of intraocular pressure (IOP).[5,6] Therefore, decreased angle width is an indirect but potentially important risk factor for glaucomatous optic neuropathy.[7]

Ocular biometric parameters measured by anterior segment optical coherence tomography (AS-OCT) and ultrasound A-scan have been identified as risk factors for angle closure, including decreased anterior chamber depth (ACD) and increased lens vault (LV) and iris curvature (IC).[2–4] Statistical models based on combinations of these biometric parameters are strongly predictive of angle width.[8,9] However, the relative and unique contributions of individual anatomic structures to decreased angle width are unclear. This is problematic because the role of these structures varies by disease subtype and treatments for angle closure, such as laser peripheral iridotomy, differentially affect these structures.[10,11] It is also unclear if population-specific differences in angle closure risk, such as between men and women, are attributable to differences among biometric measurements.[12–14] Therefore, assessing biometric determinants of angle width could help elucidate anatomic mechanisms of

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angle narrowing and enhance the clinical utility of biometric measurements for evaluating patients with angle closure.

In this study, we develop statistical models using data from the Chinese American Eye Study (CHES), a population-based study of Chinese Americans, to investigate relative and unique contributions of ocular biometric parameters to angle width.[15] We then apply these models to investigate sex-related differences in angle width. Angle width is represented by angle opening distance (AOD750), which is strongly associated with gonioscopic angle closure, and trabecular iris space area (TISA750), which is strongly associated with elevated IOP, measured 750 μm from the scleral spur.[5,16]

METHODS

ETHICS COMMITTEE APPROVAL WAS OBTAINED FROM THE University of Southern California Medical Center Institutional Review Board. All study procedures adhered to the recommendations of the Declaration of Helsinki. All study participants provided informed consent at the time of enrollment.

• **CLINICAL ASSESSMENT:** Subjects were identified from CHES, a population-based, cross-sectional study of 4582 Chinese participants ≥50 years of age residing in Monterey Park, California, USA.[15] Each subject received a complete eye examination by a trained ophthalmologist, including gonioscopy, AS-OCT imaging, and A-scan ultrasound biometry in the upright seated position.

Gonioscopy was performed under dark ambient lighting (0.1 cd/m^2) with a 1-mm light beam and a Posner 4-mirror lens (ODPSG; Ocular Instruments, Inc, Bellevue, Washington, USA) by 1 of 2 trained ophthalmologists (D.W., C.L.G.). Care was taken to avoid light falling on the pupil, inadvertent indentation of the globe, and tilting of the lens >10 degrees. The angle was graded in each quadrant according to the modified Shaffer classification system: grade 0, no structures visible; grade 1, nonpigmented TM visible; grade 2, pigmented TM visible; grade 3, scleral spur visible; and grade 4, ciliary body visible. Angle closure was defined as an eye with ≥3 quadrants of gonioscopic angle closure (grade 0 or 1) in the absence of potential causes of secondary angle closure, such as inflammation or neovascularization.[17]

AS-OCT imaging with the Tomey CASIA SS-1000 swept-source Fourier-domain device (Tomey Corp, Nagoya, Japan) and A-scan ultrasound biometry with the DGH 4000B A-scan/Pachymeter (DGH Technology, Inc, Exton, Pennsylvania, USA) were performed under dark ambient lighting (0.1 cd/m^2) before pupillary dilation. Some subjects were unable to be imaged because of availability of the AS-OCT device, clinical flow, or ability to participate.

Inclusion criteria for the study included CHES subjects who received AS-OCT imaging and A-scan ultrasound biometry. Exclusion criteria included eyes with history of medications or procedures that could affect angle width, including laser peripheral iridotomy, intraocular surgery, or corneal opacities that precluded AS-OCT imaging. One eye per subject was selected at random for analysis using MATLAB (Mathworks, Natick, Massachusetts, USA) to avoid intereye correlations between independent and dependent variables.

• **MEASUREMENT OF OCULAR BIOMETRIC PARAMETERS:** One AS-OCT image per eye oriented along the horizontal (temporonasal) meridian was analyzed using the Tomey SS OCT Viewer software (v 3.0, Tomey Corp, Nagoya, Japan) that automatically segmented anterior segment structures and produced biometric measurements once the scleral spurs were marked.

One observer (A.A.P.) masked to the identities and examination results of the subjects confirmed the segmentation and marked the scleral spurs in each image. The scleral spur was defined as the inward protrusion of the sclera where a change in curvature of the corneoscleral junction was observed.[18] Eyes with missing or corrupt images were excluded from the analysis.

Two biometric parameters describing angle width were measured: angle opening distance (AOD) and trabecular iris space area (TISA).[19] AOD750 was defined as the perpendicular distance from the TM 750 μm anterior to the scleral spur to the anterior iris surface. TISA750 was defined as the area bounded anteriorly by AOD750; posteriorly by a line drawn from the scleral spur perpendicular to the plane of the inner scleral wall to the opposing iris; superiorly by the inner corneoscleral wall; and inferiorly by the iris surface. Iris area (IA), ACD, IC, LV, and anterior chamber width (ACW) were also measured.[19,20] IA was defined as the cross-sectional area of the full length of the iris. ACD was defined as the distance from the apex of the anterior lens surface to the apex of the corneal endothelium. IC was defined as the distance from the apex of the iris convexity to a line extending from the peripheral to central iris pigment epithelium. ACW was defined as the distance between scleral spurs.

Intraobserver repeatability of AS-OCT parameter measurements was calculated in the form of intraclass correlation coefficients based on images from 20 open angle and 20 angle closure eyes graded 3 months apart. This analysis was performed using MATLAB.

Models were developed to predict the width of the temporal sector of the ACA based on temporal measurements of AOD750, TISA750, IA, and IC and shared measurements of ACD, LV, and ACW. Nasal and mean measurements were omitted to avoid issues related to intraeye correlations among biometric parameters. The temporal sector was chosen because it has more angle width measurements than the nasal sector.

Two biometric parameters were measured using A-scan ultrasound: axial length (AL) and lens thickness (LT). Vitreous cavity depth (VCD) was calculated as AL–LT − ACD.

TABLE 1. Demographics and Biometrics of the Study Population in the Chinese American Eye Study

Variable	N (Total Observations)	Overall[a] (n = 2225)	Male[a] (n = 792)	Female[a] (n = 1433)	*P* Value[b]	Adjusted *P* Value[c]	Cohen Effect Size (*d*)[d]
Age (y)	2225	59.8 (7.4)	61.0 (8.0)	59.2 (7.0)	<.001	N/A	−0.24
IOP (mm Hg)	2324	15.3 (3.2)					
Refractive error (diopters)	2312	−0.52 (2.9)					
ACW (mm)	2213	11.6 (0.39)	11.7 (0.39)	11.6 (0.38)	<.001	<.001	−0.39
IA (mm^2)	2219	1.49 (0.24)	1.51 (0.25)	1.47 (0.23)	<.001	<.001	−0.18
IC (mm)	2215	0.22 (0.17)	0.20 (0.19)	0.23 (0.15)	<.001	<.001	0.21
AL (mm)	2200	23.8 (1.32)	24.2 (1.23)	23.7 (1.32)	<.001	<.001	−0.42
VCD (mm)	2187	16.8 (1.24)	17.0 (1.16)	16.6 (1.26)	<.001	<.001	−0.31
ACD (mm)	2213	2.62 (0.33)	2.71 (0.32)	2.58 (0.33)	<.001	<.001	−0.40
LT (mm)	2199	4.46 (0.35)	4.48 (0.35)	4.44 (0.34)	.021	.55	−0.10
LV (mm)	2225	0.46 (0.27)	0.42 (0.27)	0.48 (0.26)	<.001	<.001	0.24
AOD750 (mm)	2218	0.41 (0.20)	0.45 (0.22)	0.39 (0.19)	<0.001	<.001	−0.34
TISA750 (mm^2)	2215	0.21 (0.093)	0.23 (0.099)	0.20 (0.090)	<0.001	<.001	−0.28

ACD = anterior chamber depth; ACW = anterior chamber width; AL = axial length; AOD750 = angle opening distance 750 μm from the scleral spur; IA = iris area; IC = iris curvature; LT = lens thickness; LV = lens vault; TISA750 = trabecular-iris space area 750 μm from the scleral spur; VCD = vitreous chamber depth.

[a]Values represented as mean (standard deviation).

[b]Calculated using analysis of covariance tests comparing means between biologic sexes.

[c]Calculated using analysis of covariance tests comparing age-adjusted means between biologic sexes.

[d]Cohen *d* describes the size of the difference in a given parameter between biologic sexes ($d = 0.2$ indicates sex has a "small" effect size, $d = 0.5$ indicates a "medium" effect size, and $d = 0.8$ indicates a "large" effect size). Positive values indicate that females demonstrated a higher mean, while negative values indicate that males demonstrated a higher mean.

• **STATISTICAL ANALYSIS:** All statistical analyses were performed using Stata software (v 14.2; StataCorp LLC, College Station, Texas, USA). Analyses were conducted using a significance level of 0.05.

All continuous biometric and demographic variables were described by calculating means, ranges, and standard deviations (SDs; Table 1). Intervariable correlations were assessed by calculating Pearson correlation coefficients (*r*; Supplemental Table 1).

The mean values of age and all biometric parameters were compared between men and women using analysis of covariance testing. This was repeated while controlling for age. Sex-related differences in each parameter were further characterized by calculating the Cohen effect size (*d*; Table 1).

Age- and sex-controlled univariable linear regressions were used to evaluate relationships between measurements of ACD, LV, IC, VCD, AL, LT, IA, and ACW and measurements of AOD750 and TISA750 (Table 2).

Multivariable linear regressions were used to assess the predictive value of age and sex together on AOD750 and TISA750 (Supplemental Table 2).

Separate multivariable models were constructed to evaluate the contributions of LV and ACD to angle width because the 2 parameters were highly collinear (Table 3). All models included AOD750 or TISA750 as the independent variable. Models 1A and 2A included ACD, VCD, LT, IA, ACW, and IC as independent variables. AL was excluded in favor of its components (ACD, VCD, and LT) because of high collinearity with VCD. Models 1B and 2B included AL, ACW, IA, IC, and LV as independent variables. Variance inflation factors (VIFs) were calculated to assess model collinearity; if the mean VIF of a potential model or the VIF of any individual variable within the model was >3.0, that model was discarded and a problematic variable was dropped. The contribution of each independent variable was estimated by the magnitude of standardized regression coefficients (SRCs; relative influence of variable on the R^2 statistic) and semipartial correlation coefficients squared ($SPCC^2$s; decrease in the R^2 statistic without the unique influence of variable). The R^2 statistic indicated variation in angle width explained by the model's independent variables, together with age and sex. Similar methodology was used to assess differences among determinants between men and women (Supplemental Table 3).

RESULTS

TWO THOUSAND THREE HUNDRED TWENTY-SIX OF THE 4582 subjects (50.8%) enrolled in CHES underwent AS-OCT imaging (Supplemental Figure 1). One hundred one of

TABLE 2. Univariable Linear Regression Analysis of the Relationship Between Angle Width and Potential Biometric Determinants Adjusted for Age and Sex

Dependent Variable	Independent Variable	Adjusted *P* Value[a]	Coefficient (95% CI)	R^2 Value[b]
AOD750 (mm)	ACD (mm)	<.001	0.46 (0.45–0.48)	0.56
	LV (mm)	<.001	−0.53 (−0.55 to −0.50)	0.49
	IC (mm)	<.001	−0.77 (−0.81 to −0.73)	0.42
	AL (mm)	<.001	0.071 (0.065–0.077)	0.24
	VCD (mm)	<.001	0.060 (0.054–0.067)	0.17
	LT (mm)	<.001	−0.16 (−0.18 to −0.14)	0.10
	IA (mm^2)	<.001	−0.13 (−0.16 to −0.095)	0.058
	ACW (mm)	<.001	0.061 (0.039–0.083)	0.048
TISA750 (mm^2)	ACD (mm)	<.001	0.18 (0.17–0.19)	0.41
	LV (mm)	<.001	−0.20 (−0.22 to −0.19)	0.34
	IC (mm)	<.001	−0.28 (−0.30 to −0.26)	0.25
	VCD (mm)	<.001	0.023 (0.021–0.027)	0.20
	AL (mm)	<.001	0.028 (0.025–0.031)	0.18
	LT (mm)	<.001	−0.065 (−0.077 to −0.054)	0.072
	IA (mm^2)	<.001	−0.047 (−0.063 to −0.031)	0.033
	ACW (mm)	<.001	0.027 (0.016–0.037)	0.032

ACD = anterior chamber depth; ACW = anterior chamber width; AL = axial length; AOD750 = angle opening distance 750 μm from the scleral spur; IA = iris area; IC = iris curvature; LT = lens thickness; LV = lens vault; TISA750 = trabecular-iris space area 750 μm from the scleral spur; VCD = vitreous chamber depth.

Variables are listed in decreasing order of R^2 values.

[a]Calculated using age- and sex-adjusted linear regressions.

[b]Calculated for entire age- and sex-controlled regression model.

these subjects (4.3%) were excluded based on the following criteria: a history of medications or procedures that could affect angle width ($n = 76$, 3.5%) and cases where the scleral spur could not be identified ($n = 25$, 1.1%). The mean age of the subjects was 59.8 ± 7.4 years (range 50-91 years). Seven hundred ninety-two (35.6%) of the subjects were men and 1433 (64.4%) were women. Their mean IOP was 15.3 ± 3.2 mm Hg, and their mean refractive error was −0.52 ± 2.9 diopters (D). One eye per subject was selected at random for inclusion in this study ($N = 2225$ eyes). Two hundred twenty-two of these eyes (10.0%) fit the gonioscopic definition of angle closure.

Intraobserver intraclass correlation coefficient values for A.A.P. reflected excellent measurement repeatability for all AS-OCT parameters. The intraclass correlation coefficient values were: AOD750 = 0.96, TISA750 = 0.92, ACW = 0.96, IA = 0.96, IC = 0.95, ACD = 0.98, and LV = 0.97.

There were significant sex-related differences among all biometric parameters except LT both before ($P < .021$) and after ($P < .001$) controlling for age, with all parameters being smaller in females except IC and LV (Table 1). The effect size of sex for the various parameters ranged from −0.1 (LT) to −0.42 (AL). The strongest correlations between pairs of biometric parameters were between AL and VCD ($r = 0.96$) and LV and ACD ($r = -0.83$; Supplemental Table 1).

Age- and sex-controlled univariable linear regression models demonstrated that all independent biometric parameters were significant predictors of AOD750 and TISA750 (Table 2). ACD was the most explanatory parameter for both AOD750 ($R^2 = 0.56$) and TISA750 ($R^2 = 0.41$) followed by LV ($R^2 = 0.49$ for AOD750, $R^2 = 0.34$ for TISA750) and IC ($R^2 = 0.42$ for AOD750, $R^2 = 0.25$ for TISA750).

Multivariable regression modeling demonstrated that age ($P < .001$) and sex ($P < .001$) alone were significant but weak predictors of angle width (Supplemental Table 2). For both AOD750 and TISA750, sex contributed more to angle width than age (AOD750, $SPCC^2 = 0.029$ vs 0.001; TIS750, $SPCC^2 = 0.019$ vs 0.002).

Four age- and sex-adjusted multivariable models were constructed for AOD750 and TISA750 (2 models for each) to evaluate the determinants of angle width (Table 3). Models 1A and 2A included constituents of AL (ACD, LT, and VCD), but excluded LV because of its collinearity with ACD (VIF >3.0 for both together). Models 1B and 2B included LV and AL but excluded its components.

ACD, IC, ACW, VCD, IA, and LT explained 66% of the variability in AOD750 while adjusting for age and sex (Table 3, Model 1A). The strongest determinant was ACD (SRC = 0.64, $SPCC^2 = 0.19$), followed by IC (SRC = −0.26, $SPCC^2 = 0.041$). This pattern remained

TABLE 3. Multivariable Linear Regression Analysis of the Relationship Between Angle Width and Potential Biometric Determinants Adjusted for Age and Sex

Dependent Variable	Independent Variable	Coefficient	SRC	SPCC^2	*P* Value	Dependent Variable	Independent Variable	Coefficient	SRC	SPCC^2	*P* Value
AOD750 (mm)	Model 1A[a] ($R^2 = 0.66$)	n = 2184				TISA750 (mm^2)	Model 2A[a] ($R^2 = 0.46$)	n = 2182			
	ACD (mm)	0.36	0.64	0.19	<.001		ACD (mm)	0.17	0.59	0.16	<.001
	IC (mm)	−0.34	−0.26	0.041	<.001		ACW (mm)	−0.037	−0.15	0.017	<.001
	ACW (mm)	−0.093	−0.18	0.023	<.001		IC (mm)	−0.084	−0.15	0.014	<.001
	VCD (mm)	0.02	0.12	0.011	<.001		VCD (mm)	0.0086	0.11	0.0096	<.001
	IA (mm^2)	−0.071	−0.084	0.0065	<.001		IA (mm^2)	−0.027	−0.068	0.0043	<.001
	LT (mm)	0.035	0.06	0.0022	<.001		Age (y)	0.0009	0.069	0.004	<.001
	Age (y)	0.0011	0.04	0.0013	.004		LT (mm)	0.013	0.047	0.0016	.012
	Sex	0.012	0.029	0.0008	.026		Sex	0.0027	0.014	0.0002	.41
	Model 1B[b] ($R^2 = 0.58$)	n = 2185					Model 2B[b] ($R^2 = 0.39$)	n = 2182			
	LV (mm)	−0.33	−0.46	0.1	<.001		LV (mm)	−0.15	−0.42	0.086	<.001
	IC (mm)	−0.37	−0.3	0.047	<.001		IC (mm)	−0.1	−0.18	0.018	<.001
	IA (mm^2)	−0.083	−0.1	0.009	<.001		Age (y)	0.0011	0.086	0.0066	<.001
	AL (mm)	0.015	0.1	0.0078	<.001		IA (mm^2)	−0.032	−0.082	0.0062	<.001
	Age (y)	0.0014	0.06	0.0032	<.001		AL (mm)	−0.0067	0.095	0.0051	<.001
	Sex	0.023	0.053	0.0026	<.001		ACW (mm)	0.013	0.052	0.0021	.007
	ACW (mm)	0.024	0.045	0.0016	.005		Sex	0.007	0.036	0.0012	.04

ACD = anterior chamber depth; ACW = anterior chamber width; AL = axial length; AOD750 = angle opening distance 750 μm from the scleral spur; IA = iris area; IC = iris curvature; LT = lens thickness; LV = lens vault; SPCC^2 = semipartial correlation coefficient squared; SRC = standardized regression coefficient; TISA750 = trabecular-iris space area 750 μm from the scleral spur; VCD = vitreous chamber depth.

Variables are listed according to decreasing SPCC^2 values.

[a]Mean variance inflation factor (VIF) = 1.40 (no individual VIF >3.0). LV and AL excluded from model because of VIF >3.0.

[b]Mean VIF = 1.45 (no individual VIF >3.0). ACD and VCD excluded from model because of VIF >3.0.

consistent when stratifying each model by sex and controlling for age (Supplemental Table 3).

The same independent parameters explained 46% of the variability in TISA750 while adjusting for age and sex (Table 3, Model 2A). While the strongest determinant was again ACD (SRC = 0.59, SPCC^2 = 0.16), ACW was the second strongest determinant (SRC = −0.15, SPCC^2 = 0.017) ahead of IC. This held true when stratifying age-controlled models across sexes (Supplemental Table 3).

LV, IC, IA, AL, and ACW explained 58% of the variability in AOD750 while adjusting for age and sex (Table 3, Model 1B). The strongest determinant was LV (SRC = −0.46, SPCC^2 = 0.1), followed by IC (SRC = −0.37, SPCC^2 = 0.047). This pattern remained consistent when stratifying each model by sex and controlling for age (Supplemental Table 3).

The same independent parameters explained 39% of the variability in TISA750 while adjusting for age and sex (Table 3). The strongest determinant was LV (SRC = −0.42, SPCC^2 = 0.086), followed by IC (SRC = −0.18, SPCC^2 = 0.018). ACW was the least important contributor, unlike in model 2A, where it was the second most important.

The strongest determinants of angle width were similar between males and females with a few exceptions (Supplemental Table 3). In both models of AOD750, IA was a stronger determinant of angle width in males than females (model 1A, SPCC^2 = 0.017 vs 0.002; model 1B, SPCC^2 = 0.024 vs 0.003). This was also true in both models of TISA750 (model 2A, SPCC^2 = 0.013 vs 0.001; model 2B, SPCC^2 = 0.018 vs 0.002).

DISCUSSION

IN THIS CROSS-SECTIONAL STUDY, WE ASSESSED OCULAR biometric determinants of angle width among Chinese Americans. While all biometric parameters were significantly associated with angle width on univariable analysis, ACD, LV, and IC were the strongest determinants of angle width on multivariable analysis. Multivariable models combining ACD, IC, ACW, VCD, IA, and LT explained 66% and 46% of variance of AOD750 and TISA750, respectively. In addition, women had narrower angles than men, which was explained by sex-related differences

among biometric measurements. We believe these results provide insights into anatomic mechanisms of angle narrowing and could help clinicians contextualize quantitative measurements of biometric parameters when assessing patients with angle closure.

It is important to clearly state that the primary objective of our study was to assess the relative and unique contributions of ocular structures and biometric parameters to angle width. Our objective and methods differed from those of the population-based study on determinants of angle width in Chinese Singaporeans by Foo and associates,[21] which focused on constructing a best-performing model to predict angle width. The motivation for our approach was 3-fold. First, unified information provided by multivariable models on the relative and unique contributions of known biometric risk factors for angle closure, such as ACD, LV, and IC, to angle width is sparse. This lack of fundamental knowledge is glaring because a number of biometric risk factors have been identified and the effect of treatments differ by risk factor.[11,22,23] Therefore, models that unify these disparate parameters could provide significant benefit in the development of quantitative clinical methods for assessing patients with angle closure. Second, a best-performing model of angle width would likely include anterior chamber area and anterior chamber volume.[8,9] These 2 parameters do not provide information about a specific anatomic structure. Rather, they reflect the aggregate contributions of multiple anatomic structures, such as iris and lens, and incorporate direct measures of angle width, such as TISA. Consequently, they strongly covary with the biometric parameters assessed in this study. It is intuitive that including these 2 parameters in a multivariable model would improve its classification performance, but this comes at the cost of confounding the contributions of other parameters, as was the case in the study by Foo and associates.[21] Finally, simply predicting angle width has limited clinical and scientific value, because angle width can be directly measured in most AS-OCT images.

Our multivariable models revealed important relative and unique relationships between angle width and its biometric determinants. First, ACD was the strongest unique determinant of angle width, individually accounting for 19% of the variance of AOD750. In contrast, LV only accounted for 10% of the variance of AOD750 that was not explained by other parameters. This finding supports previous studies promoting the importance of shallow ACD, especially when <2 mm, in screening protocols for PACG.[3,24] The unique contribution by ACD also helps explain why the prevalence of angle narrowing and PACG are highest in ethnic groups with the shallowest ACD, even when lens-related parameters are relatively similar.[3,25,26] Finally, it may also explain why *ABCC5*, a gene related to ACD, is the only gene affecting ocular biometrics that has been associated with PACG.[27] Second, IC is also an important determinant of angle width, with 1 standard deviation change in IC contributing to 30% of 1 standard deviation change in AOD750. In addition, the relative contribution of IC to the variance of angle width is 40% of ACD and 65% of LV, and its unique contribution to the variance of angle width is approximately 5%. These findings support mathematical models that predict a significant increase in IC secondary to pupillary block, which plays a key role in the pathogenesis of primary angle closure.[28]

The results of our univariate analyses are consistent with results from the population-based study of Chinese Singaporeans by Foo and associates.[21] Ignoring anterior chamber area and anterior chamber volume, which were omitted from our study for the aforementioned reasons, the R^2 values for the 4 strongest determinants of AOD750 were LV (0.56), ACD (0.46), IC (0.48) and AL (0.30). This closely approximates the R^2 values of ACD (0.56), LV (0.49), IC (0.42), and AL (0.24) in our population-based cohort of Chinese Americans. Age, ACW, IA, and LT are all relatively weak determinants of angle width (R^2 <0.10) in both studies. The primary difference between the 2 sets of results is that the importance of ACD and LV are switched. VCD was unique to our study and iris thickness and lens position were unique to the study by Foo and associates.[21] It is unclear if Foo and associates[21] adjusted for sex and age as we did, which may have contributed to some of the observed differences. However, it does appear that determinants of angle width are largely conserved across individuals of Chinese descent.

Women are at higher risk of angle closure compared with men, although it was unclear whether the additional risk was secondary to sex-related differences among biometric measurements or if there were other independent factors at play.[29,30] In our study, females had significantly smaller ocular dimensions and increased LV and IA, even after adjusting for age. In sex-stratified models of angle width, only the contributions of IA differed noticeably between men and women. Given that IA is a weak determinant of angle width, it appears that the contributions of key biometric determinants of angle width are similar for men and women. In addition, contributions of sex to angle width were negligible in multivariable models with biometric parameters compared with multivariable models with age and sex alone. Therefore, it appears that increased risk of angle closure in women can be explained by sex-related differences among biometric measurements. Women are also at higher risk of PACG compared with men.[30] However, we cannot draw any conclusions from our data about this increased risk because our primary outcome measures did not include the presence of glaucomatous optic neuropathy.

The prevalence of myopia has been increasing rapidly worldwide, with researchers debating whether this will affect the prevalence of angle closure and associated PACG.[31,32] One study identified that myopes constitute a significant subset of angle closure eyes and that the anterior segment biometrics of these myopic eyes resemble that of hyperopic and emmetropic eyes.[32] Another study found

that VCD is a much stronger determinant of refractive error than ACD, at least among Chinese Americans.[33] Our results add 2 more pieces of knowledge relevant to myopia and angle closure: ACD is a much stronger determinant of angle width than VCD, and AL is a much weaker determinant of angle width than LV and IC. Interpreted together, these results suggest that myopia secondary to axial, and specifically, vitreous cavity elongation alone is unlikely to affect overall angle width. Our results also support that future studies of axial myopia related to angle closure should examine the contributions of individual components of AL to refractive error.

Our study has several limitations. First, the study population consisted entirely of Chinese Americans. Ethnic variations in ocular biometric measurements exist, and the contributions of biometric parameters in our cohort could differ from a cohort of white, Hispanic, or African American eyes.[3,25,26] Alternatively, ethnic differences in angle width could be related to differences among biometric measurements, as is the case for sex-related differences. This limitation merits further investigation, although its clinical impact is blunted by the fact that the majority of angle closure occurs in Asian eyes.[1] Second, our study lacks at least 1 known biometric risk factor for angle closure, IT.[34] Unfortunately, IT measurements could not be obtained using the Tomey measurement software for half of our study cohort. Given the small individual contribution of IT in previous multivariable models of angle width, it is unlikely that this greatly affected the performance of our models.[8,9] Third, we only assessed determinants of angle width for the temporal sector of the ACA to eliminate issues related to intraeye correlations among measurements. Therefore, it remains a possibility that contributions of determinants could differ by sector. Fourth, only 1 observer graded the AS-OCT images. While intraobserver measurement repeatability was excellent for all AS-OCT parameters, interobserver variability in detecting the scleral spur could affect the generalizability of our study's models.[35] Finally, multivariable models were less predictive of TISA750 than AOD750, and approximately 50% of its variance was unexplained by our models. This is likely related to the fact that area measurements are more complex than single-point measurements of angle width and our model did not include IT, which could inform the model regarding localized iris attributes. Regardless of the explanation, further work is necessary to identify additional biometric parameters that are associated with AOD and TISA.

Quantitative measurements of biometric parameters could take on an increasingly important role in the clinical assessment of angle closure eyes as it becomes evident that qualitative disease definitions are weakly predictive of disease outcomes.[36] Biometric measurements currently have a limited role in the clinical care of angle closure patients. However, it is conceivable that the models described in this study could be applied to biometric measurements standardized using normative databases. This approach would help clinicians contextualize and interpret biometric measurements from individual eyes to identify the anatomic structures that are aberrant and contributing most strongly to angle narrowing or closure. This approach could also form the basis of studies exploring the efficacy of different angle closure treatments, such as laser peripheral iridotomy and lens extraction, on patients with particular biometric characteristics. In the future, quantitative measurements of biometric parameters could complement gonioscopy in guiding the care of patients with angle closure, especially as automated methods for quantitative image analysis are developed.[5,37,38] We hope that future studies can further elucidate anatomic mechanisms of angle narrowing and develop diagnostic tools that facilitate the clinical care of patients with angle closure.

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